ABSTRACTS

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CHEMOTHERAPY

CH1

TREATMENT OF PAUCIBACILLARY PATIENTS WITH MDT CONTAINING RIFAMPICIN, DAPSONE AND PROTHIONAMIDE

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With the introduction of MDT, there has been improved patient compliance and the duration of treatment has been greatly reduced. However with WHO recommended MDT for 6 months, the incidence of persisting activity in lesions, late reations/relapses have varied considerably and has been quite high in many of the reports. The present study was undertaken to see whether the addition of one more bactericidal drug i.e. Prothionamide could help in reducing these limitations of currently used MDT.

112 untreated paucibacillary patients belonging to Indeterminate(I), Tuberculoid(TT) and Borderline Tuberculoid (BT) types and with BI of less than 2 on the Ridley scale were treated with Rifampicin (600mg once a month), Dapsone (100mg daily) and Prothionamide (250mg daily). Treatment was stopped at the end of 6 months. The patients tolerated the drugs fairly well. 6% of the patients had early reaction which subsided with additional steroid therapy. The inactivity rate was 60% at 6 months which improved to 96% at 12 months. None of the cases had late reaction and there was one relapse in about 2 years of post treatment follow-up. The comparison of these results with those of WHO regimen and extended 12 months regimen shows that addition of Prothionamide appears to have a significant effect on clinical improvement as well as in the reduction of the late reactions.

CH2

MULTIDRUG THERAPY FOR TREATMENT OF LEPROSY PATIENTS IN NEW CALEDONIA AND FRENCH POLYNESIA. RESULTS AFTER 10 YEARS.

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Multidrug therapy (MDT), including daily administration of rifampicin, has been implemented in 1982 in French Polynesia, and in 1983 in New Caledonia, for treatment of leprosy cases. Since 1983, 100% of newly detected patients are given MDT. Until 1991, a thioamide was given in addition during the first two months for multibacillary (MB) patients in French Polynesia.

From 1982 to 1992, 365 patients were given MDT: 170 MB and 195 paucibacillary (PB). To date, 32 patients are still under MDT (20 MB and 12 PB). Of the 365 cases, 321 (88%) were compliant to the treatment. Resolution of cutaneous lesions and improvement in the local nerve damage was observed in all of the treated patients. Even in case of reaction, no residual disability of grade > 1 was notified. Among the 62 patients treated with a thioamide, 9 (15%) experienced hepatitis. No relapse has been detected in patients treated with MDT, as compared with a 30% cumulative relapse rate in MB patients treated with dapsone monotherapy in French Polynesia, before implementation of MDT.

CH3

7-YEAR SURVEILLANCE OF 657 CURED MB PATIENTS RE-TREATED WITH MDT

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Since 1983, 657 MB patients clinically cured with DDS monotherapy together with BI of 2 or more at any site smeared previously were re-treated with DDS,RFP and B663 in combination. Four hundred and eighty seven of them were males and 170 were females, their age ranged from 17 to 70 years and their disease duration ranged from 1 month to 39 years. Cured patients not re-treated were used as controls for this trail.

All patients were administered RFP and B663 1200mg each once monthly with supervision and DDS 100mg daily self-administered. This treatment was continued for 12 months and was completed within a period of 15 months. Six hundred and twenty cases (94.27%) of them completed regularly the prescribed course but 37 did not due to the occurrence of side effects or complications. Exclusive of 2 who died of non-leprosy cause and 1 migrated out of Shanghai after completion of re-treatment, the remaining 654 were followed for a period of 4-7 years (534 cases for more than 7 years), no relapsed case was identified. But there were 17 cases detected as relapses among the 137 control patients, giving an overall relapse rate of 12.41% and a mean annual relapse rate of 1.55%. Type I lepra reaction was seen in 7 cases during and after the re-treatment and was successfully controlled with steroids preparations. The authors suggest that although this study has already shown a satisfactory recent effect of re-treatment with MDT, but it is still in need of further observation.

CH4

EFFECT AND SURVEILLANCE OF 1,076 LEPROSY PATIENTS TREATED WITH MDT IN SHANDONG PROVINCE OF CHINA

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One thousand and seventy six active leprosy patients were detected in Shandong province from 1982 to 1991.Of these patients, 619 cases were MB and 457 were PB; 927 were new cases never treated before and 149 were relapsed cases after DDS monotherapy. All cases were treated with MDT until clinically inactive and skin smear negative and then received additional treatment with DDS+RFP for another 12 months. Afterwards, the patient was clinically and bacteriologically monitored annually.The results showed that the BI of skin smears was decreased by 0.7+ each year in the first 3 years. By the end of 1991, 762 of 1,076 cases reached the criteria of cure clinically and bacteriologically. The average treatment duration for cure was 53.1 months in LL, 45.5 months in BL, 42.3 months in BB,37 months in BT, 33.2 months in TT and 32.1 months in indeterminate cases.As regards the five year cured rate, there was no significant difference between the newly diagnosed and relapsed cases. the 762 cases above mentioned have already been monitored after release from treatment for a total of 2284.5 person-years. The longest period monitored was 9 years in PB and 6 years in MB. Only one BT patient relapsed. No leprosy reaction was found after stopping therapy, except neuritis with severe neuralgia occurred in one BB case.

CH5

BACTERIOLOGICAL RESPONSE OF BL/LL PATIENTS TO MDT FOR VARIED DURATION: A RETROSPECTIVE FIVE YEAR FOLLOW UP

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The analysis of five year bacteriological reports available in the hospital records of 678 LL and 180 BL patients who received WHO MDT regimen for varied duration, showed that there was a progressive reduction in the respective average Bacteriological Index(BI) by 0.75 and 0.9 index per year, irrespective of the period of therapy.

At an 18 month average duration of therapy the average BI of LL patients was 1.9+(with 36% negative patients) and that of the BL patients was 1+(with 63% negative patients). The difference observed in BI response of LL and BL patients with comparable initial BI (i.e. 3.9+ and 3.4+ respectively) was statistically significant, indicating that a proper classification is needed for any controlled drug trial.

Progressive reduction in the average BI with increasing percentage of negative patients was observed even after discontinuation of therapy in all the patients with varied ranges of duration of therapy.

In 243 LL patients, there was reduction in BI from initial 3.7+ to 1.4+(with 46% negative patients) at the end of 2 years fixed duration MDT. The subsequent follow up showed further reduction in the average BI up to 0.1+ (with 93% negative patients) at the end of third year of surveillance.

CH6

FIXED DURATION MULTIDRUG THERAPY (FDT) FOR MULTIBACILLARY (MB) LEPROSY IN INDIAN RURAL PROGRAMMES

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On the basis of the available evidence of bacteriological decline after FDT (WHO regimen) for 24 months in MB patients, the National Leprosy Eradication Programme of India has adopted this procedure as a national policy. Field level experience on operational aspects of successful practice of FDT is still lacking. In 1989 NLEP gave permission to us to study FDT in Bulsar (Gujarat) and Chittoor (Andhra Pradesh) districts. We present the methodology adopted to re-train staff in respect of newer principles of chemotherapy, field follow-up after termination of treatment, selection of sties for skin smears, ensuring reliability of smear examination and reporting systems etc.

Observations on bacteriological decline over 2½ to 3 years given below are in conformity with results reported earlier (Ganapati et al 1992).

BI at RFT*	No. of Pts	BI at First Year 4 to 5	3-4	2-3	1-2	0-1	Rendered -ve No.	%
4 - 5	1	-	-	-	-	-	-	-
3 - 4	6	1	2	-	-	-	3	50
2 - 3	11	1	-	-	3	2	5	45
1 - 2	21	-	-	1	-	10	10	48
0.1-1	59	-	-	-	-	30	29	49
Total	98	3 (3%)	2 (2%)	1 (1%)	3 (3%)	42 (43%)	47	48

*RFT : Release from Treatment

At 2nd year of surveillance 37 (88%) out of 42 cases were rendered negative and 3 (16%) were stationary and at 3rd year of surveillance 19 (95%) out of 20 patients were negative and in one patient BI was stationary.

CH7

FACTORS ASSOCIATED WITH RATE OF HEALING IN PAUCIBACILLARY LEPROSY TREATED WITH MDT

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This study was carried out in the Leprosy Control Unit, of CHAD Hospital, CMC, Vellore. 2129 Paucibacillary Leprosy Patients who were released from treatment after 6 months of WHO MDT Regimen were studied.

The effect of factors like 1)age 2) sex 3)Type 4) No. of Patches and 5) Prior treatment with Dapsone on the rate of healing of disease were analysed using Survival Analysis.

74% of the cases healed by the end of 1 year and 95% by the 2nd year. Almost all had healed by the end of 3rd year.

Age, sex and type of leprosy did not affect the rate of healing. The rate of healing was quicker among those with single lesions as compared to those with more than 5 lesions ($P < 0.05$). Interestingly those who had prior dapsone monotherapy showed a singificantly quicker rate of healing ($P < 0.001$).

Persistance of patches after 6 months of MDT does not warrant continuation of treatment.

CH8

LOW RISK OF RELAPSE AFTER PAUCIBACILLARY TREATMENT AMONG CHILDHOOD LEPROSY PATIENTS

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This study deals with the risk of Relapse in children who have undergone Paucibacillary Treatment. This study was conducted in The Leprosy Mission Hosipital, Vizianagaram of Coastal Andhra Pradesh in South India.

248 children who had completed Paucibacillary Treatment in 1985 and were followed upto 1992 were included in the study. Of the 248 children 157 were male and 91 were female. 6(2.4%) were less than 5 years of age, 89(35.9%) 5-9 years of age and 153 (61.7%) were 10-14 years. 204 were classified as TT, 33 as BT and 11 as indeterminate. 200 of them had only one patch and 48 of them had 2 patches or more.

The risk of relapse was computed after 2 years and 7 years of follow up. The two year risk of relapse was 2.016/1000 person years of risk and the seven year risk was 1.2/1000 person years of risk. This study shows that the risk of Relapse among childhood patient after Paucibacillary Therapy is very low or even negligible as compared to Adult patients after Paucibacillary Treatment.

CH9

FIXED DURATION THERAPY (FDT) IN MB LEPROSY

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The conventional WHO-recommended MDT regimen for MB leprosy requires that it be administered for a minimum period of 2 years or till the patient attains bacteriological negativity, which ever is later.

Considering the efficacy of the Combination of Rifampicin, Clofazimine and DDS, it was hypothesised that this combination administered for a period of TWO YEARS ONLY may be adequate to effect killing of M. lepra population in an infected individual and that the bacterial clearance can continue to be done by the immune system of the individual. Therefore, a trial was instituted where the WHO-recommended MDT Regimen for MB leprosy was administered for two years, and its efficacy assessed in terms of "relapse". 261 previously untreated bacteriologically positive MB leprosy patients were included.

All patients continue to have bacteriological clearance during surveillance. The rate of bacteriological clearance is similar to that of patients continued treatment till attainment of bacteriological negativity. None of these patients have relapsed as yet, during 539 person-years of follow-up.

This study is supported by UNDP/WORLD BANK/WHO SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES.

CH10

PRELIMINARY RESULTS OF THE EVALUATION OF A SURVEILLANCE SYSTEM OF SIDE EFFECTS OF MDT

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MDT leprosy treatment started as a routine in the State of São Paulo, Brazil, on July, 1991. All the newly diagnosed cases should be included and patients already under single drug treatment should be evaluated. Cases of serious adverse reactions (even death) have been reported after the implementation of the new treatment. In order to develop a better knowledge about the relationship between unexpected clinical events and MDT, a special surveillance system has been set up on May 20, 1992.

This study covers the period of time from that date to December, 1992. Cases wich have been reported and investigated were classified, following clinical, laboratory and epidemiological criteria, as confirmed, probale or discarded.

The system received 159 notifications, 84 of them (51.6%) have been considered confirmed, 55 (35%) probable and 21 (13.4%) discarded. From the confirmed cases, 43.7% were males, 43.7% in the 30 to 50 years old age group and 32.5% from 50 to 70 years old. Some 40.3% of the patients had to be admited to hospitals. The most frequent diagnoses were: 27(32.5%) cases of Influenza-like syndrome, 8 (8.6%) cases of Acute Renal Failure, 5 (7.2%) cases of Toxic Hepatitis, 11 (15.8%) association of the two diagnoses above. Out of the 83 confirmed cases, 70 (86.4%) were old patients who were switched to MDT.

The present study aims to evaluate operational difficulties on MDT implementation and also to evaluate the special surveillance system itself.

CH11

EFFETS SECONDAIRES DES MEDICAMENTS. OBSERVATIONS FAITES CHEZ DES PATIENTS HAITIENS.

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Etude retrospective de 720 dossiers de patients hanseniens suivis de 1984 a 1992, de l'Institut Cardinal Leger contre la lepre d'Haiti.

Au cours de cette communication on mettra en evidence les differents effets secondaires aux medicaments anti-hanseniens (disulone, rifampicine, Lamprene) observes chez ces patients.

CH12

" DISABILITY GRADING " OF PATIENTS IN A MDT PROGRAM - COMPARISON WITH A SIMILAR GROUP TREATED WITH DAPSONE ALONE AND FIVE YEAR FOLLOW-UP

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We reviewed the "Disability Grading" (WHO 1988), the number and severity of Reactions, Neuritis, Treatment required (use of Steroids and Thalidomide) and the prevalence of foot and stasis ulcers in about 1.000 patients that completed MDT and have been followed for 5 or more years. The RI-ISOPRODIAN regime was used in most patients (RIFAMPIN - DAPSONE - ISONIAZIDE - PROTHIONAMIDE). The same evaluations were done in a similar group of patients treated with Dapsone monotherapy. Results will be presented and discussed.

CH13

PROFILE OF RELAPSE CASES IN FIELD TRIAL OF COMBINED THERAPHY IN MULTIBACILLARY LEPROSY

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Profile of five relapase cases following two different regimens of Combined Therapy-Regimen A and Regimen B - in 1174 BL and LL cases, most of them previously Dapsone treated and skin smear negative at intake in a field based trial supported by UNDP/World Bank/WHO Special Programme for TDR at Hemerijckx Leprosy Centre, Polambakkam, South India is presented. The duration of treatment was 2 years of Combined Theraphy or till skin smear negativity whichever is later followed by 8-10 years of follow up. Out of the five relapses, one was MB type and the four being PB type relapses. Their past history, course during Combined Therapy, and Relapse profile including clinical picture, Histopathology and Mouse foot pad inoculation particulars are presented and discussed.

CH14

M.LEPRAE VIABILITY IN SKIN AND NERVE AFTER MDT AND THEIR SENSITIVITY TO ANTI-LEPROSY DRUGS

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Multi-Drug Therapy has not eliminated the problem of 'persisters' in leprosy. The THELEP trials report presence of 'persisters' in 9% of the MB cases treated with MDT.

However in a recent Bombay-based pilot study we recorded a higher incidence of viable M.leprae (30%) in peripheral nerves of treated MB cases. This study was continued to include more cases as well as to establish the sensitivity of the persisting organisms to the drugs in use.

Skin and nerve biopsies were simultaneously obtained from 20 MB cases who had completed a minimum two years of WHO recommended MDT. these were primarily tested for viable bacterial load in footpads of T200x5R (TR) mice. Inocula obtained from these footpads were repassaged into normal mice where confirmation of the growth as well as tests for sensitivity to DDS and Rifampicin were carried out.

The results obtained are discussed in light of 2-3 years follow-up of these patients.

CH15

CONTROLLED CLINICAL TRIAL OF 2 MULTIDRUG REGIMENS WITH AND WITHOUT RIFAMPIN IN HIGHLY BACILLIFEROUS BL/LL SOUTH INDIAN PATIENTS A 10 YEAR REPORT

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A controlled clinical trial of 2 multidrug regimens in lepromatous and near lepromatous cases with BI 2.5 or more on Ridley's scale was conducted. Patients were randomly allocated to the following:

a) On admission: either a 2 drug regimen of Dapsone plus clofazimine daily for 60 months or a similar regimen with rifampin and isoniazid in addition for the first 3 months followed by clofazimine and dapsone for the next 57 months.

b) At 60 months: either a 2 drug regimen of clofazimine and dapsone or dapsone alone daily.

c) At 84 months: either daily dapsone or placebo if their BI was 1.00. Those patients who had BI 1.00 continued to get the treatment allocated at 60 months.

A total of 210 patients were admitted to the study of whom 148(74%;excluding 9 deaths)were available for assessment at the end of 10 years. Clinical examination by an Independent assessor and bacteriological assessments were done periodically. All the patients showed excellent clinical and bacteriological improvement upto 10 years except one who was retreated due to reactivation.

CH16

FOLLOW UP STUDY OF 81 LEPROSY CASES TREATED BY SHORT TERM MDT IN TURKEY

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Between early 1982 and early 1984, 74 patients were taken into the short term course RMP+ETH+DDS regimen and 51 patients were taken into the short term course RMP+CLO+ETH regimen.Treatment term was 28 weeks. In first two weeks daily treatment of 600 mg. RMP was applied and then all patients received 600 mg. RMP weekly.

After completing MDT, during the last 6 years these patients followed up in the hospital or in field work. In the first group, we were able to examine 49 patients (64 %). In this group, only 3 patients had more than BI=2 on skin smears. In the second group 32 patients (63 %) were examined.In this group, only one patient had BI=5 on skin smears. Other patients who completed the trial had no m.leprae in skin smears and had no evidence of clinical activation or sign of relaps.

In this study, we discuss the effectiveness of short term MDT after a long period with bacteriological and clinical results.

CH17

TWENTY YEARS AFTER STARTING THE ERADICATION PROJECT IN MALTA

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Since the Malta Leprosy Eradication Programme was inaugurated in June 1972, 257 paients have been treated with Isoprodian-RMP. The duration of treatment was not fixed, but was determined for each patient. The medication was safe and well tolerated. To date only one patient has relapsed, 17 years after completion of MDT. Apart from the importance of leprosy eradication for Malta itself, this result is of far-reaching significance:

1. Final, relapse-free cure of leprosy can be obtained within a short time without any particular organisational procedure through the use of proper doses of antimycobacterial substances made up as fixed combinations.
2. By treating all patients with the same combination (no difference is made between pauci- and multibacillary cases) but for a varying period of time, epidemiologic eradication of leprosy is rapidly and safely obtained through the use of chemotherapy.
3. Through selection of appropriate drugs, low-cost combinations can be made up (5 - 10 US $ monthly per case).

CH18

EIGHT YEARS FOLLOW UP OF MULTIBACILLARY LEPROSY AFTER 24-27 MONTHS OF MULTIDRUG THERAPY

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During 1983, 80 untreated MB patients from Shandong and Yunan Provinces were treated with 24-27 months of MDT. These patients were examined, treated and followed annually by independent leprosy control teams of these two provinces. At the fifth year of follow-up, 100% (33/33) of patients from Shangdong and 95.3% (41/43) of patients from Yunnan have converted to smear negative. The data of clinical, bacteriological and histopathological examinations will be compared with that of MB patients treated till smear negative elsewhere in China Results at the eighth year of follow up plus their level of PGL antibody will be presented

CH19

RECAIDAS EN HANSENIANOS MULTIBACILARES TRATADOS CON MONOTERAPIA SULFONICA.

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Se estudian entre 352 enfermos multibacilares (LL) tratados con monoterapia sulfonica el número de recaidas despues de conseguirse la negativización.

Se observan un total de 33 recaidas entre 7 a 39 años despues de inactividad bacteriológica.

La recaida en 8 de los enfermos fue de la forma Dimorfa (BL y BB). Todos los casos fueron tratados con Multiterapia.

CH20

RELAPSES IN 20,091 CURED LEPROSY CASES IN SHANDONG PROVINCE OF CHINA

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A retrospective analysis on 20091 cured leprosy cases in Shandong Province of China from 1955 to 1990 is presented. Analysed with life-table method, the relapse rates for MB and PB cases were 6.48‰ person years and 4.29‰ person years respectively. The levels of the relapse rates were closely related to the therapeutic drugs used in the past. In MB patients treated with DDS and DDS+RFP, the relapse rates were 7.92%(446/5,628) and 1.07%(15/1,405) respectively. The former rate is significantly higher than the later one. In PB patients treated with thiacetazone, DDS and WHO-PB regimen the relapse rates were 12.6%(96/763), 5.4%(589/10,903)and 0.18%(2/1,101)respectively. The relapse rate in the WHO-PB regimen treated group was significantly ower than those in other two groups (U=7.70 and 11.8, P<0.001). No relapse was found neither in MB(256) nor in PB (35) cases treated with WHO-MB regimen. 96.3% of relapses in MB and 90.1% relapses in PB occurred within 15 years after cure and most of them were cured again with DDS monotherapy.

According to the analysis mentioned above, we suggest that the follow-up period for the patients cured with DDS monotherapy should be for a minimum of 15 years after release from treatment and an additional short term MDT should be considered for those who are younger than 60 years of age in order to prevent them from relapse.

CH21

SINGLE DOSE RIFAMPIN CANNOT PREVENT RELAPSE IN SKIN-SMEAR NEGATIVE MULTIBACILLARY LEPROSY PATIENTS AFTER DAPSONE MONOTHERAPY

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Between 1982 and 1985, a single dose of RMP 1500mg was administratered by 136 multibacillary leprosy patients who had become clinical and skin-smear negative after various duration of dapsone monotherapy, and then anti-leprosy chemotheray was totaly stopped. By the end of June 1992, 15 relapses were detected among the patients. The relapse rate per 100 patients-year was 2.12%, the cumulative risk of relapse at the 7th year of follow-up was 8.8% at least the same as in other studies where patients received only monotherapy. Therefore, the administration of a single large dose of RMP to multibacillary patients who had already become clinical and skin-smear negative after dapsone monotherapy could not prevent the relapse.

CH22

MULTI-DRUG RESISTANCE IN LEPROSY

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Since its introduction in 1982, Multi-Drug Therapy (MDT) is heralded as one of the most important and stimulating contributions to leprosy control. Data from routine programmes also indicate a high degree of efficacy of WHO/MDT after about 8 years of follow-up. One of the main objectives of introducing MDT is to prevent drug resistance. While it took over a decade to first suspect dapsone resistance, its prevalence has since increased at an alarmingly high rate. In a much shorter period thereafter, secondary resistance has been reported with rifampicin, clofazimine, ethionamide and prothionamide. To date however M.leprae resistance to MDT has not been observed. while 58% of currently registered patients and an estimated 2.5 million undiagnosed patients of leprosy yet remain unexposed to MDT, we report here 2 cases of lepromatous leprosy--fully treated with regular WHO/MDT who exhibited resistance with both dapsone and rifampicin in the mouse footpad. The paper discusses implications of emergence of multidrug resistance in leprosy. The need for continued surveillance and accumulation of data on multi-drug resistance in leprosy is stressed, to be certain about the prevalence and to devise strategies to effectively prevent or decelerate its spread.

CH23

PRIMARY DAPSONE RESISTANCE IN CEBU, PHILIPPINES: RECENT FINDINGS

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The use of Dapsone as monotherapy in leprosy in developing countries has resulted in the occurrence of secondary DDS resistance in patients. Exposure of the community to these individuals has brought about the emergence of primary dapsone resistance in endemic areas.

Tissue specimens taken from active lesions of 38 untreated LL-BL patients sequentially admitted to various studies were inoculated into inbred, locally-produced CBA/J mice. Dapsone sensitivity was determined by feeding the inoculated mice varying concentrations of the drug in the diet. Our results demonstrate primary dapsone resistance in 52.6% of the 38 patients tested. This is a significant increase over earlier surveys in Cebu in which 8.1% [Cellona et al, 1989] and 3.6% [Guinto et al, 1983] of patients had primary dapsone resistant leprosy. This finding stresses the importance of vigorous implementation of MDT to check the resurgence of primary drug resistant cases. Details comparing the results of the present study with those of earlier studies in the Philippines will be presented and discussed.

CH24

STUDY OF RELAPSE IN PAUCIBACILLARY LEPROSY PATIENTS IN MULTIDRUG THERAPY PROJECT IN BHARUCH DISTRICT, GUJARAT, INDIA.

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The prospective study of relapse includes paucibacillary cases of leprosy belonging to non-lepromatous group consisting of tuberculoid, neuritic and indeterminate.
6018 patients paucibacillary leprosy(till Dec.92 who had completed the prescribed period of treatment and now under surveilliance for varying periods are evaluated for evidence of clinical relapse of their disease. Paucibacillary regimen being according to WHO was rifampicin 600 mg. supervised once a month for six months and dapsone unsupervised 100mg daily for six months. The criteria applied for diagnosis of relapse

after excluding Type I reaction, were extension of existing skin lesions, appearance of new skin lesions, paresis, paralysis of previously unaffected muscles and presence of acid-fast bacilli in skin smears.
The relapse rates in these 6018 patients will be compared with relapse rates in PB patients who had received dapsone monotherapy for a minimum period of 2 years in Bharuch district using following parameters.:
a) Age, b) Sex, c) Type, d) Duration of treatment e) Prior treatment.
The findings indicate that short course chemotherapy [1]. The drugs are well tolerated and side effects are minimal. The results of the study and factors associated with occurrence of relapse, time interval and period of follow-up will be presented.

[1] using rifampicin is superior to dapsone monotherapy per se.

CH25

TREATMENT OF HIGHLY BACILLATED BL/LL CASES WITH A PYRAZINAMIDE CONTAINING REGIMEN

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Pyrazinamide has been shown to have a marked sterlizing effect in tuberculosis. A pilot trial earlier showed that it has some beneficial effect in leprosy also. We have initiated a trial in which highly bacillated untreated BL/LL cases were given Rifampicin 600mg once a month, Clofazimine 50mg daily and Dapsone 100mg daily, till the attainment of smear negativity combined with Pyrazinamide 1500mg daily in divided doses for 1 year. The progress was monitored periodically by clinical, bacteriological, BI, mouse foot pad, bacillary ATP measurements and histopathological parameters. Smears from the same sites and biopsies were repeated yearly. 25 patients on this regimen have completed the follow-up of three years after start of therapy. The patients tolerated the drugs fairly well. These patients have been compared with similar cases on same MDT without Pyrazinamide. The incidence and magnitude of reactions and nerve damage was comparable and was easily controllable with routine anti-reaction treatment. There was no growth in the mouse foot pad in Pyrazinamide and non-Pyrazinamide groups at 2 years and beyond. While about 16% of patients at 2 years and 5% cases at 3 years had detectable bacillary ATP levels in non-Pyrazinamide group, no bacillary ATP was detected in biopsies from patients on Pyrazinamide containing regimens at these time periods. By 3 years, 32% of patients of Pyrazinamide group became smear negative and mean BI fell from initial 4.6 to 0.7 whereas in non-Pyrazinamide group 6% patients became smear negative and mean BI fell from initial 4.2 to 1.3. Pyrazinamide containing regimen appears to have some role in achieving improved sterlizing effect in multibacillary leprosy.

CH26

CLINICAL TRIALS OF MINOCYCLINE IN LEPROMATOUS LEPROSY

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In our first clinical trial of minocycline 100 mg once daily for 3 months, the 8 lepromatous leprosy patients responded exceedingly rapidly both clinically and bacteriologically. After 1 week of therapy 6 of the patients had noticeable improvement observed in either skin erythema or induration, 2 showing improvement in both. After 3 months of minocycline all the patients had noticeable improvement in their skin lesions, 6 patients having complete resolution of all erythema and induration. One patient had mild transient vertigo 1 month into the trial which resolved spontaneously without the need to discontinue treatment. No other adverse reaction or laboratory abnormality was noted in the treated patients. Of considerable importance and possible significance, no patient had a lepra reaction during the trial period. Serum minocycline levels in the studied patients were as expected from the literature: 1.84 ± 0.48 μg/ml (range 1.07-2.66 μg/ml) and trough 0.43 ± 0.11 μg/ml (range 0.33-0.58 μg/ml). At 1 month 3 patients had lost viable *M. leprae* (as determined by mouse inoculation), 6 by 2 months, and all by 3 months. Because minocycline has been utilized without significant toxicity for long periods of time and for over 2 decades, the rapid clinical response and clearance of viable *M. leprae* found in this study lend strong support for its use in the therapy of leprosy.

Currently being completed is a second clinical trial of minocycline administered first as a single 200 mg dose and followed 1 week later with 100 mg twice daily for 3 months. In this trial patients on clinical grounds also improved rapidly and similarly lost viable *M. leprae* from the skin as in our first clinical trial. Results will be presented quantitating the killing of *M. leprae* by the initial single 200 mg dose and, also, after 1 week of twice daily therapy.

CH27

SHORT TERM RIFAMPICIN CONTAINING REGIMENS FOR MB LEPROSY YIELD TO HIGH RISK OF RELAPSE

L. Blanc, P. Jamet, O. Faye, S. Sow, P. Bobin

Between 1977 and 1986, 435 MB leprosy patients entered 12 different MDT rifampicin containing regimens in Institut MARCHOUX. Among this cohort, 100 relapses occured during follow-up time from end of treatment to January 1993. Relapses were diagnosed on clinical, bacteriological and histological criteria, to date 66 were confirmed by the presence of viable M. leprae in skin biopsy specimen and 21 results pending ; all the isolated strains remained susceptible to RMP. Relapse rate ranged from 2.29 (0-4.5) to 7.3 (4.8-9.8) per 100 patients year, risk of relapse at year 5 ranged from 0% for regimens of one year duration to 14% (11-17) for regimens of 4 weeks duration. Average risk of relapse at year 5 was high for the 3 regimens that duration were three months or less (8.4%), compared to the ones of one or two years duration (1.7% and 5.2% respectively). For these last regimens, risk of relapse at year 10 ranged from 7.7% (4-13) to 43% (27-57) but there was no evidence that the duration of therapy (one year versus two years) changed the risk of relapse. Time distribution of relapses for regimens having at least 10 years follow-up showed pikes at year 7 and 9. The risk of relapse was not totaly explained by the therapy. Other possible risk factors for relapse would be interesting to be analysed (Bacteriologic Index, HIV infection, Steroid therapy for reactions...).

Acknowledgment : This investigation received partial financial support from the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.

CH28

BRODIMOPRIM/DDS AND BRODIMOPRIM/DDS/RIFAMPICIN - *IN VITRO* AND *IN VIVO* RESULTS FOR A NEWLY DEVELOPED EFFETIVE MDT AGAINST LEPROSY -

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A new combination consisting of Dapsone (DDS) and the dihydrofolate reductase inhibitor Brodimoprim (BDP) has been developed for the treatment of leprosy. The combination of these two drugs shows strong synergistic inhibitory activity. This is demonstrated on *Mycobacterium lufu* as a model strain as well as on *M.leprae in vitro*. The *in vitro* efficacy has been

convincingly confirmed in mouse foot pad experiments. The combination shows a perfect fit in its pharmacokinetic properties resulting in parallel serum concentrations (~ 1:1 ratio) with a half life of ~ 24 hr. On the basis of these results, trials on previously untreated patients (=100) have been performed in Alert/Ethiopia and Asuncion/Paraguay with the following regimens: Alert, A: 200 mg BDP daily, B: 200 mg BDP + 25 mg DDS daily and in Asuncion, C: 200 mg BDP + 100 mg DDS + 600 mg Rifampicin daily. Regimens A and B were stopped after 3 months of treatment and treatment was continued with WHO MDT in accordance with the initial protocol. Regimen B shows convincing clinical and laboratory efficacy after 3 months. Treatment with regimen C was - in contrast to the initial protocol - completely stopped because of the excellent clinical results. Patients are now under relapse control. Tolerance of all 3 regimens was generally good.

CH29

PROGRESS IN CHEMOTHERAPY RESEARCH OF LEPROSY

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Since the last Congress in 1988, we have demonstrated that clarithromycin (CLARI) and minocycline (MINO) alone showing promising bactericidal activities against *M.leprae* in mice; pefloxacin (PEFLO),ofloxacin (OFLO), CLARI and MINO alone displayed very powerful bacericidal activities in lepromatous patients, with rare and mild side effects. In mice, additive effects were shown with the combinations of CLARI+ MINO and CLARI+MINO+ rifampicin (RMP); and single dose of CLARI+ MINO or CLARI+MINO+OFLO displayed definite bactericidal activity against *M.leprae*, only slightly inferior or comparable to that of single dose of RMP. The results of these studies clearly indicate that three new classes of bactericidal agents are added to the short list of antileprosy drugs. Combining these drugs with RMP may permit significant shortening of the duration of multidrug therapy (MDT) and develop a fully supervised, monthly administered MDT regimens; in addition, the these new drugs, probably in combination with clofazimine, may play an important role for the treatment of RMP-resistant leprosy.

At present, we are testing the bactericidal activities of various combinations of new antileprosy drugs in *M.leprae*-infected nude mice; evaluating the bactericidal activities of the single dose of various combinations CLARI+MINO and CLARI+MINO+OFLO in lepromatous patients; participating the multicenter field trial of one-month treatment with the combination RMP+OFLO for both MB and PB leprosy; measuring the minimal effective dosages and minimal inhibitory concentrations of OFLO and sparfloxacin against *M.leprae* in mice; and assessing the specificity and sensitivity of the PCR technique in monitoring the therapeutic effect. The methodologies and preliminary results of the studies will be discussed.

CH30

MINOCYCLINE AND RIFAMPICIN IN LEPROSY

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Twenty (20) biopsy proven, previously untreated leprosy patients were entered into the study using a 28 day course of daily minocycline (100 mgs.) and rifampicin (600 mgs.). These patients were otherwise in good health between the ages of 15 and 65, non-pregnant and non-lactating. There were 12 TT, 4 BT, 1 BB, 1 BL, 2 LL patients enrolled. The results showed clinical improvement in all patients, earlier for those in the TT and BT types and within the year for the more serious forms of the disease. The drug combination was well tolerated with no disturbance of baseline laboratory functions. Patients are still being followed-up every three (3) months for the last 2 years with no clinical evidence of relapse.

CH31

COLCHICINE IN TYPE II LEPRA REACTION AND ITS COMPARISON WITH CORTICOSTEROIDS.

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Leprosy is a scourge of the mankind which makes the individual afflicted by it not only suffer but also undergo the odium of an outcaste. Various drugs are being used in the management of the Type II lepra reaction like CLF, Steriods, Thalidomide, Levamisole etc. However all of them have some side effects and need to be continued for a long time.

We have undertaken a comparative study to assess the efficacy of colchicine and steriods in type II lepra reaction. Group A consists of 30 patients treated with colchicine and Group B consists of 30 patients treated with steriods.

Colchicine was effective in controlling mild to moderate degrees of Type II Lepra reactions within a short span of time. It also reduced patients stay in the hospital. Colchicine was more effective in controlling neuritis & arthritis as compared to steriods. Colchicine is a safe drug except GIT symptoms. Colchicine allowed continued administration of antileprosy treatment without the risk of reaction. Colchicine was not effective in controlling severe degrees of lepra reaction specially in those who were getting recurrent episodes, those who had received steriods or steriods + CLF as an anti reactional treatment in the past. In our opinion Colchicine should be tried before starting steriods in Type II lepra reaction.

CH32

OFLOXACIN-RIFAMPICIN TRIALS IN MULTIBACILLARY LEPROSY - PRELIMINARY OBSERVATIONS ON REACTIVE EPISODES

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With the object of reducing the duration of treatment in leprosy, WHO has instituted multicentre double blind controlled trials with ofloxacin and rifampicin. In this presentation we submit our preliminary observations on 58 untreated multibacillary leprosy patients with BI more than 2.0(47 had BI $\geq$ 3.0) in an "open" clinical trial. 28 patients receiving 400 mg ofloxacin and 600 mg rifampicin daily for 28 days are compared with a group of 30 patients who were administered WHO MDT for 12 months. While the object of this on-going investigation is to make long term clinical and epidemiological observations, we report here a special feature observed so far, namely the occurrence of reactive episodes over a period of 6 months to 2 years.

14 (50%) out of 28 patients have undergone reactions in the ofloxacin group as opposed to 7 (23%) out of 30 patients in the WHO MDT group. One female patient in the ofloxacin group aged 16 who underwent erythema necroticans associated with severe neuritis had to be admitted for monitored administration of high doses of steroids and clofazimine. Rest of the reactions were mild and easily controllable with steroids. 12 out of 14 and 4 out of 7 reactions were encountered in the first 6 months in the ofloxacin and control groups respectively. Mean BI in 8 patients declined from 4.5 to 2.5 in 1 year.

We conclude that:- (1) Reactive episodes may be a feature of ofloxacin-rifampicin regimen, (2) Trial designs should include precise neurological assessments in view of the possible effect of reactions on the nerves and (3) A trial group with anti-inflammatory components like clofazimine is indicated.

CH33

OFLOXACIN CONTAINING COMBINED DRUG REGIMENS IN THE TREATMENT OF LEPROMATOUS LEPROSY

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Adult untreated 23 Lepromatous leprosy and 3 Borderline lepromatous leprosy patients with a Bacteriological Index of 4+ or more were admitted into the hospital of Central Leprosy Teaching and Research Institute, Chengalpattu,

India between 1989-1991. After prescribed investigations, the patients were randomly allocated in blocks of 3 to three regimens containing Clofazimine, Dapsone and Ofloxacin with Clofazimine and Dapsone common to all. The drugs were administered orally in doses of 300 mg. once in 4 weeks and 50 mg. daily of Clofazimine, 100mg. daily of Dapsone and 400mg./800mg. daily of Ofloxacin for 56 days under supervision. Sequential biopsy results for proportion of viable M.Leprae calculated through the analysis of median infectious dose (ID50) in mouse foot-pad revealed no growth by 56th day from all patients treated with regimens containing Ofloxacin and by 28th day in regimen containing 800mg. of Ofloxacin. Moderate to marked clinical improvement has been observed in significantly higher proportion of patients treated with Ofloxacin containing regimens. No serious complications or side effects were noticed with any of the regimens requiring suspension of treatment or administration of steroids.

This study received assistance from UNDP/WORLD BANK/WHO special programme for research and training in tropical diseases (T.D.R.).

CH34

MINOCYCLINE IN LEPROMATOUS LEPROSY

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Minocycline, a tetracycline derivative, has recently been found to have bactericidal effects on M. leprae in the mouse footpads. In the chemotherapy of leprosy there is a need for new bactericidal drugs. Resistance to individual drugs in the current Multidrug Therapy(MDT) for leprosy has been reported. Furthermore, of the 3 drugs used in MDT only Rifampicin is bactericidal. The use of combined bactericidal drugs should reduce the frequency of relapses, minimize the effects of lapses in therapy as well as shorten the duration of treatment.

The present study assesses Minocycline given for 6 months to patients with lepromatous leprosy. Minocycline was given at two dose levels, and intermittently during the 1st month, followed by 100mg daily for 5 more months. Fourteen lepromatous (LL/BL) patients were admitted to the trial: 10 were new untreated, and 4 were relapsed lepromatous. Minocycline efficacy was measured in terms of clinical changes, changes in the bacterial index and histology. Determination of the levels of PGL-1 antigen was also done. Studies for viability of M. leprae by mouse footpad inoculation, and radiorespirometry were also performed. Results thus far indicate that Minocycline is very effective and the absence of significant side effects suggest it can be safely used in the treatment of leprosy.

Detailed results will be presented and discussed.

CH35

FIVE YEARS EXPERIENCE OF MDT IN AMRITSAR(PUNJAB)

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A clinicopathological evaluation of 510 new leprosy patients registered between 1982 to 1987 revealed:
1. 23.53% (120) infectious cases (Dharmendra's operational classification, 1986),
2. Majority of males (3:1), in their prime age group (21-40 years) and housewives or involved in manual labour,
3. 29.21% compliance rate of treatment [Modified W.H.O regimens with additional six months (minimum) 100mg dapsone daily for PB cases and initial intensive 2 weeks therapy with 600 mg Rifampicin and 100 mg Dapsone daily alongwith 100 mg Clofazimine EOD for MB cases],
4. 36.91%(117; 96 PB and 21 MB) clinicopathological correlation,
5. Complete clinical cure in 23.6% (26; 16 PB and 10 MB) with clinical inactivity in 74.55% (82; 73 PB and 9 MB). Two PB cases active even after 19 and 14 months therapy,
6. Untoward side effects in 13 MBMDT cases in the form of ENL in 2(6.9%), ichthyosiform lesions and/or reddish brown pigmentation of face, conjunctivae or of lesions in 11(37.93%) cases,
7. No relapse, and
8. Histological cure complementing clinical cure only in 15% (3; 2 PB and 1 MB) cases.

Strategies of leprosy eradication by 2000 AD need revision in the light of above observations, in our view.

CH36

AN OBSERVATION ON THE EFFECT OF MDT IN THE TREATMENT OF 1,095 LEPROSY PATIENTS IN SHAANXI PROVINCE, CHINA

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One thousand and ninety five cases of leprosy were treated with MDT regimen, recommended by WHO in Shaanxi province from 1987 to 1990. Eighty hundred and seventy nine cases of them (80.27%), including 695 MB cases and 184 PB patients, were clinically cured. Out of these cured cases, 103(9.41%)(MB 90, PB13) were markedly improved, 101 (9.22%) (MB 86, PB 15) were improved, and 12 MB cases (1.1%) remained unchanged. The total clinically effective rate was 98.9%, showing an obvious effect within a relative short time. In 883 MB cases treated with MDT for 24 months, the annual average decrease of BI of out patients and hospitalized cases were 0.94 and 0.91, giving a declining rate of 94.44% and 88.11% respectively. In 553 hospitalized MB cases treated with MDT, after the completion of the prescribed doses, their HI (histological index)decreased from 1.34 to 0.11, with an annual average decline of 0.62 and a decrease rate of 91.79%. BI decreased in parallel with the decline of HI. The proportion of the occurrence of type II leprosy reaction in 325 previously untreated MB cases on MDT was 24.3%, similar to that (22.58%) of 558 cases with DDS monotherapy. In the above said 558 cases 26.34% of type II leprosy reaction were seen when they were retreated with MDT. No significant difference of the frequency of typer II lepra reaction was found between pre-MDT patients and post-MDT cases, suggesting the limited effect of the routine dosage of B663 in the control of the reaction.No type I leprosy reaction was seen during the periods of treatment and surveillance. The side and toxic effects of MDT were acceptable and did not interfere the carrying out of the MDT programme.Six hundred and forty five MB and 184 PB cases were cured clinically and were followed up for 1-3 years, no relapse was detected.

CH37

THE OBSERVATION OF 328 MB CASES TREATED WITH MDT AND FOLLOW UP STUDY

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Three hundred and twenty eight MB patients were observed during the treatment with MDT (WHO regimen, 1982) for 36 months and monitored for 24 months after the end of their drug treatment. One hundred and fifty of them were previously untreated (group 1), 161 were previously treated by DDS+RFP (group 2) and the remaining 17 were relapses after cure with DDS monotherapy (group 3).

All cases were examined clinically, bacteriologically and histopathologically before, during and after MDT regularly. The observation indicated that there were satisfactory clinical improvements in all cases, macules disappearedy in 3-6 months, and nodules flattened in 3-15 months. And there was a steady fall in BI value before and even after the discontinuation of the treatment. Skin smears became negative in 110 cases 24 months after stopping the drugs. Five-year histopathological observation in 30 cases showed that all BIG(bacterial index of the granuloma), GF (granuloma fraction) and HI(histopathological index) decreased steadily. The side effects of MDT were acceptable. The authors stressed the effectiveness of MDT in reducing and controlling the frequency and severity of lepra reactions and deformities.

CH38

THE EFFECT OF MDT FOR 27 MONTHS AND POST-TREATMENT SURVEILLANCE FOR 72 MONTHS IN MB CASES

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Forty seven cases of active MB leprosy patients were regularly treated with RFP, B663 and DDS for 27 months with satisfactory clinical, bacteriological and histopathological improvements. The side effects were mild. MDT was also effective in controlling Type I leprosy reaction. After stopping MDT, there were both steady clinical improvement and steady decrease of the BI also decreased steadily approaching zero in the sixth year after stopping the medications. Histopathologically inflammatory infiltration also gradually subsided. In the period of Six years' surveillance, except 4 cases who died of non-leprosy cause, the remaining 43 cases were all cured and no relapse was detected, indicating that MDT short-term regimen was very effective in the treatment of MB leprosy patients. The authors stress the importance of implementation of MDT short-term regimen on a wider scale in order to reach the goal of basic elimination of leprosy in China by the end of the year of 2000.

CH39

OBSERVATION OF 607 PATIENTS OF MULTIBACILLARY LEPROSY UNDER SURVEILLANCE OF THREE YEARS AFTER COMPLETION OF MULTIDRUG THERAPY

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From 1984 through 1991, 607 patients of multibacillary leprosy with positive smears in 20 counties of Liangshan and Panzhihua prefectures of Sichuan province had completed MDT courses, recommended by WHO in 1982, and were under surveillance for three years. Marked steady clinical and bacteriological improvements were observed. Forty five of them were previously untreated cases with active skin lesions and BI value of 1.00 to 4.60 at the start of MDT. Their skin lesions subsided after 12 months of MDT and the annual average decline of BI in the period of five years was 0.58 and that of the first three years was 0.83. BI of 36 patients of them became negative and that of the other 9 remained positive in the third year of surveillance. A half of another 562 cases, DDS treated previously and with BI value of 0.16 to 4.66 before MDT, also had active skin lesions at the start. Their skin lesions also subsided after 12 months of MDT, and the annual average decline of BI in the period of five years was 0.31, and was 0.49 in the first three years. In the third year of surveillance, BI of 519 cases of them decreased to zero but the smears remained positive in 43 cases.

In the period of suruveillance, lepra reactions, mostly only skin reactions, were seen in 9 patients (ENL 2, neuritis 2, type I reaction 5). They were successfully controlled by steroids and did not cause new deformity.

CH40

RESULTS OF SKIN SMEARS FROM EIGHTY FOUR MULTIBACILLARY PATIENTS ON MDT MB REGIMEN RECOMMENDED BY WHO

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Eighty four multibacillary (MB) patients whose skin smears were positive were treated 24 months with the regimen of multidrug therapy (MDT) for MB patient recommended by WHO (1982) since 1987. At the end of the first 12 months of MDT there 15 (17.9%) cases whose skin smears became negative and 54 cases (64.3%) whose skin smears became negative after the 24 months of MDT completed. After that MDT was stopped and the patients were supervised once or twice a year under the doctors and technicians with physical exam and skin smears for the exam of bacilli. At the end of the first year of supervision the number of patients whose skin smears became negative increased to 63 cases (75.0%) and at the end of the second year of supervision the number of patients whose skin smears become negative increased to 78 cases(92.8%) continuously. The results observed above like some authors who introduced MDT MB regimen to MB patients until the skin smears becoming negative. That is to say that the 24 months of MDT for MB patients recommended by WHO (1982) is enough for the most of the MB patients. But the real and final efficiency of MDT for MB patients recommended by WHO will be confirmed by relapse in the future.

CH41

THE ANALYSES OF TREATMENT TIME FOR LEPROSY CASES CURED WITH DDS AND MDT IN YANGZHOU PREFECTURE, CHINA

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In the paper the data to be analysed are based on Yangzhou, China, in order to reveal the features on time distribution of the cure and to propose the appropriate time to cure leprosy patients with MDT. The leprosy cases are divided into Old PB and Old MB(treated with DDS before), New PB and New MB (never treated before). The treatment regimens include WHO MDT and Mod MDT (Modify MDT: local MDT). The method of moment is used to test for normality for the time distribution of cure. The results indicate that most of data are skewness distribution, therefore we use the median (year) of cured time to compare them. By end of the year 1990, total 14723 cases are cured by DDS with median of 11.46 years, 83 Old PB cases by WHO MDT with median of 2.09 years, 110 New PB cases by WHO MDT with median of 2.62 years, 367 Old MB cases by WHO MDT with median of 3.47 years, 58 New MB cases by WHO MDT with median of 4.43 year, 168 MB by modify MDT with median of 2.49 years. The cured median of all PB cases with WHO MDT is 2.48 years, the median of all MB cases with WHO MDT is 3.60 years. The results indicate that the optimal time to treat leprosy cases until cure: PB cases with MDT need 1.5-2.5 years, MB cases with MDT need 3.5-4.5 years. The differences between males and females in DDS and Mod MDT have high significance ($p<0.01$). It is interesting to show that the MB cases with Mod MDT need shorter time to cure than WHO MDT regimen ($p<0.01$).

CH42

A STUDY OF 315 MULTIBACILLARY CASES OF LEPROSY UNDER MDT AT JNRMH, TALA, RIZAL PHILIPPINES.

Roland C. Samson, MD, Jimmy Dayanghirang, MD.

Multidrug treatment, following the WHO regimen, was introduced at Dr. Jose N. Rodriguez Memorial Hospital, Tala, Rizal, Philippines in 1981. The main objectives were: 1. to treat all active cases admitted in the hospital, irrespective of their previous treatments; and 2. to supervise the daily intake of the MDT drugs. Since then 315 patients have finished MDT, completed the surveillance period and were released from control in January 1993.

No major problems with the use of multidrug regimen were encountered, except for the initial apprehension of patients in taking the new drugs, which was readily overcome.

This study was failed to detect any significant side-effects associated with the use of multidrug regimen. Few cases of

leprosy reaction's during the treatment have been observed. There were few complaints about dofazimine - induced pigmentation, that gradually disappeared during the surveillance period.

We are of the opinion therefore that multidrug therapy has proved successful; the drugs are acceptable to the patients and the use of MDT in leprosy control was a wise decision.

CH43

FACTOR INFLUENCING PATIENT'S COMPLIANCE TO MDT/ OMS IN RIO DE JANEIRO.

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Default from treatment for Hansen's Disease is probably one the most important reasons of the endemic status in Rio de Janeiro State, Brasil. Annual defauters rate in the last five years are around forty-five per cent.

Four hundred and eighty six defaulters were interviewed, in order to detect the most common causes of now-attendance to the supervised monthly dose in several cases leading to default before healing. Among others, profissional factors and "forgetting" the right day were frequently found. The results will be presented, analysed and discussed by the outhors in this intervention.

CH44

USE OF PGL-1 IN THE FOLLOW-UP OF MULTIBACILLARY LEPROSY PATIENTS UNDER SURVEILLANCE AFTER RELEASE FROM TREATMENT(RFT).

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Detection of IGG and IGM antibodies to phenolicglicolipid-1 by ELISA method has been used, to evaluate its usefulness in the serum diagnosis and monitoration of treatment.

A group of thirty-six multibacillary patients was followed after RFT with PGL-1 titrations by the ELISA method, on a 3 month basis. The objetive of the study was to evaluate the viability of this test in the early diagnosis of relapse. Patients were into two groups according to bacteriological positivity or negativity at the end of treatment.

It was observed that the two groups showed the expected results, already described by other authors:

Higher titrations in the BI positive group and a slow decline along the time in the two groups.

However, considerable individual variations were observed, becoming a limitation to the use of this method in early diagnosis of relapse.

CH45

TEN-YEAR COHORT ANALYSIS OF PAUCIBACILLARY LEPROSY PATIENTS WHO RECEIVED MULTIDRUG THERAPY

Thirunavakarasu S, Narayanan R, Matheus M, Lobo D, Thomas C.J.

Our institution GREMALTES based in Madras is a pioneer in URBAN Leprosy Control. We initiated MULTIDRUG TREATMENT (MDT) in 1983.

Between 1983 and 1992 - 13,250 patients received MDT, of which 11,552 are PAUCIBACILLAY (PB).

A cohort analysis of all the PB cases over the ten-year period is presented, using the following parameters:

- Treatment Regularity/Compliance
- Proportion of Drop-outs
- Proportion of Mono-lesions
- Cure rate
- Relapse rate
- Proportion of cases with complications like Neuritis/Reactions

The significance of the results, their relevance to the impact of MDT and for planning and implementation of Leprosy Control Programmes specially for URBAN areas is discussed.

CH46

FIXED DURATION COMBINED CHEMOTHERAPY IN MULTIBACILLARY LEPROSY

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The principal objective of this study is to measure relapse rates in multibacillary leprosy patients who have completed 24 doses of the combined drug regimen recommended by the **WHO** study group of 1981.

From November 1987 to January 1992, 424 new leprosy cases were included in the trial. None had previously done any antileprosy treatment and all were skin smear positive with BI of 2+ or greater. They have been receiving the treatment recommended by the **WHO** 1981 Study Group. After 24 supervised monthly doses within up to 36 months their treatment was ceased regardless of skin smear status. 240 patients have already completed the 24 doses. 96 patients have completed 2 or 3 years of followup. There have been no relapses. The followup will continue for 5 years.

This trial received financial support from **UNDP/WORLD BANK/WHO/TDR**

CH47

MDT IN MANAUS: READMISSION AFTER RELEASE FROM TREATMENT

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Between December 1982 and December 1990, 6,198 leprosy patients from the municipality of Manaus were treated with the **WHO**/1981 multidrug regimen. 32 of these patients (0.52%) needed to be readmitted to treatment.

The clinical findings that necessitated readmission to treatment are presented, and concepts of relapse and reaction are discussed.

CH48

MULTIDRUG THERAPY OF MULTIBACILLARY LEPROSY PATIENTS - A TEN YEAR FOLLOW-UP STUDY

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In 1980, 79 untreated multibacillary patients with a bacterial index ranging from 2.5 to 3.4 were chosen for the study. Of these 25 patients were dropped out for various reasons which include 8 patients who were found to be dapsone resistant. They were divided into 3 groups. One group (A 14) received daily dapsone 100mgs alone, a second group (B 19) rifampicin 600mgs and dapsone 100mgs daily and a third group (C 21) rifampicin 600mgs, dapsone 100mgs, INAH 175mgs, and prothionamide 175mgs daily.

All patients were assessed clinically for the severity of the disease and for disability. Skin smears, skin biopsies, foot-pad inoculation studies for viability of the bacilli, hemogram, liver and kidney function studies were also conducted in the beginning of the study and at every 6 months. Reaction episodes were carefully recorded. At the end of 3 years the drugs were completely stopped and the patients were carefully followed. Now, 10 years after discontinuation of therapy 1 was dead, and 20 migrated and were lost to follow up. Thirty three patients, 10 from group A, 10 from group B, and 13 from group C are available for follow up. Skin smears, skin biopsies, clinical evaluation of the disease and of the disability, were done on all the 33 patients.

The results will be presented and discussed.

CH49

FIXED-DURATION MDT IN MULTIBACILLARY PATIENTS. TWO YEARS OF SURVEILLANCE. Nery JAC, Gallo MEM, Malta AM, Viana SM, Almeida SM, Borges E, Sarno EN. Leprosy Department, Oswaldo Cruz Foundation, Av. Brasil, 4365 - Manguinhos, 21.045-900 - Rio de Janeiro - RJ - Brazil.

MDT, according to the WHO recommendation, was introduced in the FIOCRUZ Out-patient Unit. 115 had completed regularly the treatment and are now under surveillance. At the completion of MDT, all patients showed no active leprosy lesions, involution of dermal infiltrate (AFB + in the skin 55.9%) except for 11% of patients with type II reactions aspects. The BI was negative in 20% and the MI in 97,4%. When the final BIs were compared with BI of the intake, it was observed a decrease in 82,2%, increase 1.6% and no change in 16%. The neurological exam demonstrated improvement in 24.5% of the patients, worsening in 7.6% and no change in 65,2% (the majority had incapacity degree = 0). The follow-up baciloscopic exam performed in 81 patients who completed the 1st year of surveillance showed: decrease in 45.6% increase in 13.5% and no change in 27.1% when compared with the BI at the end of MDT not realized 13.5%. Among the patients who presented a negative BI at the end of MDT, 4.9% became + during the surveillance (2,45% each year). During the surveillance period 38 (46,9%) of the patient presented reactions: 29.6% in the 1st year and 6.1% in the 2nd year and 11.1% realized in first and second years. Type I reaction occurred in 15.7 % of patients only at the 1st year of surveillance and type II occurred in 76.3%. Isolated neuritis occurred in 7.8% of the patients.

Supported by grants from TDR-WHO.

CH50

INCORPORACION DE LA MULTITERAPIA EN LOS ENFERMOS DE CATALUÑA:RESULTADOS E INCONVENIENTES:

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La población enferma de Cataluña (España),inició la implementación multiterápica hace 6 años.El Trabajo realizado muestra las dificultades de su incorporación así como el resultado positivo en cuanto a la reducción de la población enferma una vez cumplido el tratamiento durante el tiempo preciso.

CH51

THE SLIT SKIN SMEAR IN LEPROSY - AN IMPEDIMENT TO MDT ?

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The launch of the World Health Organisation's two multiple drug therapy (MDT) regimens in 1982 was accompanied by the strong recommendation that skin smear microscopy of acceptable quality be a prerequisite for field programmes to implement MDT. It gradually transpired that an alarmingly small number of centres in leprosy endemic countries were capable of producing accurate and consistant results and the necessity of skin smear microscopy was questioned since it appeared that the absence of smear facilities was partly responsible for delaying the implementation of MDT in some areas. As an aid, particularly to non-medical field workers, various alternative methodologies have been adopted in order to assist in accurate classification in different programmes and a summary of the "body area rule" is presented. It is argued that, if necessary, a competent MDT field programme can be run in the total absence of a skin smear service and hence poor or absent laboratory support should no longer be allowed to impair the implementation of MDT.

CH52

PRIMARY RESISTANCE TO DAPSONE AND RIFAMPICIN

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With the objective of evaluating Primary Resistance to Dapsone and Rifampicin in untreated patients with Multibacillary Leprosy it was decided to carry out a survey with active Lepromatous Leprosy consulting at the Oswaldo Cruz Foundation. The survey was conducted between october 1989 and december 1992. During the study period, 47 skin biopsies were collected. The results showed that none of the strains was resistant to Dapsone and Rifampicin.
M.leprae recovered from 29 patients showed sensitivity to Dapsone and 25 to Rifampicin.
Four strains were non infective and the fourth was inconclusive.
The organisms from 12 patients did not infect mice and the results from 6 specimens were inconclusive because multiplication of M.leprae was observed in only few control mice.

This Investigation received finacial support from UNDP/World Bank/WHO-TRD

CH53

SURVEY FOR SECONDARY DAPSONE AND RIFAMPICIN RESISTANCE IN CUBA.

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A total of 1211 Cuban leprosy patients treated for at least 5 years were clinically and bacteriologically examined. They were being treated according to a two-phase monotherapy regimen with RMP first and DADDS afterwards. On skin smear examination 50 patients were found positive, of them, 9 showed a BI of 3+ or higher at any site. With regard to the clinical status the only cases found with clinical signs of relapse were 5 of 7 long-standing patients with BI of 4+ and 5+. A sixth patient of this high BI group who showed a good clinical condition except for a heavy infiltration of both earlobes was receiving a second RMP course when examined and biopsied for this research. These 9 patients were biopsied and susceptibility tests to RMP and DDS performed. The results showed that in 1 case the M. leprae were resistant to both drugs, the organisms from 2 other patients were susceptible to RMP but low-grade resistant to DDS. Those from another patient were susceptible to RMP and fully resistant to DDS. In 3 other cases the bacilli did not multiply in any of the mice but 1 of these strains was from the patient taking a second RMP course, therefore this strain might also be susceptible to RMP and resistant to DDS. In the last 2 cases multiplication was only observed in 2 of the controls and in 1 of the 0.0001% DDS treated mice, therefore, these experiments were not conclusive and the AFB inoculated into fresh mice to repeat the tests but failed to multiply.

CH54

RELAPSES AFTER DAPSONE MONOTHERAPY: AN ANALYSIS OF 769 CASES IN JIANGSU PROVINCE, CHINA

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From 1949 to 1988 the leprosy patients cured in Jiangsu Province totalled 41,594, of whom 1,069 cases relapsed with a relapse rate of 2.55%. This article investigated 769 relapse cases (652 males, 117 females) who had received dapsone monotherapy for 1 to 24 years with a regular treatment rate of 86.4%. The dapsone monotherapy was also given during the observation period. The interval between cure and relapse averaged 4.30 years for the MB cases and 4.69 years for those of PB. 94.8% of the relapse patients were over 25 years of age when they developed signs of relapse and the disease course was all found to be longer than 6 months. Of all the MB relapse cases, 36% had more than three skin lesions on first visit, apparently higher than the control group (26.9%). The clinical features of the MB relapse cases were mostly the reactivation of old skin lesions and the deterioration of old nerve impairment and the deformity rate was 10.79%, while a large portion of the PB's developed new skin lesions and nerve impairment,and the deformity rate was 24%. It has been shown that the main precipitating facts causing relapse are overwork, life and mental load and excessive drinking. 84.56% of the cases were detected by personnel and 13.29% by basic health care system or by the patients themselves. The authors held that the dapsone monotherapy cannot provide a solution to the problem of relapse, on which early diagnosis and treatment may have a greater effect.

CH55

AN EVALUATION OF RE-TREATMENT OF 13,477 LEPROSY PATIENTS CURED WITH DDS IN JIANGSU PROVINCE, CHINA

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In order to prevent cured patients from relapse, 13,477 cases cured with DDS monotherapy were re-treated with MDT in Jiangsu province from 1984 to 1991. Three thousand four hundred and fifty seven of them were MB and 10,002 were PB. Two thousand two hundred and twenty seven patients were re-treated with three drugs in combination and 11,250 cases with two drug combination regimen. All patients were followed once or twice a year after the completion of the re-treatment. 3,520 cases of them (26.12%) have been released from re-treatment for 5 or more than 5 years. By the end of 1991, no relapse was detected. But during the same period (1984-1991), 457 relapses were found in 22,488 DDS-cured but not re-treated patients, giving a relapse rate of 2.03% (MB 13.95%, PB 0.8%).

CH56

COMBINED CHEMOTHERAPY AND IMMUNOTHERAPY FOR TREATMENT OF HIGHLY BACILLATED BL/LL CASES

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Viable as well as dead bacilli are known to persist in BL/LL cases even after 2 years of currently recommended MDT. Our earlier studies showed that BCG had a potential immunotherapeutic effect when used in BL/LL patients. In this study, we have investigated the therapeutic response of combined immunotherapy alongwith MDT in BL/LL patients. Untreated BL/LL patients with the initial BI of 4 to 6+, were serially alloted to three treatment groups. Group I patients received a slightly modified WHO regimen (Rifampicin once a month, Clofazimine & Dapsone daily) and BCG 0.1 mg/dose. Group II cases were administered the same MDT and Mycobacterium w. (2×10^8 killed bacilli/-dose) and group III received the same MDT with 0.1 ml of distilled water. Vaccination was repeated every 6 months. Biopsies were taken from the local site of vaccination and from a distant site i.e. back. The progress was monitored periodically by using, clinical, histopathological and bacteriological-BI, mouse foot pad, ATP and other viability parameters. The vaccines were well tolerated. There were no serious side effects. In cases of combined chemotherapy and immunotherapy, no viable bacilli were demonstratable by mouse foot pad and ATP measurements at 6 months and afterwards. However in some of the control cases on MDT alone, viable bacilli could be detected even upto 2 years. With 30 months of treatment, the mean BI decreased from 4.6 to 2.45 in the group on MDT alone (control): 4.9 to 0.08 in the MDT+BCG group and 4.7 to 0.05 in the MDT+M.w group. Immunotherapy appears to have a significant effect on killing and clearance of bacilli in these cases.

CH57

INTRODUCTION OF SINGLE DOSE OF RIFAMPICIN FOR THE TREATMENT OF LEPROSY PATIENTS IN OUT REACHED AREA

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WHO had undertaken a BCG vaccine trial in Singu township of Upper Myanmar (1964-75) to see its effectiveness against leprosy. Overall prevention rate after 10 years trial period showed only about 14%.

In addition, epidemiology of leprosy was studied and incidence was not abated with the dapsone monotherapy. So combined drugs using rifampicin, lamprene and dapsone were considered for further trial.

During the trial operation, (1976-1984), patients in outreached area (about 70%) were unable to be covered with the standard trial regimen.

So, if not the best, an alternative regimen using a single supervised dose of 1500 mg of rifampicin and self administered daily dose of dapsone was introduced for 5 years.

The results were satisfactory; morphologically all of them were zero after one year and bacteriologically most of them were negative after 5 years.

And thus a feasible operation using a single dose of rifampicin per year for 5 years in outreached area was considered helpful to change the leprosy epidemiological pattern in an area where standard regimen was inoperable.

CH58

EXPERIENCE GAINED IN NEPAL WITH COTRIFAZID

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This is not a report on a trial in which a new leprosy therapy was evaluated. Such a trial had been carried out earlier in Paraguay (Ref.). The aim was to check the effectiveness of out-patient Cotrifazid treatment (Rifampicin + Cotrimoxazol + Isoniazid) under the difficult outer conditions prevailing in Nepal. Depending on the severity of the case, treatment duration varied from 2 to 6 months. The high tolerance and compliance and the excellent result of this therapy are discussed in detail. Cotrifazid, which might be termed a fixed broad-spectrum combination, offers the great advantage that no additional medication is required for treating concurrent infections often encountered in leprosy patients, e.g. tuberculosis, "atypical" mycobacterial diseases, enteritic diseases, staphylococcae etc.

Summary: So far we have not heard of any other therapy allowing to overcome such a complex of difficulties.

Ref.: A New Short-term Combination Therapy of Leprosy. E. Freerksen, A.E. Alvarenga, O. Leguizamón, Maria Victoria de Morra, L.A. Reyes, W. von Ballestrem. Chemotherapy 1991, 37, 353-363

CH59

ON THE NECESSITY OF ALTERNATIVE THERAPIES FOR THE TREATMENT OF LEPROSY

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The varying severity of leprosy is due to the large ethnic and genetic differences, the different state of nutrition, and the wide differences in age of the leprosy patients. Hence there is an urgent need for alternative forms of therapy for the treatment of leprosy.

In addition to the treatment scheme propagated by the WHO, whose advantages and disadvantages are known, fixed combinations of up to four drugs (i.e. the components have been integrated in one tablet) are presently available. These combinations are highly effective, tolerated well, easy to administer, at low cost.

A report is made on the use of "Isoprodian" (INH + PTH + DDS), "Isoprodian-RMP" (INH + PTH + DDS + RMP), "Cotrifacid" (SXT + INH + RMP), "Emdetine" (SXT + PTH + RMP), Ofloxazin + INH + DDS + RMP, and a combination of PTH and DDS in more than 1970 cases of leprosy.

CH60

BACTERICIDAL ACTIVITY OF OFLOXACIN AGAINST Mycobacterium leprae

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Sixteen patients with infiltrated lesions of lepromatous leprosy were enrolled in this trial. The microscopic examination of their lepromata yielded bacterial indexes in from 4+ to 5+ (according to Ridley's logarithmic scale) and morphological indexes higher than 70%. The histological study of the lesions revealed typical LL leprosy granuloma. Patients presented disseminated erythematous plaques, papules, nodules and macules. The mouse footpad inoculation and estearase tests were positive in all patients. Supervised multi-drug treatment (standarized by WHO) taken during at least 2 years had failed in all cases, as proven by clinical and bacteriological controls. Then, a six-month monotherapy with ofloxacin (2 daily 200 mg doses) was initiated. The drug was kindly provided by Cilag Pharmaceutical. During the progress of ofloxacin therapy, 2 patients presented type II reaction (nudosum erithema), other side-effects were absent. After 2 months treatment, only granular bacilli were found by smear examination; the estearase and the inoculation tests were negative in all 16 cases. Remission (n=7) and flattening (n=2) of the lesions was observed in the 9 patients who completed the chemotherapy. They were followed-up for 4 to 6 months and no reactivation occured.

CH61

K-130: A NEW INHIBITOR OF *M.LEPRAE* DIHYDROFOLATE REDUCTASE

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Bacterial dihydrofolate reductase is a well known target for antibacterial drugs like trimethoprim and related compounds. No compound of this type has until now become an antileprotic drug because of low effectivity. Therefore several diaminopyrimidine derivatives were sythesized with the aid of molecular modelling to derive compounds with improved properties. The aims were, 1) to increase the affinity against the target enzyme, 2) to increase the ability of permeation through the highly lipophilic nycobacterial cell wall and 3) to possibly combine two principles of folate synthesis inhibition (dihydropteroate synthase and dihydrofolate reductase inhibition respectively) by combining dapsone derivatives with a diaminopyrimidine derivative in one "autosynergistic" acting molecule.

All of these aims have been achieved successfully. Among the derivatives synthesized K-130 is the most promising. Its high activity has been demonstrated on the isolated enzymes as well as *in vitro* against *Mycobacterium lufu* (a model strain) and *M.leprae*, respectively.

The *in vitro* efficacy was convincingly confirmed in mouse foot pad experiments. On the basis of these results toxicity studies in rats and monkeys were performed at the Central Drug Research Institute in Lucknow (India), showing that the drug is safe up to the highest concentrations tested. The data have been submitted to the Indian drug contollers for permission to initiate phase I clinical trials.

CH62

GANGLIOSIDES(CRONASSIAL)& LEPROSY NEUROPATHY. A Randomized,Placebo controlled trial.

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Gangliosides are been used for the last 14 years in the treatment of various forms of peripheral neuropathies.

Method:Randomized double-blind placebo controlled trial of Cronassial conducted in 6 centres in India.Of the 120 patients who entered the trial only 114 completed it as per protocol.Only BB,BL, LL types were selected because their neural damage is similar,& an earlier open-trial suggested that these patients would benefit the most.

Other criteria for selection:1)Age between 18 & 50.(2)At least 2 nerves have moderate to severe damage as assessed with Pasricha's instruments, WHO thermal tester,skin thermometre,VMT.(3)The damage must be of not less than 2 years duration,so as to rule out spontaneous recovery.

The therapy:40mgs.Cronassial i.m.daily for 60 days.The placebo vials were identical in appearance to the drug.The patients were assessed with objective & subjective methods for sensory/motor/sympathetic loss at baseline,and after 30,60,180 days;some could be checked after 360 days. Results:the drug group showed much better results (statistically significant)than the placebo,in sensory,motor & sympathetic functions.Circa 45% of Cronassial patients recovered "in toto" all sensory modalities:touch,2-point discrimination, pin-prick,temperature,as against the placebos of which only 19% had improvement of one or two sensory modalities.The VMT score & the sympathetic functions were significantly better in the the drug-group.A follow-up of 2 years in 30% of cases showed that the placebo had a poorer score (compared to their last one)while the Cronassial group had consistent or even better results.

CH63

CLINICAL AND BACTERIOLOGICAL EFFECT OF TRYPTOPHAN-ENRICHED DIET IN MULTIBACILLARY LEPROSY - A PRELIMINARY COMMUNICATION

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Anti-leprosy effect of deoxyfructolserotonin for which evidence is available prompted trials of tryptophan-enriched diet "Nourriture Anti-Lepre" (NAL) administered to multibacillary leprosy patients to study the clinical and bacteriological effects, attributable to the enhancement of the concentration of free tryptophan as serotonin precursor in blood. A trial group of 12 MB patients with BI $\geq$ 3.0 receiving NAL 50 gms per day for 6 months was compared with 12 patients put on WHO MDT regimen and 12 others on WHO MDT along with NAL.

Assessment of photographs objectively carried out in a "blind" manner by independent observers showed that there was 75% improvement in 1 patient, 50% in 7 and 25% in 4, in the trial group. Comparable improvement was noticeable in the two other groups as well. Clinical scores assessed before and after treatment also showed perceptible decline in all the groups.

Mouse foot pad innoculations prior to the trial and six months after diet therapy showed loss of viability of M.leprae in 9 out of 12 in the NAL group.

This presentation has clearly shown that tryptophan augmentation in diet is effective against leprosy and results are comparable to the control MDT group.

CH64

ALTERNATIVE TREATMENT FOR DRUG-RESISTANT LEPROSY AND TUBERCULOSIS

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Rational chemotherapy of an infectious disease involves identifying an essential metabolic activity of the causative agent and suppressing that activity with an appropriate inhibitory compound. We discovered derepression of the enzyme, β-lactamase, in M. leprae multiplying in armadillos treated with penicillin G benzathine. M. tuberculosis has been reported to contain a constitutive β-lactamase. M. leprae is able to develop resistance against the generally used antileprosy agents. To overcome this problem, multidrug therapy is being promoted widely, and has had remarkable successes. When M. tuberculosis became resistant to individual drugs, combination therapy was adopted to treat the disease. Now multidrug-resistant (MDR) tuberculosis is spreading in many countries, especially with the emergence of AIDS. One cannot safely deny the possibility of the emergence of MDR leprosy.

Mycobacteria, in general, synthesize β-lactamase and are insensitive to penicillins and cephalosporins. We screened the effect of β-lactam/β-lactamase-inhibitor combinations on growth of M. leprae in mouse foot pads, and on M. tuberculosis H37Ra, H37Rv, M. avium, and BCG (drug-susceptible as well as drug-resistant strains). We tested four different drug combinations: ampicillin/sulbactam (Pfizer), ampicillin/YTR 830H (Taiho), amoxicillin/clavulanate (SmithKline Beecham), piperacillin/tazobactam (Cyanamid). All of them suppressed growth of the bacteria, including that of drug-resistant mycobacteria. Ampicillin/sulbactam showed better activity than the others in which the proportion of inhibitor to antibiotic is higher than in amoxicillin/clavulanate or piperacillin/tazobactam. Apparently, β-lactam/β-lactamase-inhibitor combinations could serve as effective alternative therapy for MDR tuberculosis and drug-resistant leprosy.

CH65

COMBINED DISTRIBUTION-TOXICITY STUDY OF TWO NOVEL PHENAZINES

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Clofazimine is an antibacterial phenazine which has principally been used in the treatment of leprosy. Although a very efficacious agent, its prolonged use has a number of associated problems. A number of novel phenazine agents have been synthesised to produce a more widely effective agent with less side-effects.

Two of these agents (B4090 and B4100) have been shown to be particularly promising. Before further investigation of the therapeutic potential of these compounds, we have investigated the tissue distribution and some elements of the sub-chronic toxicity of these agents as compared to clofazimine. Toxicity was measured by monitoring serum enzyme levels, routine haematology and urine analysis, including urinary NMR markers. The tissue distribution and toxicity of these newer agents in the model used are discussed.

CH66

IMPROVED HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC ANALYSIS OF SYNTHETIC PHENAZINE COMPOUNDS INCLUDING CLOFAZIMINE

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Clofazimine (B663) is an anti-leprosy agent which has also been successfully used to treat other mycobacterial diseases, including *M. avium* infection in AIDS. In an attempt to optimise and increase the therapeutic potential of B663, a number of compounds have been synthesised with different chemical substituents on the parent phenazine molecule.

We have developed a reverse-phase ion-paired HPLC procedure for the measurement of clofazimine and other phenazine compounds. The chromatographic system consists of a C_{18} column with a mobile phase of THF : Water : Acetic acid (400 : 594 : 6) with 2.5 mM hexane sulfonic acid and UV detection at 285 nm.

Phenazine compounds (B663, B749, B3954, B4090 or B4100) were extracted from biological samples into dichloromethane containing another phenazine with a suitably different retention time as internal standard. Using peak height ratios, the extraction ranges were linear in the range 0-50ug/ml.

This method uses an easier extraction protocol for phenazine agents than has previously been reported and coupled with the use of an internal standard, make this method suitable for routine analysis of these compounds from biological samples.

CH67

RELAPSES OF 1,445 LEPROSY CASES CURED WITH DDS MONOTHERAPY

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A follow-up physical and bacteriological examination of 1445 leprosy patients cured with DDS monotherapy before 1986 in 22 counties in Hubei province was carried out in 1990. Among them 35

relapsed cases were detected with a relapse rate(RR) of 2.42% (MB 31/1,084; PB 4/361).

Among 1,084 MB cases followed up,RRs in those with a disease duration less or more than 10 years were 2.58% and 10.53% respectively; RRs in those with a treatment duration of 1-6 years (555 cases)and 7-14 years (281 cases)were 4.49% and 2.14% respectively. No relapse was found in those with a treatment duration more than 15 years. As for the relationship between RR and the duration after clinical cure, it was 2.16% in 6-9 year group, much higher than that in group of 1-5 year(0.83%),but it was high up to 6.74% in those of more than 15 years after clinical cure.

The RR was likely to be closely related to the duration of contineous treatment (CT) after cure. Among 774 cases with CT of 5 or more than 5 years, 26(3.82%) cases relapsed. No relapse was detected in 254 cases with CT of more than 10 years. It was high up to 8.93% in those without CT.

The authors suggest that inadequate or irregular treatment, development of bacterial resistance to DDS and reproduction of persisters are possible causes of relapses for cured patients with DDS monotherapy.

CH68

CLOFAZIMINE DISTRIBUTION IN HUMAN MILK

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Clofazimine, (3-(p-chloroanilino) - 10-(p-chlorophenyl)-2,10-dihydro- 2-(isopropylimino) phenazine), is used in chemotherapy of leprosy. In addition it exhibits anti-inflammatory properties when used in higher doses for treating lepromatous leprosy in reactive phase. We have worked out the distribution of clofazimine in human milk as the knowledge of the amount of drug present in milk will help in deciding about the safety of breast-feeding during maternal ingestion of the drug.

Eight female leprosy patients who were on clofazimine 50 mg daily or 100 mg on alternate days for periods ranging from 6 months to 2 years and were lactating at the time of study formed the subjects of the study. 2-3 timed aliquots of milk and corresponding blood samples were collected. The drug levels were estimated by HPLC and spectrophotometric procedures.

Clofazimine is excreted in milk to such an extent as to colour the milk. The preliminary data is suggestive of a milk to plasma ratio of 1:1.5 for the drug with milk drug levels of 1.5 - 2.5 ug/ml.

The amount of drug ingested by the infants through breast-feeding (0.2 to 0.5% of maternal daily dose) is not likely to be harmful. The high liposolubility and moderate binding of the drug to plasma proteins are the key factors that may decide the distribution of clofazimine in human milk.

CH69

THE CHAULMOOGRA OIL WAS ALREADY USED TO TREAT LEPROSY BY TRADITIONAL CHINESE MEDICAL DOCTORS IN THE PERIOD OF SOUTHERN SONG DYNASTY

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It has been proved that traditional Chinese medical doctors had treated leprosy with Chaulmoogra oil even in Southern Song Dynasty (from 12th to 13th century).The following evidences are considered as major arguments, 1) Bai Yuchan(1193-1229), a famous Taoist priest, poet and doctor, treated leprosy with chaulmoogra oil and his prescription was collected in the monograph--"Jie Wei Yuan Su"written by Shen Zhiwen in the Ming Dynasty;2)Some medical works, such as "Renzhai Zhi Zhi Fang", in which the mentioned prescription was collected, were lost in the Ming Dynasty, but fortunately it had been collectecd in "Yi Fang Lei Ju" and "Xiang Yao Jicheng Fang", edited by Korean doctors in the 15th century and published by the Japanese afterwards;3)Evidences of importing chaulmoogra oil could be found in some historical literatures, such as "Si Ming Annals"; 4) Some historical relics from harbour ruins of Quanzhou Bay also provide evidences. The author suggest that the implementation of open policy in the field of trade and culture in Southern Song Dynasty resulted in the introduction and application of chaulmoogra oil and many other valuable medicinal materials.

CH70

TREATMENT COMPLIANCE IN THE SOUTH SULAWESI LEPROSY CONTROL PROGRAMME, INDONESIA

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Since 1991, the leprosy control programme of South Sulawesi Province, Indonesia, has aimed at providing all its patients in need of chemotherapy with MDT, regardless of their ability to come to the monthly clinic. Patients are allowed to send someone else to collect MDT -including the monthly dose- for them. Selected patients are treated with blister calendar packs of unsupervised MDT for up to 3 months. Although not encouraged, leprosy workers are allowed to deliver MDT to the patients' home. To assess whether this policy is in fact acceptable, urine samples of 588 patients were examined with a spot test for dapsone in the urine. Overall compliance was 78.8%.
There was no difference in compliance between patients who came to the clinic in person and those who sent someone else to collect their drugs. However, it appeared that patients who had their medication delivered at home by a fieldworker, and those being treated with blister calendar packs, were less compliant than the other patients.
Sex, age, classification, disability grade, mode of detection and duration of treatment, had no significant effect on compliance.

CH71

A BIOASSAY TO DETECT NANOGRAM CONCENTRATIONS OF RIFAMPICIN

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Mycobacterium bovis, strain 44 (BCG P_3 vaccine strain) was incubated with ^{14}C-palmitic acid in an axenic culture. Release of $^{14}CO_2$ was detected by liquid scintillation using Whatman No.42 filter paper soaked in liquifluor concentrate; PPO; Triton X 100; 4 N NaOH. Rifampicin at concentrations of 2.0, 0.2, 0.02, 0.002, 0.0002, 0.00002, 0.000002 μg/ml was added to the cultures on the first day. The evolution of $^{14}CO_2$ was monitored daily for 5 days. Rifampicin significantly inhibited the ability of BCG to oxidize ^{14}C-palmitic acid and release $^{14}CO_2$. All concentrations of rifampicin were significantly inhibitory ($p < 0.01$) after 2 days in culture (Dunnett's T test). Cultures incubated with the lowest concentration of rifampicin (2 ng/ml) showed inhibition of metabolism of BCG at the 4th and 5th days of incubation (Dunnett's T test $p < 0.001$).

This bioassay is being utilized in Ethiopia to screen extracts of plants, used in traditional medicine, for their mycobactericidal activity; and to estimate the concentration of rifampicin in various body fluids and tissues.

CH72

EFECTOS INDESEABLES PROVOCADOS POR LA RIFAMPICINA.

J.R. Gómez Echevarría, J. Terencio de las Aguas, J. López Plá.

Se estudian los efectos secundarios más importantes provocados por la Rifampicina en dosis unimensual en enfermos de Hansen tratados con multiterapia.

Se hace especial mención a los efectos secundarios renales y hepáticos.

CH73

ELECTRON MICROSCOPY, POLYMERASE CHAIN REACTION AND SERODIAGNOSIS AS TOOLS FOR ASSESSING LEPROSY TREATMENT.

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This study was done on diagnosed leprosy patients receiving the WHO regimen of treatment (MTD) for more than two years. Biopsies were taken from skin lesions and sections were prepared and stained for electron microscopy. PCR tests were done using two and four primers to increase the sensitivity of the tests. Serodiagnosis was done using (ND - O. BSA) by the indirect ELISA test.

The bacteriological and the immunological investigations showed significant results which will be discussed and presented.

CH74

THE EFFECT OF ANTILEPROSY DRUGS ON BIOLOGICAL RYTHMS

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Rythmical arrangement of physiological functions in a living organism and their disarrangement caused by endogenous factors including medicines attract an increasing attention of the investigators. The appearance of new rythms, development of desynchronoses, resulting in the formation of different pathological states and toxic complications have been described. The effect on biological rythms of DDS given by gavage to outbred white rats in doses of 2-20 mg per kg of body weight for a year was studied. Untreated animals served as controls. Total blood count and biochemical analyses of blood from caudal vein were performed monthly. The results were processed with using cosinor-analysis. All the parameters of homeostasis under investigation in control animals had their own rythms of fluctuations. Erythrocyte count, glucose and hemoglobin concentrations were changed according to circannual rythm. Rythmical fluctuations of other blood indices differed from circannual rythms. Prolonged administration of DDS caused desynchronization of the previously synchronized rythmical fluctuations of erythrocyte, leucocyte and lymphocyte counts and hemoglobin concentrations as well. In view of the evidence obtained an experimental study was begun to investigate the influence of DDS alone and combined with other antileprosy drugs on seasonal and circadian biorythms. The preliminary results suggest new potentialities of development of antileprosy multidrug regimens in terms of chronobiological factors.

CH75

Leprosy Clinical Trial of Fusidic Acid

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A clinical trial of film-coated fusidic acid (Fucidin) in leprosy was undertaken based on impressive *in vitro* activity vs. *Mycobacterium leprae* in the BACTEC system together with existing documentation of human pharmacokinetics, safety and efficacy in other infections. Untreated lepromatous patients were treated as inpatients with either A) 500 mg Fucidin daily for 8 weeks (5 patients) or B) 750 mg Fucidin daily for 4 weeks followed by 500 mg daily for 4 weeks (5 patients). Skin biopsies were taken just prior to treatment and at 2, 4, 6 and 8 weeks post-treatment. Clinical response (graded according to erythema, diffuse infiltration and size/elevation of nodules and plaques) at the end of 8 weeks treatment was judged moderate in 6 patients and marked in 3 patients. No reversal reactions were noted. Bacilli recovered from skin biopsies showed a mean decrease in radiorespirometric activity of 84%, 96% and 99.5% at 2, 4 and 6 weeks treatment, respectively. Serum phenolic glycolipid-1 titers showed a time-dependent decrease in all patients. No significant difference was noted between patients receiving 500 mg or 750 mg. Mouse footpad infectivity and PCR results are pending. Based on results obtained thus far, fusidic acid appears promising as an anti-leprosy agent.

CH76

LEPROSY CLINICAL TRIAL OF CLARITHROMYCIN

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Clarithromycin is a new semi-synthetic erythromycin derivative with superior activity, pharmacokinetics and gastric tolerance. Both by radiorespirometry and the mouse footpad assay, clarithromycin had been found to be the most active macrolide against *M. leprae*, its *in vitro* activity being roughly equivalent to that of rifampicin. Clarithromycin was evaluated in 9 previously untreated lepromatous patients with the following regimen: 1500 mg x 2 on day 1, no treatment on days 2-7, 1000 mg daily on days 8-22 and 500 mg daily on days 23-56. Skin biopsies and serum were collected just prior to initiation of therapy and after 1, 3, 5 and 8 weeks treatment. Clarithromycin was tolerated well with resolution of skin lesions by the 4th week. Serum PGL-1 antigen titers of all 9 patients declined significantly during therapy. All patient biopsies (data currently available for 6 patients) were rendered non-infectious for Balb/c mice after 2 weeks of 1000 mg/day (total of 17 doses). Radiorespirometric activity also became undetectable at this time. Clarithromycin appears to be very rapidly bactericidal and should be seriously considered in any new multi-drug regimen for leprosy.

CH77

LEPROSY CLINICAL TRIAL OF SPARFLOXACIN

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Sparfloxacin is a new fluoroquinolone which has demonstrated greater *in vitro* and *in vivo* activity than ofloxacin against *M. leprae*. Based on these findings and known human pharmacokinetics, sparfloxacin was evaluated in nine untreated lepromatous patients. Patients received a single 400 mg loading dose followed by 200 mg daily for 8 weeks. Skin biopsies and serum were collected just prior to initiation of treatment and at 2, 4, 6 and 8 weeks post-treatment. Patient response was monitored by clinical photography, serum PGL-1 antigen, radiorespirometry and mouse footpad assay. Moderate clinical improvement was noted in 8/9 patients after only 2 weeks treatment. At 8 weeks post-treatment 8/9 patients showed marked improvement. Skin biopsies became non-infectious for Balb/c mice at 2 weeks (3 patients), 4 weeks (five patients) or 6 weeks (one patient) post-treatment. Radiorespirometric activity correlated well with the mouse footpad data; all biopsies becoming negative by 4 weeks post-treatment. Serum PGL-1 antigen showed a time-dependent decline in all patients. Overall, the results with daily 200 mg sparfloxacin appear to be comparable with that found previously in trials of 400 mg ofloxacin.

CH78

MINOCYCLINE IN THE TREATMENT OF LEPROMATOUS LEPROSY - PILOT STUDIES OF POSSIBLE REGIMENS.

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Although WHO MDT covers the needs of most patients, some refuse clofazimine because of its effect on skin colour, which they fear will result in discovery of their diagnosis. Because of the relatively high incidence of toxic side-effects, including both gastrointestinal symptoms and jaundice, seen with prothionamide/ethionamide therapy, we are now using minocycline in those new patients who refuse clofazimine or reject clofazimine once their skin colour alters.

We are also using minocycline in the two year MDT course given before stopping chemo-therapy to longstanding LL and BL patients, of whom many had received thiambutosine in the past, and therefore might have developed cross resistance to the thioamides.

Side-effects encountered will be reported, and the different practical drug combinations used and the duration of treatment with the minocycline component will be discussed.

CH79

IMMUNOTHERAPY OF MB LEPROSY PATIENTS WITH THE ANTI-LEPROSY VACCINE MYCOBACTERIUM W

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Phase III immunotherapeutic trials with the anti leprosy vaccine, Mycobacterium w, have been in progress in Delhi since 1987.

Subjects inducted are untreated, BI positive, lepromin negative MB patients. In double blind study, the patients are randomly divided into 2 groups. Group I patients receive MDT+M.w vaccine i.d. every 3 months for 2 years. Group II receive MDT+placebo. At determined intervals, patients are assessed by clinical scores, BI, histopathology of lesions and lepromin reactivity. Over 400 patients have been included in the study.

Results on approximately 280 patients have been analysed and are presented. At 2 years, in vaccinated patients, lepromin conversion of 100% for BB, 72% for BL and 70% for LL has been noted. 60/109 high BI MB patients became BI=0 after 8 doses of vaccine. 82/130 demonstrated histological upgrading along the spectrum and/or complete clearance of dermal granuloma. There was slightly higher incidence of type 1 reactions, although type 2 reactions were less frequent and severe. The incidence of neuritis and deformity was less, associated with rapid regression of lesions and shortening of treatment duration. Chemo-immunotherapy, thus brings about rapid bacterial clearance and immunological upgrading without exacerbation of tissue damage.

CH80

IMMUNOTHERAPY WITH MYCOBACTERIUM W VACCINE IN MB LEPROSY PATIENTS SHOWING SLOW RESPONSES TO MDT

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Immunotherapy with Mycobacterium w (M.w) vaccine brings about accelerated regression of lesions and rapid bacterial clearance when used along with MDT in multibacillary (MB) leprosy patients. A study was done to see the effect of M.w vaccine in MB cases who were slow responders to MDT.

13 MB patients, (BL or LL), who had taken MDT from 18 months to 5 years without appreciable improvement, were inducted. Seven (5 LL and 2 BL) received MDT+M.w vaccine and six LL patients received MDT+placebo. Detailed clinical charting and biopsy were done every 6 months, BI and lepromin were performed every 3 months. The vaccine was given at 3-monthly intervals.

All 7 patients receiving MDT+M.w showed rapid fall in BI. 5 were rendered negative. Histological upgrading was seen in patients of BL and none in LL. 5 showed conversion to lepromin positivity after 2-8 doses of vaccine. These findings were in accordance with clinical improvement. Two experienced mild to moderate Type 2 lepra reaction following vaccination. None of the 6 patients in the control group recorded appreciable improvement. Some had severe reactions accompanied by neuritis.

CH81

SUBCELLULAR LOCALIZATION OF DDS AND RIFAMPICIN IN THE SKIN AND NERVE OF MULTI-DRUG TREATED CASES OF LEPROSY

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One of the important but not adequately answered questions is whether anti-leprosy drugs reach a subcellular location such as Schwann cells where there is preferential multiplication and persistence of M.leprae.

Subcellular localization of dapsone and Rifampicin was carried out in skin and nerve lesions obtained from MDT treated cases of leprosy using a immunocytochemical technique. Intracellular localization of drugs specifically in macrophages and Schwann cells was carried out with polyclonal (rabbit) anti-DDS and Anti-Rifampicin antibodies in an indirect immunoperoxidase assay.

Our study records both intra and extracellular staining in the skin and nerve lesions obtained from MDT treated MB and PB cases of leprosy. All the nerves under investigation had moderate to severe pathology; hence a broken barrier leading to free diffusion of the drug. A graded difference was seen in staining intensity in relation to integrity and cellularity of the nerve lesion. It was also noted that the drug (metabolite) persists over a long period of time (>6 mths) after stopping treatment particularly in nerves of MB patients.

CH82

INVESTIGATION OF LYMPHOEDEMA AS AN ADVERSE EFFECT OF CLOFAZIMINE THERAPY IN LEPROSY

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Pedal edema as an adverse effect of clofazimine therapy in leprosy was first described in 1990. 140 patients who were on clofazimine for the treatment of lepromatous leprosy were examined. 19 of these patients were observed to have significant pedal edema on one or both feet after the clofazimine therapy was started.

Systemic causes of pedal edema were ruled out in these patients on the basis of clinical and laboratory parameters.

Lymphangiography was done in ten of these patients. Lymphangiographic evaluation showed lymphatic block, lymph node enlargement, nodal filling defects and collateral lymphatic channel circulation.

Lymphangiographic evaluation on patients with tuberculoid leprosy showed normal lymphatic drainage.

The blockade of lymphatic vessels seems to be the probable mechanism of pedal edema in the first group of patients.

The kinetics of clofazimine and the role of the lymphatic drainage in these patients will be discussed.

CLINICAL

CL1

PREDNISOLONE TREATMENT IN LONGER STANDING SENSATION LOSS.

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Three patients were seen with late reactions involving the nerves of the hands. Prednisolone treatment was given and besides the recovery of the nerve function in the hands, they also regained most of the sensation in their feet which was lost for at least 4 to 8 years(ballpoint method).
Since then we treated all new and some old patients with nerve function loss, when willing with prednisolone, regardless the reported duration of the loss. Out of 11 patients thus treated, who had reported loss for 1 year or longer,3 did not improve or improved only slightly,4 improved moderately and 4 made good improvement. In general sensation of the feet improved more than sensation of the hands. Muscle function in general did not improve considerably. Four patients who had sensation loss on detection and could not be treated with prednisolone did not improve.
We belief that although these results need verification, there is an indication for more extensive use of prednisolone in longer standing sensation loss.

CL2

ANALYSIS OF POTENTIAL PROGNOSTIC FACTORS IN PAUCIBACILLARY LEPROSY

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With the multidrug treatment (MDT) the overall results have been satisfactory. However, the problems of residual activity, worsening of residual activity, late reactions/-relapses after the stoppage of treatment specially in case of fixed duration of 6 month regimen have been reported by several investigators. In this study, the data of over 600 cases of paucibacillary leprosy (as defined by the WHO criteria of 1982) has been analysed using multivariate statistical techniques to assess the relationship of the factors like the type and duration of treatment regimen, clinical type of leprosy, number of lesions, lepromin status, clinical type of leprosy, number of lesions, lepromin status, bacterial positivity with parameters like inactivity rates at different treatment intervals, clinical course of residual persisting activity, late reactions and relapses. These patients were treated with WHO recommended regimen of 6 month duration, modified 12 month regimens as well as Prothionamide containing regimen reported by us earlier. It was observed that the treatment duration as well as regimen had statistically significant relationship with these assessment parameters. The clinical type, immunological status, number of lesions and occasional bacteriological positivity did not have close association as reported in the dapsone monotherapy days and in some of the studies later. The significance of these findings need to be debated and investigated by further studies.

CL3

A "QUICK" VMT AND ST FOR THE HANDS COMPARED TO A STANDARD VMT AND ST.

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A "quick" Voluntary Muscle Test (VMT) and Sensory Test (ST) for the ulnar and median nerves has been used by the author in field programmes; the "quick" VMT compares left and right muscle strength for the ulnar and median

nerves while the "quick" ST uses light moving touch with the examinor's finger, asking the patient to compare sensation between areas innervated by the ulnar and the median nerves. In this study the quick tests have been compared to a more standard VMT and the ST with a ballpoint.
225 leprosy patients with WHO disability grading 0 & 1 attending the out-patient clinic of the Sitanala leprosy hospital have been tested with the "quick" VMT and ST by an experienced leprosy doctor and then independently with the standard VMT and ST by one of 3 physiotherapists from the leprosy hospital.
The results show that if the standard tests are true gold standards, the sensitivity of the quick test is poor (between 40-74%); but when the results of VMT and ST are correlated, they seems to indicate that the quick tests may in fact be more sensitive than the standard tests and they question the standard tests as gold standards.

CL4

RISK OF NEURITIS AMONG MULTIBACILLARY PATIENTS DURING MULTIDRUG THERAPY

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This non concurrent cohort study was done to estimate the risk of developing neuritis among Multibacillary patients during MDT. The cohort in the study consisted of 330 fresh Multibacillary cases without deformity or neuritis registered during 1984-1990 at The Leprosy Control Unit, Philadelphia Leprosy Hospital, Salur, Andhra Pradesh, South India. They received treatment ranging from 2 to 6 years.

All patients were assessed for evidence of neuritis during clinic visits. The data was subjected to survival analysis.

The risk of developing neuritis during treatment was 17.6%.

Adult Males had 3 times the risk of developing neuritis compared with Adult Females.

Patients with 4 or more thickened trunk nerves at detection had twice the risk of neuritis as compared with patients with less than 3 thickened nerves ($P < 0.01$).

The risk of developing neuritis was 30% greater in patients smear positive at detection as compared to those who were smear negative at detection.

CL5

INCIDENCE OF SPECIAL EVENTS AMONG PATIENTS WITH MULTI-BACILLARY LEPROSY DURING SURVEILLANCE

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During the course of surveillance we encountered interesting events among MB leprosy patients after completion of W.H.O. recommended multi drug therapy.

1) "CHANCE" SMEAR POSITIVITY: When a clinically inactive and bacteriologically negative leprosy patient (RFT) is found to be smear positive, it causes great anxiety to the physician, and the patient as well. 2.1% of patients exhibited this kind of phenomenon. Subsequent examinations turned out to be uneventful.

2) LATE LEPRA REACTION: 0.9% of MB patients on surveillance revealed evidence of lepra reactions. These manifestations responded to steroid therapy (without specific chemotherapy for leprosy).

Most of these events tend to occur during first three years of surveillance. The risk of such events, and their management is discussed.

This study is supported by UNDP/WORLD BANK/WHO SPECIAL PROGRAMME FOR RESEARCH AND TRAINING IN TROPICAL DISEASES.

CL6

TESTICULAR INSUFFICIENCY IN MULTIBACILLARY HANSEN'S DISEASE--A FIVE YEAR FOLLOW-UP STUDY

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In 1988, we reported a study of testicular function in 74 men with BB, BL or LL Hansen's disease. We reported that 37.2% (16 of 43) of those with LL disease had a low serum testosterone level and elevated serum levels of Follicle Stimulating Hormone (FSH) and/or Luteinizing Hormone (LH). Similar results were noted in 12.5% (3 of 24) men with BL disease and 14.3% (1 of 7) men with BB disease. We showed that this loss of testicular function was correlated with long-standing Hansen's disease, was not associated with immunologic Hansen's disease reactions, and was strongly associated with clinical symptoms of androgen deficiency. In this study, we present a longitudinal five year follow-up of men with multibacillary (Jopling-Ridley BB, BL, LL) Hansen's disease. Serum levels of testosterone, FSH and LH were measured approximately five years after the previous measurements. The data were analyzed to assess the number of patients who developed testicular insufficiency during the period of observation. Clinical characteristics of Hansen's disease, including antimicrobial therapy and immunologic reactions, were analyzed and compared to those cases who did not develop this endocrine problem.

CL7

PARALYSIS OF FACIAL MUSCLES IN LAGOPHTHALMOS

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In outpatients in eastern Nepal we tested the hypothesis based on clinical impression that in every clinically significant lagophthalmos also other facial muscles are involved. 46 of the 57 (81%) examined patients with lagophthalmos (mean duration 23.8 months) had involvement of at least one other facial muscle group. In patients with a gap at mild closure of 5 mm or more 27/30 (90%) had involvement of an other muscle group. In LL patients there is symmetrical, 'patchy' involvement of the facial muscles. In BT+ the ipsilateral muscles are more often involved than the contralateral muscles which is the pattern of involvement of a nerve trunk. We found that in lagophthalmos patients the upper and lower facial muscles are affected in the same proportion so that on clinical grounds we did not find support for the hypothesis that the superficial course of the facial nerve over the zygomatic bone is decisive for the pattern of facial paralysis in leprosy. We found only one patient with bilateral anaesthetic cornea and noted that the type of Bell's phenomenon and the way of

blinking are important for the functional protection of the eye in lagophthalmos. Early detection and therapy are essential in lagophthalmos to save the eye.

CL8

CLINICALY ATYPICAL RELAPSES IN MULTIBACILLARY PATIENTS

P. JAMET and P. BOBIN

During the regular and long-term follow-up of multibacillary patients included in trials for different combined treatments, we diagnosed 150 relapses.

This permit us to observe lot of cases clinicaly atypical because lesions are very mild or because they do not seem active leprosy.

Photographes presented here may incite clinicians in charge of follow-up of patients, particularly after therapeutic trials, to examine patients carefully.

CL9

LEPROSY IN CHILDREN OF MOTHERS WITH LEPROSY AND HEALTHY CONTROLS STUDIED PROSPECTIVELY FROM BIRTH.

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149 children of mothers with leprosy (MB and PB) and healthy mothers (NL) living in the same environment (80MB, 40PB, 29NL) were studied from birth up to 2 years of age (Phase 1); 89 children (mothers: 49MB, 25PB, 15NL) were reassessed at age 3-4 years (Phase 2); 86 children (mothers: 48MB, 23PB, 15NL) were reassessed at age 7-8 years (Phase 3); and 99 children (mothers: 54MB, 25PB, 20NL) were reassessed at puberty aged 13 1/2-15 1/2 years (phase 4). 3 children born to MB mothers had indeterminate leprosy by the age of 2 years; 1 child (MB mother) had indeterminate leprosy at age 4; 1 child (MB mother had indeterminate leprosy and 3 others had enlarged nerves by age 8; 15 children examined at puberty were found to have early leprosy, indeterminate (14), BT (1). At puberty 71 had a history of skin disease, 41 had clinical evidence of skin disease. Clinical findings were: 27 had no clinical signs of leprosy; 1 had skin lesions only; 28 had (slightly) enlarged nerves only; 31 had anaesthetic macules with easily palpable/slightly enlarged nerves (14 diagnosed as having early leprosy, 1 had indeterminate leprosy in Phase 3); 9 had macules without sensory loss and easily palpable/slightly enlarged nerves (1 had indeterminate leprosy in Phase 1); 1 had flattened nodules and slightly enlarged nerves (diagnosed as early leprosy); and 1 had blotchy hypopigmentation with slightly enlarged nerves. Leprosy status of the mothers of these children during pregnancy and/or lactation was: 11 active leprosy ; 2 quiescent MB leprosy; 2 PB "cured"; 3 healthy controls - 2 married to cured BT patients, 1 had a non-leprous husband.

CL10

GROWTH AND DEVELOPMENT OF CHILDREN OF MOTHERS WITH LEPROSY AND HEALTHY CONTROLS STUDIED PROSPECTIVELY FROM BIRTH TO PUBERTY

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149 children (K) of mothers with leprosy (MB and PB) and healthy mothers (NL) living in the same environment (80MBK, 40PBK, 29NLK) were studied from birth up to 2 years of age (Phase 1). Reassessments were as follows: 89 children (49MBK, 25PBK, 15NLK) at age 3-4 years (Phase 2); 86 children (48MBK, 23PBK, 15NLK) at age 7-8 years (Phase 3); and 99 children (54MBK, 25PBK, 20NLK) at puberty aged 12-15 years (Phase 4). At birth and 2 years weight, length and head circumference were greatest in NLK and least in LLK, but at 2 years LLK had the greatest growth velocity. 25/149 (17%) died before Phase 4 (LLK 24%, BLK 14%, PBK 15%, NLK 14%. Mean heights/weights at Phases 2 and 3 were 90cm/12.7kg and 113.7cm/20.1kg with no significant differences between sexes or groups of children aged 3y 7m and 7y 10m respectively. At Phase 4, mean age 13.9y, sexual development was more advanced in girls than boys and NLK › PBK › MBK. NLK weighed significantly more (girls 46.1kg, boys 36.4kg) than MBK (girls 36.8kg, boys 33.7kg). NLK (boys) were significantly taller (149cm) than MBK (136.9cm). Triceps skinfold, arm and head circumference were 7.0mm, 19.6cm, 53.6cm and 5.2mm, 19.2cm, 53.8cm for girls and boys respectively. Medical records showed hospital treatment for infections: intestinal worms /parasites 99%; respiratory 50%; ear/otitis media - MBK 26%, PBK 20%, NLK 20%; eyes all infections /trachoma - MBK 70%/37%, PBK 52%/12%, NLK 25%/0; skin all infections/scabies - MBK 67%/54%, PBK 80%/44%, NLK 75%/45%.

CL11

PREGNANCY IS A RISK FACTOR FOR RELAPSE AND NEW NERVE DAMAGE EVEN AFTER MDT

ME Duncan, T Miko, R Melsom, D Frommel.

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108 women, 87 with leprosy and 21 healthy controls, studied prospectively during pregnancy and lactation (1975-78), were reviewed with their teenage children (1990). The leprosy patients deemed "cured" had been released from treatment (RFT): 49 DDS/RFT, 33 MDT/MB/RFT, 2 MDT/PB/RFT, 3 clofazimine/RFT (DDS resistant), (4 had incomplete records). Of 87 mothers with leprosy 68% had new nerve damage following RFT, 36% had neuritis with new sensory or motor loss; 41% had stocking and glove anaesthesia (not confined to MB patients), and 6% had tender nerves. 48% patients had their new post-MDT RFT nerve damage in association with pregnancy, 45% postpartum: 82% episodes appeared to be "silent" neuritis. In addition 9% relapsed with new leprosy, 6% post partum, and 14% healthy controls developed new leprosy. These findings contrast with those at an interim assessment in 1984 when 76 mothers with leprosy had just stopped DDS or had just started MDT/MB: 47% "improved", 45% "no change", only 8% "worse". While BL patients treated with DDS were most at risk, all MB patients whether BI positive or negative at start of MDT treatment had a high risk of late nerve damage. Even among those recorded as having "No problem" a significant percentage had increased neuropathic destruction of hands and feet, some requiring surgery. This cohort review shows that nerve damage occurs after RFT even in MDT patients, especially in relation to childbirth. Most of the women in the study are still of child bearing age and could be expected to deteriorate further with subsequent pregnancies.

CL12

NERVE FUNCTION ASSESSMENT IN LEPROSY - COMPARISON OF VARIOUS CLINICAL METHODS

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In order to determine the clinical usefulness of various sensibility tests that were not commonly used at our hospital, an extended nerve function assessment (NFA) was done on 50 in- and out patients with an established leprosy diagnosis (100 hands and feet). The NFA consisted of Semmes-Weinstein Monofilament Testing (SWMT), Moving 2-Point Discrimination (M2PD), Pin Prick (PP), Position Sense (PS), Vibration Sense (VS) and Voluntary Muscle Testing (VMT). In addition the SWMT was performed on 637 hands and 634 feet of 'field patients' in order to get a better idea of the prevalence of sensory impairment as measured with the

SWMT. As the SWMT has been shown to be a sensitive test of peripheral nerve function, the other tests were compared with the SWMT. Results are reported separately for the ulnar, median and posterior tibial nerve. Test sites were the pulp of the distal phalanx of the index finger, little finger and big toe. Correllation between the SWMT and each of the other tests proved statistically significant; the closest correllations were between the SWMT, M2PD and PP for both ulnar and median nerves ($r>0.7$, F test>100, $p<0.0001$). In comparing SWMT with VMT results, the best correllation was found between SWMT and abductor pollicis brevis for the median nerve ($r=0.70$, $p<0.0001$) and SWMT and abductor digiti minimi for the ulnar nerve ($r=0.77$, $p<0.0001$). It is argued that the first tests to show nerve function impairment (NFI) are the M2PD and the SWMT. VS and PS were also absent in a significant proportion of patients. Arguments are presented that this may indicate advanced NFI. Results are compared with other data currently available.

CL13

EXTENSIVE PROGRESSIVE NEW LESIONS IN BT CASE WHILE ON REGULAR MB-MDT

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Progressive active leprosy in the form of appearance of many lesions without clinically evident Type-I reaction under MB-MDT in skin smear negative cases are seldom seen.

A case of BT type of Hansen's, with skin smear negative and multiple skin lesions was put on MB-MDT and given regularly supervised doses of MB-MDT. This case developed multiple progressive new lesions some large sized after fifth dose of MB-MDT. There was no evidence of Type-1 reaction clinically in the old lesions, no nerve tenderness, new lesions looked active and had less Lamprene induced color and ichthyosis indicating that they have appeared recently and also that patient has been consuming Lamprene regularly.

Urine/Serum for DDS, skin smear, Biopsy, CBP, VMT/ST, Chest X-ray and careful charting was done. Serial biopsies, immunological tests like ELISA - for screening antibody responses (IgG & IgM) to various M.Leprae specific antigens and lymphocyte proliferative assays to measure the T.Cell responses against the various antigens of M.Leprae and T helper/T-supressor ratios will be estimated, other tests are also planned. Resistance to MB-MDT/Type-1 reaction was considered.
(PB - Pri.DDS. Resistance reported in 1984 at Hyderabad by Pearson.)

The out come of the clinical histopathological and immunological follow up will be discussed along with its clinical implication.

CL14

CLINICAL, ELECTROPHYSIOLOGICAL AND BACTERIOLOGICAL EVALUATION OF NERVE DAMAGE AFTER REGULAR MDT IN LEPROSY

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Regular and complete MDT may not ensure cessation of nerve involvement in leprosy. Although the antigenic load may fall steadily after stopping MDT, reversal reactions are known to occur with consequent deterioration of nerve function. While recovery of nerve damage may be evident in a large proportion of cases, relapses may occur in a few.

This study of 16 cases each of multi and paucibacillary leprosy regularly treated with WHO recommended MDT attempts to correlate clinical, electrophysiological and bacteriological observations recorded at periodic intervals following stoppage of MDT. The results are discussed with a view to identify pointers indicating effectiveness of MDT in the recovery/deterioration of nerve damage in leprosy.

CL15

ONSET OF LEPROSY IN ADOLESCENCE CARRIES HIGHEST RISK OF LATER ENL

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Because studies of the immuno-pathogenesis of Type II (ENL) reactions in leprosy have been inconclusive, we re-examined the basic epidemiology of this reaction to try to identify new avenues for research into its cause(s) and mechanisms.

A cohort of 176 new, untreated patients, admitted to the McKean Rehabilitation Institute from Sept. 1984 - Dec. 1989, was followed prospectively in a study of the incidence and recurrence of reactions. Of this group, 118 were lepromatous (LL-BL); 14 of these (12%) had ENL on first admission (before treatment), 30 (25%) developed ENL during the period of follow-up, a total of 44 patients with ENL (37%). Five of these also had either a Type I reaction or reactive neuritis during follow-up.

Patients whose age of onset of leprosy (by history) was in the second decade had the highest incidence of ENL (12/17=71%) ($X^2=5.3$, $p<0.025$), with a steady decline among patients whose age of onset of leprosy was in the third through sixth decades. None of the patients whose age of leprosy was over 60 years developed ENL. The age of the patient at the time of the first episode of ENL was not correlated with the development of ENL (r approx = 0). Neither the duration of leprosy before diagnosis nor the treatment duration or regimen were significant factors in this study.

The finding that the onset of leprosy during adolescence carries the highest risk of ENL, often after an interval of several years, suggests that the factors responsible require substantial time to develop and that they may be most highly inducible around the time of puberty. The basis for these observations is not known but they suggest that maturation and senescence of human immunity, and the relationship between the immune and endocrine systems, may be areas for further study in leprosy.

CL16

LOCALISED LEPROMATOUS LEPROSY AND ITS RESPONSE TO CHEMO-IMMUNOTHERAPY.

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A 12-year old boy presented with three lesions: one each on both forearms and the third on the left leg. He was classified initially as borderline tuberculoid (BT) leprosy. Slit-skin smears and histopathology from the lesions however proved the diagnosis to be lepromatous leprosy (with BI 6+). The initial lepromin was negative. The patient was put on chemo-immunotherapy (standard multidrug therapy and immunotherapy with Mycobacterium w vaccine). Investigations after one year(15 months) of MDT and three doses of vaccine, showed a remarkable fall in the bacterial index (BI) from 6 to 0 in the lesions, a lepromin positivity of 5mm and a histological upgrading from LL to BT. Immunological

studies done at 15 months revealed a good LTT response and high levels of cytokines specifically IL-2 abd IFN-γ .
This report presents an LL patient with disease limited to a few sites. It stresses the importance of slit-smear and biopsy in all patients of leprosy as well as highlights the upgrading observed on administration of chemo-immunotherapy.

CL17

SENSIBILITY OF SKIN SMEARS IN ONE HUNDRED CASES OF MULTIBACILLARY LEPROSY

Míriam Gutierrez, Jair Ferreira, Míriam Perez

In order to establish the sensibility of skin smears in multibacillary leprosy(lepromatous - or borderline)it were reviewed one hundred new cases identified between 1976 and 1992 in a especialized outpatient unit of State Secretary-of Health,Rio Grande do Sul,Brasil.

The diagnosis was made in all cases by means of clinical examination and biopsy,with the - presence of acid fast bacilli in tissue specimens;simultaneously direct smears were collected from four sites,namely,two ear lobes,elbow and lesion.

In 33 cases the smears were negative in all-sites,thus revealing a 67% sensibility(α =0.05 CI 57.8-76.2%)for the detection of multibacillary leprosy.

The Mitsuda lepromin test was done in smear-negative cases,with 91.3% of negative or doubtful reactions,showing the value of this additional criteria in terms of classification and - treatment of multibacillary leprosy.

CL18

INVESTIGATION OF PATIENTS WITH LONGSTANDING HIGH LEVELS OF ANTI-PHENOLIC-GLYCOLIPID I AFTER RELEASE FROM TREATMENT

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Antibody levels to phenolic glycolipid I (PGLI) are supposed to be related to the bacterial load of the patient. Also, rising antibody levels after release from treatment (RFT) may be indicative for a relapse.
In a folo study 9 multibacillary (MB) patients with a high anti-PGLI level persisting for more than 5 years after RFT were examined for a possible relapse. Six patients were examined two times with 2 years intervals; 3 patients were examined once. Mean time after RFT was 8 years (range 5 - 10 years). Anti-PGLI was measured according to standard WHO-protocol. Mean level at the time of examination was 0.939 (range 0.416 - 1.494). On clinical examinations no signs of relapses were found. Skin biopsies were taken besides scars of previous treatment-follow-up biopsies; skin smears were taken from both earlobes, elbow and nates and stained with Fit-Faraco-Wade staining: in all samples no acid-fast material was found. At the more recent examinations nose swabs were taken, on which a polymerase chain reaction (PCR) based on the M.leprae specific sequence of the gene encoding for 36 kD antigen, was performed. In 2 of the 7 investigated samples a positive signal was found; in 2 patients at 9 respectively 10 years after RFT. There seemed to be no relation between anti-PGLI level and PCR-positivity. It appears that there is a group of patients with longstanding high anti-PGLI levels after RFT who show no signs of relapse. As PCR from nose swabs remain positive in some cases its value in detecting relapses may only be by longitudinal examinations.

CL19

LIQUEFYING NODULAR PANICULITIS CAUSED BY MYCOBACTERIUM LEPRAE:

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Liquefying nodular panniculitis (LNP) is a rare condition described by Shaffer in 1938. Its etiology has not been clarified yet. The disease is characterized by multiple erythematous subcutaneous nodes that undergoes liquefaction and consequent discharge of an oily liquid. The disease develops to hypopigmented, atrophic and depressed scars due to necrosis of subcutaneous fat. The authors report a case of a Wirchow type leprosy with atypic features and clinical characteristics of LNP with 30 years of evolution.

CL20

THALIDOMIDE -- A CLINICAL STUDY OF 33 CASES OF TYPE II LEPRA REACTION.

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Thalidomide is N-phthalyl-glutamic-acid-imide, a mild sedative, causing two serious side effects - Neuritic symptoms and characteristic foetal anamolies, for which it was withdrawn from the market in 1961. It is indicated in Type II Lepra Reaction.

This study consists of 33 patients, all males, suffering from repeated Type II Lepra Reaction and treated with Thalidomide. All the patients responded extremely well to Thalidomide with minimal side effects. Cases were selected carefully due to limited supply and difficulty in getting the drug.

Considering the factors such as Recurrent Reaction, Steroid dependency, side effects of steroids, other associated infections like Pulmonary Tubereulosis, Strongyloidiasis, Cardiac disease etc., the patients were selected for Thalidomide. With the help of competent staff and careful selection of cases, morbidity due to Type II Lepra Reaction can be considerably reduced.

The paper will be discussed in detail at the time of presentation.

CL21

NATURAL HISTORY AND CLINICAL FEATURES OF REVERSAL REACTION IN HYDERABAD, INDIA

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A retrospective survey of the notes of all patients attending Dhoolpet Leprosy Research Centre during 1985 was done to establish the frequency, timing and clinical features of Reversal (Type 1) reactions. 494 case notes were examined and clinical evidence of a reversal reaction was found in 44 cases (10.9%). Reactions were commonest in borderline patients with 11.4% and 14.8% of BT and BL patients developing reactions. Presentation in reaction was common with 41.3% of patients having signs of reaction at the time of diagnosis. 43.1% of patients had only skin lesions, 22.7% had both skin lesions and neuritis whilst 31.8% had only neuritis. The ulnar nerve was the most commonly involved nerve. Skin reactions were commonest in the first month of treatment, neurological reactions were commonest in the first six months of treatment. However late reactions may occur up to 7 years after the start of treatment. Recurrent reactions occurred in 30% of patients and may be frequent. Steroid treatment produced improvement of both skin lesions and neuritis, but improvement occurred in only 50% of neuritic episodes. This study raises several practical points for clinicians working with leprosy patients.

CL22

FACTORS AFFECTING RISK OF TYPE I REACTION AMONG MULTIBACILLARY PATIENTS

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Availability of information on factors associated with risk of Type I reaction should facilitate designing a high risk approach in the care of individuals with Hansen's disease. With this in view, a historical cohort study was carried out on fresh multibacillary cases initiated to MDT since 1985 at the Leprosy Control Unit of Christian Medical College, Vellore, India. 633 of them had no evidence of type I reaction or visible deformities at start. Risk of reaction was calculated among them using survival analysis and the adjusted Relative Risks (RR) were computed using multivariate techniques.

The overall risk of reaction during the first and 2nd years were 54/1000 and 19/1000 respectively. The cumulative risk of reaction by the end of 6th year was 106 per 1000. Presence of thickened nerves at registration (RR = 4), BI positivity (RR = 2) and palmoplantar anaesthesia (RR = 2.4) were associated with risk of reaction. The probability of reaction increased with number of patches. Individuals aged less than 40 had greater risk of reaction when compared with those aged more than 40. 18.6% the patients who had reaction finally developed visible deformities.

CL23

REACTIONS IMMUNOLOGIQUES OBSERVEES A L'INSTITUT CARDINAL LEGER PENDANT UNE PERIODE DE 8 ANS.

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Institut Cardinal Leger contre la lepre (HAITI).

Sur une population de 720 patients enregistres, 55 ont presente un etat reactionnel:

35 erythemes noueux lepreux
23 reactions reverses

1) la repartition des etats reactionnels selon l'age, le sexe et le type clinique

2) les variables telles que la periode moyenne d'apparition des symptomes, le rythme des poussees, l'influence et la duree de l'hospitalisation et le traitement.

CL24

CLINICAL STUDY OF LEPRA REACTIONS IN 123 CASES TREATED BY MDT.

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An attempt was made to investigate the incidence & behaviour of lep. reactions in a group of 123 case treated during the last few years with MDT. Classification of the cases is as follows :T.T.8 (6.5 %), B.T.47 (38.2 %). B.L. 21 (17 %), L.L. 47 (38.2 %).

47 Lepra reaction cases were recorded, of which 20 belong to type one & 27 to type two. Of the first group only 2 cases suffered from 2 episodes of reversal reaction, while 12 of the second group had more than one attack of type 2 reaction.

Four cases with type 2 R. developped severe bullous pustular lesions with toxaemia & tendency to relapse while under M.D.T.A. mild chronic recurrent type of E.N. lesions occured in 4 cases. Crops of few small subcutanious nodules appear 2-4 days after the monthly dose Of Rifampicin, & clear up in 10 to 14 days. (Herx Hiemer Like Reaction)

The above observations suggest that MDT had little effect in preventing or ameliorating lepra reactions. One of the study cases developed type 2 R.after a complete 2 years course.

Coloured slides and tables are available to demonstrate different types of reactions and their follow up for periods from two months to several years.

CL25

REVERSAL REACTION IN MULTIBACILLARY LEPROSY PATIENTS FOLLOWING MDT WITH/WITHOUT IMMUNOTHERAPY WITH A CANDIDATE ANTILEPROSY VACCINE, MYCOBATERIUM W.

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Immunotherapy with a candidate antileprosy vaccine, Mycobacterium W was given in addition to standard multidrug thereapy (MDT) to 53 multibacillary lepromin negative patients belonging to BB, BL and LL types of leprosy (Vaccine group). An equal control group received MDT and injunctions of micronised starch as placebo. Both the vaccine and placebo were administered intradermally every 3 months. The patients were evaluated at determined intervals by clinical, bacteriological and histopathological parameters and lepromin testing. Reactional eposodes were analysed with reference to incidence, onset, frequency and severity dur[illegible] and after release from treatment (RFT).-ing. Incidence of reversal reaction(RR) was marginally higher in vaccine group (22.6%) vaccine group vs. 15% control group). All cases with history of downgrading type 1 reaction developed RR during therapy. Most episodes occurred within first year of commencement of therapy-half developed within 3 months. Late reversal reactions(after RFT) were observed in 3.8% of case in both groups. Half the reactors in control group and 1/3rd in vaccine group had repeated reactional episodes. Incodence of neuritis associated with RR as well as isolated neuritis were equally frequent in both groups.

CL26

SIGNIFICANCE & MANAGEMENT OF REACTIVE PATCHES IN LEPROSY TYPE 1 REACTION

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In this study 350 cases of Type 1 reaction have been included. There are from the leprosy patients registered at Dhoolpet Leprosy Research Centre, Hyderabad during the period 1984-1992.

All cases were classified according to Ridley Jopling Classification, Charting done carefully, skin smear taken, VMT done routinely and biopsy taken in most cases.

These cases were analysed as regards to classifications, presentation of reaction with regard to leprosy treatment.

Local effect of these reactive patches on the skin involved, hair and underlying structures will be mentioned. Significance of the Location and size of reactive patches to the nerves damaged ulnar/median/C.peroneal/facial will be dealt.

All these cases received similar treatment given on an outpatient basis with semistandardised steroid regimen with good result in most cases. Results will be presented.
Appropriate color transparencies will be shown.

CL27

STUDY OF LATE REVERSAL REACTION IN PAUCIBACILLARY PATIENTS, AFTER MULTI DRUG TREATMENT - ITS INCIDENCE RATE, TIME OF ONSET, MODE OF PRESENTATION AND MANAGEMENT.

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The occurance of the reversal reaction in letrosy has been recognised for long but there has been very little information about clinical epidemiological and natural history of Late Reversal Reaction in paucibacillary patients.

The study comprises of 3500 patients of paucibacillary leprosy (tuberculoid, neurtic and borderline - tuberculoid) detected by different methods in multidrug therapy project in Bharuch district. These cases completed Multi Drug Treatment during the year 1989-90 and also completed the prescribed 2 years surveillance period in the years 91-92. These 3500 patients contributed to a total of 7051 person - years of risk (PYR). The number of patients who developed reversal reaction was 19 giving an incidence rate of 2.69 per 1000 person - years of risk. The criteria applied for dignosis of reversal reaction clinical and bacteriological after excluding relapses with therapeutic doses of steroids. The results of the study will be presented.

CL28

CYCLOSPORIN TREATMENT IN REVERSAL REACTION.

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Reversal reaction in leprosy is usually described as a classic example of type IV hypersensitivity reaction. Therefore, treatment with corticosteroid is considered the main stay of treatment. However, in some patients, corticosteroids are poorly tolerated.
Two patients with reversal reactions are described. One patient on prednisolone developed a steroid cataract and had to be treated with cyclosporin. The patient responded well. The other patient had a difficult to control diabetes and his reversal reaction too responded very well to cyclosporin. Although cyclosporin has been described for treating ENL, this treatment did not work in our hand. However, as expected it was effective in reversal reaction. The mode of action and side-effects of cyclosporin will be discussed.

CL29

NEOPTERIN AS A MARKER FOR REACTIONAL LEPROSY.

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Reversal reaction (RR) is supposed to be a delayed type hypersensivity reaction; the pathogenesis of erythema nodosum leprosum (ENL) is not clear but CMI may play a role. Neopterin, a product of gamma-interferon activated macrophages was measured in sera from leprosy patients and controls from the Phillipines It appeared that neopterin levels were increased in RR and ENL compared to untreated TT/BT and BL/LL patients. (Hamerlinck et al. Exp. Derm. 1992; 1:101) Therefore, we studied sera of patients with RR and ENL who had increased serum neopterin levels.
Retrospectively, sera were examined before, during and after reaction.
Six patients were studied with 4 episodes of RR and six episodes of ENL. In 3 out of 4 RR episodes, the reversal reaction parallelled the increase of serum neopterin level and the same was observed in 4 out of 6 ENL episodes.
It appears that, by means of longitudinal investigation, increase in serum neopterin levels correlate with the occurrence of RR and ENL and therefore may be helpful in differentiating between RR and relapse.
As neopterin is produced by gamma-interferon stimulated macrophages, the results supports the hypothesis that CMI plays a role in ENL.

CL30

LATE REVERSAL REACTION IN PAUCIBACILLARY PATIENTS, AFTER M.D.T. - ITS INCIDENCE RATE, TIME OF ONSET, MODES OF PRESENTATION

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While the occurrence of reversal reaction in leprosy has been recognised for long, there has been very little information about clinical epidemiological and natural history of late reversal reactions in paucibacillary patients.

A total of 2972 patients of paucibacillary leprosy (Tuberculoid and Borderline Tuberculoid) detected by different methods at Sivananda Rehabilitation Home, Hyderabad, in its Urban Leprosy Control Unit, who had completed M.D.T. during the years 1986-1990 and also completed the prescribed 2 years surveillance period were included in this study. The number of patients who developed reversal reaction was 23, giving an incidence rate of 3.9 per 1000 person-years of risk. The criteria applied for diagnosis of reversal reactions were clinical and bacteriological after excluding relapses with therepeutic doses of steroids. The late RR has been studied in relation to variable like age, sex, type of disease and number of skin and nerve lesions. An attempt has also been made to identify the relation between length of treatment with M.D.T. and development of late RR and the risk factors for RR

CL31

OPHTALMIC FINDINGS OF LEPROSY CASES THAT WERE DIAGNOSED AT ISTANBUL LEPROSY HOSPITAL

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Ophtalmic examinations of 21 leprosy patients whose first diagnosis were established in Istanbul Leprosy Hospital, were performed by slit-lamp and results are reported below.

The average age of patients was 23,71±1,8 and average disease duration was 5,71±0,63 years.

66,66 % of cases had bilateral corneal nerve thickening, 57,14 % had m.leprae infiltrate in the right eye and 61,90 % in the left, 9,52 % had bilateral pannus, 33,33 % had subepithelial scar in the right eye and 28,57 % in the left eye.

52,38 % of cases were still on anti-leprosy treatment. 14,28 % of patients had bilateral uveitis. All patients having uveitis had subepithelial scars and two of them had completed their treatment Two of the uveitis cases had nerve thickening and opacity. None of them had pannus.

CL32

THE EXTENT OF LEPROSY RELATED DISABILITIES IN TURKEY

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Turkey has a national population of aproximately 55 million and there are 3502 registered leprosy cases at the end of 1992.

In this study, realized between january 1986 and january 1993. 711 leprosy patients were evaluated according to their age, sex, province they live, classification of their disease and disability using WHO grading.

The average age of patiens was 50,07±13,50 and average disease duration was 25,97±13,29.

50 % had lagophtalmos, iritis or keratitis in both eyes and 9,4 % had severe loss of vision or blindness.

37,4 % had ulcer, mobil claw fingers or slight absorbtion. 18,1 % had wrist drop, stiff joints or severe absorbtion.

43,25 % had plantar ulcers, clawed toes, foot drop or slight absorbtion in both feet, 10,4 % had contractures, severe absorbtion or amputations.

CL33

OCULAR STUDY OF HANSEN'S DISEASE AT A DERMATOLOGICAL HOSPITAL. THE PREVENTION IN OUR HANDS.

Fernando Oréfice, Leticia Boratto

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

This study is based on the observation of 363 patients bearing different types of Hansen's disease.

In examining a patient we had no previous knowledge as to the type of leprosy to expect. Therefore we were able to study all patients without the danger of being influenced by a previous diagnosis.

The protocol was brokendown as follows: visual acuity, facial muscle function, eyelashes, lacrimal apparatus, pupil, ocular motility, cornea, sensibility, Schirmer test, a study of the anterior segment of the eye with slit lamp.

This study encompasses 363 patients, brokendown as follows: Virchowiane (275), Tuberculoid (57), Indeterminate (29) and Dimorphos (2)

Age ranged from 18 to 82. There were 229 men and 134 women. 183 caucasians, 157 dark skinned and 23 black.

CL34

STUDY OF OCULAR LESIONS IN LEPROUS OUT PATIENTS

Lilian Monteiro, Wesley Campos, Fernando Oréfice, Maria Aparecida Grossi

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais - Belo Horizonte - Minas Gerais - Brazil.

In this study, 997 leprous out patients were examined, 528 of which (53%) were of the Lepromatous type, 199 (20%) of the Borderline type, 167 (16,8%) of the Tuberculoid type and 103 (10,3%) of the Indeterminate type.

314 patients (31,5%) showed ocular adnexa lesions and 389 (39%) showed eyeball lesions, and these manifestations were more common in Lepromatous Leprosy and increased according to the age of the patient and the duration of the disease.

Sight threatening lesions were rare findings and this was in part considered due to the early systemic treatment.

CL35

DACRIOCISTOGRAPHYCAL STUDY OF PATIENTS BEARING HANSEN'S DISEASE

Leticia Boratto, Fernando Oréfice, Liliana Werner.

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

A dacriocistographical study of 200 patients were performed in order to detect an early damage of facial nerve in patients bearing Hansen's disease.

This study was performed in two groups of patients: those with the disease and those without it, each group with 100 patients..

The authors concluded that this type of exam brings no diangnosing help in detecting an early damage of the VII nerve.

CL36

USE OF CLOFAZIMINE IN PATIENTS WITH OCULO-CUTANEOUS ALBINISM IN BEARES OF VIRCHOW'S FORM OF HANSEN'S DISEASE.

Wesley Campos, Fernando Oréfice, Maria Aparecida Grossi, Carlos Rodrigues..

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

It is reported a case of one patient with oculo-cutaneos albinism, tirosin + , with Hansen's disease, treated with multidrug therapy (MDT).

The patient was treated with Clofazimine (one of the drugs used in MDT) for two years and it was not noticed any pigmentation of the skin and mucosa.

If Albinism is a congenital disease with a failure of the formation of a normal amount of melanin and if Clofazimine can produce increased pigmentation, would the metabolism of Clofazimina be correlated to melanin?

Could this correlation explain why this patient did not become pigmented?

CL37

CONJUNCTIVAL AND SCLERAL PIGMENTATION DUE TO CLOFAZIMINE

Wesley Campos, Maria Aparecida Grossi, Lilian Monteiro, Fernando Oréfice.

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

The authors present a case of a patient with Hansen's disease and that had used Clofazimine as therapy, daily, during 9 years, in a total dosis of 324 g.

This patient presented a very intense ocular pigmentation, mostly at conjunctive and scleral.

The exam at slit lamp showed a very "suis generis" aspect of the ocular pigmentation.

The authors also comment on differential diagnosis and the difficulties of finding Clofazimine's crystals with optical microscopy and mention a method where they can easily be reconized.

CL38

PSEUDO ACUTE ABDOMEN DUE USE OF CLOFAZIMINE

Frederico Discini, Maria Aparecida Grossi, Wesley Campos, Fernando Oréfice

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

The authors present a case of pseudo acute abdomen in a patient with Hansen's disease after the use of Clofazimine (multidrug therapy) for a period of five years.

Several exams were performed and the video laparoscopy showed a different impregnation of parietal peritoneum and omentum with dark spots tha at fresh microscopic exam revealed clofazimine's crystals.

The authors emphasize that it is important to pay attention to the possibility of Clofazimine to simulate a sugical picture and that this picture should be included in differential diagnosis of acute abdomen , mostly in countries where Hansen's disease is endemic and Clofazimine is used as therapy.

CL39

BILATERAL IRIDOCYCLITIS CAUSED BY MYCOBACTERIUM LEPRAE DIAGNOSED THROUGH PARACENTESIS.

Wesley Campos, Fernando Oréfice, Maria Aparecida Grossi, Carlos Rodrigues.

Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

The authors carried out anterior chamber paracentesis in a patient bearing Hansen's disease who presented bilateral iridociclitis.

The paracentesis was performed in out patients.

The aqueous humor was studied through Ziehl-Nielson colouring method and the result was the isolation of Mycobacterium leprae at anterior chamber.

This study shows that Mycobacterium leprae is on of the causes of uveitis in Hansen's disease and so it is worth while to look for it in patients bearing this kind of disease.

CL40

ANALYSIS OF LAGOPHTHALMOS AMONG 2,144 CASES OF LEPROSY

Yan Liangbin Zhang Guocheng Li Wenzhong

Institute of Dermatology, CAMS, Nanjing, China

Two thousand one hundred and fourteen cases with lagophthalmos among 14,257 cases of leprosy in 11 counties in Yangzhou Prefecture were analysed. The results were as follows: 1214 cases had uni-lateral lagophthalmos, and 900 had bilateral lagophthalmos. The prevalence of lagophthalmos was 14.83% comprising 72.92% of all eye complications in leprosy(2114/2666). In the lagophthalmos group, 51.61% of the cases had loss of sensation of the cornea(1,91/2,666), which was higher than that in the non-lagophthalmos group. The eye complications in leprosy varied with age, type of leprosy and duration. For PB cases, 58.93% of the cases had lagophthalmos within four years after the onset of the disease. For MB cases, 69.95% of the cases had lagophthalmos over 10 years after the onset of the disease, most of them were bilateral lagophthalmos. The approach to eye complication prevention has been proposed according to the findings. Emphasis was laid on the early detection and treatment of eye complications.

CL41

EVALUATION OF PRE-CORNEAL FILM IN LEPROSY

ALAMPUR SAIBABA GOUD

SIVANANDA REHABILITATION HOME

KUKATPALLY , HYDERABAD

The number of registered cases of Leprosy was 3.7 millions in 1990. 25% of them have got ocular involvement and may be 5% do have blindness. The present study aimed at investigating the pre-corneal tearfilm abnormalities in patients of various types of Leprosy. The study was conducted on 500 eyes of patients attending Sivananda Rehabilitation Home. The patients were subjected for Schirmer's Test, 1% Rose Bengal Test, Tearfilm break up time with Fluroscein and Conjunctival impression cytology. It is observed that tearfilm abnormalities are important factors contributing for corneal morbidity. This work has been carried out at Sivananda Rehabilitation Home, Kukatpally, Hyderabad.

CL42

DERMATOGLYPHIC ASPECTS IN LEPROSY PATIENTS AND THEIR RELATIVES IN ALBANIA

M.M.Nakuci & M.Nakuci

(Clinic of Dermatology, Tirana, Albania)

Genetic predispositions in leprosy are demostrated in some works with pedigris, prasens of the "specific" genes in HLA (DR$_2$) etc) sistem. We have study aspects of dermatoglyphics in 29 leprosy patients, 44 relatives persons and 110 health persons (group of control).

In 1097 fingers of health persons there are : 62.2 % Loops, 30.8 % Whorls, 6.6 % Arches. In 269 fingers of leprosy patients there are : 71.1 % Loops, 23.7 % Whorls, 4.8 % Arches. In 440 fingers of relatives 62.7 % Loops, 31.8 % Whorls, 5.5 % Arches. If in the leprosy patients the Loops are higher ($t=2.8, p < 0.05$) the Whorls ans Arches are lower ($t=2.4, p < 0.050$ in comparing with the group of control.

Important is that the thirt finger in the leprosy patients the Loops there are (very higher) 77.8 % in comperation with health persons, which have 64.5 % ($t=2.95, p < 0.05$).

Furuhara index (F=100xW/L) is for the health persons 91.83, in the leprosy patients is 36.55 (very low), in the relatives 58.18.

In the study of triradiuses: t'(n=200) 24 %, in health persons; t'(n=52) 50 %, in leprosy patients; t'(n=88) 62.5 % in relatives. There are significant diferences ($t=3.4$, $t=6.5$)

The conclusion is that :

1. This date confirm genetic predisposition of the leprosy patients for this disease.
2. This method can apley in the control of the people in the endemic zones to know the predisposition of this populations for leprosy.

CL43

LEPROSY IN CHILDREN

Virendra N Sehgal

Department of Dermatology and Venereology, Lady Hardinge Medical College, New Delhi, India

A study of 161 leprosy children / 3,184 patients had indicated an incidence of 5.06% amongst leprosy patients in an urban setting with a boy : girl ratio of 2.6:1. Children were largely immigrants from neighboring endemic states of Uttar Pradesh and Bihar. The mean duration of disease was 1.2 years for paucibacillary and 2.8 years for multibacillary leprosy. The expression was either a macule or a plaque. Most of the cases belonged to indeterminate, borderline tuberculoid or borderline borderline, with polar groups being distinctly uncommon. Thus emphasizing again the incomplete nature of expression of the disease spectrum in children. Single lesions over the exposed areas of the body were more frequent. Reactions and deformities were uncommon. The limitation of slit-skin smear was once again exposed. In only 55.3% of the cases was clinicohistopathologic correlation obtained.

CL44

A CLINICAL ANALYSIS OF 187 CHILDREN LEPROSY

Wu Yongzan

Xiuying Leprosy Hospital, Haikuo, Hainan Province, China

Xiuying Leprosy Hospital was established in 1933. The accumulative number of hospitalized patients is 1,073 including 187 children patients (0-14 years of age), accounting for 17.4%. Of these children patients, 41(21.9%) and 146 (78.1%) were detected before and after the fifties respectively; males 112 (59.9%), females 75(40.1%), male/female=1.5,1; MB 110(58.8%), PB 77 (41.2%); household contacts 37 (19.8%), contacts outside the household 26 (13.9%), infection resource unknown 124 (66.3%); the average age of onset of the disease was 10.9 years, the youngest was 4.8 years and the oldest was 14 years; the average duration of disease was 3.3 years, the shortest was 1 month and the longest was 11.3 years; the extremities were the first sites of apearance of skin lesions in most cases (71.2%); 83 cases with Grade I-III disabilities with a disability rate of 44.38%. 73 cases (PB 49, 67.1%; MB 24, 32.9%) cured with 2-5 year DDS monotherapy and 96 (PB 22, 22.9%; MB 74, 77.1%) cured with more than 6 year DDS monotherapy. There were 21 relapsed patients (MB 17, PB 4) with a relapse rate of 11.2%.

CL45

AN ANALYSIS OF 70 NEWLY DETECTED LEPROSY PATIENTS

Liu Houjian Zhao Tian'en Zhang Yuxian Li Yongshi

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Linyi Prefecture was one of the leprosy highly endemic prefec-ctures of Shandodng province. By the end of 1990, the accumulative number of registered leprosy patients was 9594, the peak prevalence was 10.5/10000 in 1959. On the basis of an active implementation of leprosy control programme over more than 30 years, both the preva-lence and incidence have considerably decreased reaching the criteria the goal of basically eliminating leprosy required, and there were only 100 active cases by the end of 1990. In recent years, the case detection rate was also reduced, only 70 new patients were detected from 1987-1990. Of these patients: male 55, female 15; the average age of onset of the disease was 38.75 years; the average age at the time diagnosed was 43.5 years; MB 39 (55.17%) and PB 31 (44.29%), MB:PB=1.26:1. The average duration is 2.97 years in MB and 2.1 years in PB. most of them were lately diagnosed with a duration of more than 2 years. Most new cases (85.71%) were detected by skin clinics, the rest by clue survey and self reporting. 42(60%)cases were found in the villages where with leprosy patients and 28 cases (40%) in villages where no leprosy patient was found in the past. Thus we should not only pay attention to the supervision of villages with leprosy patients, but also to the villages with no leprosy patients. Of these 70 cases, 13 were detected from patients' families. At the time diagnosed, 9 of them developed deformities. This high disability rate may be related to late case finding (average>2 years) indicating that disability prevention and rehabilitation should be very important components of the leprosy control programme in the future.

CL46

LEISHMANIASIS DIFUSA AMERGICA DE REPUBLICA DOMINICANA PARTICIPACION DEL PERSONAL AUXILIAR DEL PROGRAMA DE LEPRA EN EL DESCUBRIMIENTO DE CASOS

Huberto Bogaert, Rafael Isa Isa.

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Se describen las características clínicas, patológicas, epidemiológicas y terapéuticas de una forma de leishmaniasis cutánea propia de la República Dominicana. Todos los casos, 32 en total, presentaron prueba de leishmanina negativa. Descubiertos en el período 1974-1992, por el personal médico y paramédico del programa para el control de la lepra, especialmente en la región Este del país. Una investigación en población sana de áreas endémicas mostró 156 pruebas de leishmaninas positivas entre 893 personas a las cuales se les practicó la prueba.

Pruebas de inmunofluorescencia indirecta practicadas en 510 personas de áreas endémicas mostraron títulos po--sitivos en 183.

CL47

HYPERSENSITIVITY TO DAPSONE, RIFAMPICIN, AND CLOFAZAMINE, IN A LEPROMATOUS LEPROSY PATIENT

K Sathish Kumar, Jacob Samuel, Sunderarajan, & Arunthathi S

S L R T C Karigiri, Tamilnadu, India 632 106

Allergic reactions to individual drugs are not uncommon but a hypersensitive response to several drugs which are different in their constitution and their mode of action is quite rare.

Multi-Drug Therapy (MDT) consisting of Dapsone, Rifampicin and Clofazamine is the main-stay of anti-leprosy treatment in the past few years, on which the hopes of leprosy control have leaned heavily. To the best of our knowledge allergic reactions to all these three drugs have not been observed or reported in any one patient.

We report here a male lepromatous leprosy patient who developed erythema, scaling and exfoliation of the skin, when administered MDT therapy. Provocative tests with each of these drugs, individually, elicited the same severe cutaneous allergic response, demonstrating that the hypersensitivity involved all these three drugs.

We discuss and present the alternative treatment plans evolved in the management of this patient.

CL48

DAPSONE INDUCED PULMONARY EOSINOPHILIA

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Dapsone induced hypersensitivity is not unknown, but to the best of our knowledge, pulmonary eosinophilia induced by Dapsone, without any cutaneous allergic manifestations has not been reported.

A lepromatous leprosy patient, known to have a history of repeatedly developing wheezing and fever whenever he was treated with dapsone for his leprosy, had a high eosinophil count (36%) and an absolute eosinophil count of 3,300/cumm while being otherwise symptom free, on admission to SLRTC, Karigiri.

When a challenge dose of dapsone was administered under supervision, the patient become acutely ill with wheezing and fever. His eosinophil count also rose up sharply, thus confirming the occurrence of a dapsone induced pulmonary eosinophilia without any accompanying cutaneous reactions.

We present our experiences in the management of this patient.

CL49

SYSTEMIC LUPUS ERYTHEMATOSUS IN A LEPROMATOUS LEPROSY PATIENT : A DIAGNOSTIC AND THERAPEUTIC PROBLEM

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The clinical and laboratory features of Systemic Lupus Erythematosus (SLE) manifested in a forty three year old male lepromatous leprosy patient, after induction with Dapsone .

Although two totally different clinical entities, leprosy and SLE share features which are similar, which pose difficulty in diagnosis and therapy. The differentiating of nephritis occurring due to erythema nodosum leprosum from that occurring due to SLE is often difficult. Since Dapsone cannot be used, carefully modulated alternative therapy to treat leprosy has to be formulated.

We present guidelines in the diagnosis and management of these two diseases jointly occurring in a patient.

CL50

STUDY OF FUNGAL INFECTION IN HANSEN'S DISEASE

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Six cases Hansen's disease (four of B.T. Hansen's disease and two of T.T.) were studied for fungal infection which they developed during the rainy seasion July/ August'85. They developed Tinea infection also on the anesthetized patches. In these cases branched, septate, mycelia were seen microscopically. An interesting phenomenon was that the anesthetized patches which were not showing any sign of pain, temperature and touch, were showing signs of much itching. Scratch marks were very noticeable on the patches. These cases responded to anti-fungal treatment of grisovine plus local application of one of the imidazole anti fungal group of drugs.

CL51

ZOSTER-FORM BORDERLINE-LEPROMATOUS LEPROSY.

Jane T.Yamashita,Mitie T.L.R.F.Brasil,Renée Jabur,Regina M.C.Fortunato,Nilceo S.Michalany,and Osmar Rotta

Dermatology Unit, Escola Paulista de Medicina R.Botucatu,740 04023900, São Paulo,SP,Brazil.

RJG is a 32-year-old dark-skinned man with 8 month history of cutaneous lesions. He presented multiple and infiltrated lesions with symetrical distribution.

The feature of the cutaneous lesion localized at medial face of left thigh and leg was unusual. It was an erythematous infiltrated plaque with a linear disposition. The edge was irregular, polymorphic, well-defined in some areas an poorly demarcated in others.

The histopathology of the lesion showed thinned epidermis, with inflammatory-cell infiltrate separeted from epidermis by a narrow zone of collagen. The infiltrate was represented by foam-cells, some forming large nodules throughout the dermis with little epitelioid-cells. Bacterial index of skin smear was 5+ and lepromin reaction 3mm.

CL52

KERATOSIC PRESENTATION ON TUBERCULOID LEPROSY

Jane T.Yamashita,Mitie T.L.R.F.Brasil,Renée Jabur, Ana C.C.Sauwen,Nilceo S.Michalany,Osmar Rotta.

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RCS is a 49-year-old white woman with a 4 month history of paresthesia on the left foot.

On physical examination, she had three erythematous infiltrated plaques localized at medial face and heel of the left foot. The main characteristic was the surface of this lesion, that was dry, keratosic and with loss of sensation in the skin lesions and enlarged left common peroneal nerve.

The histopathology showed hyperkeratosis with psoriasiform acanthosis and a tuberculoid granuloma in the mid-dermis. The Ziehl-Neelsen stain showed that the fast-acid bacilli was absent in the histopathological examen. The skin smear examen was also negative and lepromin reaction was 9.5 mm. The culture for mycobacteria was negative, showing that there was not association with other mycobacterias.

The reason for presentation is the unusual keratosic form on tuberculoid leprosy.

CL53

ASPECT CLINIQUE DIFFERENTIEL DE LA LEPRE EN HAITI.

Gyliane Woel, Claude Pean, Raymond Bernardin.

Institut Cardinal Leger contre la lepre (HAITI)

Presentation iconographique des principales pathologies cutanees pouvant constituer des pieges en pratique courante de dermatologie.

CL54

ASPECTS CLINIQUES PARTICULIERS DE LA MALADIE DE HANSEN EN HAITI.

Florence Desvarieux, Claude Pean, Nicole Bellard, Gysette Blanc, Marleme Dambreville, Florence Foucauld, Claude A.Leveille,Real Charlebois.

Institut Cardinal Leger contre la lepre (HAITI)

Cas no 1 - Femme, de 54 ans.presentant un placard erythemato squameux de couleur violine a resolution centrale localise au dos du pied droit, accompagne d'une lesion satellite angiomateuse.

Cas no 2 - Homme, de 70 ans, avec de multiples nodules dissemines d'aspect dyshidrosiforme au niveau des doigts. (Diapo)

Cas no 3 - Femme, de 52 ans, lepromateuse avec de multiples nodules en grappe de raisin sur le nez et dissemines sur le corps.

Cas no 4 - Femme, de 20 ans, avec des lesions a type d'erytheme polymorphe de la paume des mains.

Cas no 5 - Aspect zoniforme des lepromes nodulaires observe chez un patient lepromateux de 44 ans.

CL55

LOCALIZATION OF SINGLE LESIONS IN LEPROSY.

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In this paper the authors study the sites of single lesions in 317 leprosy patients registered at two outpatient units in Rio de Janeiro, Brazil.

The preferencial sites of lesions in the population studied, was the body's uncovered and most exposed areas.

Paucity of lesions in covered sites, even when considered the percentual body area occupied by these regions favours this impression; also the significant ocurrence of dorsal lesions more common in men than women reinforce this point of view.

Predilection of facial lesions in the age group under suggests that another factors, besides exposition, interact in the distribution of lesions sites in this group.

Important differences were found when compared with data from other places and times. If vascular distribution, Langhan's cells rates and body temperature were considered as universal factors, one conclude that the exposition factor, related to social ecological and cultural characteristic should play a major role in the localization of single lesions in leprosy patients, wich do not depend of transmisson's more.

CL56

CLINICAL ASSESSMENT OF MONOLESION LEPROSY CASES

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The epidemiological significance of mono-lesion as well as the clinical followup of such lesion is still unexplained satisfactorily. It is generally observed that many of mono-lesion cases might later on convert into more progressive form of cases if left untreated.

The objectives of the investigation was to study 1) the clinical behaviour of mono-lesion cases 2) relapses.

A retrospective analysis of 829 mono-lesion Paucibacillary (PB) cases was done without following any sampling techniques.

Results :

Out of 829 cases which were treated with WHO-PB-MDT regimen for 6 months, 562 (67.8%) were found to be inactive at Release From Treatment (RFT). From the remaining 267 cases active at RFT, 264 (98%) attained inactivity at Release From Surveillance (RFS). Out of 3 cases, 2 patients dropped out during surveillance period and were lost for followup. One patient who relapsed attained inactivity after restarting MDT for 6 months.

Conclusion :

From the above study it may be derived that mono-lesion cases may be easily treated by the routine WHO chemotherapy. Therefore for field and operational purpose, the management of such cases does not appear to be cumbersome. The number of relapses in the study seems to be negligible so as one may not be alarmed about it from the public health point of view.

We also present data pertaining to large size monolesions as well as those involving single nerves in relation to PB as well as MB regimens.

CL57

CLINICAL AND HISTOLOGICAL PICTURE OF VERY EARLY INDETERMINATE AND BT LEPROSY IN ADOLESCENTS

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19 children born to mothers with leprosy and healthy controls (NL) were diagnosed clinically as having early indeterminate or BT leprosy at puberty. Their mothers' classification during pregnancy/lactation was: 6LL, 4BL, 3BT active, 3BT "cured", 3NL. There were 11 girls and 8 boys, average age 14 years, puberty grading (Tanner) 2.3 for both sexes. 15/19 had a past history of skin diseases and 6/19 had clinical evidence of skin disease. Number of leprosy skin lesions seen per child: 1 (7), 2 (6), 3 (3), and 3 had 7,10 and 11 lesions each. Size of lesions: ‹=10mm (26:47%); 11-20mm (18: 33%) and ›20mm (11: 20%); range 4x4mm - 50x70mm. Type of lesions: flat hypopigmented macule with hazy edge (34 - 1 was slightly oedematous, 3 also had "goose-pimples"); flat hypopigmented macule with defined edge (2 - 1 was shiny); slightly raised hypopigmented macule (1); reddish/ coppery macule (8 - 4 were shiny); flattened nodules (10 - 1 patient only). The largest lesions were seen on the buttocks and thighs. Light touch sensation in lesion: lost (14), reduced (19), intact (18), variable (4). Site of lesions: trunk (34: 62%) - buttocks 11, back 8, chest 8, scapular 6, hip 1; upper arm -› elbow (10), thigh -› knee (7), forearm (2), face (2). Condition of nerves: just palpable (2), easily palpable (3), slightly enlarged (10), definitely enlarged (4). Number of nerves easily palpable/enlarged per child: 1 (8), 2 (6), 3, 4 or 5 nerves (1). Biopsies were indeterminate leprosy with AFB seen (8), early BT (1), "consistent with, not diagnostic of early leprosy" (7). Fernandez results were - (4), (2), + (4), ++ (7); Mitsuda readings were - (1), (1), + (3), ++ (6), +++ (1).

CL58

CLINICAL-HISTOPATHOLOGICAL CORRELATION IN PATIENTS SUSPECTED OF HAVING LEPROSY

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A retrospective study was carried out in order to analyse the correlation between clinical and histopathological diagnosis in patients biopsied at the "Alfredo da Matta" Institute for Tropical Dermatology. It lasted from January to December 1991, and was restricted to patients suspected of having leprosy.

The authors sought to determine the coincidence in percentage terms of clinical and histopathological diagnosis; between granulomatous inflammatory process findings and positive Mitsuda reactions , as well as between the detection of AFBs in tissue sections and in slit skin smears.

CL59

BONE INFARCTION AND LEPROSY

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Among 50 patients with leprosy, 12 (24%) had radiographic evidence of bone infarction in feet and/or hand. Fifteen lesions were recorded with a marked predominance to the upper extremity (80 p. cent were located in the hand). Considered asymptomatic, these lesions were painful only in two cases (both located in hand's phalanx). X-Rays disclose encasulated calcifications, and bone sclerosis.

We think than these lesions are due to a vascular pathogenesis like aseptic necrosis, and they are a - kind of specific bone change due to invasion of bony vessels by the bacteria.

These were found to have highest incidence in the lepromatous type of leprosy, and with the longest -- duration of the disease.

CL60

TUBERCULOID LEPROSY ASSOCIATED WITH PULMONARY TUBERCULOSIS

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The authors present a clinical case of association of tuberculoid leprosy and pulmonary tuberculosis involving a 17-year old female Mulatto student from Goiás, Brazil.

In October 1990, after presenting symptoms of infection of the upper airways, she was diagnosed to have pulmonary tuberculosis.

After 1 week of treatment with a triple drug schedule (isoniazid , hydrazide and rifampicin), the patient presented skin lesions of a progressive nature. After 4 months, 3 nummular, erythematous-desquamating hypoesthesic lesions with infiltrated borders were observed on the face and upper limbs at the Dermatology Service of FMRP-USP.

The diagnostic hypothesis of tuberculoid leprosy was raised and the following laboratory tests were performed:

. Lesion bacilloscopy: negative

. Mitsuda reaction: positive (20 x 20 mm + central necrosis)

. Histopathology: tuberculoid leprosy.

The triple schedule was maintained and 100 mg/d dapsone was started.

The reason for this presentation is to suggest that infection with Mycobacterium tuberculosis may have altered the immunological equilibrium of the patyient and triggered the skin manifestations of leprosy.

CL61

Dapsone-Induced Lupoid Photodermatitis in Leprosy

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The authors present a clinical case of dimorphic tuberculoid (DT) leprosy involving a 66-year old woman who had been using dapsone for 8 months when infiltrations of a violaceous color started on her face and papulo-erythematous-violaceous, desquamating lesions started in areas of the upper and lower limbs exposed to sunlight.

Laboratory tests:

Blood count: white cells, 4,900/mm³ with 23% eosinophils; hemoglobin, 11.2 g/100 ml.

Determination of LE cells and of antinucleus factor (ANF): negative.

Latex test: +. C-Reactive protein (CRP) measurement: negative.

Skin biopsy: Epidermal atrophy with liquefaction of the basal layer. Areas with gaps at the dermo-epidermal junction. Dermis with a chronic perivascular infiltrate, with deposition of fibrinoid material around the vessels.

Direct immunofluorescence of skin biopsy: Fringe-like linear IgG, IgM, C3 and fibrinogen deposit in the basement membrane zone.

The clinical and laboratory aspects and the involution of the lesions promptly occurring after the discontinuation of dapsone, with only residual hyperchromia left, led to a diagnostic hypothesis of dapsone-induced lupoid photodermatitis.

CL62

HISTOID LEPROSY AT WESTFORT HOSPITAL, SOUTH AFRICA

Lars Wentzel

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Six patients with histoid leprosy were seen over a period of twelve years. Four patients had never been treated before, and two responded to dapsone monotherapy. Three developed ENL. A low incidence (2,3% of all LL cases) and a homogeneous histopathologic picture were found.

CL63

STUDIES ON SERUM -ANTITRYPSIN INHIBITORY CAPACITY OF LEPROSY PATIENTS

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Modified Eriksson's method was used to evaluate serum -antitrypsin inhibitory capacity (-AT) of 60 healthy subjects(control group) and 55 patients with leprosy, including TT 15, Borderline group(BB, BT, BL) 30, LL 10. The results showed that the values of serum -AT were 1.21 ± 0.15 mg/ml for the control group, 1.18 ± 0.26 mg/ml for TT (compared with control group, no significant difference, P) 0.05), 1.02 ± 0.28 mg/ml for Borderline group (compared with control group, significant difference, P (0.01), 0.78 ± 0.42 mg/ml for LL(compared with control group, significant difference, P (0.01). Furthermore, the value of -AT decreased gradually from TT to LL. The authors believe that -AT deficiency may play a role in pathogenesis of leprosy, thus purified -AT preparation or drugs capable of elevating -AT may be useful for the treatment of leprosy.

CL64

RBC IMMUNO-ADHEREING FUNCTION IN LEPROSY PATIENTS AND THEIR HOUSEHOLDS---A PRELIMINARY STUDY

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Eighty one leprosy patients and their household members were monitored with RBCC3bRR, RBCICR, RFER, RFIR and CIC. The results showed that there was a significant difference of the values of RBCC3bRR, RBCCICR, RFER and RFIR between the patient group or household group and the healthy controls. There was no significant difference of values of RBCC3bRR, RFER and RFIR between the patient group and the group of household members, but significant difference of the value of RBCICR was found between the two groups just mentioned. The results also showed that the values of RBCC3bRR, RBCICR, RFER and RFIR in household members of LL and BL patients were abnormal as compared with those of healthy individuals. In this study, the authors investigated and discussed the possible mechanism of abnormal RBC immuno adhereing function in leprosy patients and their household members and its possible clinical significance, emphasizing the importance of monitoring leprosy household members in the strategy of leprosy control.

CL65

THE CLINICAL SIGNIFICANCE OF ANTI-PHENOLIC GLYCOLIPID (PGL-I) ANTIBODY IN MULTIBACILLARY LEPROSY PATIENTS

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With NT-P-BSA as antigen, ELISA was used to detect anti-PGL-I antibodies (IgM) in MB patients with different clinical status of disease and different durations. The following were the results: the average OD value (OD) of 154 healthy individuals was 0.11 ± 0.08 ($X\pm SD$) with 0.27 as the cut off point of positivity and a positivity rate (PR) of 4.6%, the initial OD of 30 previously untreated patients was 0.71 ± 0.30 with a PR of 96.7%; OD and PR of 40 cases after 12 doses of MDT, 26 cases after 24 doses of MDT and 52 clinically cured cases were 0.53 ± 0.25 and 85%, 0.37 ± 0.21 and 65.4%, and 0.20 ± 0.17 and 62.9% respectively; OD and PR of 19 relapses were 0.53 ± 0.22 and 84.2%. The OD of active case was remarkably higher than that of cures, and there was also a significant difference between OD of cures and healthy persons. The annual mean falls of OD and BI of patients on MDT were 0.28 and 0.65 respectively, showing a reduction of the average OD value and PR with the increase of duration of the treatment and with the decrease of BI. The sensitivity and specificity of NT-P-ELISA were 96.7% and 95.4% respectively and have been proved stable and reproduceable, suggesting this test might be helpful in detecting the clinical status of MB cases, evaluating the effect of MDT and predicting the possibility of relapse.

CL66

THE METHOD FOR QUALITY CONTROL AND ITS APPLICATION IN LEPROSY SKIN SMEAR EXAMINATION

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Five Workshops on Skin Smear Examination were conducted in Guangdong province since 1989. Every participant was required to take tissue fluid from active leprosy skin lesions (4-6 sites for each patient). Totally 81 slides including 476 smear spots were examined. All the participants and more than two experienced technicians read these slides with double blind method. The findings of the experienced technicians were used as the criteria to assess the quality of slide preparation, staining, slide BI value and BI value of each smear spot. "Three Contents Assessment Method" (TCAM) (Slide preparation, staining, slide BI value) and "Modified Three Contents Assessment Method" (MTCAM) (modified by adding BI value of smear spots) were used to evaluate the quality of skin smear made by 51 participants. According to MTCAM, the results were: grade A 31.4%, grade B 29.4%, grades C and D 19.6% each, but according to TCAM grade A was 76.5%, grade B 19.6%, grade C 3.9% and grade D 0%. All slides of grade D assessed by MTCAM were reassessed by 10 freshmen with TCAM, the results were changed as follows: grade A 30%, grade B 50%, grade C 20% and grade D 0%. The authors suggested that TCAM, if used for skin smear quality control, could not fully reflect the quality of bacteriological examination. MTCAM might be pre-ferable.

CL67

THE RELATIONSHIP BETWEEN ANTI PGL 1 ANTIBODY (IgM) LEVEL AND RELAPSES IN THE CURED LEPROSY PATIENTS

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Three hundred and thirteen cured leprosy patients (MB 171, PB 142)were clinically, bacteriologically and serologically monitored for 2 years in Guangxi Autonomous Region. ELISA and MLPA with NT-P-BSA as antigen, were used to detect PGL-1 (IgM). Sera from 235 local healthy people (OD+2SD=0.24) served as the cut-off point of ELISA, the positivity threshold of MLPA is≥1:32.

The results showed that: 1)the anti-PGL-1 antibody (IgM) were detectable over a considerable period of time in leprosy patients after cure. The mean OD value of 171 cured MB for ELISA was 0.133 with a positive rate of 15.79%(27/171), much higher than those of the PB, the latter being 0.086 and 3.52%(5/142)respectively. 12.87% (22/171) of cured MB was regarded as MLPA positive, but all cured PB were MLPA negative. 2) 2 (7.4%) relapses from cured MB were detected in 27 NT-P-BSA-ELISA positive cured MB patients. Furthermore, the levels of specific antibody in the sera of both cases steadily increased right before relapses appeared, but no relapsed case was found in 291 NT-P-BSA-ELISA negative patients.

The results suggested that relapses were more likely to appear in cured patients with positive serological results.

It may be helpful in early detection of relapsed patients or in relapse prevention if close observation is given to those whose OD value is relatively high.

CL68

LEPROSY BACILLI IN SMEARS FROM NASAL MUCOSA

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Smears from the nasal mucosa of 171 newly detected multibacillary leprosy patients were taken over a five year period in the LEPRA Control Project in Malawi. The smears were taken on the day the patients were detected and at the same time as the initial standard slit skin smears which were taken from at least four sites.

The Bacillary Index (BI) of the nasal mucosa smear is compared with the highest BI of the slit skin smears. The comparison shows a mildly positive correlation (r=0.42). A majority (approx. 75%) of the patients for whom the highest BI of the slit skin smears is 4 or less has a negative nasal mucosa smear. On the other hand patients with a BI of 5 or 6 tend to have a positive nasal mucosa smear (65 to 70%).

Of the 171 patients 85 had a positive nasal mucosa smear. Of these, 55 could be followed until the nasal smear became negative. The majority (62%) became negative during the first six months of treatment with the standard WHO multidrug regimen.

CL69

HEMATOLOGIC DATA OF OLD PATIENTS WITH LEPROSY

Shigeru Matsui[1], Sunao Tanaka[1], and Tsugio Nakazawa[2]

National Leprosarium Kuryu Rakusen-en[1] and Gunma University[2], Gunma, Japan

Hematologic values, in a retrospective three-year(1989-1991) longitutudinal study, were analyzed for 315 old leprosy patients who were 163 males(ranged in 47-90 years of age, 70.9±8.3) and 152 females(47-101, 71.6±9.1). Patients were selected based on long-term records confirming their forms of leprosy, medical treatments and present other illness. Hemoglobin level (Hb), RBC count and hematocrit(Ht) began to decline in male patients in the sixth decade and in female in the eighth decade of life. WBC count were not statistically different. Hb values for lepromatous form were lower than those of tuberculoid form and decreased significantly with advancing age.

Sex	Age	n	Hb (g/dl)	RBC (10^6)	Ht (%)	WBC(10^3)
Male	50-59	13	14.6±1.0	4.59±0.32	43.4±2.6	5.6±1.5
	60-69	63	13.8±1.4*	4.36±0.46	41.3±3.7	6.2±1.2
	70-79	60	13.5±1.5*	4.27±0.49*	40.7±4.3*	6.0±1.2
	80-89	23	13.5±1.6*	4.31±0.49	40.1±4.7*	6.0±1.3
Female	50-59	13	13.4±1.0	4.36±0.35	40.5±3.2	6.3±0.8
	60-69	45	13.4±1.0	4.31±0.34	40.0±2.9	5.9±1.2
	70-79	62	13.2±1.0	4.23±0.35	39.4±3.1	5.7±1.2
	80-89	28	12.8±1.2**	4.10±0.44**	38.6±3.4	5.8±1.3

Values are mean±SD. *:$p<0.05$ vs. fifth decade, **:$p<0.05$ vs. sixth decade using the paired Student t test.

Sex	Age	n	Hb (g/dl)	Lepromatous	Tuberculoid
Male	47-69	78	14.0±1.4	13.9±1.4 (n=72)	15.2±1.1 (n=6)
	70-90	85	13.5±1.5*	13.3±1.4*(n=72)	14.7±1.7 (n=13)
Female	47-69	59	13.4±1.0	13.4±1.0 (n=45)	13.4±1.0 (n=14)
	70-101	93	13.1±1.1	12.9±1.1*(n=70)	13.5±1.0 (n=23)

*:$p<0.05$ vs. under 69 years group

CL70

ETUDES DE L'INDICE BACTERIOLOGIQUE CHEZ LES PATIENTS MULTIBACILLAIRES

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Institut Cardinal Leger contre la lepre (HAITI)

Seront consideres:

1) les variations de l'IB chez les patients multibacillaires reguliers au traitement.
2) les variations de l'IB dans les cas de non compliance au traitement.
3) les variations de l' IB dans les cas d'abandon du traitement.

CL71

THE ROLE OF SKIN-SMEAR EXAMINATION IN PAUCIBACILLARY LEPROSY

Devanbu V, Salim A. Khan, Lilly Ravikumar, Nobleraj A, Lobo D.

It is an established fact that Skin-smear will be NEGATIVE in the large majority of Paucibacillary (PB) leprosy cases. Thus the Diagnosis of PB leprosy is mainly based on Clinical criteria.

Inspite of this known fact, a routine Skin-smear is advised in PB cases before and at completion of treatment as per WHO guidelines.

Over a period of thirty months commencing 1990, a total of 5394 PB smears were done in our institution, out of which only TWO (2) were found to be POSITIVE. Thus 99.95% of the smears were NEGATIVE. A detailed analysis of the PB cases who under-went skin smear is presented.

The need, relevance and cost-effectiveness of this exercise is discussed, along with its role and importance in the planning of future Leprosy Control Programmes, taking into due consideration the scarce laboratory facililties worldwide.

CL72

POLYMERASE CHAIN REACTION EN LA LEPRA.

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Se ha utilizado la técnica de la PCR detectando el gen groEL mediante nested-PCR y con los primers 18K-1 y 18K-3 en 25 biopsias de enfermos de lepra comparandolo con estudio clínico, bacteriológico, histopatológico e inmunológico.

Se presentan los resultados preliminares obtenidos y se hacen consideración de la importancia de esta técnica para detectar formas paucibacilares, casos iniciales y diferenciar las recaidas de las reversal reactions. También puede ser útil en el estudio de la transmisión de la lepra en los contactos y no contactos de areas endémicas.

CL73

BACTERIOLOGICAL AND IMMUNOLOGICAL STUDIES ON ACTIVE LEPROSY IN CAIRO

Sawsan H.M. El Tayeb, Abd-El Hamid A. Mohamed, Jiri Kazda,* Ez - El Regal Khamis, Nehad El Shabrawy, Ezat M. Nasr.

Al Azhar University, Medical College Egypt, *Research institute Borstel Germany.

In spite of efforts done by WHO and the Egyptian Ministry of Health, still there are many sporadic new cases of leprosy. This study was done on 26 active patients examined clinically, skin and nervous system. Bacteriological investigations were done including the bacteriological and morphological indices. Polymerase chain reaction (PCR) was done on biopsies using two or four primers. T- cell subpopulations and the ratio between T helper and T suppressor were determined. Specific humoral immunity was done by determining the PGL antibodies using the indirect ELISA test.

The results of these investigations and their significance in classifying leprosy will be presented.

CL74

HEMATOLOGICAL AND BIOCHEMICAL INVESTIGATIONS ON ACTIVE AND TREATED PATIENTS.

Sawsan H.M. El Tayeb, Ezat M. Nasr, Abdel Hamid A. Mohammed, Ez El Regal Khamis, Nehad El Shabrawy.

Al Azhar university, Medical College, Egypt.

Hematological investigations as blood hemoglobin, total and differential leucocytic count, and biochemical investigations as liver and kidney function tests, were done on active and treated patients. The results were compared with those done on apparently healthy control age-matched persons.

It was found that mild to moderate anaemia was present. Hemoglobin level was affected with the intensity of the bacterial load. Treated patients had a higher hemoglobin level than the under treatment patients. All the biochemical result showed non significant increase or decrease values compared with the control group.

Details and Data results and their statistical analysis will be discussed and presented.

CL75

SERUM LACTOFERRIN IN LEPROMATOUS LEPROSY PATIENTS

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The serum concentrations of lactoferrin were determined by competitive enzyme immunoassay in sera of 16 healthy volunteers and 38 lepromatous leprosy patients. Out of these leprosy patients 25 were without any sign of reactions and 13 were suffering from type-II of reaction. The mean lactoferrin levels in both types of patients (1.89±1.26 ug/ml; 3.29±1.80 ug/ml respectively) were observed to be significantly higher than those in healtny volunteers. The serum lactoferrin levels were found to be associated with bacterial load ($p<0.02$). Majority of lepromatous patients without reactions (64.0%) had normal levels whereas 62% of lepromatous leprosy patients suffering from reactions showed a significant increase in the levels of lactoferrin. These findings suggest that rise in lactoferrin levels is associated mainly with occurrence of reactions in lepromatous patients. The results and their possible use in prognosis and understanding the pathogenesis of type-II reactions would be discussed.

CL76

EFFECT OF MULTIDRUG THERAPY ON PLASMA LEVEL OF HIGH DENSITY LIPOPROTEIN CHOLESTROL (HDL-C) IN PATIENTS OF LEPROMATOUS LEPROSY

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Increased plasma level of HDL-C have been reported in lepromatous leprosy to the extend that a negative test has been used to exclude diagnosis of lepromatous leprosy (Kumar et al, Int J. leprosy 1989-p 392)

In this study HDL-C estimations were performed in 50 patients (32 males & 18 Females) of Lepromatous leprosy, taking plasma HDL-C level as 28-71 mg/dl in men & 34-91 mg/dl in women as range of normal value, of 50 cases (mean age 48.02 ± 5.7 years and mean weight 42 ± 6.04 Kg) who received multi drug Therapy & declared free of disease (as per WHO tech. report

1982) HDL-C remained high in 41 (82%) Cases, decreased in 9 cases, of which, became normal in 7 cases.Nutritional status and weight improvement was noticed in last two groups. Relapse rate remained 5% in 1st group and nil in other two groups.

It is openied that HDL-C plays an important role not only in disease process but also has role in relpase of lepromatous leprosy. We suggest to give trial of lypolytic drugs along with MDT in cases of lepromatous leprosy.

CL77

ADAPTATION HORMONES AND AUTOSENSIBILIZATION TO CONNECTIVE TISSUE IN LEPROSY

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37 LL patients (16 active and 21 inactive cases) were assayed for antibodies to collagen (ABc) and elastin (ABe) with using latex-agglutination method, and for hypophyseal somatotropic hormone (HSH), hydrocortisone, triiodothyronine (T3), thyroxin (T4), and for T-cell suppressor activity (TSL) with using RIA. 22 otherwise healthy persons were used as controls. In active patients ABc and ABe levels were significantly elevated remaining such in some cases after 10 years and more of their clinical inactivity. In leprosy patients blood levels of hydrocortisone and T3 were high while T4 and HSH were in the normal range. There was a strong relationship of the titers of the antibodies studied and TSL-activity and hydrocortisone and T3 levels. More elevated concentrations of endogenous hydrocortisone in leprosy patients were correlated with low titers of ABe and increased TSL-activity. On the contrary, high levels of T3 in leprosy patients were accompanied by decreased TSL-activity and increase in ABc and ABe titers. Based on the correlations found out, optimal prophylactic and curable measures for treatment of auto-sensibilization to connective tissue in leprosy might be selected.

CL78

THE FREQUENCY AND CLINICAL FEATURES OF ERYTHEMA NODOSUM LEPROSUM IN HYDERABAD, INDIA

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Erythema nodosum leprosum (ENL) is a well recognised complication of multibacillary leprosy. However few data exist as to the frequency and natural history of this phenomenon. We report here a retrospective case note study of all multi-bacillary patients registering with our clinic over the twelve year period 1980 to 1992. During this time 2742 multibacillary patients registered with the clinic, 48% were LL and 52 % BL. Overall 22.1% (range 10.7%-57%) of LL and 2.7% (range 0-6.5%) of BL patients presented with ENL. Of the 1985 cohort 32% of LL and 9.3% of BL patients have devloped ENL. Details of the time course and clinical features of the disease will be presented and the impact of Multi-Drug Therapy on the frequency and presentation of ENL in our clinic will be discussed.

CL79

AGRANULOCYTOSIS SUPPOSED CAUSED BY CLOFAZIMINE IN A LEPROMATOUS PATIENT

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This abstract is about a case of agranulocytosis in a lepromatous patient who was under treatment for leprosy and, after months of treatment with 2 doses administrates clofazimine, rifampin, dapsone, developed agranulocytosis and needed hospitalization in C.T.I.

After discharge from the hospital, he used only dapsone without a problem but when clofazimine was used (50 mg/day) he developed agranulocytosis and needed C.T.I. again.

Now he is only treated with 100 mg/day of dapsone and he has been stable for 6 months.

CL80

POSSIBLE ROLE OF OFLOXACIN IN ARRESTING REVERSAL REACTION

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Reversal reactions are not a very uncommon phenomena after the implementation of Multi Drug Therapy.

Differentiation from Relapse was made on Clinical grounds, histopathology and trial with steriods. During its treatment with steriods the period ranges at times upto one year with a gradual tapering of the steriods.

In some cases it appears during Multi Drug Therapy and in some when the treatment is completed. The paper discusses the use of Ofloxacin in combination with Dapsone over a period of thirty days in five patients, where the steriods could be cut off within three months. This raises a possibility as to whether a Reversal Reaction occurs purely due to the immunological aspect or an element of Rifampicin resistant organism have a role to play.

Thus the addition of Ofloxacin along with the steriod cover definitely helps, and another interesting aspect was that the prospect of nerve damage also is reduced.

CL81

APPLICATION OF ELECTROACTIVATED SOLUTIONS FOR TREATMENT OF OSTEOMYELITIS IN LEPROSY PATIENTS

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Electroactivated solutions which are successfully applied in surgery and stomatology (S.A. Alekhin, 1992) are proposed for using in leprosy as well. Recently valid evidence for effectiveness of such solutions in treatment of infected wounds in nine-banded armadillos inoculated with M.leprae has been obtained (A.A.Juscenko, 1992). The results of treatment of 46 leprosy patients with ostemyelitic foot lesions are presented. The patients were 35 - 65 years old. Osteomyelitis was confirmed roentgenologically. In 38 patients bone damages were accompanied by plantar neurotrophic ulcers, which were perforated in 8 cases. Pathogenic coccal flora was isolated in 43 cases. In the course of the treatment minor surgical operations were done on osseous and soft tissues of foot if indicated. We applied electroactivated physiological solution (0,85% NaCl) after electrodialysis of various duration and specified current parameters. In cases of secondary infection ulcers were washed with anolyte, i.e. the fraction (pH<7) with marked bactericidal properties. As inflammation subsided anolyte was substituted for local catolyte (pH>7), i.e. the fraction with rege-nerating properties. Clinical observations showed that applications of electroactivated solutions resulted in a more rapid dis-appearance of foci of infection with healing of ulcers. In addition, these solutions are free of allergic complications.

CL82

THE EXPERIENCE OF USING REFLEXOTHERAPY IN LEPROSY PATIENTS WITH CHRONIC NEURITIS

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Prospects of using reflexotherapy in leprosy patients are discussed. The results of reflexotherapy of 68 leprosy patients suffering from chronic neuritis are presented. The age of the patients ranged from 25 to 72 years old, the duration of their illness was 6-42 years. 28 patients were given acupuncture according to inhibitory method with using biologically active points of common and local action. One course of reflexotherapy consisted of 10-12 procedures, the number of courses made up to 2-3. 18 patients were given 8-12 procedures of pharmacopuncture with aloe extract introduced into the points of acupuncture. 10 patients were administered auricular acupuncture of prolonged action (the needles were left in the floor of the auricle for 7 days). Points AR:28, 51, 55 and the points of pain locus were used. The treatment lasted for two or three weeks. 12 patients received 10 procedures of transcranial electroanalgesia, i.e. electrostimulation of opioid structures of CNS. By clinical observations, reflexotherapy arrested nerve pains and improved general condition with increase in movement activity of limb joints and muscle strength. A significant increase in blood levels of beta-endorphines in leprosy patients was noted that might partially account for the beneficial effect observed. The data obtained suggest usefulness of reflexotherapy as an addition to other rehabilitation measures for leprosy patients.

CL83

RESULTS IN SEROLOGICAL ASSAYS FOR DETECTION OF PREVALENCE THE ANTIBODIES TO HIV-1 LEPROSY CASES IN RIO DE JANEIRO, BRASIL.

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Sera from 1030 leprosy patients were tested for HIV-1 antibodies. These patients are on treatment or under surveillance at two the outpatients unit in Rio de Janeiro, Brasil.

All sera were screened initially using Elisa Recombinat HIV-1 antigens(ABBOT). Positive tests were confirmed further both by using Elisa Virostika anti-HIV (ORGANON) and by Imunofluorescency - cells K37/3 (GERMANY). In this study we considered positive reactive in all 3 tests. Control group consisted of blood donors, matched by age and sex.

HIV-1 seropositivy rates were 0,29%(3/1030) among leprosy patients. Those 3 seropositivy cases are males, means of age 41 years old and lepromatous on MDT treatment. In the interview these patients refer only the sexual transmission as risk factor for HIV infection.

In this paper prevalence of HIV infection among leprosy patients dont seem to differ of the general population.

CL84

BORDERLINE TUBERCULOID LEPROSY IN AN HIV+ PATIENT; CLINICAL, HISTOLOGIC, AND IMMUNOHISTOLOGIC EVALUATION

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Despite a HIV seropositivity rate among leprosy patients similar to that of the general population, little data exists relative to the effects of HIV infection on the clinical and immunological response to Mycobacterium leprae. A 52 year old HIV+ white homosexual man presented with several erythematous, anesthetic, annular plaques. Histology was consistent with borderline tuberculoid leprosy and M. leprae was detected by PCR. The lesions responded rapidly to MDT. The percentage and absolute number of CD4+ peripheral blood lymphocytes (PBL) was decreased (98/mm3) with an increased percentage of CD8+ cells. Immunohistochemical analysis of a cutaneous lesion revealed a marked increase in CD1a+ epidermal cells, HLA-DR+ cells, and CD25+ cells. The intradermal granulomata consisted principally of CD4+ cells surrounded by a mantle of CD8+ cells, with less than 5% CD22+ cells. There was upregulation of several adhesion molecules on PBL and in the lesion. For example, ICAM-1 was strongly positive in the epidermal basilar layer and concomitantly increased with CD11c in granulomata. These findings demonstrate that concurrent HIV infection in paucibacillary leprosy patients does not alter the general character of the *in situ* inflammatory cell infiltrate. Moreover, peripheral and *in situ* adhesion molecule expression appears predominantly influenced by the mycobacterial infection.

CL85

NEOPLASTIC TRANSFORMATION OF CHRONIC ULCERS IN LEPROSY.

Niyi Awofeso. Ag. Director,

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Neoplastic transformation of trophic ulcers though infrequent, may have a fatal outcome, especially if diagnosis and treatment are delayed.

Trophic ulcers are common in patients with leprosy, yet leprosy workers are commonly ignorant of the fact that neoplastic changes may develop in such ulcers. There is insufficient literature on the subject even in standard textbooks of leprosy.

Although neoplastic transformation of chronic plantar ulcers is said to be rare, the fact that, for instance 2 patients were detected within 4 months from among 23 patients admitted for care at the NTBLTC, Zaria is a reminder that this unpleasant complication does occur.

Since the prognosis becomes poorer with delay in diagnosis, it is important that health workers, and especially those looking after leprosy patients should remember the possibility of malignant change in patients with refractory plantar ulcers. In addition, this condition should be emphasised in textbooks and handbooks on leprosy.

Most importantly early diagnosis and effective treatment of leprosy patients will prevent malignant transformation of trophic ulcers.

CL86

HEPATITIS C AND HEPATITIS B VIRUS SERUM MARKERS IN GREEK LEPROSY PATIENTS

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Hansen's Disease Center, Athens, Greece

In previous studies increased prevalence of hepatitis B among leprosy patients has been noted. In order to estimate the frequence of hepatitis B and hepatitis C in Greek leprosy population this seroepidemiological study was carried out. Serum samples from 71 leprosy patients were assessed

for HBs Ag (ELISA, Abbott),whereas in 53 samples from the same original population HCV seropositivity was also assessed (ELISA, Abbott, 2nd Generation). HBsAg seropositivity (5,6%) did not differ between leprosy cases and healthy control. HCV seropositivity was found 18,9%. A most significant difference was observed between patients and healthy controls (A 0.00LI). Total seropositivity rates revealed a statistically significant difference (p 0.02) between the prevalence of HCV and HBV. It is concluted that the prevalence of hepatitis C is increased among Greek leprosy patients. In both form of hepatitis, seropositivity rates do not differ between paucibacillary and multibacillary forms of leprosy.

CL87

THE CURRENT EYE HEALTH CARE DELIVERY SYSTEM FOR LEPROSY IN LEPROSY ENDEMIC ZONE OF EASTERN INDIA

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Social stigma had kept the leprosy sufferers away from the general hospital and private clinics for opthalmic care. Till upto late eightys of this century the leprosy patients can avail the facilities of the general hospital eye O. P. D. and hospital indoor only by concealing their disease (specially in cases of patients with deformity). Their eye care were mainly adopted by the weekly eye clinics of the leprosy home and hospitals and the field clinics which were conducted by P. M. W., non opthalmologist Medical Officer and in a very few instances by the opthalmologist.

But now after the successful campaign of M. D. T. the after care patients with or without deformity get admitted and stay in the general hospital indoor and in the mass eye camp just beside other non-leprosy patients. They are also being treated or operated in the same OPD & operation theatre respectively. At the same time most of lthe leprosy hospitals have their own ophthalmologist leprologist with special training in ophthalmic aspect of leprosy. In private clinics the eye specialist also examine the leprosy patients without much hesitation. This is really a great turn out in context of the socio medical aspect of this disease which certainly allows more specialist ophthalmic care for the sufferers and prevents the blindness from leprosy in a far better way.

CL88

RELATION OF SKIN LESIONS WITH DEFORMITIES IN NON LEPROMATOUS LEPROSY

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The skin lesions and their relation to nerve involvement resulting in deformities is studied in 176 non lepromatous cases (with 310 nerves involved) of GMLF's Referral Hospital at Wardha. It is very interesting to note, that the deformities are more when the skin lesions are over the anatomical course of nerves in case of non lepromatous cases. The severity of deformity also increases with the size of skin lesions. The patches in reaction definitely induce some deformity or other in hands, feet, eyes and face when they are present in the vicinity of the nerves supplying these parts.

CL89

THE EFFECT OF HIV INFECTION ON CLINICAL RESPONSE OF LEPROSY PATIENTS TO MULTIDRUG THERAPY IN KENYA

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A case control study was undertaken in Western Kenya to determine the effect of HIV-1 infection on cure rate, development of adverse drug reactions, deveopment of type I or type II reactions and occurrence of relapse among leprosy patients who had been treated with WHO MDT.

Cases were HIV positive patients who were put on MDT between July 1989 to April 1990. Controls were leprosy patients who were HIV negative at the time of the study. Cases and controls were matched on age, sex, time of diagnosis, clinical classification and geographical locality. We enrolled 18 cases and 18 controls into the study.

Preliminary findings were that HIV positive leprosy cases were more likely to present with reactions than controls at the time of follow-up (OR = 4.8, X^2 = 1 p = 0.4). At the time of follow-up 15/18 controls were found to have achieved clinical cure as opposed to 9/18 (50%) of the cases, the difference being statistically significant (X^2 = 4.4 p = 0.04). Relapse/retreatment rate was found to be higher among cases (28%) as opposed to controls (5%) (OR = 6.5 X^2 = 3 p = 0.07).

These findings would no doubt have implications on the national control programmes which are implementing MDT in areas where both diseases are endemic.

CL90

HUMAN IMMUNO DEFICIENCY VIRUS (HIV) AND LEPROSY

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In countries with endemic tuberculosis and which are now being confronted with a HIV epidemic there is an increase in the number of patients with tuberculosis. This, however, is not the case for leprosy, although in these countries the number of individuals infected with M.leprae is similar to that infected with M.tuberculosis.
HIV specifically attacks T helper cells, which are essential for immunity to infection. Therefore, theoretically it is possible that HIV infected patients with a concomitant infection with M.leprae may provide M.leprae the opportunity to multiply. The leprosy spectrum is determined by the Cell-Mediated Immunity (CMI) towards M.leprae. The same is true for M.tuberculosis, but because it is basically toxic, after infection it causes spontaneous inflammation and granulocyte activation. M.leprae is definitely non-toxic and does not generate an initial response.
For leprosy to become clinically manifest, the CMI must recognize the bacillus and initiate a hypersensitivity reaction. During a HIV infection, this may well not be possible. The bacilli multiply without causing clinical disease. We present a HIV infected patient who developed clinical signs of leprosy, which disappeared within a few weeks. The theoretical aspects of the HIV epidemic on the incidence of leprosy are also discussed.
We expect an initial decrease in leprosy which can been seen in many countries in which HIV infection is widespread and which is commonly attributed to BCG vaccination or Multiple Drug Therapy (MDT) programs. Thereafter we expect an increase of leprosy infections among those not infected with HIV.

CL91

MALIGNANT TRANSFORMATION OF CHRONIC PLANTAR ULCERS IN LEPROSY PATIENTS

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The malignant transformation of chronic plantar ulcers may be suspected when clinical signs are present ; nevertheless, pathological examination is necessary for diagnosis of certainty. Even so, the histological differenciation between carcinoma and pseudo-epitheliomatous hyperplasia may not be easy.

The authors report on 22 cases of chronic plantar ulcers suspected of malignant degeneration in ancient leprosy patients : 13 of them were shown to be effectively carcinoma while the rest were pseudo-epitheliomatous hyperplasia.

Accurate diagnosis is most important since the line of treatment differs according to the nature of the lesion : amputation in case of carcinoma, deep local excision in case of hyperplasia (dependining on healing possibility and functionnal capacities of the foot). In case of carcinoma, the regional lymphnode dissection should not be systematically considered.

From available data in litterature, it is difficult to ascertain whether the malignant transformation of plantar ulcers is frequent. Nevertheless this possible event should be kept in mind and, also, should be remembered during training courses for health workers in leprosy control programmes or in non specialized health programmes when integration of vertical programmes is planned.

CL92

SQUAMOUS CELL CARCINOMA IN CHRONIC ULCERS OF LEPROSY PATIENTS

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An analysis is presented of case histories of 38 consecutive cases of squamous cell carcinoma (SCC) in chronic ulcers of leprosy patients treated between 1981 and 1990 at McKean Rehabilitation Centre, Northern Thailand. The study included 37 individual patients; 29 males and 8 females. The average age was 60 years, the average duration of the ulcer was 12 years. Four patients (11%) had histories of SCC on other extremities. Metatastic spread was observed in 2 cases (5%), both instances leading to death. The commonest site of involvement of SCC was the foot, but it was seen on the knee in 1 patient and on the hand in 2 others. The incidence rate of SCC in the group at risk (leprosy patients with disability grading 1 and 2) was 0.79:1000 per year.

A case-control study was performed with the objective to identify factors associated with the development of SCC in plantar ulcers of leprosy patients. No associations were found between the development of SCC and factors concerning race, profession, place of origin, duration of leprosy, type and duration of leprosy chemotherapy, presence of bone involvement and type of ulcer care given. The only statistical valid finding was that the duration of the ulcer was significantly lower in the group with malignant change.

It is concluded that SCC in chronic ulcers in leprosy patients cannot be considered rare and emphasizes the need for an active policy of disability prevention in leprosy programmes. Factors other than ulcer duration need to be searched for, in order to identify factors influencing malignant change in plantar ulcers of leprosy patients.

CONTROL AND ERADICATION

CO1

ON THE ROLE OF THE GOVERNMENT IN LEPROSY CONTROL

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Before the founding of the People's Republic of China, the local governments of Yulin paid little attention to the prevention and treatment of leprosy. Leprosy transmission developed more and more seriously. Not long after the founding of New China, the local governments of Yulin have been not only involved in leading, planning and implementing leprosy control programme and have provided with necessary resources including manpower, lands and funds, and also have mobilized the whole society to support the work against leprosy. As a result the transmission of leprosy was soon controlled and in 1990 this disease was basically eliminated as a public health problem in all cities and counties of this region. Both the incidence and prevalence rates of the disease dropped sharply. The results of the research showed that different attitudes toward leprosy of different governments made the results completely different. The more the government is involved, the faster leprosy will be eliminated. Based on the findings in the research, the authors realize that leprosy is mainly a social disease. For the time being and also in the future, the important factors are the attention, involvement and support of the community and the go-vernemnt, especially in the third world countries where leprosy is seriously endemic.

CO2

THE DISABLED LEPROSY PATIENT AS PARTNER IN LEPROSY CONTROL: STIGMA AS SIGNPOST.

Rien Verhage

N. S. L., Bukuru, Nigeria.

The strategy of accelerated implementation of MDT presupposes the political commitment to: the allocation of resources, a well motivated leprosy control organisation and a relatively stable political and social environment.
The result of this strategy in N. Nigeria will be a sharp decline in the prevalence of leprosy from 15 to 1.7 per 10 000 inhabitants by the end of 1995. The side effects of the diminished visibility of the leprosy problems are likely to create three counterproductive problems: diminished political commitment and funds, diminished motivation of leprosy control staff due to lack of career prospects, and diminished care for "cured" leprosy patients with disabilities. The most common solutions like integration of leprosy control into PHC or combination with TB control do not address sufficiently the problems of care of disabled patients, the motivation of health personnel and the instability of the political and social environment. In addition or as alternative to these solutions the systematic participation of (ex)leprosy patients and patient associations is discussed. The experience with (ex)patients as voluntary leprosy workers has shown that they could become powerful

partners in leprosy control and could contribute greatly to the sustainability of leprosy control in the next decade.

CO3

COMPREHENSIVE LEPROSY CARE PROJECT, "BORSAD MODEL" - A NEW APPROACH TO LEPROSY ELIMINATION

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The Comprehensive Leprosy Care Project envisages the combination of governmental efforts and specialists brought under one roof through international assistance to develop a new approach where a leprosy patient at any stage of the disease process needing medical, surgical or rehabilitative care is offered an opportunity to overcome the disease. In rural field situation at Borsad taluka in Gujarat (population 3,70,000) not only MDT but an integrated deformity care programme was undertaken. The workers were trained to deliver comprehensive services consisting of (a) simple exercises (b) prefabricated splintage (c) identification of early neuritis, reactions and relapses for medical or sugical intervention (d) care of insensitive extremities (f) recognition of handicap and required economic assistance and (g) rehabilitation of advanced deformed patients by Modulan grip aids.

During the past four years of its existence the project has detected 485 new patients, started MDT in predominantly monotherapy area, provided deformity care services to 408 patients (including those released from treatment or cured) through training of existing staff and systematically worked towards integration of deformity and rehabilitative care services with chemotherapy distribution, thereby maximising the chances of elimination in true sense. The detailed observations will be presented.

CO4

A COMPARATIVE STUDY ON THE EFFECTIVENESS OF DIFFERENT METHODS OF CASE DETECTION IN NORTH INDIA

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The Leprosy Mission (TLM) India, New Delhi 110 001 TLM Hospital, Muzaffarpur (Bihar) and TLM Hospital, Naini, Allahabad (U.P) India.

This study was conducted in two endemic areas, Muzaffarpur and Naini in North India. The main objective of the study was to analyse the effectiveness of Mass Survey as compared with rapid surveys (RS) for case detection in leprosy. The results were analysed in relation to the man hours spent on the survey and the profile of the cases detected such as age, sex, type, deformity rate and bacteriological index, etc.

A population of 9,892 in 6 villages were first covered by Rapid surveys by a team of para medical workers and then the same population was subjected to mass survey by a second team. Preliminary findings showed that 35 new cases were detected by the rapid survey giving a case detection rate of 3.5/1000. 8.34 man hours were spent to detect a case. By the conventional survey 58 cases were detected giving a case detection rate of 5.8/1000 which took 13.5 man hours per case detected. More male cases were detected by rapid survey (1.7:1) than in the mass survey (1.2:1). More adult cases were detected in mass survey (7.4:1) than in the rapid survey (4.8:1). More single lesions were detected in the mass survey (1.5:1) than in the rapid survey (0.9:1). The relative merits of these case detection methods will be discussed and presented.

CO5

GUIDELINES AND STRATEGIES OF THE PROGRAMME FOR THE CONTROL AND ELIMINATION OF HANSEN'S DISEASE IN BRAZIL IN THE PERIOD 1990-1994

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The proposal of governmental action for the effective control of Hansen's Disease between 1990-1994 will be presented.

The governmental plan of action, called "National Emergency Plan", used epidemiological and operational criteria to stratify Brazil into priority areas, with the objective of having an impact on the endemy through activities of disease prevention, early diagnosis and ready treatment with MDT/WHO.

Results obtained in the plan's first three years will be presented and debated.

CO6

ERRADICAR LA TRANSMISION DE LA LEPRA PARA 1994: POLITICA PARA LA ACCION EN MEXICO.

José Rodríguez-Domínguez MD, MPH, Lucía B. Yáñez Velasco MD, MSc; Francisco Castellanos García MD, MPH.

En 1989 el Gobierno Mexicano emitió la política de eliminar a la lepra como problema de salud pública cortando su transmisión mediante incorporación de los 16,700 enfermos prevalentes y los nuevos casos a los esquemas de poliquimioterapia (PQT o MDT) recomendado por la OMS.

Se implementó un plan entre el Gobierno de México y dos organizaciones internacionales de ILEP (SMHF y ALM) para intensificar acciones de salud y de atención primaria.

La distribución de los enfermos con lepra abarca casi todo el territorio nacional, pero el 80% de los casos se concentra en 10 de los 32 estados que conforman al país; por lo que se consideró prioritaria a esta área geográfica, para iniciar la primera fase de localización e incorporación al tratamiento de los enfermos. Las principales dificultades para lograrlo han sido renuencia al tratamiento y no localización de casos; por ello se diseñaron estrategias de capacitación en leprología, de promoción y fomento de la salud usando como lema la curabilidad de la lepra; implementación de un programa de rehabilitación de incapacidades; supervisión continua y evaluación periódica.

Actualmente se encuentran 9,000 enfermos recibiendo tratamiento y 2,900 han concluido la vigilancia postratamiento.

La tasa de prevalencia del país al iniciar la PQT era de 21 X 10,000, actualmente ha bajado a 1.8. Para 1994 se pretende bajarla a menos de 1 X 10,000 hbs.

CO7

EVOLUTION OF THE ILEP INFORMATION SYSTEM FOR LEPROSY CONTROL PROJECTS 1966 - 1993

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This abstract presents the historical development of the information system used by Members of the International Federation of Anti-Leprosy Associations (ILEP) for the annual monitoring of leprosy projects.

Its evolution parallels the policy direction of leprosy field programmes over the last 27 years and incorporates all the major

advances in leprosy control introduced during this period. The modifications in the information system reflect the changes from the early welfare programmes sponsored by ILEP Members, through institutional care, ambulatory treatment, to systematic Survey-Education-Treatment programmes and the present day leprosy control programmes based on the use of Multidrug therapy. The changing pattern of the organisation of leprosy work in the field, from small/local projects often private, to national government programmes is also one of the factors which have considerably influenced the development of the system.

The objectives and components of the current ILEP information system are described. This system provides for, information on project formulation (the ILEP A questionnaire), annual medical and financial reporting (the ILEP B questionnaire) and the use of indicators for monitoring progress with MDT.

The future development of the system will be outlined.

CO8

RAPID PHOTO SURVEY AS A TOOL FOR CASE DETECTION IN LEPROSY IN URBAN AREAS

Lobo D, Mathews M, Alexander M, Nambudripa K, Thirunavakarasu S, Leo Pandiaraj, Jayaraman R.

Intensive whole-population survey is the main mode of case detection in India. This method is time-consuming and requires abundant manpower. It is difficult to employ this method in Urban areas since it requires house-to-house enumeration and complete EXAMINATION of the population. Hence a RAPID PHOTO Survey was tried as a case detection technique in Madras. This technique involves:

- Household visits and enumeration
- Display of Flash-cards depicting early signs
- People with suspected early signs to report to the nearest clinic.

This survey was conducted in 85 Divisions with a population of 2.1 million and showed the following:

- Population coverage : 92%
- House hold coverage : 94%
- Total manday-Daily Coverage : 3771/522
- Cases detected - MB/PB :1332/52/1280
- New Case detection rate : 0.68/1000

The survey was completed by 44 para medics in six months. Advantages/Disadvantages discussed.

CO9

COMPARITIVE CASE-OUTPUT THROUGH DIFFERENT CASE-DETECTION METHODS IN URBAN AREAS

Mathews M, Alexandar M, Thirunavakarasu S, Lobo D, Kothandapani G, Maria Dominic I.

In Urban areas and metropolitan conglomerates, it is impossible to employ an uniform method of case-detection for the entire population.

Madras City has a population of approximately 4 million of which 2.1 million population is covered by our institution GREMALTES for leprosy control work.

Over a six-month period in 1989, we employed three methods of case-detection:

a. Intensive whole population survey
b. Rapid photo survey
c. Health camps

The case-output was as follows:

Method	Pop. Covered	Case-output		
		PB	MB	Total
Intensive	269,096	642	27	669
Rapid Photo	1,969,019	1,280	52	1,332
Health Camps	12,531	44	02	46

The advantages/disadvantages and cost-effectiveness of each of the above methods is discussed along with their role and relevance while planning Urban Leprosy Control Programmes.

CO10

BETTER COMMUNITY PARTICIPATION IN LEPROSY

Indira Alatkar

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A microlevel experiment was carried out during April 1985 to March 1987 for intensive health education through **Individual approach**, to imbibe the scientific knowledge about Leprosy in people and to erase the superstitions, misconceptions and stigma attached to the disease

The Sector wather (K), Dist. Satara, (Maharashtra) was selected with total population, 25000 distributed in 10 villages. Intensive health education with special stress on personal contacts, was given with the help of visual aids. After two years successive efforts following spectaculer results were noticed.

1) New case detection through **VOLUNTARY REPORTING**, increased from **40% to 80%**.

2) Increase in **clinic attendance** from **60% to 95%**.

3) **Survey absentee** reduced from **25% to 5%**.

The details about the methods adopted are discussed in my paper. Hence in developing Countries, to have a **KAP** change, individual approach is extremely effective.

CO11

RAPID VILLAGE SURVEY (RVS), AN ALTERNATIVE METHOD IN THE ESTIMATION OF LEPROSY PREVALENCE

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This study aimed to find an alternative method which is valid,simpler,quicker and less expensive to replace the total village survey for the estimation of leprosy prevalence in rural community.

40 rural villages were (cluster) randomly selected. WHO case definition was used. Found cases would be confirmed by leprologist. Standardization of examination methods were done before the survey. Rapid village survey (RVS) was executed by one medical doctor and 5 staff. The village headman was visited one week prior to RVS. He annouced objectives, appointment and place of examination for RVS. Focus group discussion with village leaders by one team member would be done in the afternoon as soon as the team entered the village. Suspected cases from this gossip technique would be traced. Registered cases (known cases) and their contacts would also be traced. Announcement by using loudspeaker on the survey car moving through the village with precise content was done to inform those who had symptoms of leprosy to report voluntarily. Total village survey (TVS), consisted of 10 staff, was used as gold standard method one week after RVS. TVS would be informed to villagers after completion of RVS. Registering of all inhabitants, examining all inhabitants and tracing of absentees up to 3 consecutive visits in one month period were main activities of TVS, meeting for cooperation with representatives of all households would be executed the night before TVS.

The surveys were done in Khon Kaen province, Thailand in late 1990. Inhabitants examined by TVS were 20,815 which was 99.6% of target population and absentee was only 0.4%. Leprosy cases found by RVS was 22 compared to 24

by TVS. Reason of two cases missing by RVS was temporarily left the villages. The statistical analysis showed no significant of different between the two methods(p value > 0.1). Total cost ratio (TVS: RVS) was 2.8: 1. The RVS thus was proved to be a sufficient valid, simpler, quicker and less expensive method which should be an alternative tool in leprosy prevalence survey.

CO12

HOW TO REDUCE LEPROSY PREVALENCE IN NEPAL

Baral, J. P. and Louhenapessy, Andy A.

Leprosy is prevalent in the Kingdom but not equal ly distributed,more in Terai Districts and Hill Districts in Western&MidWestern Regions.Leprosy control started since early 1960 with a prevalence of 10/1000,after a sample survey in 1961(WHO & Government).In 1966 Leprosy Control Programme was started as a Pilot Project till 1980.About 19 districts have the prevalence more than 13/10000 in 1990/91(country prevalence 12/10000).MDT was used since 1982,first started in Leprosy Hospitals and few clinics gradually expanded to all almost all clinics/health posts.Leprosy control activities in the field and hospitals were carried out by HMG(His Majesty Government)and NGOs.Epidemiological patron in the last 6 years:1986/87 to91/92, prevalence rate from 13.7 to 12.1/10000,Case detection rate from 3.6 to 3.2/10000,MDT coverage 33 to 67%.
Action plan to improve leprosy control activities for more better achievements are:
Training programmes for DPHO(District Public Health Officer),Leprosy supervisors and Basic health workers was put as first priority;improvement of the services in clinics/health posts,supervision from National and Districts level will be done more systimatically and frequently to the district leprosy supervisors and clinics/health posts workers in the field.Distribution of leprosy drugs will be maintained regularly.

CO13

A MODEL FOR ERADICATION OF LEPROSY FROM RURAL SOUTH INDIA AT AMBILIKKAI DURING LAST THREE AND A HALF DECADES AMONG 1.5 LAKHS OF POPULATION BY INDIGENOUS INITIATIVE AND EFFORT STARTED IN 1965 LATER ON SUPPORTED BY ALM.
(1) FIRST PHASE OF IMPLEMENTATION 1965-1984 A PERIOD OF MONOTHERAPY, NUMBER OF PATIENTS TAKEN TREATMENT AFTER BASELINE SURVEY-4364. NUMBER OF PATIENTS DISCHARGED CURED, ARRESTED AND ABSENTEES -2468. PREVALANCE RATE CAME DOWN FROM 29 to 12/1000 AND INCIDENT RATE 12 to 4/1000. NUMBER OF PATIENTS LEFT OVER 1896.
(2) SECOND PHASE OF MODIFIED MDT. 1984-87 GIVEN ONLY FOR POSITIVE (BL AND LL)-186 CASES (BECAUSE OF LIMITED FUNDS). 60% OF 186 CASES WERE CONVERTED NEGATIVE IN THE FIRST YEAR ITSELF. WHEN WE RECEIVED MORE FUNDS AND DRUGS FROM ALM, MODIFIED MDT WAS GIVEN FOR THE REMAINING KNOWN NEGATIVE CASES (BB.BT.TT) OF THE WHOLE PROJECT AREA.
(3) THIRD PHASE OF REGULAR MDT(PULSE REGIME) AFTER ANOTHER EXHAUSTIVE SCHOOL AND GENERAL RESERVEY AND CIRCUITS PLANNED TO COVER WHOLE AREA COMPLETELY WITH GOVERNMENT FREE DRUG SUPPLY AND INCENTIVE SUPPORT. MDT COVERAGE 100% AND CLINIC ATTANDANCE 96%. PREVALANCE RATE DROPPED TO 2.4/1000 AND INC RATE 1.4/1000. INC, RATE IN CHILDREN 3/1000. DEFORMITY RATE 2.5/1000. INTEGRATED APPROACH ADOPTED THROUGH 24 MINI HEALTH CENTRES. COMMUNITY HEALTH WORKERS CASE-HOLDING, LEPROSY PARAMEDICAL WORKERS CASE-SURVEY, DETECTION AND SURVEILL - ANCE. HOPING TO ERADICATE ALMOST ALL CASES OF LEPROSY AND MAKE INC.RATE DROP TO ALMOST NIL/1000 BY TURN OF THE CENTURY (2000 AD).
(4) FOURTH PHASE OF PLANNING REHABILITATION OF THE TREATED IS ALREADY TAKEN UP THE HAND-CAPPED AND ALSO SURVEILLANCE OF ALL TREATED.

CO14

UTILIZATION OF BARANGAY* HEALTH VOLUNTEERS IN THE IMPLEMENTATION OF THE LEPROSY CONTROL PROGRAM

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National Leprosy Control Program, Philippines

The Philippine Department of Health integrated leprosy services with MDT as the main approach in 1988. After 1 1/2 years of implementation, problems in case finding, case holding, surveillance, and information dissemination arose due to inability of the health services to cope with the time and personnel requirements. In an effort to find alternatives to the situation, the writer and 2 Regional MDT Coordinators did a study to find out if and how involving the volunteer health aides in the program would have an effect on the success of the program. The group set the criteria for selection of the town where the study was to be conducted and used evaluation indicators set by the National Program.

Cabugao, Ilocos Sur, with a Prevalence Rate of 4.5 per 1,000 and a Case Detection Rate of 1.5 per 1,000 was chosen as the study site. At this time, 7 Rural Health Midwives are implementing the health program with 17 Barangay Health Workers helping them. A 2-week training (with the supervisors) and a house-to-house survey of the barangays in the town preceded the actual year of involvement.

Data gathered at mid-year and at the end of the study period attest to the hypothesis that involvement of these volunteer workers did have a positive effect, not only in the Leprosy Control Program, but also in changing the community attitude towards the disease and the patients and their families.

Proponents of the study recommended a replication of this support method to other hyper-endemic areas.

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* Village

CO15

EFFICIENT PROGRAMME MONITORING, DEVELOPMENTS FROM THE MURLEP PROJECT

Elink Schuurman M, Pinitsoontorn S, Bijleveld I, Srisaenpang S, Metaphat C, Chaipar W, Chirawatkul A.

MURLEP is a multidisciplinary health systems research project for the improvement of management of leprosy and tuberculosis control programmes. It is situated in the Khon Kaen Province, Thailand, started in September 1989 and is planned to end in August 1994. It is the result of an agreement between three parties: the Khon Kaen University, the Ministry of Public Health and the Netherlands Leprosy Relief Association (NSL).

Efficient monitoring of disease control programmes follows the principle of measuring general programme performance first. Only if this general performance (i.e., case finding coverage and cure rates) is below a preset acceptable level, monitoring of contributing factors is warranted. If general performance is satisfying only few details of the programme need to be monitored, saving and time and money.

In the past three years MURLEP has developed tools for the monitoring of the general performance and tools which identify the most important contributing factors to low performance. Flow charts are attached to the tools, indicating the remedial actions for improvement of the programme.

The tools are presently being field tested by the local health personnel (partly by general health workers and partly by leprosy and tuberculosis programme supervisors), and evaluated on feasibility and usefulness by the research team.

The tools and the system for use are explained in the paper. In a second MURLEP paper the results are presented of the development of another tool, the Rapid Village Survey. This survey method can replace the total village population survey method used in the usual cluster sample prevalence survey and is much quicker and cheaper.

CO16

INTEGRATION OF EYE CARE IN LEPROSY CONTROL IN NORTHERN NIGERIA

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The prevalence of blindness is generally estimated as to be 2-2.5% amongst leprosy patients. Potentially eye sight threatening lesions may develop in as many as 20% of the patients.

Primary eye care services are in short supply or absent in Northern Nigeria and therefore leprosy patients with eye complications have hardly any options for treatment, except within the leprosy services. In 1992, as an answer to this need a flexible, organisational framework has been developed for the integration of eye care in the leprosy control programmes of 11 states in Northern Nigeria, making optimal use of available manpower and functioning health systems. In this presentation the following essential features are discussed and illustrated: 1) regular, standardized training and supervision of primary health workers and workers in the secondary and tertiary health care level, 2) an appropriate and efficient referral system and 3) the maintenance of a distribution system for standardized equipment and medicines.

CO17

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National Tuberculosis and Leprosy Programme Tanzania TB/Leprosy Central Unit, Dar es Salam Tanzania.

PROS AND CONS OF COMBINING TUBERCULOSIS AND LEPROSY CONTROL ACTIVITIES (BASED ON THE 15 YEARS EXPERIENCE OF THE NATIONAL TB-LEPROSY PROGRAMME IN TANZANIA).

The NTLP (National Tuberculosis and Leprosy Programme) in Tanzania was the first of its kind ever established. It has been successfully operating for 15 years.

Registered prevalence for Leprosy dropped from more than 50,000 cases in 1978 to less than 5000 in 1992. Case detection rates show a steady decline as well, whereas - in the wake of the ongoing HIV endemic in this country - TB notification rates are steadily increasing.

It will be demonstrated which aspects of both diseases could be successfully combined and which not. Simultaneously the advantages and disadvantages of such a combination will be illustrated. Finally some aspects of cost effectiveness of TB and Leprosy Control activities will be discussed. (Costs per death averted, average costs per case treated, overall economic impact).

CO18

IMPLEMENTATION OF LEPROSY CONTROL PROGRAMME THROUGH BASIC HEALTH CARE NETWORK

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Since 1960s a network for leprosy control at county to village level has been developed and gradually perfected by integration of leprosy control into primary health care service in Fujian Province. This network has played a very important role in the fight against this disease. The main task of the network is case finding and implementation of MDT. Through this network, 68.3% of the total number of new cases were detected, and 95.9% of the total number of patients on MDT were visited and supervised at home. Furthermore, one healthy member in each patient's family was appointed as supervisor for MDT. In the recent years, through the efforts of basic health workers and patient's family members, 2,684 patients received MDT with a coverage of 97.5% and regularity rate of 95.4%, 2,411 (89.8%) of them had completed the prescribed MDT course. The basic health workers, together with leprosy professionals, have been very active also in propaganda on the knowledge of leprosy, reporting of suspected cases, implementating post-treatment surveillance and patient's hand, foot and eye self care programme.

CO19

COST AND EFFECTIVENESS OF INTEGRATING LEPROSY WITH PRIMARY CARE

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The objective of the study was to estimate the extra cost and the extra effectiveness possible by adding a primary care component to a leprosy control programme. The study included two tribal sub-centres (pop. 17,175) of the control unit. The area is unique because of its cultural and geographic isolation. The infant mortality was 120/1000 and immunization coverage was 4% at start in 1987. The source of data included the mobile clinic records from 86 - 92. Pre and post cross sectional surveys are also done in the intervention and control villages. The outcome measured was the no. of non-leprosy service contacts which ranged from 1034 - 3423 per year. This included chronic diseases (e.g. TB, RHD, STD, epilepsy) immunization and antenatal care. The extra cost incurred was an average of Rs.12,500 ($420) per year mainly for drugs The intervention area showed improvement in immunization coverage from 4% to 25% compared to control area along with improvement in other indicators of health care. 264 leprosy patients were treated during six years. The leprosy control activities showed steady progress as indicated by general surveys and attendance of patients. The study illustrates affordability and sustainability of integrated leprosy control in a tribal setting. This study is of relevance to health policy relating to integration of leprosy with primary care services.

CO20

THE SIGNIFICANCE OF TAKING CARE OF LEPROSY IN-PATIENTS WITH COMPLICATIONS IN GENERAL HOSPITAL

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In the 1980s, thanks to recent advances in knowledge of leprosy, patients have been no longer isolated in leprosaries and leprosy hospitals as before, they enjoy domiciliary fashion of ambulatory treatment schemes. However, a number of leprosy patients with complications must still be sent to the leprosy specialized units. That's why, the dermatology department of Viet-Tiep general hospital has been determined to hospitalize temporarily all the above-said cases.

The care and treatment for leprosy in-patients have created more favourable conditions for the dermatology department whose Head is also Dean of dermatology of Haiphong medical college to contribute valuable experiences to early detection of leprosy patients to treat them with the best success and to prompt discovery and effective treatment of leprosy reactions in order to avoid nerves damage, thus preventing disability for leprosy patients.

Doctors' and nurses' ordinary attitude and behaviour towards leprosy patients as towards patients of other skin diseases have set a shining example for all patients and students. So the department has become a new model for teaching medical students on leprosy, and also a city center of training, health education and communication on leprosy.

CO21

INTEGRATION OF A LEPROSY-TUBERCULOSIS-ONCHOCERCIASIS-CONTROL-PROGRAMME INTO A PHC-PROGRAMME IN THE FOREST REGION OF GUINEA

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The integration of a leprosy control programme with two other vertical programmes (tuberculosis and onchocerciasis) and then into a primary health care programme is exemplified with our experience in the Forest Region of Guinea. Work started in 1981, when a leprosy programme was started in a pilot area. In 1986 the leprosy programme was expanded into one of the four regions of the country. A year later the tuberculosis programme, and with the adventure of ivermectine an onchocerciasis component was added. Starting from 1989/90 the national leprosy control programme was discussed. Our team took an active part in the formulation of the programme and especially the technical manual. In 1991 finally the tuberculosis control programme was formulated. Experiences, difficulties and statistical data are presented.

CO22

EVALUATION OF MDT IMPLEMENTATION FOR LEPROSY CONTROL IN BENDEL STATE OF NIGERIA (1985 - 1990)

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MDT as recommended by the WHO was introduced in the above geographical area in October 1985 as a pilot project in one clinic. By December 1988, the whole treatment centres in the State had been fully covered. A total of 5,662 patients entered the register during this period. Known prevalence dropped by about 85% but the incidence remained the same. The number of treatment centres was reduced from 136 to 53 at Dec. 1990. Factors that accounted for the fall in this prevalence are discussed. Relapses have been few, the reasons and the place of H.E. are also discussed. The results have shown the effectiveness of the WHO MDT regimen and the fact that the known pool of active leprosy cases can be drastically reduced within a short period with this regimen.
The programme was supported by the GLRA.

CO23

SAMPLE SURVEY OF LEPROSY AFTER THREE YEARS OF MDT IN BHAVANI TALUK OF PERIYAR DISTRICT TAMILNADU SOUTH INDIA

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A sample survey of Bhavani Taluk was undertaken in March 1992 by the Voluntary Health Services Leprosy Project 3 years after MDT was introduced. 10% of the population was taken for the sample. A population of 45781 was enumerated and 41554 was examined. The design of the study consisted of stratifying the three sectors according to the prevalence and classifying the villages by the size of the population. Villages were selected by random sampling. The survey was completed in 36 days. 377 active cases were detected. 288 cases were new. 5.55% were bacteriologically positive for AFB. The child rate was 13.54% among new cases. Whereas according to the programme the prevalence has come down to 3.45 from 13.09, according to the sample survey the prevalence rate is 9.07 with a prevalence of new cases of 6.93. This is much higher than the expected ten fold reduction of prevalence under MDT. Independent assessment of NLEP units is advisable before integration to avoid return of the situation prior to MDT following accumulation of undetected cases.

CO24

TRENDS IN PREVALENCE AND OTHER RATES DURING A DECADE OF MULTIDRUG THERAPY IN BHUTAN

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Bhutan introduced MDT in 1982, following the WHO regime. A marked decline in prevalence has been seen during the past decade, from 4 per thousand to 0.3 per thousand. However, programme planning demands that the trends in incidence are also known. This study, based on a review of all casenotes for the years 1982-1992, documents the decline in prevalence, and relates it to changes in case detection rate, lepromatous rate, child rate and deformity rate.

A preliminary study indicated that the decline in prevalence was much clearer than the improvements in other rates over the same period, but that evidence of encouraging trends might be emerging. The completed study, covering some 3500 patients, will allow more definite conclusions to be drawn, and will provide evidence of the approach of a genuine state of control.

In view of the need to plan for integration of leprosy control into primary health care, the likely epidemiological developments and the future caseload need to be estimated as far as possible. The practical implications of the findings for programme planning in Bhutan, and in other newly low-endemic situations, will be discussed.

CO25

TREND OF LEPROSY IN MULTIDRUG THERAPY AREA OF MYANMAR

Kyaw-Tin, and Hla-Htut-Lwin

Leprosy Control Programme in Myanmar was started in 1952 with intensive case detection and Dapsone monotherapy. Of the country's 14 states/divisions, six divisions constituted 91.6% of the total registered cases in 1982 and were designated as hyperendemic areas. In these divisions WHO Multidrug Therapy was introduced in 1988. The MDT delivery was by the Vertical staff but was integrated into the activities of the Basic Health Staff (BHS) during second half of 1991.

Epidemiological indicators were calculated from the annual reports (1982 to 1991) of the Leprosy Control Programme.

Among the registered cases, Number and Prevalence rate declined progressively but was more marked after introduction of MDT. The Multibacillary rate declined but was more marked two years after introduction of MDT. The Multibacillary proportion increased after introduction of MDT. There was decrease in under 14 year proportion.

As for the new cases, Number and Case detection rate declined but increased again one year after introduction of MDT and the increase was more dramatic after integration into the BHS. There was increase in Multibacillary proportion. The under 14 year proportion fluctuated but the 1991 figure was lower than the 1982 figure.

Possible reasons for the findings are discussed.

CO26

COSTING OF LEPROSY CONTROL PROGRAMMES BEFORE AND AFTER INTRODUCTION OF MDT

Jeyakumar Daniel & Cornelius S Walter.

Figures from 20 leprosy mission centres in India were obtained. The cost per patient treatment prior to and after the introduction of MDT was studied.

The number of patients in these centres prior to the introduction of MDT varied between 258-2947 with an average of 1652 patients. The budget of the leprosy control programmes varied between Rs.86,000 to Rs.3,89,700 and the average budget Rs.200,278. The cost per patient treated varied from Rs.59/ patient per year to Rs.366/ patient per year, with the total average cost as Rs.136/. per patient per year.

Due to decrease in case load after MDT was started, the number of patients in these centres varied from 109-1446 with an average of 526. The budget of the leprosy control programme varied from Rs.111,800 - Rs.6,96,500 with an average cost of 423,327. The cost per patient increased from Rs.136 prior to MDT to Rs.1054 per patient/year.

Analysis of these results are leading to measures to optimise unit costs and make leprosy control measures more cost effective. These will be presented and discussed.

CO27

IMPLANTING MULTIPLE DRUG THERAPY IN SAO PAULO - BRASIL - STRATEGIES, OPERATION AND RESULTS

Wagner Nogueira, Marcia R.Buzzar, Otilia S.J. Gonçalves, Heleida N.Metello, Zenaide L.Lessa

The implantation of Multiple Drug Therapy in São Paulo, starting from recommendation of the Ministry of Health, had as its starting point the identification of health'unities for regional reference and upgrandin of Human resources.

At State level, health sub-regions were motivaded for the implantation through the employment of ludo and pedagogical techniques with emphasis in the work team and integral attention to the client. Next, the sub-region filled up a pre-established agenda with a situation diagnosis for the sub-regions, after, wich a regional reference team underwent a training program designed to reorganize services to implant the therapeutic scheme. The unit which was trained, in a three month period implanted the therapeutic and, as a following step, executed the expandion with trainment for the other health unities of the sub-region.

Results show that therapeutic schemes were implanted in only 18 health unities in 1990, passing to 392 in 1991 and 569 in 1992, with an increase coverage to 2,8% in 1990 to 61,6% in 1991, and 91,2% in 1992.

CO28

MDT FOR LEPROSY IN 8 FRANCOPHONE COUNTRIES OF WEST AFRICA : TEN YEARS IMPLEMENTATION (1982-1991)

The 8 National Leprosy Control Managers, Report prepared by A. Tiendrébéogo and L. Blanc
Institut MARCHOUX BP 251 BAMAKO MALI

WHO MDT is used in 8 Francophone Countries of West Africa since 1983. Starting with pilot projects in each country, MDT implementation was extended since 1988 trough national leprosy control programmes. During the ten years (1982 to 1991), prevalence rate of leprosy decreased from 49.7 to 9.7 per 10.000 (5 fold decrease). Detection rate during the same time increased a little from 1.2 to 1.4 per 10 000.

The drop of prevalence rate ws partly due to drug activity and mainly to efforts to clean regis - ters based on systematic skin smears for all MB patients and on WHO leprosy case definition. MDT impact on the prevalence rate started in 1990, but was small because the average MDT coverage was only about 20% for the region.

In order to enhance MDT implementation in the 8 Countries, Institut MARCHOUX organised annual meeting of national leprosy programme managers since 1991. During the first meeting, target of 75% MDT coverage in average for the 8 States was decided for the end of year 1993. Guidelines for leprosy control programmes were given, technical standards were defined, and needs were analysed by NGO's. In December 1991, MDT coverage reached 45% ranging from 8 to 97% depending upon Countries. It is reasonable to think that MDT coverage will reach the target by the end of 1993.

CO29

DRUG SUPPORT TO THE USE MULTIDRUG TERAPY/WHO IN BRAZIL BETWEEN 1986 AND 1992

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Six years after the oficial implementation of MDT in Brazil (1986-1992), an analysis allowed us to see the difficulties found in the area support of supplies needed for the treatment of the 250,066 registred patients.

Brazil, a continental country, with a prevalence of 17 cases per 10,000 population, with out a policy for the national production, distribution and control of drugs, and with the central level monitoring three drugs manufactured by different laboratories, had to obtain support from the Sasakawa Memorial Health Foundation.

This paper shows and discusses the programmed use and the coverage reached in supplying medications, under the monitoring of the central, state and municipal levels.

The table presents the impact on the country's epidemiological picture with the assessment of registered patients and the determination of the number of patients requiring drugs for their treatment.

CO30

THE IMPLEMENTATION OF MULTIDRUG THERAPY IN PROJECTS SPONSORED BY ILEP MEMBERS 1984-1991

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In 1982, the Members of ILEP, the International Federation of Anti-Leprosy Associations, agreed a resolution to make provision to implement MDT regimens, notably in the framework of national programmes. Of patients worldwide under chemotherapy 20 % are treated in ILEP sponsored projects. Statistics illustrating the

implementation of MDT in these projects at the end of 1991, the latest reporting year for which complete data are available, are presented in detail.

Using graphics and diagrams data are presented showing the increase in MDT coverage in ILEP supported projects from 1984 to 1991 and the dramatic drop in patients registered for chemotherapy due to the policy of discharging patients after successful MDT treatment. In 1984, 8 % of the 1 273 221 patients registered for chemotherapy in projects sponsored by ILEP Members were receiving MDT. At the end of 1991, 60 % of the 636 742 patients registered for chemotherapy were receiving MDT.

Trends in the registration of new patients for treatment from 1985 to 1991 are illustrated. During 1991, 89 % of the 155 697 new patients registered for chemotherapy were put under MDT. Among the new patients starting MDT during 1991, 35 % were MB and 64 % were PB.

Limitations in the collection of the data from the field are outlined.

CO31

PROSPECTS OF GLOBAL ELIMINATION OF LEPROSY AS A PUBLIC HEALTH PROBLEM BY THE YEAR 2000

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The World Health Assembly (May, 1991) approved a resolution about the global elimination of leprosy as a public health problem by the year 2000. It took into account mainly the marked decrease of prevalence suggesting that it was the success of MDT that has brought such a drastic reduction.

In randomized multicentric trials MDT schemes were not superior to DDS alone. Unless follow-up studies provide better results the present findings do not confirm that the world reduction of prevalence was due to MDT. Instead two other causes should be considered: 1) When MDT was adopted (1982) the duration of treatment and follow-up was considerably shortened: six months for paucibacillary cases and only two years for the multibacillary; previously the duration was respectively 3-5 years and 5-10 years. The antecipated release from control of all cases caused automatically a dramatic decline of the prevalence and apparently not the MDT. 2) The improvement of the control programmes in order to implement MDT.

The A. also analysed two other factors and related conditions: 1) Difficulties in implementing the MDT and the control programmes; 2) Socio-economic, cultural, historical, political, demographic and ecological factors, education and related conditions.

In the light of the above it does not seem possible to achieve the global elimination of leprosy as a public health problem by the year 2000, unless a very effective vaccine or drug become available in the very near future. Nevertheless the relevant praiseworthy effort of WHO, Governments and Non-Government Organizations will be of great benefit to countries and populations.

CO32

PROJECTION OF DEMAND FOR LEPROSY SERVICES IN INDIA, AFTER WHO-MDT

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Quantitative analysis of published data suggests that eighteen years after the introduction of WHO-MDT (1991 Indian guidelines) in a high-incidence Indian district:

a. The number of patients receiving MDT will be only a tenth of the initial number (of all registered patients before the introduction of MDT.)

b. The number of patients on either MDT or post-MDT observation will be only two-thirds of the initial number.

c. The total number of persons in either of the above classes plus the respective numbers:

i. diseased and awaiting treatment, or

ii. disabled by leprosy,

will probably be double the initial number, and almost certainly no less than 125% of the initial number.

Rational planning of health services should anticipate the increasing demand for leprosy-specific activities other than anti-microbial chemotherapy, including:

A. Earlier detection of progressive and disabling forms of leprosy, which usually remain inapparent for some time.

B. Expert 3-monthly monitoring of nerve function with anti-inflammatory treatment as soon as necessary.

C. Retardation of the progressive disabilities which generally follow the sensory loss of leprosy.

CO33

DECLINING OF LEPHOSY IN MALUKU INDONESIA AFTER INTRODUCING MDT IN 1982

Ristianto Sugiono, H.Sugiono Tanamal and Andy A.Louhenapessy

Leprosy was known in Maluku Province, Indonesia since last century, until now still prevalent but not equally distributed. More patients found in Ambon town, North Maluku, Kei Islands in S.E.Maluku and Central Maluku. Epidemiological situation since last 1982/83 was: Prevalence rate from 41.8 to 12.0/10000, Case Detection rate from 2.8 to 0.6/10000, MDT coverage from 2.3% to 93%, Cure rate from 5% to 89% and cumulative MDT coverage from 12.8% to 78.5% (1982/83 to 1991/92). Leprosy patients were treated since early 1950th in several leprosy hospitals/leprosaria in N.Maluku, Central Maluku, Ambon town and S.E.Maluku.
Leprosy Control Programme (LCP) started since 1969 in Ambon town and Central Maluku, 1970 in North Maluku, and in 1971 in Kei Islands S.E.Maluku, used Dapson and Lamprene until 1982 started with combined regimen introduced by WHO October 1981.
In the first few years after the introducing of MDT the coverage was still limited to very active cases and in hyperendemic districts/sub districts due to limited stock of drugs.
The MDT Programme in Maluku Province was carried out by Government Health Staff and workers assisted by the WHO, Ciba Geigy, Danish Save the Children Organization, NSL and Sasakawa Memorial Health Foundation.
Effort is made to continue strengthen the activities to achieve the goal 1 per 10000 by the yera 2000.

CO34

TEN YEARS OF MULTIDRUG THERAPY IN ZIMBABWE

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A national Leprosy Control Programme based on WHO recommended Multidrug Therapy was implemented in 1984.

From 1986, a gradual integration of control into Primary Health Care was initiated after training of health workers from the districts.

The results have shown a decline in incidence (Case Detection) and prevalence. The child proportion (< 15 years) in new patients has fallen whilst the MB proportion has increased.

The results also sho that although we are now in the elimination phase (<1/10 000) the integration into PHC may have resulted in a decline in diagnostic skills as evidenced by the patients diagnosed already disabled (>50% of new cases have more than WHO grade 1 diability).

As this requires specific attention, a special project for disability prevention has been initiated. Such a decentralised health care programme demands an extra strong supervision and extensive training when the incidence drops in the elimination phase.

CO35

D E L E N D A L E P R A
ORGANIZATION OF THE STRUGLE FOR ERADICATION OF LEPROSY IN ALBANIA

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Since 1944-1992 (50 years) we have treated 88 cases of leprosy (67 LL, 17 LT, 4 LI). Long period of incubation of leprosy (30-40 years) present for us the duty to control 612 houshold, 988 neighbourhood 1-2 time a year for long time clinicaly and serologicaly. Also we must to control all the people in endemic areas one time in two years. In this we can to find early the patients oligosimptomatic or subclinic leprosy. With ELISA method, which we have applied before, we have diagnosed 7 contact persons with DO above 20 %, raised levels of anti-PGL-1 IgM antibody specific markers for infection of leprosy.

SCEMA OF THE PROGRAM

I. DIAGNOSTIC	II. TREATMENT	III. PROPHYLAXIS
1. Clinicaly control of the patients 1-2 time/years,for all life 2. Control of realtivs and neighbourhood. 3. Control of the people in endemic zones. 4. Serologic control with ELISA patients and contact persons.	1. MDT under surveillance 1-2 years for the new patients. 2. MDT antirecidivans for short period 1-2 mounth every two years,if needs them. 3. MDT for the persons with ELISA DO above 20 %, like paucibacilar leprosy.	1. Earlyer discovering of the patients and treat them rigorously and free of charge. 2. Improve the economic and hygienic condicions of lives. 3. Chimioprophylaxis with Rifadine 25 mg/kg.W. a single dose. Repeat them after 2-3 years (?) 4. Education.

CO36

FORMULATION OF A NEW LEPROSY CONTROL PROGRAMME IN REPUBLIC OF YEMEN AS COOPERATION BETWEEN GLRA AND MOPH.

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Yemen Republic is the land of the Queen of Shiba. Historically known as the "Arabia Felix". It has an area of about 5,30,000 sq.km. and a population of about 12.5 million. It is the most densely populated country in the Arabian Peninsula.

Leprosy in Yemen is well documented since 650 AC with very interesting stories.

Inspite of the two large Leprosariums built since 1940 the country lacked a programme for leprosy control up to 1990.

In 1989 an agreement between GLRA and MOPH brought to the country its first NLCP.

Passing on geographical distribution of 2320 cumulative registered patients in the old register of City of Light Hospital a pilot area was chosen to start the programme actively by the beginning of 1991.

After two years of support by GLRA to the NLCP a real implementation for MDT has been achieved and a three fold increase in the detection rate is resulted.

The article will discuss the situation of leprosy, policy applied in field activities and the fight against the stigma of leprosy in Yemen.

CO37

COMMUNITY-BASED LEPROSY CONTROL PROGRAM
A CASE STUDY IN NAKHONRATCHASIMA PROVINCE, THAILAND

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Village leaders and village health volunteers from Ban Rai, Nakhonratchasima province were trained to have knowledge in leprosy diagnosis, referral for leprosy treatment, and self-care for deformity prevention. In the training process, field trip were set up for trainees to have a site visit at the leprosy colony where trainees could experience real cases of leprosy patients. The preliminary results of these intervention are 1) some trainees had the awareness of the leprosy problem in their community and have compassion to those patients with disabilities whom they saw in the leprosy colony. As a result, when they come back to their community, they provide health education to their community. Some refer cases of leprosy to the Leprosy Center. 2) Patients with deformities organized themselves for occupational training in their village.

CO38

CHINA LEPROSY SURVEILLANCE SYSTEM

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The China Leprosy Surveillance System is a specialized system under Department of Epidemic Prevention of MOPH. Its responsibility is to monitoring leprosy prevalence on a country-wide level, to predict the trends of the disease and to evaluate the leprosy control programme. It is based on institutes of dermatology at county level, which are responsible for recording and reporting data of leprosy cases. It comprises three components : 1) A recording and reporting network over the country. 2) The forms to collect data, togerther with guidelines and menuals of procedures. 3) Computer equipments and software. The system uses 4 individual forms specially designed for Optical Mark Reader (OMR): 1) New patient form : for active patients and new patients detected annually since Jan. 1, 1990; 2) Follow up form : for the cases under treatment and surveillance since Jan. 1, 1990; 3) Relapsed form: for relapsed cases on annuallies; 4) Old patient form: for cases cured, died, transferred out, left by end of 1989. Special training courses had been given to leprosy workers at various levels, in such a way that they accurately fill in forms. This system using OMR is of great advantage for entering the data into the computer more accurately and with high speed. It takes only a second per patient form; more than 6 000 forms can be entered per day. The reading error is less than 1/1 000 000 marks. More than 400 000 leprosy cases data have been entered into the computer by the end of year 1992.

CO39

IMPACT OF A VERTICAL PROGRAMME ON LEPROSY IN LALITPUR 1986-1992 : EPIDEMIOLOGICAL AND MANAGERIAL IMPLICATIONS

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Anandaban Leprosy Hospital was established in Lalitpur, south of Kathmandu in 1957. In the early years a few mini surveys were carried out but in general case finding was passive and relied on a hospital based programme. From 1986-1990 a mass intensive survey was carried out. Out of a population of 210358 enumerated, 179811 were examined(85.4%) and 162 new cases were registered. A further 72 patients presented voluntarily during the survey period. After the survey was completed the team visited every patient who had ever been registered at Anandaban in order to do a post treatment surveillance check, update registers, examine healthy contacts and check their antibody

status. The team also did rapid school surveys in the north of the district. A further 47 patients have been registered in 1991-92(NCDR 1/10000) of whom 41 presented voluntarily and the rest were found during the school/contact surveys. At the end of 1992 there are 56 patients still on treatment (registered prevalence of 2.2/10000). A number of the leprosy control staff have been relocated to other parts of the programme and the focus of the control programme has been redirected. This could serve as a model for other areas with trained staff who are no longer able to be fully employed in leprosy control.

CO40

DRUG RESISTANCE IN NEPALI LEPROSY PATIENTS

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Due to difficulties associated with regular attendance for leprosy treatment in Nepal, one third of registered patients still receive monotherapy. Also, undiagnosed leprosy patients may receive rifampicin for tuberculosis without other anti-leprosy drugs. To assess the extent of dapsone and rifampicin resistance, this study was undertaken at a leprosy referral hospital.

Over a 4½ year period, 106 outpatients with B.I.≥2+ were studied for drug resistance using the mouse footpad technique of Rees. Subjects were previously untreated or relapse cases, or those who showed unsatisfactory response to multi-drug therapy. In 20 cases there was no growth in control mice.

Of 59 biopsies from previously untreated patients, 5% showed dapsone resistant strains. Of 27 biopsies from previously treated patients, 41% demonstrated dapsone resistant strains.

8% of 86 biopsies tested for primary rifampicin resistance initially showed growth, but the M.leprae were sensitive on subsequent passage. From the two biopsies tested for secondary resistance, no rifampicin strain was demonstrated.

Primary dapsone resistance in Nepal is present at a low level, but may be expected to increase as 41% of treated cases tested exhibited secondary dapsone resistant strains. Rifampicin resistance was not confirmed.

CO41

LUCHA ANTILEPROSA EN LA REGION SUROESTE DE LA REPUBLICA DOMINICANA PROGRAMA MODELO CON PARTICIPACION DE LA COMUNIDAD

Huberto Bogaert, Sócrates Canario y Rafael Isa Isa.

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La lucha antileprosa en la región Suroeste de República Dominicana se desarrolla en 4 provincias con una población de 309,000 habitantes,presentando niveles críticos en cuanto a pobreza se refiere. La unidad dermatológica Suroeste ejecuta un programa modelo con participación de la comunidad y coordinación con las diferentes estructuras de salud del área.

Todas las metas programadas en lo que se refiere a descubrimiento de casos nuevos, revisiones a enfermos de lepra, tratamiento a enfermos, consultas dermatológicas por auxiliares y por médicos, contactos intradomiciliarios y extradomiciliarios, censos escolares etc. se vienen cumpliendo rigurosamente. La unidad tiene 595 enfermos de lepra inscritos. 327 han sido dados de alta; 210 están activos en control; 36 enfermos multibacilares en tratamiento y 83 sin tratamiento; 54 enfermos paucibacilares en tratamiento y 37 sin tratamiento.
No hay enfermos renuentes y solo dos están perdidos.

CO42

RECIDIVAS EN ENFERMOS DE LEPRA MULTIBACILARES Y PAUCIBACILARES TRATADOS CON TRES DROGAS REPUBLICA DOMINICANA OCTUBRE 1982 DICIEMBRE 1992

Rafael Isa,Huberto Bogaert,Freddy Simonó,Sócrates Canario.

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Se hace una revisión de los 4,992 pacientes tratados con tres drogas en el período octubre 1982 a diciembre 1992 para determinar el porcentaje de recidivas que se han presentado al finalizar la multiterapia. Se dividen los pacientes por forma clínica y de éstos los que están en revisión posterapéutica y los que han sido dados de alta por curación. Se precisa además el lapso en meses transcurridos antes de la presentación de la recidiva, el esquema de tratamiento recibido, el número de lesiones que presentaba el paciente al examen inicial y el sexo al cual pertenece. Se observa que la frecuencia global de las recidivas es del 0.22% con 0.20% en pacientes multibacilares y 0.23% en paucibacilares.

De los once enfermos que han presentado recidiva, dos pertenecen al sexo femenino.

CO43

COMPUTERIZED MONITORING OF LEPROSY PROGRAMME

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For improved monitoring both at the macro and micro levels some of the important components like treatment, prevention and care of disability and epidemiological and operational changes, currently available softwares are not found to be suitable. Hence the following softwares were developed.

1.Computerised Central Registry :

To overcome multiple registration and problems of follow up of patients and to arrive at more accurate macro epidemiological picture, this software was designed. The Cross-notification facility is one of the important features. This simple software helps programme managers to obtain data on a large scale for better planning especially for metropolitan leprosy programmes.

2.Prevention and care of Disability :

This is a micro monitoring system useful for monitoring services needed and services offered to deformed leprosy cases for prevention and care at the field level.

3.General management of Leprosy :

This is specially designed to monitor individual leprosy patients during MDT and surveillance to track reaction and relapses.

All these three softwares were designed by using foxbase package.

CO44

STRENGTHENING OF ACTIVE CASE-FINDING STRATEGIES AND CLINICAL STUDY OF HOUSEHOLD LEPROSY CONTACTS IN MEXICO.

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Leprosy in Mexico has a prevalence of 0.20/1000 inhabitants. Most cases (95%) are distributed in 18 hyperende-

mic States located on the West coast and central part of the country. In order to reinforce early diagnosis and case-finding strategies included in the National Programme for Leprosy Control, a field project was carried out in Sinaloa State, a hyperendemic leprosy area on the Pacific coast. Patients from several endemic areas of the country were also studied in a specialised hospital in Mexico City. A total of 125 leprosy patients were diagnosed by trained dermatologists and were classified according to the Ridley and Jopling criteria.

Household contacts of patients were thoroughly studied and immunological and mycological investigations were performed when necessary. Fungal infections caused by dermatophytes were found to be a common skin condition posing problems in the differential diagnosis with leprosy. Health education activities for patients, their relatives, medical/paramedical staff, and for the community were carried out in order to emphasise the importance of early diagnosis and application of strategies directed to break the transmission of leprosy. Correlation of clinical, epidemiological, laboratory and anatomical findings was carried out to identify precise problems in the control of leprosy. Specific recommendations from this study were included in a field trial aiming at the elimination of leprosy in Mexico.

CO45

THE NATIONAL LEPROSY ELIMINATION PROGRAMME OF PAPUA NEW GUINEA, FIRST YEAR OF IMPLEMENTATION

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In the 1960's and 70's, leprosaria in Papua New Guinea were progressively phased out as dapsone therapy became available. After independence in 1975, the services were decentralized to the provinces including the health services. Reorganization of the health services was completed in 1983, with tuberculosis and leprosy consolidated into one program within the integrated health services.

Review of epidemiological data at the end of 1988 showed that the declining trends in the prevalence of leprosy in the country could be further influenced by the introduction of MDT. The National Leprosy Elimination Programme was initiated to eliminate leprosy from PNG by the year 2000, established on the revised strategy for leprosy elimination based on MDT.

The main program phases are: mobilization and planning; implementation; consolidation; and, surveillance. Two teams were formed to carry out the phased introduction of the program in the 20 different provinces of the country as part of the program implementation. This paper covers the first year of the implementation phase of the program.

CO46

UPGRADING OF HUMAN RESOURCES FOR HANSEN'S DISEASE CONTROL ACTIONS IN THE STATE OF SAO PAULO - BRAZIL - DURING 1988 TO 1992.

Heleida N.Metello, Zenaide L.Lessa, Wagner Nogueira , Marcia R.Buzzar, Otilia S.J. Gonçalves

Since the State Secretary of Health of São Paulo started the Special Program Group for Hansen 's Disease, in August, 1988, priorities were set up for reorganization of Hansen's Disease control actions . Upgrading of Human Resources was one of these priorities and, since then, training programs were developed regarding the perfecting of assistance to patients of Hansen's Disease, intensified with the integration of actions with the Instituto Dr. Lauro de Souza Lima(Bauru)

More than 5.000 technicians from the 65 administrative sub-regions of the State were upgraded during this period and avaluation of the distribution of such personnel by kind of training and institution responsible for the training can be made by maps.

Central level for Hansen's Disease control in the state of São Paulo, based on this avaluation, which is routinely and permanently performed, which is participation in the programmed trainings to meet the needs for all sub-regions.

CO47

SITUATION DIAGNOSIS AND REORGANIZATION OF SOCIAL ACTIONS FOR HANSEN'S DISEASE IN THE STATE OF SAO PAULO - BRAZIL

Otilia S.J. Gonçalves, Heleida N. Metello, Wagner Nogueira, Zenaide L. Lessa, Marcia R.Buzzar

Since the state Secretary of Health created the Special Program Group, priorities reorganization of control actions were stablished, including among these upgrading of Human Resources.

Therefore, it was possible to identify the need for social actions, starting a process of mobilization of social workers in all the State through meetings per greater region in attention to clients of health services and, especially, patients of Hansen's Disease.

This process is already in course for five years,ensuing evalution and organization of some important aspects for social accompaniment including routins attention. The register of social actions is made in appropriated charts, with a special agenda,ensuing the sistematization of these data, evaluation of social data and lines of research.

Two yarly meetings are made per sub-region, in a total of 10 per year, and one State Encounter for Evaluation per year. In the year of 1993, will be presented. The group sharing the efforts and results obtained. This process envolved socail workers,acting at local, regional and central level.

CO48

PROJECT FOR IMPLANTING INTEGRATED HEALTH ATTENTION CENTRES FOR REHABILITATION IN THE 65 HEALTH SUB-REGIONS OF THE STATE OF SAO PAULO - BRAZIL FOR THE PERIOD OF 1993 A 1995.

Wagner Nogueira Marcia R.Buzzar, Heleida N. Metello, Otilia S.J. Gonçalves, Zenaide L. Lessa

Implanting Integrated Rehabilitation Centers is a need which has been felt since the start of the Unique Health System in São Paulo.

The existence of services designed to the assistance of deficiencies, in general,is adequate to the new sistem, and the existence of specific Rehabilitation Services for Hansen's Disease patients is no longer justifiable.

An agendá of meetings between the Hansen's Disease Program and the Programs of Mental Health Worker's Physical Handicaps was met, establishing the need for implanting regional reference services for each of the 65 sub-regions of the State of São Paulo.

The regions for 1993 were priorized and proceedings for selection of the sub-regions for the years 1994 and 1995 were established. These procedures include sensibilization for the problem elaboration of regional situation diagnosis, selection of regional reference unities and, upgrading oh Human Resources for services as well as formal and informal leaderships of the cities where the services will be implanted.Resources for implanting this program were requested to non governmental entities.

CO49

MAINTAINING A NATIONAL HANSEN'S DISEASE PROGRAM IN A BUDGET-DEFICIT REDUCTION ERA

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The National Ambulatory Hansen's Disease Program (NAHDP) provides Hansen's Disease (HD) related outpatient medical services to patients living in the continental United States and in the Territory of Puerto Rico. Services are provided by the Federal Government through third party reimbursement contracts with medical facilities throughout the country. A decrease in the Ambulatory HD Care budget, for HD care, has necessitated an assessment of these Programs and the development of multiple options for optimum service delivery.

Our HD contract with the Texas Department of Health, with its multiple service delivery systems, may well serve as a model for the near future.

CO50

SURVEILLANCE SYSTEM FOR LEPROSY
A FIELD APPROACH

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Leprosy control programme in West Africa was using in 1989 a surveillance system concieved during the seventies. This system was adapted to a vertical programme using dapsone monotherapy and specialised nurses. With the introduction of MDT and programme integration in peripheric health centers the system was no longer efficient. In order to get complete and reliable data for programme and leprosy evaluation, a health center based information system was elaborated. Six essential indicators were selected, necessary information to collect identified and two simple forms containg only these informations developped. Treatment notebook allowed calculation of prevalence rate, detection rate, proportion of disable and proportion of MB patients among new cases, proportion of compliant patients, MDT coverage in order to avoid form compilation. An annual statistic form was used to convey these informations from peripheric to intermediate and central level.

Sensitivity and specificity of data collected by the surveillance system were evaluated in two urban health centers of Nouakchott (Mauritania). Depending upon items, sensitivity ranged from 50% to 100% and specificity from 76% to 100%. Evaluation showed 100% form completion by health centers nurses.

CO51

ROLE DE L'AGENT DE SANTE DANS UN PROJET DE CONTROLE DE LA LEPRE; EXPERIENCE D'UNE ANNEE

Gysette Blanc, Florence Desvarieux, Claude A. Leveille, Claude Pean.

Evaluation du travail des agents-lepre dans un programme vertical de lutte contre la lepre a Port-au-Prince (HAITI) sur une periode d'une annee. Des parametres tels que le nombre de contacts intra et extra-domiciliaires, le nombre de visites (passages repetes) , le nombre de frottis bacteriologiques seront evalues. Des facteurs socio-economiques et culturels seront aussi discutes.

Institut Cardinal Leger contre la lepre (Haiti).

CO52

INVOLVEMENT OF SCOUTTING MOVEMENT IN LEPROSY CONTROL

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The work of Bharat Scouts and Guides in leprosy awareness and health education during last few years has helped leprosy control work in India. The world scouts have adopted this work as a model and one of their activities specially for regions which are known for leprosy endemicity. Scouting as one of the voluntary activities of schools in India has been an effective educational movement. Nearly twenty different activities are undertaken by scouts and guides for helping leprosy control i cluding case detection in schools.

With the help of appropriate health education material in hand nearly 1.5 million scouts and guides are getting involved in leprosy control activities for their own schools and for the community.

Scouting movement is an example of role of organised youth groups in leprosy control activities. Examples of work will be presented with the help of slides.

CO53

SOCIAL ACTION FOR LEPROSY ERADICATION
AN INEXPENSIVE INDIAN MODEL

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Making use of the fundamental principles of Social Work, a community based action programme was initiated for controlling leprosy in Nilgiri District of Tamilnadu.

Based on this encouraging experiment the following methodology was found effective.

- The Social Worker had identified the community to be involved in this process as target community.
- Established rapport with the community by familiarising with them through a known voluntary organisation in the community.
- Interacted with the community and made them aware the role and functions.
- Motivated the community and made them interested in leprosy control and eradication work.
- A core group was formed comprising deeply committed volunteers who are interested in leprosy eradication work.
- A Madar Sangham (Mother's Group) and a youth group was formed as core group.
- Provided training to the core group members to identify cases of leprosy within the community.
- Core group members conducted Health Education Programmes and referred leprosy cases which were identified for treatment to the nearby leprosy centres.

This model is found less expensive and highly effective which had brought about the formation of a fundamental core group in the community that could take up continuous community based action programmes towards leprosy eradication.

CO54

LA PLANEACION ESTRATEGICA DE MERCADOTECNIA UTILIZADA PARA ERRADICAR LA TRANSMISION DE LA LEPRA EN MEXICO.

Alberto Barocio (Ciba Geigy México) y Francisco Castellanos (Coordinador Nacional del Programa Contra la lepra - Secretaría de Salud, México)

Teniendo como objetivo la erradicación de la transmisión de la lepra en México para

1994, se están realizando acciones que permitan el cumplimiento de la meta.

Dichas acciones, estructuradas dentro de un plan estratégico de acción, han sido sustancialmente apoyadas dentro de un marco social.

La planeación estratégica de mercadotecnia incluye lugares o plazas de acción; promociones basadas en fuertes campañas dirigidas a los diferentes públicos objetivo, que abarcan publicidad y relaciones públicas, el producto y el costo-efecto del programa integral.

Así, se desarrolla el análisis de cada una de las áreas de la mercadotecnia utilizada, el por qué de los mismos y su importancia dentro del contexto del programa tendiente a erradicar la transmisión de esa enfermedad.

Se abarca, de manera específica, la promoción de la campaña y su plaza de acción, como pilares dentro de la planeación estratégica de mercadotecnia social.

CO55

ACTIVE SEARCH FOR LEPROSY PATIENTS BY PARAMEDICAL PERSONNEL IN ALTO AMAZONAS PROVINCE, LORETO REGION, PERU. NOVEMBER 1987 - DECEMBER 1989.

Eduardo Falconi, Pedro Legua, Ciro Maguiña and Gilma Ruiz.

Instituto de Medicina Tropical "Alexander von Humboldt" de la Universidad Peruana Cayetano Heredia and
Centro de Investigación en Salud "Dr. Hugo Lumbreras Cruz" del Instituto Nacional de Salud, Lima, Perú.

Leprosy was not considered a public health problem in Alto Amazonas. In order to perform an active search for leprosy patients, the working area was divided in two parts: Yurimaguas (the capital) and the rest of the province (rural area), with a total population estimated in 109.700 inhabitants.
For the field work, five male auxiliaries (with no previous training in health) were trained on leprosy during six weeks. Emphasis was put on the recognition of early stages of the disease. For the work in Yurimaguas, three health auxiliaries and one nurse (females) were trained. Additionally, short training courses (one week) were done for health auxiliaries and promotors of the whole province. The area was combed house by house, visiting every village and examining the dwellers. The paramedical workers detected early leprosy cases, with no obvious signs of nerve involvement, including infiltrative lesions without evidence impairment of sensation. They detected 45 confirmed cases in the field and 43 in Yurimaguas, 11 leprosy suspect cases and they had three diagnostic errors. Leprosy patients were concentrated around the most populated areas.
The population examined was 72,341 inhabitants, by the end of theperiod, total registered patients were 101, which makes a prevalence of leprosy for the area of 1.4 per thousand, a public health problem according to WHO standards. Well trained regional paramedical personnel is a most useful human resource for field work as an intervention model for the control of leprosy and other prevalent disease.
(These paper was financially supported by Red Barnet-Denmark).

CO56

LEPROSY CONTROL PROGRAM (LCP) IN ALTO AMAZONAS PROVINCE LORETO REGION, PERU. OCTOBER 1987 - SEPTEMBER 1990.

Pedro Legua, Eduardo Falconi, Ciro Maguiña and Gilma Ruiz.

Instituto de Medicina Tropical "Alexander von Humboldt" de la Universidad Peruana Cayetano Heredia and
Centro de Investigación en Salud "Dr. Hugo Lumbreras Cruz" del Instituto Nacional de Salud, Lima, Perú.

Registered patients in the LCP were evaluated and for two years, an active search for leprosy cases was performed in the whole province. Through this activity new patients were identified and old patients were engaged again when a active disease was shown. Patients were treated with WHO recomended regimens (MDT). Results were as follows:

	Old Cases	New Cases
Number	58	43
Age: mean in years (range)	52 (21-94)	47 (9-82)
Sex: males	43 (74%)	32 (74%)
females	15 (26%)	11 (26%)
Means of detection:		
- Search + contact tracing	8 (14%)	26 (61%)
- Self reproting	25 (43%)	10 (23%)
Diagnosis: - Multibacilary	33 (57%)	20 (47%)
- Paucibacilary	25 (43%)	23 (53%)
Illness duration: mean (range)	19y (2-42)	3y (2m-21)
Nerve trunk involvement:	53 (91%)	38 (88%)
- Enlargement only	14 (26%)	15 (39%)
- Paralisis	23 (43%)	9 (24%)
Normal hands	22 (38%)	24 (56%)
Normal feet	22 (38%)	25 (58%)
Normal eyes	25 (43%)	26 (60%)
Complications during treatment	27 (47%)	19 (44%)
- Type 1 or 2 reactions	13 (22%)	2 (5%)

Prevalence of leprosy in the province was 1.4 per thousand The active search for leprosy cases allows the detection of patients in early stages of their illness and with less physical
[illegible]

CO57

EPIDEMIOLOGICAL IMPACT OF MULTI-DRUG THERAPY OF LEPROSY IN BHARUCH DISTRICT GUJARAT, INDIA.

N.K. CHOPRA, MRS.M.P.TRIVEDI AND R.K. GUPTA

The epidemiological impact of multi-drug therapy project in Leprosy erradication program in tribal Bhruch district (Gujarat) was measured covering population 1296451. The Multi-Drug Therapy project commenced on 1st March 1989 with financial assistance of Government of India and World Health Organisation. The prevelence rate at commencement of project on 1st March 1989 was 4.76 per thousand population which declined to 2.15 per thousand population till Dec. 92. 11447 cases of leprosy are brought under Multi-Drug Therapy during last 4 years. 8393 (73.33% cases of Leprosy are released after adequate treatment as per recommended by W.H.O.

The results of MDT and in built system of delivering the therapy almost at the door steps have instilled confidence in patients and hence very high rate of attendance and drug compliance i.e. 92%,only 15 PB cases relapsed after surviellance of 2 years.

Dispite annual surveys and health education, some cases are missed each year are detected late. Incidence rate, relapse rate, deformity rate, MB rate and other epidemiological parameters will be presented.

Hence MDT is very effective tool in National Leprosy erradication program and the study showed that MDT can be implemented in tribal rural urban population with high rate of compliance.

CO58

STUDY OF FIELD TRIALS OF COMBINED CHEMOTHERAPY AND FIXED DURATION COMBINED CHEMOTHERAPY IN MULTIBACILLARY LEPROSY IN MDT PROJECT BHARUCH DISTRICT GUJARAT, INDIA.

N.K. CHOPRA, DISTRICT LEPROSY OFFICER, DISTRICT PROJECT OFFICER. BHARUCH

The main object of MDT is 1) to prevent drug registers and presisters 2) to achieve the more rapid arrest of transmission of the disease. 3) to prevent relapse. MB cases were treated as per regiman recommended by World Health Organisation. Treatment was continued for minimum of two years or till bacteriological negativity

which ever is later. Total 4355 M.B. patients were included in the study till Dec.92. 1181 MB cases were positive prior to MDT. 237 (20.06%) patients were positive after 24 months pulsed therapy. No case of relapse has been reported.

The persistant strains of M.leprae are not significantly reduced by present day Chemotherapy. The benefits of extended Chemotherapy till bacteriological negativity need to the evoluated. This can only for ascertained by measuring relapse rates after fixed duration Chemotherapy.

351 newly detected untreated bacteriological positive MB patients were studied with fixed duration 2 years pulsed therapy as per W.H.O. Only 137 (39.03%) MB patient who have completed 2 years treatment show gradual bacteriological clearance even after cessation of Chemotherapy. During 570 person- yers follow up no relapse and encountered.

CO59

SKIN DISEASE DIAGNOSTIC, TREATMENT & EDUCATION (SDDTE) CAMPS : A TOOL FOR COMMUNITY EDUCATION IN TRIBAL DISTRICT BHARUCH (GUAJRAT) INDIA.

N.K. CHOPRA Mrs. M.P. TRIVEDI AND R.K. GUPTA

71 Skin disense diagnostic, treatment and education camps were organised in prepratary and intesive phase of M.D.T. Project in forms of Local Festivals in different rural and tribal villages in Bharuch district during 1989-92.

The idea was basically used for bringing opennes for diagnosis. The secondly obejctive was new case detection. The gathering in the camps usually comprised of patients, their relatives, teachers, onlookers and the NLEP-PHC functionaries. Case selection and demonstration for differential diagnosis was used as a method of Health Education. The method used to increase community's knowledge "from known to unknown" 167 leprosy cases (82 New and 65 old) including 13 deformed cases were detected in these camps. 3505 other skin ailment cases were alsobenefited The services offered was free of charge. The role of community was vital in such camps as they were the organisers and NLEP functionaries were helpers and guides. Primary health were system was mainly responsible for diagnostic facilitation.

CO60

AN EXPERIMENTAL STUDY OF INVOLVEMENT OF GENERAL HEALTH WORKERS IN LEPROSY WORK.

S.K.BANDYOPADHYAY

Although the NLEP in India has been functioning for over 3 decades as a vertical programme, the ultimate objective of the programme is to integrate it with general health services so that separate vertical programme is not necessary.

In Balarampur Unit of Gandhi Memorial Leprosy Foundation in India, on an experimental basis, the staff of a primary health centre were involved in leprosy control work in addition to their routine health care activities. In 1988, 41 general workers were first given a short-term training in medical and social aspects of leprosy and the areas of the programme in which they could participate. Annual meetings of these workers were held for 4 years in which the progress made by general health workers was reviewed and additional inputs related to their participation in this programme were given.

A questionnaire was prepared in 1992 and administered to the 41 health workers to assess the role played by these workers in the leprosy control activities in their area. The data was tabulated and is discussed. It was observed that 25 out of 41 health workers have participated in active case detection. 100 cases were suspected by the health workers of which 98 were confirmed and brought under treatment. The participation of these health workers in health education, absentee persuasion, and counselling the patients in various socio-economic situations were discussed based on the data tabulated.

CO61

THE IMPORTANCE OF THE EXAMINATION OF ALL FAMILY MEMBERS IN FIELD WORK

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Because of the endemic situation found in São Gonçalo municipality, and the diagnosis of LL in a two year old boy, we decided to make a home visit to examine the other family members. In a family of twenty five people , we diagnosed thirteen with leprosy. In other words, more than 50% of the family members had the disease.

CO62

EPIDEMIOLOGICAL AND ECOLOGICAL ASPECTS OF LEPROSY: AN ANALYSIS OF MAJOR DIMENSIONS OF DISEASE ECOLOGY AND HEALTH CARE MANAGEMENT

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The total number of leprosy cases in the country is estimated to be around 4 million cases based on the average prevalence rate of 5 to 6 per 1000 population Of the cases reported in India 60% of the cases are actually new and 40% are old undetected cases. A majority of the cases were noticed in the adult age group as against 25% of the cases reported in the age group below 14 years. The present study is an attempt to analyse the spatial distribution of Leprosy in Tamilnadu(India) state with reference to epidemiological and ecological parameters and to observe intra-regional variation in relation to disease ecology and different types of leprosy and health care utilization under various types of treatment and associated variables. An attempt is also made to identify the major dimensions and to map out the same. The study was based on the medical statistics reported at various leprosy control units of the different districts of Tamilnadu. The data were analysed with the help of factor analysis to identify the major dimensions of ecology of leprosy and health care system. The epidemiological and ecological perspectives of spatial pattern of paucibacillary types of leprosy has identified seven major dimensions viz., Case History of Paucibacillary type,(22.56%),Disease prevalence (15.85%), Need for Lab.Technician (12.9%), Population and Case detection rate (9.30%), Curative efficiency of MDT on Paucibacillary (8.10%),Efficacy of Medical Treatmentand personnel (7.35%) and treatment effect.

CO63

"DEFORMITY CARE CLINICS" - A NEW APPROACH TO INTEGRATE 'CARE AFTER CURE' CONCEPT IN ROUTINE MDT PROGRAMME

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Under the "Borsad Model" of Comprehensive Leprosy Care Project sponsored by Government of Gujarat and Ciba-Geigy Leprosy Fund in a population of 3,71,000 inhabitants, spread over 96 villages with low endemicity, this new approach was experimented. All workers were trained in basic deformity care delivery. Wherever the MDT clinics were held at drug delivery points (DDP) all patients release from treatment with sensory motor loss were called in subsequent 2 hours to begin "deformity care clinic". Travel cost of patients was defrayed by paying the incentive in cash for attendance. The patients were then taught on taking care of anesthetic extremities, ulcer care, proper application of splintage and studied for requirement of grip aids or MCR sandals. By this approach it was feasible to render and integrate "Care after Cure" services in better way. The data of 408 patients in need of such services was analysed and will be presented.

CO64

COMBINED TUBERCULOSIS/LEPROSY DETECTION PROGRAMME IN AN URBAN METROPOLITAN CITY - A PILOT STUDY

Leo Pandiaraj, Nambudripad K, Jayaraman R, Lobo D, Matheus M.

Many countries including India have well established VERTICAL infra-structure and manpower for Leprosy Control.

With declining trends of leprosy prevalence and case-load, many such programmes are faced with the problem of under-utilisation of staff and over-stretching of resources.

Inorder to tackle this problem, our institution decided to combine leprosy with Tuberculosis (TB) Control. As a first step, a pilot survey for detection of Leprosy and TB was conducted in four Corporation divisions with a total population of approximately 100,000. The summary of results are:

Population covered so far	:	24,448
Number of new leprosy cases detected	:	41
Number of old treated leprosy cases	:	203
Number of TB symptomatics detected	:	73
Number of old treated TB cases	:	20
Number of TB symptomatics confirmed	:	06

The survey was conducted by 4 para medics over a period of 22 weeks. The results and importance of the survey in planning combined Leprosy/TB programmes is discussed.

The survey is ongoing and the results up to July 1993 will be presented.

CO65

INTEGRATION OF LEPROSY CONTROL PROGRAMME INTO PRIMARY HEALTH CARE. 4 YEARS PRELIMINARY STUDY. OGUN STATE OF NIGERIA.

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Ogun State Leprosy Control Programme, Nigeria

The aim of the 4 years preliminary study was to analyse the problems associated with integration of Leprosy Control into Primary Health Care and to find practical solutions.

The study was conducted in Ogun State of Nigeria with 2008 registered leprosy patients within 15 local government areas in an area of 16762 square kilometers with a total population of 2½ million.

During this study the existing problems with the vertical leprosy control programme, segregated leprosy patients' community, leprosy health workers, government general health workers, problems in the community at large and managerial problems were analysed.

The national health policy, the network system of the PHC in the state and logistics were studied. In the process of a step by step integration the problems found at various levels were treated. The results were positive and and encouraging.

CO66

INTEGRATION-FOLLOW-UP STUDY OF GENERAL HEALTH STAFF TRAINED IN LEPROSY IN WARDHADISTRICT - INDIA.

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: Gandhi Memorial Leprosy Foundation, P.O.Hindi Nagar, WARDHA - 442 103, Maharashtra - INDIA.

In India, leprosy services were vertical & aloof from general health services for over 4 decades. Several suggestions were made to integrate leprosy with general health services. A few attempts were also made in this directions.

A pre-requisits for integration is the training of health staff in basic medical and social aspects of leprosy and an initial follow up of their performance to understand their achievements and difficulties hindering their participation. This enables to evaluate, modify the course content and also the expectations from them concerning leprosy work.

The Gandhi Memorial Leprosy Foundation conducted a one day orientation course in leprosy for 330 health staff at 27 primary health centres level. Medical and social aspect of leprosy were covered and method of participation by health staff was decided after mutualconsultations.

After one year, a detailed questionnaire was framed and administered to evaluate the knowledge of health staff in leprosy, assess their participation and the difficulties by them in this work. 130 workers have responded to the questionnaire. Detailed observations about their responses were tabulated and discussed.

CO67

THE APPLICATION OF CONTROL THEORY IN THE MANAGEMENT OF MDT

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ABSTRACT This peper presented the preliminary analysis and summary of the application of cybernetics in the management of MDT. Many operational problems of MDT implementation were also discussed by the combination of the cybernetics and its application.

The theoretic basis of this article is the advance control, field control and feedback control of the cybernetics, of which the most important one is the field control. The application of cybernetics in the MDT implementation aims at the regularity of treatment, especially the supervised intake and the daily self intake of drugs. The more the levels of the control, the higher regular treatment rate will be. In addition,

the scientific management can help in the improvement of both the personnel and the basic health system.

The enhancement of initiative and responsibility of all the people concerned, including the patients themselves, by the scientific management is also the task of the control. The more the measures of control, the better quality the MDT will have.

The International Conferrence on the Basic Health System in Alma Ata, 1978 called for the integration of leprosy control into the basic health care services, which makes it necessary that the leprosy control activities should be supported by the community. This peper proved that the scientific management of MDT contributes to the increase of quality and effect of the leprosy control but also aides to the integration of the leprosy control activities into the basic health care services.

CO68

THE NATIONAL LEPROSY CONTROL PROGRAMME OF BHUTAN: FACTORS IN A SUCCESSFUL MDT PROGRAMME

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National Leprosy Control Programme, Bhutan

Bhutan is a small mountainous country in the eastern Himalayas. Designated "least-developed" by the UN, it has extreme constraints of terrain, communications, finance, and trained personnel.

The National Leprosy Control Programme was constituted in 1982, and has been supported by two NGOs. MDT was introduced at the same time, and has proved very successful in reducing the prevalence of the disease. It is clear in retrospect that the success was largely due to the care taken in establishing the programme at the outset.

This presentation will document the preparatory steps taken, and the structures and policies within which the programme has functioned. Now that more is known about the effectiveness of MDT, some of the requirements may be proven to be excessively rigorous; these areas will be identified and discussed.

CO69

THE EPIDEMIJOLOGICAL IMPACT OF MDT ON LEPROSY IN GUANGDONG PROVINCE

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A province-wide comparative analysis of leprosy data of DDS monotherapy period (DDSP) of 1982-1986 and that of MDT period (MDTP) of 1987-1991 was reported.

The cure rates of the DDSP and the MDTP groups were 52.68% and 66.23% respectively with an increment of 25.72% (66.23%−52.68%/52.68%) in the MDTP group, but in the period of dapsone monotherapy of 1952-1986, the highest range of such increment was 10% only.

The prevalence rates in the DDSP and the MDTP groups were reduced by 44.55% and 59.26% respectively, and they were reduced either by 13.71% and 20.11% annually in the average in the DDSP and MDTP groups respectively.

The age specific incidence rate of 0-14 year group was decreased by 38.06% in MDTP as compared with that in DDSP.

After the implementation of DDT for 5 years, the number of medium endemic counties (prev.rate≥0.1-0.99‰) decreased from 12(1986)to zero and the number of non-endemic counties increased from 56 (1986) to 98, including 31 counties with a prevalence (0.01‰.

The results showed that the implementation of MDT has given a positive impact on leprosy control in Guangdong province.

CO70

ON THE COST-EFFECTIVENESS OF MDT FOR LEPROSY

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The authors reviewed WHO/MDT Programme and studied its feasibility. The authors also analyzed the effects of the MDT Programme implemented in Guangxi and found that RMB 1,050 yuan was needed to be invested for one-year-treatment for one MB leper and RMB 250 yuan for every six-month treatment for one PB leper in this province. The prolonged one-year treatment of all the leprosy patients in Guangxi costs RMB 320,000 yuan and at the same time we have to pay 9,000-14,000 yuan more for the management of liver damage caused by the drugs. In all, at least 329,000 to 334,400 yuan will be used more than necessary. The authors realize that the WHO-MDT Programme is adequate and practical and the way of investment should be changed. Instead of implementing prolonged treatment, the limited funds should be used to develop the three-tier health network, to improve the training of health workers at the basic level, to increase necessary equipments for strengthening the quality control of MDT and to standardize our work strickly according to the criteria approved by the Ministry of Health. The authors emphasized that the MDT regimens should be implemented individually. The patient should be released from treatment and be monitored immediately when the disease recovered to the required criteria for stopping drugs, if not, the additional treatment is still necessary, otherwise it is also a waste of money.

CO71

THE IMPACT OF MULTIDRUG THERAPY ON EPIDEMIOLOGICAL TRENDS OF LEPROSY IN GUIZHOU, CHINA

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Since 1986, with the great assistance from ALM International and WHO, the multidrug therapy (MDT) recommended by WHO has been introduced into Guizhou province, China to treat all patients suffering from active leprosy. By the end of 1991, MDT coverage rate had reached 100 %. After 6 years, a remarkable decrease of leprosy prevalence rate from 2.4 per 10,000 in 1986 to 1.1 per 10,000 in 1991 (linear regression curve: $Y=18.47-0.0243x$, $P<0.001$) and of leprosy mean annual detection rate from 0.221 per 10,000 in 1986 to 0.122 per 10,000 in 1991 ($\overset{-1}{(}$ power regression curve : $Y = (1992.028\,X^{-1})^{3.91\times10^{-1}}$, $P < 0.05$) has been observed. On the basis of the fact that the relapse rate was nil in Guizhou patients put on MDT, our results may suggest that the implementation of MDT has cause a decrease of prevalence rate and detection rate for leprosy because of interruption of transmission of the disease by MDT.

CO72

ACCELERATED PROGRAMME FOR MDT IMPLEMENTATION

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In the four Northern States of Bihar, Madhya Pradesh, Uttar Pradesh and West Bengal the MDT implementation has been the slowest. To

accelerate it a programme was undertaken by the Government and the Leprosy Mission India in 10 Districts of these 4 States to estimate the magnitude of the problem.

A special team of 15 field staff lead by a Medical Officer covers each district in 4 months to screen old cases and conduct a chase survey after a 2 day orientation programme. With the help of local NLEP Staff cleaning up of the registers where all the patients who are inactive, cured, self healed, died, left, wrong diagnosis and double entries are removed. In addition a quick round of health education through the streets of the villages is done and new cases of leprosy identified.

The results obtained in the first 3 districts showed that 72% of all the villages were visited and 85% of 6.5 million population covered and 9,430 new cases detected giving a case detection rate of 1.7/1000. Out of 6,103 old cases on monotherapy 22.5% were found to be active, 17.2% cured and inactive and 6.8% died or left. 53.5% of the cases could not be contacted. The results of the full study will be analysed and presented.

CO73

RESULTS OF MDT IMPLEMENTATION IN THE MILE FOUR LEPROSY CONTROL PROJECT, ABAKALIKI, ENUGU STATE, NIGERIA

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The Leprosy Control Services of Mile Four Hospital (Catholic mission hospital) in Abakaliki Zone, Enugu State, Nigeria cover an area with a population of over 1 million (1992). The implementation of WHO Multiple Drug Therapy (MDT) for leprosy started in 1984, replacing Dapsone monotherapy. In 1987 the overall MDT coverage was 98%. Between 1985 and 1991 the number of registered leprosy patients decreased from 2371 to 962 (respective prevalence rates per 10,000 population, 21.1 and 7.31). The case detection rate (CDR/10,000) was 2.6 in 1985 and 3.1 in 1991. The proportion of children diagnosed increased from 19.3% in 1985 to 25% in 1991. Possible epidemiological and operational reasons for this will be discussed.

The outcome of MDT treatment was determined in a review of 629 records of patients who started MDT between January and June in four consecutive years (1986 - 1989). Preliminary results of this cohort analysis of treatment outcome indicate that overall, 87% of PB patients and 83% of MB patients completed their treatment, and that MDT was successfully implemented.

CO74

THE IMPACT OF THE IMPLEMENTATION OF MDT/WHO ON THE CONTROL OF HANSEN'S DISEASE IN BRAZIL, IN THE PERIOD 1986-1992

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The multidrug therapy regimen for the treatment of Hansen's Disease, recommended by WHO in 1982, was gradually implemented in pilot units in Brazil, since 1986.

We present the implementation strategy for this therapeutic regimen in the country, and its monitoring using specific indicators, up to decision of making this the only regimen in the country, starting in 1991.

We will present and debate the main epidemiological and operational indicators which are essential for the "National Programme for the Control and Elimination of Hansen's Disease" between 1985 and 1992, a period coinciding with the National Programme's restructuring and the implementation of MDT/WHO.

CO75

TEN-YEAR COHORT ANALYSIS OF MULTIBACILLARY LEPROSY PATIENTS WHO RECEIVED MULTI DRUG THERAPY

Renuka Ramakrishnan, Narayanan R, Devanbu V, Lobo D, Ramanujam R.

Our institution GREMALTES based in Madras is a pioneer in URBAN Leprosy Control. We initiated Multi Drug Treatment (MDT) in 1983.

Between 1983 and 1992 - 13,250 patients received MDT, of which 1698 are Multibacillary (MB).

A COHORT analysis of all the MB cases cover the Ten-year period is presented, using the following parameters:

- MDT Coverage
- Treatment Regularity/Compliance
- Proportion of Drop-outs
- Skin Smear Status
- Cure Rate
- Relapse Rate
- Proportion of cases with complications like Neuritis/Reactions

The significance of the results, their relevance to the impact of MDT and for planning and implementation of Leprosy Control Programme is discussed.

CO76

MULTIDRUG THERAPY IN THE STATE OF AMAZONAS 1982 - 1992

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Amazonas is an enormous state with an extremely low population density. Half of its people live in the capital, Manaus , and the rest are evenly divided between the towns of the interior and the rural zones. Multidrug therapy in Amazonas was started in 1982, and the authors set out to evaluate its impact on the endemic leprosy situation 10 years after its implementation. The leprosy prevalence has come down to 5.1 cases per 1,000 population from 10.6 in 1982. By December 1992 a total of 20,217 patients were on or had completed MDT.

The proportion of new cases presenting with deformities fell from 12% of those diagnosed in 1982 to 6.4% in 1992.

CO77

EPIDEMIOLOGIE ET POLYCHIMIOTHERAPIE
APPLIQUEES AU PROGRAMME DE LA LEPRE EN TUNISIE

La Tunisie, pays méditérranéen située au Nord est de l'Afrique, la lèpre a une prévalence de 0,03‰ malgré cette faible endémicité le besoin d'entreprendre une action de lutte contre ce fléau a été rendu nécessaire par la prédominance de la F. lepromatjuse et l'existance de foyers dispercés.
De ce fait un programme de lutte antilepreux a débuté en 1985 avec l'aide du C.I.O.M.A.L. qui a pour objectifs :

- Sur le terrain par la formation d'une équipe médi--cale mobile qui a pour tache : la prise en charge des malades, le dépistage, l'examen des contacts, la distri--bution et la surveillance de la PCT.
- Au centre hospitalié de traiter les complications de la maladie et de réunir tous les donnés sur lesmalades dans un fichier central.

Jusqu'en 1992, 200 cas sont fichés et répertoriés.
Les régions les plus concernées sont Mahdia 60 cas, Medenine 51 cas, Sfax 45 cas.
61 % des malades sont des lepromateux.
16 % sont âgés de 60 - 64 ans.
La contamination reste essentiellement familiale.
20 % ont une invalidité au degré 3.
Tous les malades sont sous PCT Rifadine, Disulone ou Fanasil, Lamprene.
Deux shémas thérapeutiques sont préconisés. 30 % des malades sous Rifadine, dose unique 30 mg/kg supervisée pour les patients des régions montagneuses d'accès dif--ficile et ceux nécessitant de grandes distances à par--courir. 70 % des malades sous Rifadine 1200 mg/mois (6 mois supervisée), associés aux 2 shémas DDS-Lamprene en auto traitement.
Les résultats après 7 ans sont pratiquement identiques avec un contrôle clinique et surtout bactériologique régulier.

CO78

MARTINIQUE : Evaluation de 1980 à 1992 de la polyantibiothérapie (PAT) ou polychimiothérapie (PCT) traitement de la LEPRE

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J. GROSSET, H. SANSARRICG,
R. BELLANCE, C. DALLOZ, P. PINVILLE-LOGER,
P. RENE-CORAIL, JC. SAINT-ZEBY, V. SCAT
J. MAGDELEINE, JC CAROLINA, A. LEOTURE

D'abord la mise en route de cette nouvelle approche thérapeutique a necessité une démarche communautaire grâce à la participation du personnel soignant et de beaucoup d'actions sociaux afin de prendre en compte le versant culturel. Puis avec l'aide du laboratoire de bactériologie du CHU Pitié Salpêtrière de PARIS la surveillance des malades nous a fait évoluer dans le choix des antibiotiques, en raison de la fréquence des résistances double ; de leur association et la durée du traitement.
Enfin cette maladie infectieuse touchant la peau et les nerfs a permis la constitution d'équipes médicales regroupant des médecins spécialistes hospitaliers et des médecins de famille.

CO79

PATIENTS COMPLIANCE AND DRUG TRIALS: AN ANALYSIS OF EFFICIENCY OF MONOTHERAPY AND MULTIDRUG THERAPY(MDT) TREATMENT

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The spatial pattern of distribution of leprosy in different districts of Tamilnadu has been analysed to understand the health situation of Tamilnadu and its status in recent years before and after the implementation of MDT. The present study has made an attempt to highlight the importance of MDT in controlling the prevalence rate of leprosy in most part of the distri-cts of Tamilnadu compared to Monotherapy treatment. The study was based on the statistics collected from all district leprosy units of Tamilnadu. The data were analysed with the help of a multivariate statistical technique Factor analysis to identify the major dimensions. A questionnaire survey was also employed to collect the patients compliance in relation to monotherapy and MDT treatments. The Monotherapy has identified 8 major dimensions and these were on Case History of Monotherapy, Inefficiency of Monotherapy treatment, Treatment awareness, Examined population and Detection rate, Irregular treatment Effect, Persistence of disease under monotherapy treatment, Susceptibility of children to disease under monotherapy. Whereas the MDT treatment has idenfified eight major dimensions and these explained the case history of multidrug therapy, Curative efficacy of MDT, Treatment Awareness, Disease cycle, Examined population and Treatment efficiency, Treatment effect and susceptibility of school Children. The patients compliance towards the preferance of MDT was strongly felt due to short duration of treatment and quick improvement in deformity status, MDT programme was perceived to be highly satisfactory among males aged 35 to 64 years (60.7%) than the females who aged 14 to 34 years (47.9%). More than 50% of the patients of either sex have had their regular drug supply under MDT.

CO80

LONG-TERM EVALUATION OF A PROVINCE-WIDE CLUE SURVEY FOR LEPROSY IN LIAONING

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Based on the effective health education activities, a provincewide clue survey was carried outfrom 1977 to 1978 in Liaoning province. Through this survey, 4,882 suspected cases were reported, among them 54 new leprosy patients, including 19 multibacillary (35.2%) and 35 paucibacillary (64.8%), were diagnosed.

The survey was completed in the end of 1978. From that time on to the end of 1991, various modes of leprosy case finding, including small scale clue survey, focus survey, examinations of patients' households and contacts, dermatological consultations and rewards for reporting suspected individuals, were carried out actively and contineously in order to detect leprosy patients as early as possible. The results of the past 13years showed that the number of newly detected leprosy cases has reduced significantly.

During the period of 1979 through 1991, the total number of newly detected patients in the whole province was 65, only 13 of them were late cases. We probably can say that the reported province-wide clue survey had detected 80% of the patients(52/52+13) existed at the time the survey was implemented, and only 20%(13/52 +13)were missed, most of them may be because of their absence when the health education was given, or their symptoms might have been very slight.

In the period of 20 years before and 10 years after the implementation of the province-wide survey, the incidence rate of leprosy of Liaoning province decreased by 94% and 93% respectively. It is evident that the province-wide clue survey accelerated (facilitated) the declining incidence rate of leprpsy in Liaoning province.

CO81

AN EVALUATION OF THE ACHIEVEMENTS OF COMMUNITY-BASED LEPROSY CONTROL FOR 35 YEARS IN CHENGGU COUNTY, SHAANXI PROVINCE, CHINA

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Since 1956, along with the principle of"Prevention First and Active Treatment on Community Basis", comprehensive measures of leprosy control, consisting of "Health Education, Survey, Treatment, Prevention, Management, Research", were caried out in Chenggu County, Shaanxi province. The accumulative number of registered leprosy patients was 1,300. Excluding cured (1,050, 80.77%), died and migrated cases, there were only 11 active cases at the end of 1990. The prevalence reduced from 2.1‰ in 1958 to 0.022‰ in 1990.

The average incidence rate of 5 years decreased from 20.07/100000 of 1956-1960 period to 0.42/100.000 of the period of 1986-1990. The incidence of children (0-14 years of age) also declined from 7.75/100.000 to 0.12/100.000 of the above mentioned periods. The number of villages with patients diminished from 559 to 7. A programme of disability survey and health education of prevention of disabilities has been implemented. The above facts strongly indicated that Chenggu County, as a high endemic county(prev. rate >1‰) in the past, has become non-endemic (prev. rate (0.05‰). It is expected that the goal of basic elimination of this disease could be reached in this city in 1995 according to the prediction with exponential function.

CO82

AN ANALYSIS OF RELAPSES AMONGST 21,878 CURED LEPROSY PATIENTS

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By the end of 1991, the accumulative number of registered leprosy patients was 28,458 in Fujian province, among them 21,878 cases (MB 7,195 PB 14,683) were cured with monotherapy, and 728 (MB 598, PB 130) of them relapsed. the relapse rate of cured MB (8.31%) was much higher than that of cured PB(0.88%). The average duration from cure to the occurrence of relapse of MB (7 years and 9 months) was much longer than that of PB (5 years and 7 months). As time went on, the relapse rate increased and the number of new cases reduced. The proportion of relapsed patients among active cases increased from 0.10% (1957-1961 period) to 5.63% (1987-1991). The existing disabilities of 247 (33.9%) of 728 relapsed patients worsened. Disability-worsening of relapse was more common in PB (44.6%). Since 1986, 2,352 patients (MB 1,161 PB 1,191) have been cured with WHO/MDT, no relapse was found up to now. The authors emphasize that preventing cured cases from relapse and detecting relapses early are very important to leprosy control.

CO83

COHORT STUDY IN THE LEPROSY CONTROL PROGRAMME IN AMAZONAS

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The authors present a cohort study of leprosy patients detected and registered in the state of Amazonas in 1988.

Clinical, laboratorial and epidemiological aspects of leprosy, as well as some of the Leprosy Control and Elimination Programme's operational aspects are discussed in with reference to the national norms and protocols.

CO84

IMPROVING PATIENT COMPLIANCE - A MULTICENTRE EVALUATION OF THE 'DDS TILE TEST'.

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Previous longitudinal studies of drug default in Bombay using the 'DDS Tile Test' and counselling of defaulters showed improved drug compliance from 35% to 87% (Naik et al., Ind. J. Lepr., 1990, 62, 305). A similar study was launched in field condition in rural areas with the participation of leprosy centres (98 Government and 14 non-government). During one year, 2959 urine samples were examined for DDS presence using a 'DDS Tile Test Kit' by paramedical workers. 284 (9.6%) urine samples were found DDS negative, suggesting default or poor compliance.

Analysis of information returned by 52 leprosy centres showed that though 90% of the paramedicals used the 'kit' for the first time, they could perform the simple "Tile Test" well in field conditions and counselling of patients on the basis of results of the Tile Test helped to improve drug compliance of patients.

The paramedical workers judged the kit too cumbersome to carry to the field and suggested modifications in container. They also felt less utility of the test, particularly with the drop in case number in MDT districts. The collection of urine from female patients was also difficult. However, the Tile Test could be satisfactorily performed in the treatment centre itself where more patients attended.

CO85

INFLUENCE OF MULTIDRUG THERAPY ON SMEAR POSITIVE CASES IN TALUKA PANVEL.

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Panvel Taluka has its unique features, such as surrounded by costal and hilly area where the residents are uneducated, in low socio-economic group of tribal and fishermen community and generally males among them are out of homes six months in year to earn their liveligood. At the other hand there are several developed and developing big industrial packets in same Taluka, where residents around are highly educated, economically well setteled but under the influence of constant influx of semi and unskilled persons.

MDT was initiated in Panvel Taluka in 1990. The comparison of newly detected cases in pre and post MDT era in centres having different regional and population set up was made. During last 5 years (1988-1992), total 1597 new cases (234 MB and 1363 PB) registered by conventional methods of SET. The analysis showed that there is a no change in child rate, deformity rate and smear positive cases rate in newly detected cases in pre and post MDT era but bacterial quantum based on B.I. of smear positive cases (n=166) reduced considerably after MDT and brought to the negligible state irrespective of regional and population variation. It is further noticed that the results are more impressive in area of educated and stable population.

CO86

CURRENT SITUATION OF HANSEN'S DISEASE CONTROL PROGRAMME IN THE AMAZON REGION OF BRAZIL

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MoH-BRAZIL/PAHO/OMS

THE NORTHERN REGION, WITH 9.30% OF BRAZILIAN POPULATION AND 22.36% OF REGISTERED CASES OF LEPROSY (1991) IS THE LARGEST REGION OF THE COUNTRY.
THE GEOGRAPHIC AND UNDERDEVELOPED CHARACTERISTICS OF THIS REGION PLUS THE INADEQUATE CONTROL STRATEGIES CERTAINLY WAS RESPONSIBLE FOR THE ACCUMULATION OF INFECTED CASES OF LEPROSY.
EVEN WITH AN INTENSIFICATION OF THE ACTIVE SEARCH FOR NEW CASES IN THE MAIN STATES OF THIS REGION FOR OVER THAN A DECADE, AND THE HIGH MDT COVERAGE THIS REGION IS STILL RESPONSIBLE FOR THE HIGHEST DETECTION RATE (53.94/100000HAB) AS WELL AS FOR THE HIGHEST PROPORTION UNDER 15 YEARS OF AGE (17.36%).

NEVERTHELESS, THIS REPORT REMARKS CONCERN THE PERSPECTIVE RELATED TO OPERATIONAL IMPROVMENT OF YHE PROGRAMME ACTIVITIES WHICH HAVE BEEN COMING TRUE. IN MOST STATES THE PROPORTION OF DEFORMED NEW PATIENTS IS LOWER THAN 5% AND THE MDT COVERAGE IS THE HIGHEST IN THE COUNTRY.

FOLLOWING THE AMAZON AND ACRE STATES EXPERIENCE THE MACRORREGIONAL SUPERVISION IS PROVIDING ADVICE TO THE STATE MANAGERS WITH AIM OF ACHIEVING NOT ONLY THE SHORT TERM TARGET OF ELIMINATING LEPROSY BY THE YEAR 2000- DECREASING PREVALENCE RATES THROUGH CLEANING OF FILES, BUT ALSO CONSOLIDATING THE STRATEGIES TRIGGERED IN ORDER TO CHANGE THE ENDEMY'S TREND IN A LONG TERM.

CO87

SITUATION OF LEPROSY ELIMINATION IN THE AMERICAS

Clovis Lombardi

Par. American Health Organization, Caracas, Venezuela

Presentation of the latest available data on the epidemiological and operational situation of leprosy control in the endemic countries of Latin America, through indicators such as Prevalence Rates, Detection Rates, MultiDrug-Therapy (MDT Coverage, Cumulative MDT Coverage, etc.
Comments on the several organizational aspects of national leprosy control programs and other related items as research and training.
In connection with the descriptive picture presented, projections concerning the possibility of reaching at regional, subregional or country level the targets of elimination of leprosy as a public health problem from the Americas, according to the PAHO/WHO Regional Plan of Action.

CO88

THE INTERN.L.CONGRESSES AND OTHER OUSTANDING EVENTS IN THE STUDY,EPIDEMIOLOGY AND ELIMINATION OF L.(with bibliografy and fotgs.of nearly all)

BALIÑA LUIS M. and VALDEZ RAUL P. Hospitals Argerich and de Clinicas,av.Alvear 1890 (1129) Buenos Aires,Argentina

1873G.A.Hansen starts the scientific era.
1897 I Int.Conf.about L.(Berlin)Virchow Prés."L.

is producedby a microbe,not hereditary and is possible to prevent it"
1902 II Int.L.Conference on L.(Bergen)Pathologists and dermatologists under the honor.Presid.Hansen
1923 III Intern.L.Congress(Stras) a meeting that provokes the birth of ILA.Pres.E.Janselm,vicepres V.Heiser and the journal"Lepra"(P.Lee & H.W.Wade
1938 IV Int. L.Congress(Cairo)The indian european classification and the south american with Ind. form.Native chaulmoogra seeds as centuries ago.
1947 R.G.Cochrane Ist. edition:reference book.
1948 V Int.L.Congress(La Habana)Pres.A.Oteiza Setien;ILA'sH.W.Wade.With sulphones L. enters in the chemotherapic age.(Faget) Stanley Stein(founder editor starts with"the Star"a unique campaign.
1953 VI Int.L.Congr.(Madrid)Pres.F.Contreras,ILA's H.W.Wade.Thiosemicarbazones,B.C.G.,leprosaria to be replaced by out -patients clinics.
1958 VII Int.L.Congr.(Tokio)Compulsive internation banned as institutionalization of patients children.Pres.of ILA:J.M.M.Fernandez:B.C.G.and relatio L.-T.B.
1963 VIII Int. L.Congr.(Rio de Janeiro) L.a dìsea se like all others,the term leper has to be avoided.1968 IX Int.L.Cong.(London)Physical rehabilitation (Brand) and psychological (Hasselblad)Inoculation of the mouse foot-pad(Rees and Shepard)

1973 and 5 more events are presented

CO89

LEPROSY CONTROL IN KARAKALPAKSTAN

T.Eschanov, V.Idunov
Republic Antileprosy Dispensary, Nukus, Karakalpakstan

For Karakalpakstan Republic leprosy presents a main problem of the regional pathology. More than 20% of the total amount of leprosy cases in the former USSR are registered here, while a population of the Republic is only 0,3%. Three phases may be followed in the organization of leprosy service in Karakalpakstan endemic area. The 1st phase continued till 1933 when no case recording was kept and no special measures were taken. The 2nd phase was from 1933 to 1963 when every efforts were directed towards setting up a leprosarium, active case-finding,isolation and treatment of leprosy patients.During that period active case-finding through mass surveys of the total population was initiated.The 3d phase (from 1963 up to now) is characterized by a well developed network of antileprosy institutions (Karakalpak Branch of Uzbek Institute for Study of Skin and Venereal Diseases, 2 leprosy dispensaries, 5 leprosy rooms and a specilized sanatorium for children of leprosy parents. Current antileprosy service is based on a continuous and multidisciplinary approach to implementation of leprosy activities: active case-finding, hospitalized and outpatient treatment of leprosy patients with post-treatment surveillance and epidemiological control of leprosy foci and their sanation. Effectiveness of such an approach is proved by more than 10-fold decrease in leprosy incidence, leprosy prevalence being decreased in average by 2% annually.

CO90

LABOR DEL LABORATORIO NACIONAL DE REFERENCIA DE BACTERIOSCOPIA DE LEPRA DE CUBA.

Odelaisy Suárez Moreno, Ancel González Secredo, Reynaldo Gil Suárez.

Instituto "Pedro Kourí". La Habana. Cuba.

Este trabajo muestra la estructura y funcionamiento del laboratorio nacional de referencia de Lepra y de sus laboratorios de la red nacional, también se describe la retroalimentación de la información que se deriva del trabajo tanto de los laboratorios de la base como el propio laboratorio rector y el apoyo que se brinda con estos resultados al Programa Nacional de Control de la Lepra en Cuba.

CO91

FOURTEEN YEARS OF HD CONTROL IN ACRE STATE.

William John Woods, Leia Borges Marques, Alvaro Romero.

Secretaria de Saúde, Acre State, Brazil.

The most remote of all Brazilian states Acre had an average prevalence of HD 0f 10.5/1000 for over 20 years. With no roads and only river travel most patients were attended once a year. The prevalence in 1992 fell to 3/1000.

The factors involving this change and the importance of assistance from non

governmental agencies is discussed. The implantion of MDT, even in remote areas and a 5 year follow up of patients not included in MDT is presented. The rehabilation, prevention of deformities and education programmes mentioned.

Co-operating with the State Government team are DAWH, Germany, ALM, USA and AIFO, Italy.

CO92

MDT IN REMOTE AREAS OF THE ACRE STATE.

William John Woods, Maria do Socorro Lins Brasiliense, Silvano Renzo,* Luiz Ferreira+

Secretaria de Saúde, Acre state Brazil
* AIFO ,Italy. + University of Amazonas.

The Acre state, which is the most inland of all Brazilian states has few roads and almost all travel had to be done by taxi plane or river. To attend HD patients living on the river Juruá alone take 12 weeks, travelling daily. The difficulty to implant MDT is discussed.

The monthly supervised dose was released for self adminstration and patients were attended by para-medical workers at 3 monthly intervals. To iniciate MDT and to realease from treatment each patient was evaluated and orientated by the medical supervisor. To iniciate MDT in these circumstances took 3 years and involved travelling on 30 different rivers.

The clinical results compared with a sample of 50 histopathological exames have been satisfactory.

CO93

A Health Education Intervention in Cuba to diminish the delay in diagnosis of leprosy.

Vivianne de Rojas, Olenia Hernández, Reinaldo Gil.
Institute "Pedro Kourí", Havana, Cuba.

Early diagnosis of leprosy is important to establish treatment, prevent disability and eliminate the patient as a source of infection. In a previous study we demonstrated that in 2 cities with different prevalence rates: Guantánamo (Gt) high and Havana City (HC) moderate, the diagnosis took longer in the latter due to a low index of clinical suspicion among primary health care (PHC) doctors (15.5 months HC, 5.5 Gt). In Gt the patients sought medical attention 5 months after the initial clinical manifestations while in HC they did so during the first month. These findings allowed us to design 2 different interventions: in HC to increase physicians index of clinical suspicion; and in Gt, to encourage the patient to seek medical care at the onset of symptoms. During almost 2 years we gave lectures, seminars and used participatory techniques with PHC doctors. We also utilized posters illustrating the first symptoms of leprosy. In Gt we used posters, leaflets, mass media and group dynamics to spread 3 messages: leprosy is curable, leprosy is not contagious if the patient is under treatment and deformities are avoidable. We also developed a poster campaign with the aim of easy recognition of the first symptoms of leprosy. With every message we emphasized the need to seek inmediate medical attention. In HC, the in Gt, the number of consultations for skin disorders were increased. This intervention also led to considerable gains in knowledge about leprosy among the people in the community.

CO94

IMPLEMENTATION OF MDT IN A LOW ENDEMIC REGION AN OPERATIONAL STRATEGY

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One of the district in Kerala State, with a population of 10,70,629 (1991 census) has been taken up for this study. The literacy rate in this region is high.45 PHCs,2 LCUs and 2 ULCs exist in the district, but there was a GROSS deficiency of manpower in the leprosy centres.

A 2 days task oriented training in leprosy was instituted for staff of the PHCs and the **existing** vertical leprosy control programme. Facts about leprosy and a schedule of an extensive network of Skin camps spread out all over the region, were widely publicised through mass media and during a Rapid Enquiry Survey, during which PHC health workers were instructed to identify all suspected cases of leprosy.

The Survey was completed within 15 days, and 57.3% of the total population was contacted. Suspects were reviewed by a well trained medical team, at subsequent skin camps. 12,619 skin cases including those with Hansen's disease were screened and 603 leprosy cases were detected. 62% had active leprosy lesion and 38% had inactive lesions.

MDT was initiated on the day of screening. Further treatment delivery was entrusted to the PHC STAFF and DLO. This programme was completed within a period of two months.

This methodology may be adopted to implement MDT in uncovered low endemic areas, utilising the existing Primary Health Care facilities. However, the health staff may require further training. The cost effectiveness of this strategy is to be worked out.

CO95

IMPACT OF MULTI DRUG THERAPY ON THE FIELD WORKERS IN LEPROSY AND THEIR FUTURE PROSPECTS.

*R.D.Kharkar K.Nagaraj G.S.Mane

Maharashtra Lokahita Seva Mandal, Bombay, India.

With the successful implementation of Multi Drug Therapy on a large scale the active case load has started falling drastically with this tool, leprosy eradication by 2000 AD seems to be a possibility. This is because of the sincere efforts put in by the leprosy workers with this goal in mind. All the same a sense of insecurity now seems to be creeping into the workers as to what would be their future with leprosy work coming down.

The Maharashtra Lokahita Seva Mandal is a Multi faceted organisation not only dealing with leprosy but also other projects like T.B. Control and Community Development aiming at serving the slum population with as much benefits it can offer. The paper discusses a Pilot Study where integration of a select Leprosy workers was done in T.B., Community Welfare Schemes and Rehabilitation

This experiment has definitely boosted the confidence of the workers and helped in driving out the feeling of insecurity and giving them ideas about reaching newer horizons after their success story in Leprosy.

CO96

LUTTE CONTRE LA LEPRE AU ZAIRE 1987 - 1991

Mputu Luengu Boyau, Bureau National de la Lepre, Zaire

Actuellement, la lutte contre la lèpre sur le terrain se fait grâce aux Infirmiers des centres de santé et par les Infirmiers des équipes spécialisées. Actuellement, notre stratégie repose essentiellement sur l'intégration de la lutte contre la lèpre dans les soins de santé primaire, et l'application de la polychimiothérapie (PCT) O.M.S. Cette approche va entraîner, nous en sommes convaincus une augmentation de la couverture du programme lèpre et de la PCT/OMS, deux pilliers nécessaires à la réussite du programme lèpre.

En 1991, la couverture des activités antilépreuses était de 33%, cela veut dire que nous ne couvrions qu'un tiers du pays, et pourtant celle-ci était respectivement de 62% en 1988 et 61% en 1989.
Le départ massif de nos collaborateurs en 1990 et le retrait de l'appui de certains O.N.G. dans une bonne partie du pays ont conduit le pays à cette situation.
La couverture de la PCT/OMS au Zaïre en 1991 était de 53% et pourtant celle-ci n'était que de 7% en 1987 et de 27% en 1988. Ceci est donc le résultat de notre nouvelle stratégie de lutte contre la lèpre lancée en 1988.

CO97

EPIDEMIOLOGICAL CHANGES IN AN URBAN LEPROSY CONTROL PROJECT-15 YEARS OBSERVATIONS IN BOMBAY

CR Revankar, RR Pai, D Girija, SS Deshpande, KL Gandewar, VV Pai, Nirmala Hiwase & R Ganapati

Bombay Leprosy Project, Vidnyan Bhavan, 11 VN Purav Marg, Sion-Chunabhatti, Bombay 400 022. India.

Leprosy control in metropolis and other developing cities in endemic countries, is becoming a major public health problem. Due to heterogenicity in socio-economic conditions with artificial living habits, health practice behaviour etc., the epidemiological trends in leprosy could vary from rural areas. No studies are yet available on impact of MDT intervention in metropolitan cities. A retrospective analysis of 15 years field data was undertaken in Bombay Leprosy Project with special reference to prevalence rate, new case detection rate, child rate, monolesion case rate, deformity rate and smear positive rate.

Between 1977 and 1991, a total of 11,062 cases were registered from a population of 1.8 million essentially from slum population in a well defined area in the city. Till 1981, patients were treated with dapsone monotherapy. Since 1982, all the new cases were brought under WHO-MDT. The following changes are observed before and after introducing MDT.

The active registered prevalence rate reduced from 17/10,000 to 6/10,000 population. However, the new case detection rate was ranging between 4/10,000 and 5/10,000 without showing an appreciable change. The child rate was ranging from 27% to 29%. Smear positive MB rate reduced from 12% to 8%. Though disability rate was showing a decline among new cases, the cumulative total showed increase. The implications of these observations are discussed.

CO98

SIXTY YEARS OF LEPROSY CONTROL IN SOUTH-EASTERN NIGERIA: THE UZUAKOLI EXPERIENCE

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Leprosy Referral Centre, Uzuakoli. Abia State, Nigeria.

Founded in 1932 as a settlement for lepers, the Uzuakoli leprosy centre was second only to Itu in an area which was "One of the most heavily infected regions in the world" (J.A.K. Brown 1960). The paper outlines the operational strategies adopted by the pioneer leprologists including Drs J.A.K Brown, T.F. Davey and S.G. Browne from the 30's through the 60's in combating the seeming epidemic. Sixty years and many developments later, we review the leprosy situation in Imo and Abia States- two states in the area which have all along maintained reasonable control services disrupted only by the Nigerian civil war. The paper presents and compares prevalence figures, case detection rates as well as proportion of diseased children and reaches the conclusion that the WHO elimination goal is feasible in this area. More importantly the figures indicate a decline in the rate of transmission of infection in the community. Several factors in our view contributed to this welcome development. These include the segregation villages, the sulfone era, 100% MDT patient-coverage as well as high and increasing BCG coverage. Finally, the paper turns attention to a very important issue: ways and means of consolidating and sustaining the gains so far made. The following approaches are proposed: (a) Functional integration through 'empowerment' of general health staff. (b) Renewed vigour in public awareness activities to further reduce stigma and encourage community participation. (c) To encourage committed and dedicated individuals to form indigenous Non-governmental organisations (NGO's)

CO99

EXPERIENCES WITH EVALUATION OF LEPROSY CONTROL

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Experience has been gained in the evaluation of more than 30 leprosy centres in over 10 countries in Africa, Asia, the Far East and the Western Pacific regions. The different methods used in evaluation include questionaires, field visits and sample surveys. The evaluation covered epidemiological aspects both descriptive and analytical, operational and organisational/administrative/economic aspects.

Disease patterns and secular trends over periods of time were also studied in high and low endemic regions in relationship to period after MDT was implemented and MDT coverage.

It was seen that the functioning of the traditional indicators depended considerably on the methodology used in leprosy control and traditional interpretations of these indicators can be misleading.

These issues are analysed and presented in the paper.

CO100

CHANGE IN LEPROSY PROFILE IN A HYPER ENDEMIC BOMBAY SLUM OVER 15 YEARS

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At the 11th International Leprosy Congress, Mexico City, we presented (Ganapati et al, 1978) the challenges posed by leprosy in an overcrowded Bombay slum with 3812 population. Our subsequent efforts at leprosy control in urban slums including leprosy colonies (Ganapati et al 1989) indicated that although a leprosy colony concentrates huge reservoir of infection, it was relatively easier to achieve success in reducing the quantum of infection, the same degree of success was not possible in a vast slum with 80,000 population, due essentially to logistic difficulties.

We report here the radical change in the leprosy profile assessed through survey in a slum with about 3000 to 4000 population referred to above over a period of 15 years.

Survey Year	Families visited	Enumeration	Examination	% Examined	PB	Cases MB (+ve)	Total Cases	PR**
1977	729	3812	3178	83	68	11	79	25
1992	801	4113	3653	89	4*	Nil	4	1

*All 4 patients had monolesions and had migrated from other slums **PR: Prevalence expressed as Rate per total slum population enumerated.

This transformation was brought about by promoting attendance of all the patients in the slum at a nearby "integrated" clinic and a special drive made to reach treatment to infectious reservoirs in the community through adequate training of staff. Rapid increase in the population density in large urban slums posing logistic problems is the crucial factor in overcoming lerposy transmission.

CO101

PRELIMINARY EVALUATION TO MEASURE THE FUTURE EFFECTS OF DECENTRALIZATION ON THE CONTROL OF HANSEN'S DISEASE IN THE METROPOLITAN REGIONAL AREA OF BELO HORIZONTE, MINAS GERAIS-BRAZIL FROM 1990 TO 1992

Maria Ana Leboeuf, Aparecida Grossi, Salete Santiago

Coordenação Estadual de Controle de Hanseníase, Secretaria de Estado da Saúde de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

The authors discuss some of the epidemiological and operational aspects in the detection of new cases of Hansen's disease in the metropolitan region of Belo Horizonte, Minas Gerais, Brazil. Changes are discussed in relationship to the municipalization and decentralization of health services with started in 1990.

The use of this preliminary evaluation is a baseline for measuring the future impact of training health care workers and decentralization of Hd control in the municipality of Belo Horizonte.

CO102

CONTROL AND ELIMINATION OF LEPROSY
A RURAL/URBAN STRATEGY ANALYSILS

T. Jayaraj Devadas, Thomas Abraham, Director GLRA/ALES Regional Secretariat, 4 Gajapathi Street Shenoynagar, Madras 600 030

Control and elimination are not synonymous. The two terms indicates two phases of activities towards eradication of the disease. Multi Drug Therapy is no doubt essential for the control and elimination of lepros in rural and urban settings. However, there are some varying factors needing attention.

This analytical study covers a population of 10 million in 5 urban and 5 rural leprosy control projects situated in endemic regions in India. Findings are as follows:

- Varying socio economic conditions of the population have a direct influence on the incidence of leprosy. On analysing the cases detected it was found that the cumulative case detection rate was 8.4°/°° in urban and 1.8°/°° in rural areas.
- It was observed that the urban/rural case load per worker though differs numerically (76 and 14) the work load is found to be similar since the rural workers have to cover a larger area for better case holding.
- It was found that the coverage of the population examination was found better in rural in comparison with the urban areas.

The strategy of Survey, Education and Treatment holds good for Urban as well as Rural areas.

CO103

LEPROSY ERADICATION PROGRAMME IN METROPOLITAN CITIES : A CRITICAL EVALUATION

R.S.Misra, C.Indira, S.Dayal, S.Yashodhara, H.V.Nayak, U.Saxena & V.Ramesh.
URBAN LEPROSY CENTRE, SAFDARJANG HOSPITAL, N. DELHI

Rapid industrialisation and population migration to urban areas in search of job opportunities has shifted a sizable leprosy problem to these areas, which demand for an urgent need for tackling it effectively to make the goal of leprosy eradication a success. A retrospective analysis of an Urban Leprosy Centre data with a large attendance of new and follow-up patients from a pre-MDT year (1983) is compared to three-year MDT period (1989,1990,1991) and its impact on various aspects of the disease-pattern are studied.

The observations reveal that the total clinic attenders per annum have increased (1983-332, 1989-480,1990-435,1991-440). PB leprosy has shown an upward trend(1983-48.2%,1989-54.0%, 1990-57.5%, 1991-58%)while MB has gone down. Childhood leprosy has nearly doubled and deformity rate has remained static. The most depressing aspect is that only 20% patients take treatment regularly. Number of patients coming from an endemic state have registered an increase from 14.1% to 31.3% showing a cause for concern in the matter of implementation of the MDT programme. The implications of these findings are discussed and a coordinated plan of action is suggested for effectively combating the problem of leprosy in these areas.

CO104

A TRIAL BASED ON PGL-I SEROLOGY FOR LEPROSY CONTROL. PRELIMINARY RESULTS.

Elba Gonzalez-Abreu and Angel B. Gonzalez.

Institute "Pedro Kouri", Havana, Cuba.

The trial area is the city of Trinidad, Cuba, and 2 other small neighbor villages with an estimated population of 46000 inhabitants. The number of leprosy patients registered on 31 December 1992 was 69 for a prevalence rate of 1.5 per 1000. Leprosy cases have been detected every year in the last decade. This city is being used as a pilot area to test a control strategy based on PGL-I serology which consists in performing serological tests by ELISA to the whole population above the age of 9 years as well as clinical examination, lepromin and bacteriological tests and follow-up of those showing anti-PGLI antibody levels above the cut-off value which was established at an O.D.=0.200. The administration of chemoprophylaxis to some of these individuals is included in the follow-up scheme. The interest in testing this strategy is based on the expectation of finding actual and potential M. leprae "transmitters" which would lead to an earlier administration of chemotherapy and of chemoprophylaxis and, in this way, to an effective cut of the chain of transmission. To date, 10848 individuals have been tested for PGL-I antibody. Of them, 660 (6%) showed O.D. readings higher than 0.200 and, among these, readings higher than 0.500 were observed in 43 (0.39%) individuals. Results of the serological tests performed on the whole study population as well as of the clinical examination, bacteriological and lepromin tests on seropositive individuals will be presented.

CO105

LEPROSY CONTROL PROGRAM IN SANTA FE PROVINCE, ARGENTINE REPUBLIC: RESULTS AFTER 30 YEARS

Victor Merlin, Adolfo Dalla Fontana, Silvia Paredes, Amira Lehrer and Mónica Recarte

Sanitary Dermatology Control Program, Santa Fe, Argentina

The Leprosy Control Program in Santa Fe Province was launched in 1962. A partial evaluation after 30 years leads to the following conclusions:

Epidemiological facts: (1) The geographical distribution is uneven, with major prevalence in the northeastern zone (6,6 per 10.000 population); (2) A

progressive decline in the incidence has been documented during the last 20 years; (3) Two facts have been observed in association with the falling incidence rates: an increase in mean age at onset (44/52) and an increase in the proportion of multibacillary forms among new cases (43%/64%); (4) There is a high proportion of cases (83%) without any antecedent of infective contact; (5) Intrafamiliar transmission is higher among consanguineous contacts. It suggests the importance of genetic factors; (6)The disease in the zone is not at all associated with poverty.

Operational features: (1) Selective integration is being implemented in highly endemic areas: (2) MDT has been introduced since 1982. The current coverage is about 45%; (3) A high percentage of cases is under private assistance (44%). This sector is not yet adequately integrated; (4) Case holding, defaulters retrieval, training of personnel and research have been so far the main activities of the Program; (5) Active case finding activities have been somewhat neglected and are still to be reorganized.

CO106

LONG-TERM EFFECT ON PATIENT DETECTION AFTER 30 YEARS OF LEPROSY CONTROL IN PREFECTURES OF TWO PROVINCES IN CHINA, 1980-1992

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Ran Shun-Peng, Wenshan Prefectural Institute of Dermatology, Yunnan 663000

Weifang of Shandong and Wenshan of Yunnan were highly prevalent for leprosy in the 1950's. Due to differences in geographical condition and socio-economic development, the decline of prevalence is 99.3% (0.9 - 0.006/1000) in Weifang and 93.7% (1.42 - 0.09/1000) in Wenshan; the decrease of detection rate during this period in Weifang is 99.9% (23.6 - 0.005/100,000) and 91.7% (69.9 - 5.8/100,000) in Wenshan. The endemicity of leprosy in Wenshan appears to be still in the level of 1960's of Weifang. The features of patients detected between 1980-1992 of these two prefectures will be presented, their differences and solutions discussed.

CO107

A BENEFICIARY STUDY OF LERPOSY SERVICES AMONG THE TRIBAL AND NON TRIBAL POPULATION IN THREE SELECTED DISTRICTS OF MADHYA PRADESH, IN INDIA

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The tribal population constitutes 7.7% of India's population. In the selected leprosy endemic districts the tribal population is 18.5% in Raipur,12.6% in Durg and 25.3% in Rajnandgaon. A beneficiary study of leprosy services conducted in the above three districts indicate that the prevalence rate of leprosy and Annual New Case Detection Rates are less among tribal community compared to the non-tribal community in all three districts. The awareness of both tribal and non-tribal community is good in general regarding curability of the disease, availability of the treatment at the nearest place, visits of the leprosy workers to the villages and activities undertaken by the workers in the villages. 80-100% of the patients are taking treatment regularly and 91-100% of the patients are living with their families. While level of leprosy awareness in general is slightly less in the tribal people in Durg & Rajnandgaon districts in comparison to non-tribals, this gap is wider in Raipur district.This may be due to intensive health education campaign conducted in Durg & Rajnandgaon districts by DANIDA assistance. Both tribal & non-tribal community members& patients have inadequate knowledge and awareness about cause of leprosy. Although majority of tribal and non-tribal people say Allopathy is the best treatment available for leprosy(84-100%), a small percentage of people still feel Ayurveda and Homeopathy as better remedy for leprosy.Women in tribal areas & girl students in both tribal & non-tribal areas are less aware about leprosy compared to the male groups of the same villages/schools.

CO108

SELF-ASSESSMENT TOOLS IN MONITORING OF LEPROSY CONTROL PROGRAMMES.

Henk Eggens

Leprosy Control Programmes collect, analyze and report with different purposes and in various manners. Most Leprosy Control Programmes stress reporting upward toward a higher hierarchical level. The new ILEP-B form and the proposed WHO-surveillance report are examples of reporting tools. In addition, importance should be given to methods of self-assessment of intermediate and peripheral levels of the Leprosy Control Programmes, for two main reasons: expected increase of management capability and improved quality of data collection.

Epidemiological indicators can be used (such as defined in the reviewed ILEP-B form), but also essential operational indicators, necessary to monitor programme support activities (such as logistics, training).

Self-assessment is done comparing indicator values of Leprosy Control Programme units (eg clinic, district, province or national level) in three ways:

1. With a set target or a range;
2. In time (comparing the unit now with earlier periods);
3. In place (comparing this unit with other units).

Self-assessment tools facilitate this comparison by forcing the transformation of data into interpretable information. Typically this implicates:

1: Transformation of data into proportions or rates. Where it is useful, proportions of targets reached are used.

2: Presentation of information in tables and graphs.

Possible standard formats are proposed, some of them to be used in conjunction with the current ILEP-B form. The inclusion of the use of these tools in management protocols is stressed.

CO109

ANALYSIS OF 1096 NEWLY REGISTERED CASES OF LEPROSY FOUND IN JIANGSU PROVINCE, CHINA

Ren Xianwu, et al.

Jiangsu Institute of Dermatology, CHINA

ABSTRACT 1096 cases of leprosy newly detected in Jiangsu province from 1983 to 1987 were analysed and compared with those from 1976 to 1979. The results showed that the incidence of leprosy during 1983 to 1987 decreased by 64.8% compared with that during 1976 to 1979, of which the proportion of lepromatous leprosy increased and the proportion of children declined . The early detection rate increased and the diagnosis level improved. Voluntary consulting,reporting by non personnel and consulting at the outpatient department for leprosy, the three ways became the main approach of case detection.The average interval between the time of making diagnosis and the time of starting treatment was eight days. 99.82% of patients accepted treatment, and stadium shortened. These data proved that the leprosy control activities in Jiangsu province were successful and effective.

CO110

FIVE-YEAR EVALUATION OF A PROGRAM OF CHEMOPROPHYLAXIS FOR LEPROSY USING A SINGLE DOSE OF 25 MG/KG RIFAMPIN

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In January-February 1988, a program of chemoprophylaxis for leprosy was implemented in French Polynesia : 2,786 (98.7 %) inhabitants of the Southern Marquesas, a remote archipelago, and 3,144 South Marquesan "emigrants" in other islands and their families were given a single supervised 25 mg/kg dose of rifampin within 4 weeks.

During the subsequent 5 years (February 1988-February 1993), 2 leprosy patients were detected in the treated population (instead of 8 expected patients if no chemoprophylaxis were given), the first, 4 months and the second, 21 months after chemoprophylaxis, respectively. In addition, a case of lepromatous leprosy was observed in a South Marquesan "emigrant" who had not been given prophylaxis because he was not known by the leprosy control unit.

During the same period, a decrease in detection rates for leprosy in the entire population of French Polynesia has been observed, which makes difficult the interpretation of findings. Nevertheless, according to our present data, the effectiveness of chemoprophylaxis with a single dose of 25 mg/kg rifampin may be estimated at 50 %.

Those results, and the financial and logistic constraints raised by such a program (in which entire eligible population could not be included despite careful preparation), lead us to conclude that chemoprophylaxis, even with a single dose of rifampin, cannot be considered for leprosy control.

CO111

THE REASONS WHY LEPROSY IS DIFFERENT IN ERITREA WHEN COMPARED TO THAT OF ETHIOPIA

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Leprosy in Eritrea is almost dying and we have very few patients when compared to that of Ethiopian patients. The indigenous leprosy patients in Eritrea are of majority lepromatous while that of Ethiopia are more of tuberculoid type of leprosy. The incidence of leprosy in Eritrea is 0.002/10,000 of the population and while that of Ethiopia is 0.9/10,000. In Eritrea no patient is discharged from treatment, but after completion of MDT the patients are put on dapsone monotherapy for life even the practice of keeping patients on the register did not increase the number of patients more than that of Ethiopia patients. The prevalence of leprosy in Eritrea is 0.04/10,000 and that of Ethiopia is 50/10,000 of the respective population.

Now Eritrea is facing the challenge of organizing a combined control programme of leprosy and tuberculosis in such a away that the programme will be integrated to the basic health services under the district health management.

The above points will further be discussed in detailed.

CO112

PREDICTIVE VALUE OF GELATINE PARTICLE AGGLUTINATION TEST (GPAT) IN LEPROSY CONTROL

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GPAT using semi-synthetic trisaccharide antigen (manufactured by FUJIREBIO INC,Japan and provided by WHO) has been applied to 1,030 apparently normal people, including 680 household contacts and 350 people living in areas exempt of leprosy .

After 4 years of following-up (1988-1992), some interesting conclusions have been made by the authors :

1.GPAT was positive in 20% of household contacts as compared to only 3.1% of apparently non contact people .

2.Among 135 household contacts showing positive GPAT, 17 have developed leprosy after 4 months to 3 years (12.8%), while among 884 people with GPAT negative, none (0%) has developed the disease during the same period .

3.Of these 17 cases, 16 (94%) belong to PB group (I, T, BT) . Only one case who had very strong reactivity has developed L type of leprosy .

4.In children under 15 years , a high title of antibodies constitutes a valuable indicator of high risk in developing the disease : 63.1% of them developed clinical leprosy within 3 years period, while it was only 7.7 % in adults .

5. 100% leprosy patients' children showing GPAT positive at serum dilution of 1:64 or over, have developed leprosy .

In conclusion, GPAT can be used in field conditions as a practical tool for early diagnosis and assessement of leprosy epidemiological trend, and also as an indicator for chemoprophylaxis .

CO113

PRELIMINARY EXPLORATION OF LEPROSY RELAPSE SURVEILLANCE WITH IMMUNOLOGIC ASSAYS

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This paper describes the use of serologic(GPAT,PGL-ELISA)and lepromin tests as a screening procedure for the detection of suspected cases, and for the follow up of clinical relapse. Since 1989, 1,658 cured cases were screened in Weifang Prefecture, Shandong Province and the combination of PGL-IgM (+) and lepromin (-) was assumed as a risk factor for relapse. The results showed the positive risk factor in cured casses was 24.6%(174/707) for MB and 3.9% (37/951) for PB. During 3 successive years of follow-up, it was found that the relapse rate of risk factor(+) was 9.8% (17/174) for MB and 16.2% (6/37) for PB.The total relapse rate of risk factor (+) was11.0% (23/211), whereas the relapse rate was only 0.28% (4/1447)in the 3 other combination groups.The relative risk of risk factor (+) was 39.5.

The result of screening reflects immunologic status in cured cases after chemotherapy.PGL-IgM level tends to subside and there is a ability to restore cellular immunity with the passing of years after cure in MB cured cases. The negative correlation between the levels of PGL-IgM and intensity of lepromin reaction suggests that the combination of these two tests may not only indicate the capability of eliminating M.Leprae but also provide a practical tool for screening cases in risk of relapse. The majority of cases with clinical evidence of relapse had high PGL-IgM. It is to be noted that 5/7 relapses had rising PGL-IgM in 3 successive years prior to relapse,whereas in PB relapses no rising of PGL-IgM level was detected. Hence, cured cases with high PGL-IgM level or rising PGL-IgM in successive years but without evidence of clinical manifestations should be monitored carefully in order to detect relapse early.

CO114

BASIC ELIMINATION OF LEPROSY IN SHANGHAI, CHINA

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Shanghai, the biggest city of China, covers an area of 6,185 square kilometers with a population of over a 12 million. By the end of 1991, the accumulative number of leprosy patients diagnosed was 5,424.Exclusive of those who died,migrated and lost of track, there were 3,136 patients who remained on the register, including only 29 active cases. The prevalence was reduced to less than 0.01‰ and the mean annual incidence of the period of recent five years was declined to less than 0.5/100,000 on county or district

bases since 1988 and were confirmed by experts from MOPH after their 10-day field evaluation.

In the past 40 years, under the leadership of the government and the support of the whole society, leprosy control programme has been implemented successfully and fruitfully in Shanghai by leprosy professionals at different levels. Systematic health education activities for the public, contineous training of health workers of different categories, early case detection through various methods and timely treatment of patients, including the provision DDS-cured patients with re-treatment with MDT, and development a well-organized health care network at different levels in particular, were main components of the comprehensive measures set up by leprosy control programme. Together with the improvements of the standard of living of the people and their health care services, the implementation of above mentioned comprehensive measures resulted in progressive reductions of prevalence, incidence and detection rates to 0.0023‰, 0.02/100,000 and 0.02/100,000 respectively in this big city at the end of 1991.

CO115

AN ANALYSIS OF 392 LEPROSY CASES NEWLY DETECTED IN 1985-1991 IN SOUTH-EAST PREFECTURE OF GUIZHOU PROVINCE

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In 1985-1991 392 leprosy patients newly detected in South-East Prefecture of Guizhou Province were analysed. Two hundred and fifty five of them were MB (LL 193, BL 30, BB 32) and 137 were PB (BT 20, TT 106, I 11), males 258, females 134, their age ranged from 6 to 78 (11 of them less than 14). One hundred and ninety seven cases(50.26%) detected had a duration of 2 years, 63.77% of them came from the villages which had leprosy patients previously and 86 of them from patients' family. Regarding the mode of case detection, 234 cases (59.69%), 86 (21.94%), 25(6.38%) and 47(11.99%)were found through or by clue survey, household contact examination, patients' neighbour examination and skin clinics respectively. The disability rates among newly detected patients were 30.6% (1985), 22.6%(1986), 21.6%(1987), 20%(1988), 18.51%(1989), 13.3%(1990), and 12.6%(1991). The authors emphasized the importance of; 1) not neglecting the population of non-focal villages because there were 132 new cases detected in the past 7 years; 2) intensifying health education to the general health workers and to the community to keep them more aware of early signs of leprosy.

CO116

EPIDEMIC AND CONTROL OF LEPROSY IN TIBET

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Leprosy is an old disease in Tibet. It has a long history of more than 1,400 years. From 1952 to 1991 there 3,491 leprosy patients were detected and 2, 160 cases were cured.By the end of 1991, the number of active cases was 868 and the prevalence rate was 0.4 per 1000 was one of the most high epidemic area in China at that time.

The distribution of leprosy in Tibet is not uniform. In the east and south-east parts of Tibet are high epidemic areas. In the north and west parts are low and/or non-epidemic areas. The other parts are middle epidemic areas of leprosy.

There are 72 counties in Tibet. By the end of 1991 there 33 (45.8%) counties had no active cases of leprosy and the leprosy was controlled in these counties. But there were 6 counties still in the range of high level of epidemicity and the prevalence rate was over 1 per 1000.

Since 1987 the multidrug therapy (MDT) recommended by WHO was implemented in the places of Tibet where leprosy patients had.By the end of 1991 the coverage rate of MDT was over 90% and the most of the patients were treated regularly.

The problems of leprosy control in Tibet are difficulties of transportation,lake of medical and financial resourses. Because Tibet has a area of 1.2 million square kilometers with a total population of 2.1 million. If these problems could be solved the possibility of basic eradication of leprosy in Tibet by the end of this century would be able to realize.

CO117

THE ANALYSES OF DELAY FOR 19472 LEPROSY CASES IN YANGZHOU PREFECTURE, CHINA

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The median of delay in 19472 cases is 1.9 year (23.3 years with 95% upper limit and 37.3 years with 99% upper limit). The shorter delay, i.e.median less than 2 year, is observed with the following case-finding methods: dermatological clinics, group surveys, contact examination,voluntary and notification.General surveys have the longest delay (median>5 years). The TT and LL cases have longer delay (>2.2 year) and BB shorter delay (<1 year).The delay in females (2.0 year)is significantly longer than in males (1.8 year, $0.05 > p > 0.01$).The results show that earlier case-finding may be important for prevention of deformities, ulcers and keep patients' ability to work. The older patients in 45 and 65 age group have the longest delay (>4.2 year). Recently the delay has been shortened.The cases detected in the first two years represent 80% of all cases and 99% of the cases detected within 10 years since 1985. The study suggests that the health education and popularizing knowledge of leprosy may improve case-finding in the early stages of the disease. At present more than 80% cases are detected by dermatological clinics, general hospitals and basic health units.As a consequence integrating leprosy control within general health care should be strengthened in order to detect more leprosy cases in the early stages. Case-finding can be accepted as early if a case is detected within 2 years of onset and if deformities are less than grade II.

CO118

HANSEN'S DISEASE AND ITS ELIMINATION

Maurice J. de Mallac

The term elimination enjoys, as it were, quite a Janus-faced perspective in the case of Hansen's disease. Thus, the decision of the 44th WHA attendant to "the global elimination of leprosy as a public health problem by the year 2000" bespeaks an 'outward' political pronouncement as strikes a familiar chord in line with the slogan "Health For All by the Year 2000" of the previous decade, grave doubts being, incidentally, entertained from many quarters as to the timely implementation of the latter.

As regards the 'inward' perspective, is one naive enough to believe that eliminating Hansen's disease in a given region from a public health standpoint would, by the same token, remove stigma, solve the magnitude of disability and/or deformity, facilitate the social re-insertion of patients in its integrality ?

The danger that the connotation elimination be taken at its face or 'outward' value is all there, while the 'inward' consequences of Hansen's disease be left to their own devices. Moreover, one cannot from an epidemiological view point speak of eliminating Hansen's disease when its control, the root and bark of the whole issue, demands that it be carried out to its all-round conclusions over, more likely, decades to come. Shouldn't it be more appropriate, then, to delete that rather misleading term elimination, since, however unwittingly, underpinning the central perception of Hansen's disease as underplaying the complexities of its realities as has been observed elsewhere ?

CO119

AN IMPAIRMENT SCORING SYSTEM

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For the purposes of evaluation of disability control activities in a leprosy programme it is important to monitor year to year change in levels of impairment in numbers of present and former patients in a district. In this paper an impairment scoring system suitable for the purpose is described.

Some uses of impairment scoring are:
1. To draw attention to inconsistencies in the recording of impairment and thus to any need for retraining of staff in recording skill. For example, staff may have illogically recorded that toes have regrown or that sensation lost for 20 years has recovered.
2. To identify any patients losing or regaining sensation or strength, and to monitor both the extent of change and the effect on nerve function of neuritis treatment.
3. To assess the effectiveness of self-care in patients with insensitive limbs through monitoring year to year change in the prevalence of wounds, cracks and bone loss.

Activities can also be scored, for example the category of protective footwear each patient is using at review or the duration and starting dosage of Prednisolone courses.

Examples are given of the application of impairment scoring in various countries and projects. A demonstration computer programme, based on scoring, is described.

CO120

EVOLUTION OF THE LEPROSY ENDEMICITY IN BENIN (1982-1992)

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4 : Association Française Raoul Follereau (A.F.R.F.).

With the generalization of new combined treatments (PCT), the leprosy endemy has been declining considerably since the 1980's, particularly since 1988. Recently (1992) the prevalence has been estimated at 0.22 p.1000 versus 3.18 p.1000 in 1986.
Presently 1,429 patients have been enrolled (MB: 39.7%, PB: 60.3%). Among them 8.6% are children under 15 year of age.
As far as case-finding is concerned, new cases have been increasing from 541 in 1986 to 1,023 in 1992, due to systematic active case-finding in the neighbourhood of MB patients. Among new cases, 23.5% are MB patients and 11.9% are children under 15.
New regimen is presently available within the whole country and coverage is 100% on Dec. 31, 1992.
Compliance to treatment is 95% and regularity to PCT 97%.
Integration of leprosy control activities in the primary health care structures has been achieved. All health agents have been trained or retrained between 1990 and 1992, thank to A.F.R.F. These two factors are responsible for the good results notified since the last 5 years by the national program of leprosy control.

CO121

LEPROSY AND CHILDREN: FUTURE PERSPECTIVES

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With the effective MDT programme for leprosy control in India the prevalence rates are declining. The child incidence rate appears to be high i.e. around 13 per cent of the total number of patients. Review of literature indicates a variety of issues involved in leprosy among children ranging from clinical, epidemiological, psychological and rehabilitation aspects.

With the time bound goal of elimination of leprosy as it affects children is of significance. The issues under discussion are : (a) case finding methods for approaching each and every school going and out of school child, (b) labeling of child cases in view of possibility of self healing leprosy in the context of social stigma, (c) ratio of PB & MB cases among children and its implications from control (d) primary health care approach and integration of case finding methods with other MCH services, (e) need for epidemiological studies, (f) role of NGOs, (g) problems of street children (h) social mobilisation.

Puolished review of literature and unpublished proceedings of a National workshop on leprosy and children in India will be presented.

CO122

LEPROSY CONTROL PROGRAMME IN LORETO REGION, PERU. OCTOBER 1990 - MARCH 1992

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The LCP in Loreto was reactivated in Iquitos (The capital city) and the provinces of Ucayali and Requena, while maintained in the province of Alto Amazonas.
Theoretical and practical training courses were delivered to health auxiliaries and 3 nurses in the region. An active search for leprosy patients started in Ucayali and Requena, combine the rural area nouse by house with local health personnel. Patients were treated with WHO recommended regimens.

A total of 22,338 persons were examined and 52 new leprosy cases were found, 20 PB and 24 MB. From these, 19 were from Ucayali, 18 from Requena, 9 from Alto Amazonas and 6 from Iquitos. Additionally, 62 old leprosy cases were readmitted to the LCP. Prevalence rates for leprosy were 4,5/1000 in Ucayali and 2,1/1000 in Requena. By the end of the period there were 324 patients under control (127 PB, 197 MB), 184 receiving treatment and 140 under surveillance.

The LCP in these areas has been reactivated and the active search has been performed by local paramedical health personnel (from the official health system), who additionally gave support to other health problems, within a Primary Health Care approach. According to WHO standards, observed prevalence rates for leprosy in these areas, represent a public health problem.
(These paper was financially supported by Red Barnet-Denmark)

CO123

SOME POINTS ON THE ELIMINATION OF LEPROSY

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To make it possible to monitor adequately the WHO Resolution to eliminate leprosy, some basic concepts and indicators should be further clarified.

1. **Prevalence.** In some MDT programmes, the reduced number of registered cases is not necessarily due to MDT. It is the result of removing from the registers those patients who had been cured but who, prior to MDT, had never been removed from the registers. The extent of this problem and its causes should be investigated.

2. **Distribution**. Because of the well-known uneven distribution of leprosy, it seems necessary to clarify the level of population to be used as denominator to monitor the decrease in prevalence and incidence rates (e.g. total population of a country? Only the population of endemic areas?).

3. **Incidence**. Decreasing incidence is the only true indication of progress towards elimination. Reports from a number of countries show declining incidences following MDT programmes. It is essential to assess the real impact of MDT and other factors in these situations.

The points outlined above will be discussed along with some other relevant issues (definition of cure, under detection of cases at the maintenance phase of MDT programmes, and problems in "difficult areas").

It should be possible to agree on standardized concepts and indicators to allow adequate monitoring of progress in the elimination plan. The demonstration of progress would in turn be a great stimulus for those engaged in this effort.

EPIDEMIOLOGY

EP1

THE STUDY OF APPLYING TWO-STAGE CATALYTIC MODELS TO COMPARISON BETWEEN LEPROSY AGE-SPECIFIC PREVALENCE RATES

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The Two-stage catalytic models can be used to simulate the distribution of age-specific prevalence rates of some infectious diseases and age-specific positive rates of some indicators, to measure their "force of infection" and "force of eliminiting disease". It is certainly significant for researching and evaluating the prevalent features of infectious disease and the effect of the disease control programme. In this paper the author uses an improved two-stage catalytic model(LogTCM) developed by the author which is transformed in an equation to simulate age-specific prevalence rates of leprosy in Yangzhou Prefecture in 1985 and to analyse the results in comparison with 1975.The results of the study confirm that the parameters "a" and "b" in the model represent the force of infection and the force of eliminiting disease respectively, by vertical section of leprosy endemic situation and leprosy control. By analysing and comparing the practical leprosy prevalence rates and the parameters of the catalytic model, it becomes clear that the prevalence rates are positivity related to parameter "a" and inversely related to parameter "b" and "k"(a/(a-b)). Catalytic models may be used to fit and analyse the epidemiological data in various periods,regions or populations.

EP2

EPIDEMIC SITUATION OF LEPROSY AFTER MDT IMPLEMENTATION AND PREDICTION OF BASIC ERADICATION IN YANGZHOU PREFECTURE

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Yangzhou Prefecture of Jiangsu Province was one of the former leprosy hyper-endemic area in China, which had once the highest prevalence rate of 1.88‰ in 1973. Since 1983, all the active cases were treated with MDT recommended by WHO.At the end of 1990, 1176(MB 621 and PB 555) patients have been treated with MDT. Through the comparative analysis of the theoretical endemic indicators of 1983-1990 calculated by the mathematical models of DDS mono-therapy (1973-1982) and the actual indicators, the results showed that the detection and prevalence rates after MDT were usually higher than the thoretical ones (difference between theoretical and observed values, $\triangle Y>0$) and $\triangle Y$ values declined significantly after 1989, moreover $\triangle Y$ was less than 0 in some counties. However, the incidence rates of leprosy after MDT introduction were lower than the theoretical rates calculated, which means the effect of MDT on epidemiology would be presented significantly in 5 years. The time trend of this area have been fitted with the exponential function models($Y=e^{a+bx}$) with $b<0$ and $R^2>0.8558$ except one county with R^2 of 0.6027.

Through the results the authors suggested that the short-term endemic situation of leprosy can be predicted using the mathematical models fitted by the complete date of past years. The prediction results showed that leprosy will be basically leradicated by 1997 in Yangzhou Prefecture.

EP3

MEASURING EPIDEMIOLOGICAL IMPACT OF MULTIDRUG THERAPY IN LEPROSY CONTROL AREA

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Given the increased acceptance of MDT and greater political commitment, there are great hopes that the transmission of leprosy could virtually be stopped over a period of time. However, the expectations have not been fully realised, perhaps because the epidemiological impact depends on several other host and environmental factors that need assessment and proper management.

MDT has been in vogue for over a decade in Gudiyatham Taluk (400,000 population) and its epidemiological impact is measured through annual screening of a sample population. Leprosy newly found among those normal in the previous year are labelled as incident cases and other new cases discovered in the area considered case detections. During the decade, deaths, births and migrations have resulted in qualitative and quantitative changes in the population under study. These have been carefully monitored and documented. Using actuarial methods and Cohort analysis, as well as linked cross-sectional data, the epidynamics of leprosy within geographically defined areas and time-trends in incidence of leprosy are determined and associated with relevant factors. After substantial initial declines, current rates are around 1/1000 with no further significant reductions. Possible reasons for this scenario and implications for future reductions are discussed

EP4

ASSOCIATION OF LEPROSY AND TUBERCULOSIS BETWEEN 1902 AND 1991 IN FRENCH POLYNESIA.

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From 1902 onwards, notification and lifelong follow-up of leprosy patients has been systematic in French Polynesia. Since

1960, notification of tuberculosis is mandatory. Leprosy case detection rates per 100,000 decreased from 50 in 1902 to 25 in 1959 and to 8 in 1991. Tuberculosis case detection rates per 100,000 decreased from 568 in 1960 to 25 in 1991.

From 1902 to 1959, 673 cases of leprosy were detected. Of them, 89 (13 %) died from tuberculosis. Mortality from tuberculosis between 1901 and 1930 was 21 %, and decreased to 8 % between 1931 and 1959. From 1960 to 1991, 350 new cases of leprosy were detected. Of them, 12 (3 %) developed tuberculosis.

From 1902 to 1959, mortality from tuberculosis occurred significantly more frequently in multibacillary patients (13 %) than in paucibacillary (4 %, Relative Risk (RR) = 3.2, $p = 0.003$). From 1960 to 1991, incidence of tuberculosis seemed more frequent in multibacillary patients (RR = 3, $p = 0.07$), whatever the sequence of detection of the two diseases.

Our study suggests that lepromatous patients share factors of susceptibility to mycobacterial diseases with patients developing tuberculosis.

EP5

THE APPLICATION OF OPTICAL MARK READER (OMR) TO CHINA LEPROSY SURVEILLANCE SYSTEM

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Computers have been widly applied to various domains. The first step is to input the data into a disk in order to rapidly process a vast amount of data. Up to now in many fields, data are slowly entered into the computer by hand. A slow input of data is not appropriate with the microcomputer may process them quite rapidly. It produces a bottleneck, which makes the use of the computer irrelevant. The application of Optical Mark Reader (OMR) to input data is a way to solve this problem. The China Leprosy Surveillance System uses the OMR to enter the data of leprosy cases. It is a good start in order to solve this problem. The data of leprosy cases must be coded in a set of number "0-9" and the codes of each item have to be located on the special form for leprosy case in blank marks. While the different forms are automaticly passed the gap in the reader of the OMR, the codes of data can be read by the sensors in the reader and then are transferred into computer in a character string. Soon afterwards the string are divided into many parts and sent to different databases as fields by programme control. In this way to input data are processed more rapidly and more accurately. One form takes only a second, more than 6 000 forms can be processed per day, and the reading error is below 1/1000000 marks. The method of inputing data with OMR provides a powerful tool to input a large amount of data not only in leprosy epidemiology, but also in other fields.

EP6

A TWENTY YEAR FOLLOW-UP STUDY OF INCIDENCE RATES OF LEPROSY IN DDS PROPHYLAXIS AND CONTROL GROUPS

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DDS was believed to be a good prophylactic tool around 60's & 70's. 2 Experiments were conducted in India to assess this. During 70's & 80's, a few studies suggested that DDS has inhabitory effect on CMI.

The author has analysed the post-prophylactic data of incidence rates during last 20 years in the project of Gandhi Memorial Leprosy Foundation where DDS as prophylaxis was given for 8 years to 1 group of 9200 (L), for 4 years to 8829 (L.W) and 18674 (W) were kept under placebo. The analysis was done to assess whether DDS exerted any prophylactic value or was inhibitory to CMI.

In the 20-year period, 153 cases occured in L (mid-term population 5120), 171 in L-W (5361) and 354 in W (11103) groups. The respective cumulative incidence rates were 29.8, 31.8 and 31.8. No significant differences were noticed in incidence rates. DDS did not seem to have either prophylactic value or inhibitory effect on CMI.

Further detailed analysis of age-type occurance, deformity & relapse rates and responses to treatment were made and discussed.

EP7

LEPROSY AND HIV IN TANZANIA

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Association between TB and HIV is well documented in Tanzania. A TB/HIV study was conducted between 1992 and 1993 during which time all available new leprosy patients were tested for "HIV" virus, as control.

Over 300 leprosy cases were studied from some 12 Regions. The results were compared with existing blood donors or antinatal mothers blood samples as well as with the TB patients blood.

The paper will present the results and discuss implication of HIV with regards to leprosy in Tanzania. Preliminary results so far shows however no significant difference between leprosy and blood donors / antenatal mothers. Detail analysis might show some difference. This will be reflected in the details and paper discussions.

EP8

THE EPIDEMIOLOGY OF HANSEN'S DISEASE IN THE ENGLISH-SPEAKING CARIBBEAN AND SURINAME: CURRENT STATUS AND TRENDS

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Hansen's Disease is still endemic in some Caribbean countries. This paper documents the current epidemiology of Hansen's Disease in 19 countries which are served by the Caribbean Epidemiology Centre. According to World Health Organization guidelines, based on estimated prevalence, this disease can currently be considered a 'public health problem' in two of these countries: Suriname and St. Lucia. In other words, their populations can be considered to be at significant risk of infection. However, there is uncertainty regarding the amount and sensitivity of case detection in the other countries. Active transmission is still occurring, evidenced by the continued detection of new cases aged less than 15 years. Patients are still suffering disabilities due to lateness of diagnosis and treatment. Thus, in pursuing the goal of leprosy elimination in CAREC member countries, the definition of elimination and the steps taken to attain the goal will require careful deliberation.

EP9

LEPROSY AND SOCIO-ECONOMIC DEVELOPMENT : BETWEEN AND WITHIN COUNTRY COMPARISONS

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Leprosy disappeared from Northern Europe before effective chemotherapy was available, probably as a result of social, economic and environmental improvements. The current downward trend in the occurrence of leprosy in some rapidly developing countries may also be the result of socio-economic improvement as well as due to the impact of chemotherapy.

Current leprosy data and socio-economic, health, education and population data from 158 countries has been analysed. Significant correlation is noted between leprosy prevalence and incidence, and many socio-economic indicators. The relationship is log-linear and such that, for example, no country with a Gross National Product of more than US$5500 per capita has a leprosy prevalence of greater than 4 per 10 000. MDT coverage is correlated with leprosy prevalence but shows no relationship with incidence. A similar analysis within Malaysia has shown MDT coverage to be related to leprosy prevalence but not to incidence, however housing standards were closely related to incidence.

These between country and within country analysis demonstrate the relevance of socio-economic development to the decline prevalence and incidence of leprosy.

EP10

STUDIES OF TRENDS OF HANSEN'S DISEASE IN BRAZIL

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The study of trends Hansen's Disease in Brazil has been used to assess the endemy's evolution and estimate targets for the annual programming of control activities.

We used the historical series of detection rates for the country, the macroregions and each unit of the federation, from 1973 to 1992, applying the exponential adjustment method. For each region, we built three curves of the endemy's trend, corresponding to the periods 1973-1981; 1982-1992; and 1973-1992.

The authors discuss the influence of operational factors from the Programme for the control and elimination of Hansen's Disease on the results shown and the validity of using these curves in assessing the endemy's evolution in the country.

EP11

EVOLUTION OF THE LEPROSY DETECTION RATE IN ANJOUAN (COMORES) FROM 1981 TO 1992

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Intensive case finding and combined treatment regimens for all patients were introduced in Anjouan in 1981. The mean yearly detection rate (not taking into account the unknown increase in population) during successive 4 year periods was for 1981-84: 9 per 10.000, for 1985-88: 4.8 and for 1989-92: 5 per 10.000. The MB rate during the same periods was 20, 34 and 30 respectively. The % of children (< 15 yrs) at diagnosis among PB declined from 57 to 52 and 49; among MB it was 23, 30 and 13. The disability rates at diagnosis decreased 10 fold. However, between 1989 and 1992 the yearly detection rate declined steadily from 6 to 3.8/10.000. These figures together with the decrease of the proportion of leprosy in children may indicate that after 10 years of intensive antileprosy activities the incidence of the disease finally declines.

EP12

LEPROSY PREVALENCE IN RUSSIA

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In 1992 in Russian Federation (population - 150 million) 1104 cases of leprosy were registered. Additionally, about 100 patients from other countries of CIS also received multidrug therapy in Russia.There are 4 leprosy centres for approximately 500 beds, responsible for outpatient treatment, post-treatment surveillance and other activities on leprosy control. Among the patients 34% are males and 66% are females. The patients aged over 50 years old prevail. In 1961-1965 on the whole Russian territory in average 73 new leprosy cases were registered annually,and for the last five years' period of 1986 - 1990 - only six new cases per year. Multibacillary forms prevail (56%0).Formely the Lower Volga and some territories in the North Caucasus as well as Yakutia in Siberia were considered as leprosy endemic foci. Sporadic leprosy cases were found out throughout the whole country. In nowadays only Astrakhan region (population - 1 million) situated in the delta of the Volga is of epidemiological significance: here 550 cases are on the register, i.e. 50% of the total amount of leprosy patients. In the south of Russia, excepting Astrakhan region, another 400 cases are registered, and there are totally 150 cases in central, north and eastern regions. Retrospective computerized analysis of the annual rates of leprosy prevalence, incidence and mortality suggest that provided the trends found out have retained,by 2000 epidemiological situation in Russia will remain unchanged.

EP13

LEPROSY IN THE FORMER USSR

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Leprosy was never a major problem of public health in the former USSR. The highest number of leprosy cases was registered in 1964 and equaled 7436 patients. In the period of 1950-1964 annually 250-600 new cases of leprosy were registered. Sulphones were implemented into the practice of leprosy treatment in 1952 in the USSR. In 1970 chemoprophylaxis of contacts of multibacillary leprosy patients was introduced.Since the middle of 1960 leprosy incidence has been continuously declining. In 1990 only 15 new leprosy cases were registered. For the last 50 years over 20 governmental decrees and guidelines on leprosy control have been issued. On the begining of 1991 in the republics of the USSR 3976 leprosy patients were registered: Russian Federation - 1152, the Ukraine - 75, Byelorussia - 2, Kazakhstan - 1185, Uzbekistan - 1003, Tadjikistan - 166, Turkmenistan - 141, Kirgizia - 33, Azerbaijan - 104, Armenia - 40, Georgia - 21, Moldova - 6, Latvia - 22, Lituania - 1, Estonia - 25. There are 12 antileprosy centres where 974 cases were treated as inpatients and 1576 - as outpatients (the rest 1426 patients were under surveillance). With desintegration of the USSR active case-finding, survey and treatment activities have worsened, but Leprosy Research Institute is trying to avoid a severance of professional relations between leprosy centres. Today's economic hardships adversely affect the care of the patients and surveillance of leprosy contacts and every efforts are required to escape worsening epidemiological situation.

EP14

10-12 YEARS FOLLOW-UP OF HEALTHY CONTACTS OF LEPROSY CASES USING FLA-ABS AND LEPROMIN TESTS

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In leprosy, the risk factors and course of the disease in the healthy contacts is not known with certainty. At CJIL, Agra more than 1000 healthy contacts of different types of leprosy patients attending the OPD of the Institute have been followed-up for 10-12 years. Their initial lepromin status and positivity for M.leprae specific antibodies by fluorescent antibody absorption test (FLA-ABS) was recorded. During this follow-up of more than a decade, a large number of contacts have developed disease ranging from tuberculoid to lepromatous types. Various risk factors including the predictability to get disease either using FLA-ABS, lepromin alone or in various combinations has been statistically evaluated. Analysis of the results indicates that FLA-ABS test is a very sensitive test for monitoring the subclinical infection in the community specially the childhood contacts. It was also observed that by the combination of FLA-ABS and lepromin tests, the relative risk can be better predicted than using these tests alone. The contacts with initial FLA-ABS positivity and lepromin negativity were found to be at significantly higher risk in compared to other groups. FLA-ABS positivity was observed to appear before lepromin responses in many childhood contacts and is thus a more sensitive method for detection of subclinical infection in this age group.

It is concluded that FLA-ABS test is a highly sensitive test which can be used for monitoring the transmission of disease. Alongwith lepromin testing, this can be used for detecting the contacts at higher risks of developing the disease.

EP15

A SEREEPIDEMIOLOGICAL STUDY OF LEPROSY IN HOUSEHOLD CONTACTS AND HEALTHY POPULATION BASED ON ELISA USING ND-O-BSA AND PGL-I AS ANTIGENS

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Using the ELISA assay of detecting antibodies to ND-O-BSA(A-ND)and PGL-I(A-PGL), a seroepidemiological study of leprosy was carred out in 723 leprosy household contacts(HCP), including 1632 healthy persons in endemic areas (EHP)in Yunnan Province and 131 healthy persons in nonendenic area (NHP). The seropositive criteria were identified by EHP and NHP respectively, namely EHPC and NHPC. For A-ND and A-PGL, EHPC were 0.23 and 0.225, NHPC were 0.14 and 0.17. According to NHPC, the seropositive rates for A-ND and A-PGL were 20.19% and 15.21% for HCP, 15.13% and 9.38% for EHP, presenting a significant difference between HCP and EHP for both antibodies. According to EHCP, the seropositive rates for A-ND and A-PGL were 6.36% and 8.44%, respectively. Among the three groups of populatioon, the mean antibody levels were not significantly different between HCP and EHPC, and significantly different between others. According to NHPC, the relative risk (RR) of HCP and EHP were 4.04 and 3.02 for A-ND positive, and 3.04 and 1.88 for A-PGL positive. According to EHPC, RR of HCP were 1.27 and 1.88 for A-ND and A-PDL. The results of the study suggested that the detection of antibody was a useful tool for epidemiological research, but was questionable as a serological tool for early diagnosis of leprosy.

EP16

STUDY ON LEPROSY SERO-EPIDEMIOLOGY IN CHINA

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We reported the results studied by sampling survey on leprosy sero-epidemiology in different provinces in China. The provinces selected were: Jiangsu (Baoying, Gaoyou), Shaanxi (Chenggu, Giyuan), Hunan(Chengbu, Shangzhi), Hubei(Tianmen, Jianshi) and Liaoning(Benxi). A sum of 5,861 samples, including household contacts(HC)1,083, matched random population(MR) 452, random population(RP)3,171 and normal controls(NC)380 from endemic area and non-endemic area for leprosy (ENC 95 and NNC 285). The above samples, except those using Ms-ELISA in Benxi, were all detected by PGL-I-ELISA for antibody against PGL-I.

The results indicated that:

1. cross section studies: 1)The order of positive rates (PR) was HC>MRP>RP>ENC>NNC; 2) Ig level increased gradually from that of HC to that of LL, but in BT≈TT, IgG>IgM and in LL≈BL IgM >IgG; 3) PR was 29.1% in the group aged 15-25 more than those in the other age groups and was higher in HC contacted with MB than in those contacted with PB, and the PR were relative to blood relationship and type of index cases contacted and so on.

2. longitudinal studies: in weakly positive HC, a minority of them, antibody level became strongly positive, a majority of them—negative, in strongly positive cases, there were no case who turned to be negative and two of them have developed clinical leprosy(BT and BL). In 19 cases of them (lepromin test $-\sim\pm$), except those with increased antibody levels, AFB in blood or skin smear have been found in some cases.

EP17

DETECTION OF LEPROSY INFECTION BY SEROLOGY AND POLYMERASE CHAIN REACTION. AN EPIDEMIOLOGICAL STUDY IN SOUTH SULAWESI, INDONESIA.

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A population based study was carried out in two adjacent villages in South Sulawesi, Indonesia. The prevalence of clinical leprosy was 10.0 per thousand inhabitants. A total of 1015 serum samples were examined. IgM antibodies to phenolic glycolipid-I (PGL-1) were demonstrated by the gelatin particle agglutination test (MLPA) and by indirect ELISA test. PGL-I-IgG and Lipoarabinomannan-B (LAM-B) antibodies were measured by indirect ELISA. IgM antibodies were present in 32 % of the population, with the highest prevalence in the younger agegroups. The seropositivity rates in females were consistently higher than in males. PGL-I-IgG and LAM-B antibodies were found in 6.7 and 11.6 % of the population respectively, and no age related pattern was observed. There was no difference in IgM and IgG seropositivity between household contacts of leprosy cases and non-contacts. Nasal swabs from 1228 persons were examined by polymerase chain reaction (PCR). The presence of Mycobacterium leprae was demonstrated in 7.8 % of the swabs. No relation was found between the PCR and the serological results.

EP18

SPATIAL ANALYSIS OF THE ORIGINS AND RISKS OF ARMADILLO LEPROSY.

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Nine-banded armadillos are highly endemic natural hosts of leprosy but the origin of their infection and risks they present to man has been unclear. In addressing these issues we've examined nearly 1400 armadillos from across the southern US and elsewhere using histopathology, PGL-1 serology, and PCR for a 360 Bp *M. lepraespecific* DNA fragment. Leprosy is absent among those US armadillos that arose as a segregated population in the state of

Florida but it is widely distributed among all others. There are no directional trends in its prevalence distribution that might suggest a nidus. Leprosy appears to be indigenous to armadillos. Both the detectability and transmission of armadillo leprosy appear to be affected by the environment. Antibody prevalence rates are highest in low lying habitats and average 15%. In regards to man, a review of US registry data since 1894 indicates that familial contacts have been the principle source for leprosy transmission. But analysis of recent patient histories in Texas, Louisiana and Florida suggest that contact with infected armadillos is an increasingly important associable risk factor. Leprosy remains rare among US citizens, but contact with armadillos may be a factor in its persistent low incidence in this country and armadillos can be useful models for studying environmental variables in leprosy transmission.

EP19

INCIDENCE RATES OF LEPROSY DECLINE WITH INCREASING DURATION OF SCHOOLING AND WITH IMPROVING STANDARDS OF HOUSING IN KARONGA DISTRICT, NORTHERN MALAWI

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Although factors related to the poverty complex have long been postulated to be risk factors for leprosy, detailed relevant data are scarce. Confirmation of an association might clarify mechanisms of *M. leprae* transmission, and even provide a target for control programmes. We studied incidence rates of leprosy in more than 80000 individuals in Karonga District, Northern Malawi, followed for an average of five years. Leprosy rates were inversely related to increased duration of schooling and to improved standards of house construction as defined by data collected at the start of the study. Examination of these trends within strata defined by age and sex and adjusted for prior BCG vaccination suggested that the association with housing was a function of living conditions in early, rather than later, life (although confidence intervals were wide). Implications of these results for the natural history of leprosy will be discussed.

EP20

NEW SIMULATION MODEL FOR PREDICTING INCIDENCE AND PREVALENCE TRENDS IN SEVAGRAM AREA OF DISTRICT WARDHA - MAHARASHTRA - INDIA

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Epidemiometeric models are useful tools for studying dynamics of disease in populations. Simulation model that is used in this paper has been developed newly, with the Data from Sevagram Leprosy Control Unit,District Wardha in State of Maharashtra, India, run by Gandhi Memorial Leprosy Foundation. It was assumed that man is the only source of infection and natural events such as death, migration and birth have been considered in the model.The data is collected for the annual status of each individual that existed in the Unit anytime between follow-up period from 1952 to 1990 and followed up through annual surveys under SET plan. From this well coded data annual transit probabilities for changes of status of individuals from one year to next year are calculated annually. The probabilities were simulated on a cohort of population classified for sex. This generated sex specific incidence and prevalence rates, from 1952 to 1990. The mathematical eguation based on experience of rate from 1952 to 1990 would be used to predict trend of Leprosy in the area.

EP21

EFFECT OF NATURAL DEMOGRAPHIC CHARACTERS ON INCIDENCE OF LEPROSY - A CASE STUDY.

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The data is maintained in Sewagram Leprosy Control Unit of District-Wardha in Maharashtra India through annual surveys for leprosy .

Of the twentyseven villages the data from one village in Sewagram Leprosy Control Unit for over a period of 40 years is collected on the natural demographic characters such as death, emigration and immigration, birth both for population and cases of leprosy. Same is analysed as a case study in this paper to find out the effect of these natural forces pertaining to population and existing cases on incidence of leprosy with a further view to 1) estimate relationship between increase in population and incidence of leprosy ,
2) compare the effect of natural forces on general population and case of leprosy,

3) compare incidence in original population that existed in first survey of 1952 followed up over 40 years and that in subsequently added population.

Both age and sex composition of population is considered to establish effect of these factors also.

EP22

ANALYSIS OF FACTORS AFFECTING LEPRA EPIDEMIC WITH STEPWISE REGRESSION MODEL

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The basic data were taken from the records in Bose Prefecture of Guangxi from 1956 to 1992, with lepra morbidity (y_1) and case rate (y_2) as dependent variables, the per capita gross value of industrial and agricultural production (x_1), per capita national income (x_2), proportion of agricultural population (x_3), proportion of public health personnel (x_4), average annual temperature (x_5) and average annual rainfall (x_6) as independents. Multiple regression model of y_1 and y_2 were built with stepwise regression method, respectively. The simple correlations between each variable and independents in the model were analyzed. It is illustrated that population, economy and air temperature have effects on lepra epidemic in varied degrees, among which x_4. X_2 and x_3 have greater effects on y_1, x_1 and x_3 have more obvious effects on y_2.

Key words: Multiple regression; stepwise regression; partial regression coefficient; morbidty; case rate.

EP24

THE ANALYSES OF LOGISTIC REGRESSION FOR 593 MB CASES WITH WHO MDT OR MODIFY MDT IN YANGZHOU PREFECTURE, CHINA

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Five variables of the AGE at beginning MDT, SEX, delay(DL), treatment regimen(TR) and delay of treatment(DLTR) from detection to beginning MDT are used in the analyses of logistic regression. Ages are divided into 3 levels: <=35, 35-50 and >50, sex with 2 levels: male and female, DL with 2 levels:<=2 and >2 years,TR with 3 levels: Old MB (treated with DDS before) and New MB (never treated before) with WHO MDT, and MB with Mod MDT (modify MDT: local MDT), DLTR with

3 levels:<=2, 2-10 and >10 years.The cured time is a dependent variable which is divided into 2 levels: <=3.6 (median of cured time) and >3.6 years. The results in single factor show that above 36- age group has high Odds 1.666 in comparison with young age group (Odds = 0.6002), differences between males and females (males Odds=1.188), and delays (<=2 year Odds=1.0815) show no significance (p>0.05). Mod MDT has the highest Odds 4.2533 compared with New MB (Odds= 0.20) and this indicates the longest time to cure. The cases in group of 2-10 year delay of treatment has an Odds 2.280, but DLTR less than 2 year indicates the lowest treatment efficiency(Odds=0.255). In multiple factors, the male MB with Mod MDT in medial age group has the highest Odds of 3.580. It means that the cases in the group have the shortest cured time in median in contrast to New MB cases in young age group with WHO MDT(Odds=0.3237).

EP25

TREND OF LEPROSY DURING THE MDT ERA

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The known facts about leprosy are that: 1) the only known source of infection is a case of leprosy; 2) the mode of transmission in leprosy is unclear; and 3) the incubation period is long i.e. 2 to 5 years or more. In the absence of any primary prevention measures, it becomes obvious that the only possible area of intervention is by attacking the known source of infection i.e. a case.

S L R T C Karigiri, in Gudiyattam Taluk, (population 570,000) has been implementing a leprosy control programme, with intensive case finding activities, since 1962, with Dapsone monotherapy; MDT was introduced in 1982. In such a situation, one would expect a reduction in new cases of leprosy in the community. This has reduced the workload considerably, in terms of treatment delivery.

However, Incidence Rates reveal a slow decline over ten years, while the New Case Detection Rates among the various sections of the target population show a minimal reduction. The available data suggest that the quantum of disease transmission in the community has not changed appreciably.

EP23

THE ANALYSES OF STEPWISE REGRESSION AND INDICATORS FOR REFLECTING LEPROSY DECLINE IN YANGZHOU,CHINA

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Total 19478 cases have been detected(1949-1990) in Yangzhou Prefecture located in East of China with 9 200 000(1990) population. The aims are to explore the relationship between some indicators and leprosy epidemiological trends as well as to identify the most important indicators for monitoring leprosy decline. The methods consist in a stepwise regression using 35 independent variables which are divided into two categories : registered and retrospective variables (the date of onset according to patients' complains), and 4 dependent variables : retrospective incidence rate, retrospective prevalence rate, registered prevalence rate,detection rate. The results show that the most important indicators with high significance(F test:p<0.0001) are: registered prevalence rate, detection rate, mean age at detection or onset, the proportion of cases at<=14 age in total new cases, the median of delay,cured number in current years, the proportion of MB in registered cases,the proportion of cases with disabilities (II/III) at detection or in registered cases, prevalence rate, incidence rate. In order to calculate these indicators, the following data should be collected: sex, date of birth,date of onset, date of detection,date of beginning MDT, date of completed MDT, date of cured, date of relapsed, type of leprosy, disabilities grade and population in the area.

EP26

STUDY OF LEPROSY IN CHILDREN IN MULTI DRUG THERAPY IN BHARUCH DISTRICT GUJARAT INDIA

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Multi-drug therapy project commenced since 1st March 1989 with financial colloboration of Government of India and W.H.O. Total no of patients brought under MDT till December 92 are 11447 (4513 old active area + 6934 new detected cases) No of child below 15 years detected between commencement of MDT and till Dec. 1992 are 1378,(12.01%), of which 187 (13.57%) are M.B. and remaining 1191 are P.B. (86.34%). Amongst P.B. most of the cases were indeterminate and tuberculoid.

Child incidence rate& childhood rate are one of the most vital epidemiological parameters for impact of MDT for leprosy control. These parameters are studied in relation to prepratory, intensive and maintenance phase of MDT. The study showed that child incidence rate which was at commencement of MDT was 21.19% and after 3 years of intensive face in the year 91-92 which increased to 28.9% Childhood rate in the year 1988-89 in prepratory phase was 16.25% and it was increased to 23.89%. in the year 91-92.

The other vital epidemiological parameters e.g. the deformity rate, MB rate Bacteriological conversion rate, Age sex and cast factors will be presented.

EP27

AN ANALYSIS OF THE INCIDENCE OF LEPROSY FOR LEPROSY CONTACTS AFTER MDT IN LIANGSHAN AND PANZHIHUA PREFECTURES, SICHUAN PROVINCE

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MDT has been successfully implemented in Liangshan and Panzhihua Prefectures for 5 years. Two-hundred-twenty-five new leprosy cases were detected among the leprosy contacts from 1987 to 1991; 131 of them were HC of MB 12 were HC of PB,and 94 were non-HC; the ratio for risk for MB HC, PB HC, and non-HC being 13:3:1. The case detection rate gradually reduced annually in the above three kinds of contacts. The annual average declining speeds were 29.9%, 41.1%, and 40.2%, respectively. Both age at onset of disease and proportion of MB among the newly detected cases were obviously increased year by year. The results of the epidemiological analysis indicated that MDT was very effective in interrupting the source of infection and in decreasing the incidence of the disease.

EP28

THE PROTECTIVE ROLE OF BCG IN HANSEN'S DISEASE

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All studies carried out to evaluate the effectiveness of BCG on Hansen's Disease have demonstrated a statistically significant protection, in spite of variations among the different populations. Recent studies have confirmed this protection, particulary againts the multibacillary forms of the disease.

This paper presents a survey of the past 21 years in the Pernambuco State Central Hansen's Disease Register. Data were grouped by age, sex, and clinical form. Among these, 192 Hansen's Disease patients born since 1971, when ID BCG against tuberculosis was implemented, were examined.

The next phase of the study was the application of a statistical model to the collected data, studying the relationship between vaccine status and age, clinical form, and HD contact.

EP29

THE LEPROSY IN ALGERIA.

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Leprosy is not a problem for public health in Algeria. For one century (from 1888 to 1987) a maximum of 259 cases were reported, 25 only of them were algerians, and 51 caught the disease in Algeria.

In july 1988, a couple from Tlemcen (West Algeria) and living in Mali, came to our service for consultation for the same type of lesions, non pruriginous achromic spots of 0,5 cm of diameter. These lesions reside on the forearms, the legs and the feet. A biopsy of an injury was practised and the histological examination shows the presence on the derm of perianexial and perivascular discret infiltratis made of histiocytary cells with clear cytoplasm. The aspect is compatible with an indeterminate leprosis. Although the Hansen's disease is not a problem for public health in Algeria, the geographic situation of the country (several neighbouring countries) imposes a continnous surveillance, because of multiple exchanges with the neighbouring countries where there is a high leprous endemicity .

EP30

THE ACTUAL STATE OF LEPROSY IN THE BALTIC STATES

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The Baltic States, which until recently were republics of the former USSR, are now independent states.
This fact permitted the possibility to conduct research into the situation of leprosy after the political change.
The actual presence of leprosy will be demonstrated by overhead slide- projection.
Of the three Baltic States only Lithuania is free of leprosy at present, while in Latvia as well as in Estonia leprosy is endemic.
Diagnostic as well as therapy of leprosy were influenced by the political an economic situation of the former USSR.
Contacts with leprologists abroad were not possible. The only very limited possibility of continued education, advanced training, and research existed in Astrakhan (in the south of the USSR).
In Estonia a "prophylactic therapy" was executed. The sociological problems of the patients are aggravating. The clinical picture of leprosy with complete statistics will be presented.

EP31

The Relationship between Leprosy Incidence and Economic Development

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Abstract

There was a problem puzzled us for a long time when we tried to find out the environmental factors that influence leprosy incidence , why leprosy in Norway was exterminated before any special anti-leprosy drug was found and why high leprosy incidence always occurs only in poor-economic area . In Guangzhou area , leprosy incidence is greatly decreased in past ten-odd years along with steadily economical development. Although multi-drug treatment (MDT) is used in recent years, it is important for curing active patients , but it is not important for influencing leprosy incidence . We took the regression analysis between economy and leprosy incidence on the basis of data from 1981 to 1989 , the result is satisfied . The relative coefficient R reaches 0.9429 for the logarithmic model with examining value p($r=0.9429 > r_{0.05}=0.798$) =0.01 (n=8) . With this model, we made a prediction, showing that leprosy incidence will decrease to below 0.5/100,000 by 1998 in Guangzhou area according to economic development trend and goverment plan . Our research maybe also suggest that it was along with economic development in Guangzhou area that leprosy will be exterminated in near future just as a Chinese saying "daybreak will be coming whether cock call it or not".

EP32

MICRO LEVEL ANALYSIS OF LEPROSY IN VADODARA DISTRICT

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Leprosy is a widespread in the rural areas of India with hardly very few districts in the country being free from this disease. With the introduction of MDT in Vadodara district, the prevalence rates show a declining trend. However there are still pockets of high prevalence that form the focus for the spread of the disease. The continuance of the disease in this areas is a result of various socio-cultural factors. The present study is an attempt to analyse the behaviour of the disease at the micro level with a view in preparing strategies for the total elimination of this disease.

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EP33

AN ANALYSIS OF FAMILIAL CLUSTERING OF LEPROSY INFECTION USING THE MODELS OF THEORETICAL PROBABILITY

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A total of 1,522 samples from 435 families in two leprosy-endemic counties within Yunnan Province of China were tested for anti- M.leprae antibody based on ELISA using ND-O-BSA as antigen.

For the purpose of the epidemiological analysis, the 95% percentile value of OD (0.14) from the samples of healthy population was defined as the operational breakpoint OD value for leprosy infection. The distribution of leprosy infection in families was analysed using the theoretical models of Possion, negative binomial and logarithmic distributions, respectively. The results showed: that 1)in the different age groups, the introducing rates had significant difference (P=0.007) and the highest rate was 42.22% at 20-30 years of age, which indicated that the family members at this age were most likely to bring the infection into their families; 2) the actual distribution of infection in families was consistent with the negative binomial and logarithmic distributions, but not with the Possion one, which showed that the leprosy infection was significantly clustered in families. In this paper, the implications of these results for the epidemiology and control of leprosy in population, especially in families, were discussed as well.

EP34

EPIDEMIOLOGICAL SURVEY OF LEPROSY IN YICHUN PREFECTURE OF JIANGXI PROVINCE, CHINA

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Based on the related data available about leprosy patients registered in the past 30 years, an epidemiological survey was carried out in 10 counties of Yichun Prefecture, Jiangxi Province in 1990. The results of this survey showed that the prevalence rate was 0.083‰. The lepers detected mainly lived in the plain regions along the railways and rivers and in the area around the cities and towns, distributed in clusters. Frequency distribution of lepers in those villages appears Negative Binomial distribution instead of random distribution. Aggregation exponent K was 0.7278. There was a significant difference between prevalence rate and population density (P <0.05) and the linear regression equation was y=33·3638x-237·04.

EP35

PROFIL EPIDEMIOLOGIQUE DE LA LEPRE EN HAITI

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Les auteurs etudierent les differents parametres epidemiologiques de l'endemie lepreuse au niveau de deux centres de reference en Haiti.

EP36

HANSEN'S DISEASE IN CHILDREN IN THE STATE OF AMAZONAS, BRAZIL, 1980 TO 1990

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Amazonas has high rates of detection and prevalence for Hansen's Disease, showing that this condition is a major public health problem in the State.

The authors discuss the disease's epidemiological behaviour in children under 15 years of age, using the historical series of detection rates from 1980 to 1990 and other indicators for this age group.

EP37

THE DWELLING AT THE SITE OF LEPROSY TRANSMISSION.

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In areas with higher prevalency of leprosy quality of life for the most part of the population is below recommended standards, with inadequate health services and poor sanitary conditions. This papers analyses the contribution of several characteristics of dwellings and households to the definition of leprosy. Dwellings with diagnosed cases of ilness are compared with randomly selected dwellings located in the same urban area, in the outskitrs of the Metropolitan Area of Rio de Janeiro. The paired analysis of patients with their neighbors revelead an association with age and educational level as a measure of socioeconomic status. In the group of dwellings and households distant form the focus area, age and type of house are the probable differencial factors in relation to dwellings and households with diagnosed cases of leprosy. The dwellings is a fundamental unit at ecological and individual levels, while age and educational level are determinants of leprosy morbidity in this area.

EP38

PREVALENCE RATE OF LEPROSY IN KHULNA,SOUTH OF BANGLADESH

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Since there was not any leprosy control program in the south of Bangladesh by 1986, the prevalence rate of leprosy in this area still unknown. This report is about the result of a case detecting activity which was done from February to June 1992 both for villagers and for slum dwellers in Khulna municipal area and to give a some idea of the prevalence rate of leprosy in the south of Bangladesh.

Khulna is the biggest city in the south of Bangladesh with 1.2 million population, which has expanded along the west side of the big river, Rupsha. It can be divided into two characteristic area from the point of public health: (1) industrialized or commercial areas in the heart of city and (2) village areas in the peripheral. A case detecting activity was carried out in these different areas parallelly with the same method. The same team member had been involved in this program for 5 month.

The number of total population who were checked from February to June 1992 was 19,032 and 127 cases were found to be leprosy. The overall prevalence rate was 6.67 per thousand population. The numbers of villagers and slum dwellers checked were 15,791 and 3,241 and the members of cases found were 87 and 40 respectively. The prevalence rate in villagers was 5.51 and that of slum dwellers was 12.34, which was extremely high but of the same order of that of the slum in Bombay.

EP39

A STUDY OF PREVALENCE OF CHILD LEPROSY IN ILOCOS NORTE, PHILIPPINES (1986 - 1992)

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This is a retrospective study of the prevalence rate of child leprosy in Ilocos Norte, one of two pilot provinces in the country that started MDT. The writer did a records review of all the new cases 14 years and below detected during a 7-year period from 1986 to 1992.

MDT was started in Ilocos Norte during the third quarter of 1985. It had a prevalence rate of 34/10000 in 1985. In 1988, it went up to 46/10000. In the last 5 years, the case detection rate has not gone down (average 2.7/10000) and cases of child leprosy have been cropping up through the years.

In the study we noted the age, sex, type or classification and deformity grading on admission. From a total of 82 children diagnosed as leprosy, 3 (3.6%) belonged to the 0-4 age group, 31 (38%) and 48 (58.5%) to the 5-9 and 10-14 age group, respectively. More males were affected than females, 43 (52.4%) versus 39 (47.5%). Forty-eight (58.5%) were MB and 34 (41.4%) were PB. For both sexes, 75 (91.4%) did not have any deformities, 4 (4.8%) had Grade 1 and only 3 (3.6%) had Grade 2 deformity.

The proportion of children to the total new cases detected every year fluctuated. In 1986, 19 out of 145 cases (or 13.1%) were detected. There was a decrease in 1987, 9/119 (7.5%). For 1988, 18/124 (14.5%); 1989, 12/127 (9.4%); 1990, 6/123 (4.8%); 1991, 10/110 (9%) and 1992, 8/106 (7.5%).

The writer would like to investigate further other areas and find out common factors in the circumstances surrounding child infection.

EP40

SAMPLE SURVEY FOR PREVALENCE OF LEPROSY IN THREE SLUMS OF DELHI, INDIA.

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Union Territory of Delhi has conventionally been treated as a low endemic area for leprosy prevalence.Most of the estimates regarding the prevalence of the disease have been based on old and obsolete surveys or on a few voluntary reportings by patients themselves in an advanced stage of the disease with deformities setin,to the urban leprosy Centres. The high social stigma against the disease in areas like Delhi, which has a large slum population comes in the way of early diagnosis,treatment and rehabilitation of the afflicted persons.There is no proper estimate of leprosy cases in Delhi since no systematic surveys to detect these cases were carried out in the past.We have conducted a Sample survey door-to-door,in three resettlement slum colonies in North Delhi,sponsored by Damien Foundation.The prevalence of leprosy has been 3.13/1000 population examined. Hence it was expected that there may be many leprosy cases in the area and need for surveying larger groups.

EP41

A TEN YEAR FOLLOW UP STUDY ON LEPROSY CONTACT POPULATION BY PGL1 SEROLOGY FOR THE EARLY DIAGNOSIS OF LEPROSY.

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In 1983, a program to follow up the family contacts of leprosy cases has been implemented in French Polynesia, to assess the usefulness and applicability of PGL1 serology in a leprosy control program. A total of 1201 contacts (666 female and 535 male) have been included in the study: 704 of them entered the sudy between 1983 and 1985, 419 between 1986 and 1989, and 78 between 1990 and 1992. The IgM anti-PGL1 dosage was performed by ELISA test using the natural synthetic trisaccharide NTP. As determined on normal polynesian sera, the specificity was of 98% and the sensitivity of 95% for multibacillary (MB) and 35% for paucibacillary (PB) patients.

The IgM anti-PGL1 seroprevalence determined on the initial sera was of 17%. It was significantly higher among female than male (20% versus 15%, p= 0.02). The median time of participation was 93 months among the seropositive and 100 months among the seronegative individuals. From 1983 to 1993, 4 out of 209 (2%) seropositive contacts developed the disease (1I, 1BT, 1BL, 1LL), as compared to 10 out of 992 (1%) seronegative contacts (4I, 3BT, 1BB, 2TT). Of these 10 patients, only 3 (3I) converted to seroposivity when leprosy was diagnosed. The risk to develop leprosy was not significantly higher among seropositive than among seronegative groups (2% versus 1%, p= 0.2). The median time to externalize the disease was longer (but not significantly) among the seronegative than the seropositive patients (27 versus 17 months, p=0.3). The total number of leprosy cases detected in the studied population represented only 15% (14/94) of the total new cases detected between 1984 and 1992 in French Polynesia.

In conclusion, this 10 year prospective study clearly shows that IgM anti-PGL1 serology is not effective for the early diagnosis of leprosy among high risk population. Therefore, in most of the endemic countries, this test cannot be recommended for a leprosy control program.

EP42

A LONGITUDINAL STUDY OF THE PREDICTIVE VALUE OF THE LEPROMIN RESPONSE AND ANTI-PGL-1 SEROLOGY IN CHILDREN.

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One thousand two hundred seventeen children from municipal schools of Bombay (low socio-economic status, age 10-15 years) were clinically examined for leprosy, tested with lepromin and the blood was collected by pin-prick (blood spot) for PGL-1 antibodies determination. All the children were clinically examined every six months for evidence of leprosy for the next 3 years. The children showing either lepromin negative status (n=116) or PGL-1 Ab positive status (definite positive n=64, borderline n=94) or lepromin negative along with PGL-1 Ab positive status (definite positive n=4; borderline n=23), total n=301 were clinically and serologically examined more frequently.

There was no statistical difference in PGL-1 Abs positivity rate in male and female children. Twelve new cases developed during the study period of which 11 were of mono lesions (TT) and only one BT (female). (7 females and 5 males). Statistical evaluation showed that lepromin negativity alone or PGL-1 Abs positivity alone were not useful as predictors for developing clinical leprosy. However when taken together, these two parameters identified a high risk group.

EP43

A SPONSORSHIP PROGRAMME FOR LEPROSY AFFECTED CHILDREN.

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This study deals with 455 children (below 15 yrs.) who were suffering from polyneuritic or smear positive leprosy and were registered at a leprosy hospital in Bombay during last 13 years. Of these, 122 were registered before MDT and 333 after introduction of MDT. A sponsorship programme in the form of giving help for school fees, books and school uniforms was introduced in 1982 for these children and further supported with initiation of personality development classes in 1987. The inputs of this "social service" has further improved the doctor-patient relationship.

In spite of the reduction due to MDT in the total number of patients on the register, the proportion of children with polyneuritic or smear positive leprosy has not changed (18%) indicating continued infection in Bombay. The sponsorship programme which provided

opportunity for personality development enabled 126 children to complete their education upto secondary school level (55%) and also improved regularity of drug intake and completion of MDT in 78% as compared to 44% in the pre-MDT era. It was necessary to continue the sponsorship and personality development programme for at least 3 years for each student (cost per child $ 10 per year). This appears to be a cost-effective approach for prevention of dehabilitation. Such simple "Social service programme" has potential of multiplication in several cities in hyperendemic area.

EP44

DETECTION OF M.LEPRAE-SPECIFIC ANTIGEN WITH M-DOT-ELISA IN SERA FROM HOUSEHOLLD CONTACTS OF LEPROSY PATIENTS

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The results of detecting M.leprae-specific antigen-phenolic glycolipid I(PGL-I) with our modified method—M-Dot-ELISA are reported. The sera were from 75 cases of household contacts of leprosy patients (HC), all previously seropositive in Gelatin Particle Agglutination Test (MLPA) and ELISA. Results indicated that: 1) 14/75 (21.3%) were antigen positive, among them, in HC of MB, 14/16 (87.5%) were antigen positive, in HC of PB, 0/16 were antigen positive, in HC of unknown types of leprosy patients, 2/16 (12.5%) were antigen positive, thus the rate of positivity in HC of MB was markedly higher than those in HC of PB. There was significant difference (P<0.001) between them; 2) Positive rates and levels of PGL-I in HCs were associated with levels of antibody against PGL-I in s era from HCs. There were significant differences in antigen positive rates and levels between weak and strong antibody positive groups of HC (P<0.001). 3) PGL-I were all negative in sera from either 10 controls or 10 nonleprosy patients who were previously anti-PGL-I antibody positivein MLPA and ELISA.

EP45

SEROEPIDEMIOLOGICAL ASSESSMENT OF LEPROSY IN CULION, PHILIPPINES

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Culion Sanitarium was once the biggest leprosarium in the Philippines, founded as a segregation colony for Hansenites in 1906. Since then the communities of Hansenites and non-Hansenites have grown and at present the latter outnumber the former.

Although the number of patients coming from different provinces has diminished significantly, there was an increasing incidence among the endogenous population as shown by the 7.5/1000 rate in 1987 following a survey done prior to the start of the MDT program in Culion. This is a reflection of an active transmission going on in the resulting intermingled populace. The extent of transmission and infection going on before 1987 was a big question, however treatment of active cases, which are potential reservoirs of infection have been addressed by the MDT program with a resulting decline in incidence and prevalence after 5 years, although new cases are still arising from the community.

This study monitors the efficacy of MDT, determines relapse rates and measures PGL-I antibody and antigen level of the general population allowing early diagnosis and treatment using ELISA technology in support of the goal of eradicating leprosy in Culion Island.

Household enumeration, numbering, mapping of target population ages 5 years and above are considered Culion residents (6 months residency) were included in the study. Population were classified as index case and contacts (household and community).

7567 baseline serum (90% target population) were examined. 13% of community contact (CCC) and 11% of household contacts (HHC) were ELISA (+). Negative contacts are followed-up annually while positive contacts are examined bi-annually for 4 consecutive years.

Through this cohort study, high risk contacts will be identified and new knowledge in leprosy epidemiology may be generated.

EP46

A PROSPECTIVE IMMUNOEPIDEMIOLOGIC STUDY USING MlSA AND ELISA FOR ANTIBODIES AGAINST PGL1

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About 11,000 individuals selected through cluster sampling in the field area of C.L.T.R.I and investigated for skin response to MlSA and antibodies against PGL1 by ELISA were followed for periods varying from 2 to 3 years for occurence of leprosy. A total of 104 cases were detected (90TT,7BT,5Pn,2BL). Risk ratio for factors like age, sex, contact status, ELISA for anti-PGL1 positivity, MlSA positivity and combinations of ELISA and MlSA were calculated. Contact status, MlSA &ELISA (both -ve) and MlSA -ve were found to be significant risk factors for disease (RR 2.74, 1.64 and 1.58 respectively). Eventhough the follow up period is not sufficiently long to make conclusive remarks it appears that response to MlSA and ELISA for anti-PGL1 antibodies may not be of much use as predictors of clinical disease, at least not as much as the easily identifiable factor of contact status, in high endemic population.

EP47

The role of anti-*Mycobacterium leprae* PGL-I antibodies in assessing the contacts of leprosy patients in a low endemic area.

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The role of anti-*M.leprae* phenolic glycolipid (PGL-I) antibodies in the serodiagnosis of leprosy is still uncertain. Although some studies suggest that seropositive contacts of leprosy patients have an increased risk of developing leprosy, the situation is less clear in community studies. In high endemic regions seropositivity is higher in 5-15 year olds and is not associated with the subsequent development of leprosy. This suggests that seropositivity is a marker of subclinical infection rather than clinical leprosy. We have studied the value of screening with anti-PGL-I antibodies in contacts of leprosy patients in a low endemic region. The leprosy control program in the Lalitpur District of Central Nepal has been active since 1962 and multi-drug therapy (MDT) was introduced in 1983. Between 1986 and 1990 a mass intensive survey detected 234 new cases (case detection rate 2.2/10,000/year). In 1991-1992 past patients were re-examined and finger prick samples collected from the 159 index cases and 403 of their healthy contacts. Anti-PGL-I IgM antibodies were measured by ELISA. Of the index cases, 55 had received MB-MDT, 93 PB-MDT and 11 DDS monotherapy alone. Twenty percent (8/39) of those who were receiving or who had stopped treatment in the last 3 years were seropositive while 2.5% (3/120) of those released from treatment earlier were seropositive. Of the 503 contacts, 93 were <15 years. There were no new cases of leprosy found in the contacts and only 4 (0.8%) were seropositive. On review 6 months later these 4 contacts had no evidence of leprosy and had become seronegative. The index cases of the antibody positive contacts had been released from therapy 1-8 years before and were seronegative. The low seropositivity rate in the contacts may be related both to the inactivity of the index cases and to the effective control program in the district which had reduced the background rate of subclinical infection in the community. These data indicate that the role of the anti-PGL-I antibody assay for screening contacts in a low endemic area is very limited.

EP48

USE OF PGL-IMMUNOASSAYS IN SEROEPIDEMIOLOGICAL STUDIES OF MYCOBACTERIUM LEPRAE INFECTION IN MALAYSIA

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Results from a three year national seroepidemiological study involving about 40,000 individuals selected by stratified sampling showed that PGL I immunoassay can be used as a

screening tool in a leprosy control programs. Seropositivity to PGL I antigens correlated with the prevalence rate of a defined population. The use of M. leprae specific antigens, such as PGL I, in immunoassays could thus be used as an indicator of exposure to M. leprae. individuals with subclinical infection had higher antibody titers and could be identified from those who had been exposed and became immune. High antibody titers, especially of the IgM class, were found in higher frequencies among individuals staying in high prevalence communities and in leprosy patients. IgG antibodies were found in significant quantities in individuals staying in low prevalence communities and in leprosy patiens treated over a long period of time. A gelatin particle agglutination test (MLPA) which detects IgM-anti-NT-BSA was used as a field test in the seroepidemiological studies in Malaysia and was shown to have very good concordance with the reference ELISA test.

EP49

A NATURAL ECOSYSTEM FOR LEPROSY RELATED CHEMOAUTOTROPHIC NOCARDIOFORM BACTERIA; TRANSMISSION OF LEPROSY BACILLUS TO HUMANS FROM FOSSIL FUEL RICH SOIL:

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Global maps were prepared for the incidence of leprosy and distribution of fossil fuels in different countries. This allowed comparison of these two parameters. A correlation has been found to exist between the prevalence of leprosy and distribution of fossil fuels (FF) and their surface soil seepages at global, regional as well as individual country levels. This could be accounted for by the occurrence of FF metabolising soil-bacteria which were indistinguishable from those isolated from human leprosy cases. The factors which appeared to determine the final outcome of the endemicity of leprosy, could be : a man-to-man, and soil-to-man infections. These in turn, seemed to depend on overcrowding, consanguinity and clustering of populations, quality of living standards and hygiene, and mode of tilling of lands assessed on the basis of comprehensive information. The origin of leprosy in the world, as well as, that of indigenous leprosy cases in the "leprosy-free" countries like USA and Russia, can be considered to be due to a soil-to-man infection. The possibility of indigenous origin of leprosy in different FF rich countries of the New World, independent of being imported from outside, explains the numerous findings of leprosy-like faces and figures in various paintings, and engravings on metals and stones, and pottery works etc. in the pre-Columbian Maya and Inca civilisations and the Aztec empire in the Americas. These had been accurately recorded by early Jesuit missioneries as frequent occurrences of florid leprosy among the Mayan and Incan Indians who must have had this infection long before Columbian era.

EP50

ASSOCIATION OF GEOGRAPHIC FACTORS WITH LEPROSY INCIDENCE RATES IN KARONGA DISTRICT, NORTHERN MALAWI

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Within an area of high leprosy incidence, geographic variation in incidence rates may be associated with socioeconomic factors, or with environmental factors which influence either transmission of *M leprae* or the acquisition of protective immunity. We studied the association between leprosy incidence (adjusted for age, sex, prior BCG vaccination, ecological zone, house construction and duration of schooling) and location of residence at the start of the study in more than 80000 individuals in Karonga District, Northern Malawi. Average follow-up was five years. Leprosy incidence was not associated with proximity to rivers, but there was some evidence of lower rates among individuals living within 1 km of the shore of Lake Malawi (rate ratio=0.66, p=0.075). There was strong evidence for higher incidence rates with increasing distance from the main roads in the district; at least some of this effect appeared to be socioeconomic. Although incidence rates were lower in the vicinity of the district "capital", there was no significant association with proximity to smaller "towns". The relation of these results to geographic variation in naturally acquired DTH to *M leprae* antigens, which is strongly associated with protection against leprosy, will be discussed.

EP51

LEPROSY IN ISFAHAN

A PRONVINCE OF IRAN

Ali Asilian - Ali Momeni - M. Meghdadi - Shariati and Sh. Enshaie

Leprosy is a chronic Tropical disease that frequently in volve skin, peripheral Nerve and Nasal Mucosa.

According to WHO estimatation there are about 15 Millions lepric patients all over the world and about 60% of them are living in Asia.

In Iran there have been cases of Leprosy in several provinces however, in Isfahan, Native dermatologists and pedtalists of infectious diseases belive that Leprosy specialists is not present in Isfahan,area.

We began an investigation either to approve or rull out this idea.

We searched the records about all of the registle-red patients In Leprosy registered center were 21. 14 of whom were Afghan, one was Iraqie, and the reminder were Iranian who were infected in othere provinces and then migrated to Isfahan.

Ihe analysis the results proved that.

There are not any eases of lepresy in Isfahan residential areas at the present time.

EP52

THE IMPLICATIONS OF DELAYED-TYPE HYPERSENSITIVITY TO M LEPRAE SOLUBLE ANTIGENS AND TO TUBERCULIN FOR NATURAL AND VACCINE-DERIVED IMMUNITY TO LEPROSY

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We report incidence rates of leprosy among 58,618 individuals in Northern Malawi as a function of age, sex, prior BCG status and prior delayed-type-hypersensitivity (DTH) to several different M leprae soluble antigens (MLSA) and to tuberculin (RT23, 2 IU). Though no relationship was evident with prior DTH to MLSA antigens produced by the initial protocols, a strong negative relationship with leprosy risk was evident with prior DTH to MLSA antigens which had been prepared with a later protocol including centrifugation at 105,000 g. The

association was restricted to individuals without prior BCG scar. Leprosy risk was also negatively correlated with prior DTH to tuberculin in unvaccinated but not in vaccinated individuals. Age/sex/BCG scar-adjusted prevalence of DTH to the MLSA antigens was inversely related to prevalence of leprosy within different ecological areas. Naturally-acquired DTH to mycobacterial antigens may be a stronger correlate of protective immunity to leprosy than is DTH induced by BCG vaccination.

EP53

INTRAFAMILIAL TRANSMISSION OF LEPROSY IN VELLORE TOWN, INDIA

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Intrafamilial risks in leprosy reported mostly from rural areas are likely to be different in urban setting due to several socio-demographic and environmental factors. Urban sample surveys are expensive and frustrating due to problems of stability, cooperation and logistics. In this paper we describe a hospital based study done from 1968 to 1991 to determine risks and extent of intrafamilial transmission in relation to characteristics of index cases and contacts in urban areas. Families were examined annually by doctors. Person-years of followup were used for calculation of incidence rates.

Of the 120 index cases 44% were MB. 410 contacts were registered and followed up. 14 contacts developed leprosy of whom 12 were under 15 years of age. 83% were detected during the first 5 years. The incidence rate (IR) per 1000 was 5.1 with no gender bias. The IR was 7.3 and 2.8 among contacts of MB and PB leprosy ($P < 0.05$). Importance of active surveillance by hospital based survey is emphasized and may be designed to focus on persons below 15 years, with intensive followup for first 5 years. This model is feasible and can be integrated into general health service of any hospital.

EP54

DETECTION OF *MYCOBACTERIUM LEPRAE* NASAL CARRIAGE IN A LEPROSY ENDEMIC POPULATION.

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In order to better understand the role of *M.leprae* nasal carriage in the maintenance of infection reservoirs and transmission of leprosy, we applied a polymerase chain reaction (PCR) detecting a 531 bp fragment of the *pra*-gene of *M.leprae* on nasal swab specimens collected through a total population survey from individuals living in an area endemic for leprosy. False-positive reactions were controlled by the application of dUTP/UNG. False-negative reaction were monitored using a modified control. A total of 1228 nasal swabs specimens were analysed; 7.8% were found positive. No clear age-related pattern could be revealed. It was found that only 3.1% of the households was associated with 27% of all PCR-positive individuals. The results of this study further add to the already available evidence that infections occur readily throughout the endemic population. Assuming that the specific and sensitive detection of *M.leprae* DNA through PCR indeed reflects the presence of bacilli, this is to our knowledge the first time that *M.leprae* nasal carriage has been specifically detected at the population level.

EXPERIMENTAL

EX1

EARLY IMMUNOLOGICAL RESULTS OF EXPERIMENTAL M. LEPRAE CHALLENGE OF MONKEYS AFTER ATTEMPTED IMMUNIZATION WITH LIVE BCG OR BCG + HEAT-KILLED M. LEPRAE.

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Groups of 10 rhesus monkeys (RM) and 7 sooty mangabeys (SM) were immunized and boosted with either live BCG alone or BCG + low dose heat-killed M. lepraе (LD HKML) or BCG + high dose (HD) HKML. These plus an unvaccinated group were challenged with live ML and studied immunologically and clinically at intervals before and after vaccination.

Blastogenic responses of blood mononuclear cells (MNC) to lepromin (lep) and Rees soluble protein antigen (Ag) were initially baseline, but increased in BCG + HKML groups after vaccination. Lep skin tests of BCG + HKML groups of RM 2 months postvaccination were strongly positive in all 20 RM.

Changes were observed in the following blood MNC subsets by flow cytometry after monoclonal antibody (Ab) staining: CD4, CD8, CD4/4B4, CD4/2H4 and CD16.

Ab profiles to ML-specific phenolic glycolipid-I (PGL-I) Ag by ELISA showed elevated IgG and little IgM in groups receiving BCG + HKML compared to others. We previously reported that this pattern is present in leprosy-resistent monkeys.

These results together with histopathology suggest that BCG + HKML or BCG alone have a protective anti-leprosy effect. Long term follow-up is in progress to determine if this will result in protection against progressive, disseminated leprosy.

EX2

LEPROSY IN PHILIPPINE CYNOMOLGUS MONKEYS [MACACA FASICULARIS]

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Nonhuman primate models of leprosy provide valuable information on the pathogenesis of leprosy in humans.

We initiated leprosy studies in 23 Philippine cynomolgus monkeys to determine their susceptibility to the disease. The animals were infected with either human or mangabey-derived M. leprae.

Acid fast bacilli [AFB] have been detected in nasal smears of 4 of the animals 9 to 50 months postinoculation. One of the 4 animals died 14 months after inoculation from causes unrelated to leprosy and histopathologic evaluation confirmed lepromatous lesions in the nasal mucosa of the animal. In 2 of the 4 animals, an increase in anti-PGL-I antibodies [IgM] correlated well with the appearance of AFB in nasal secretions. No lesions are apparent at the cutaneous inoculation sites. The colonization of the nasal mucosa with M. leprae in the absence of other clinical manifestations implicate the nose as a primary site of infection in this species. Additional details of the experimental disease will be presented along with the results of an ongoing survey for naturally-acquired leprosy in wild-caught Philippine cynomolgus monkeys.

EX3

RECONSTITUTION OF *M. leprae* IMMUNITY IN SEVERE COMBINED IMMUNODEFICIENT (SCID) MICE

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SCID mice have an autosomal recessive mutation that prevents the formation of functional B and T lymphocytes. We found that SCID mice infected with *M. leprae* developed a significantly ($P < 0.05$) more profound footpad infection than BALB/c mice. To test whether *M. leprae*-immune T cells can confer protection against infection with leprosy bacilli, groups of SCID mice were reconstituted 24 hours prior to *M. leprae* footpad infection both with a BALB/c-derived *M. leprae*-responsive T cell line, which produces gamma interferon upon stimulation with *M leprae*, as well as *M. leprae* non-immune T cells. The transfer of *M. leprae*-immune T cells resulted in a significant ($P < 0.03$) reduction in the number of *M. leprae* found in the footpads of infected SCID mice, and to levels, also, lower than that found in mice receiving *M. leprae* non-immune T cells ($P < 0.03$) and normal BALB/c mice ($P < 0.05$).

Flow cytometric analysis of spleen confirmed effective reconstitution with both CD_4+ and CD_8+ T cells. *In-vitro* lymphokine production and the proliferation of spleen cells from the reconstituted mice established that the donor cells had maintained their functional activity for the duration of the study (275 days). While spleen cells from non-reconstituted SCID mice upon stimulation with Con A failed to incorporate tritiated thymidine or produce detectable levels of cytokines, reconstituted SCID mice incorporated tritiated thymidine (stimulation index 9.6) and produced interferon gamma and IL-4 (41-72 ng and 600-800 pg per 10^6 cells, respectively).

These experiments demonstrate that *M. leprae*-immmune T cells home effectively, function, and control *M. leprae* infection in SCID mice.

EX4

ON THE POTENTIAL OF THE SCID MOUSE AS AN ANIMAL MODEL FOR LEPROSY

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The SCID (severe combined immunodeficient) mouse lacks both B and T cells and tolerates cells transferred from other species including man, the principal host of *M. leprae*. A series of experiments were carried out to determine if this animal is susceptible to infection with the leprosy bacillus. It was determined that SCID mice are susceptible to inocula of highly viable bacilli. Dissemination can be observed beyond the footpad. However, SCID mice may be able to resist inocula of less viable organisms better than conventional mice. Other investigators have shown that SCID mice have highly active natural killer (NK) lymphocytes producing amounts of interferon-γ capable of activating macrophages to destroy intracellular bacteria. Results will be presented on the effects of treatment to abrogate NK cell and macrophage function at the time of injection of *M. leprae* on the growth of the organism in both SCID and congenic normal mice possessing an intact immune system. Preliminary data should also be available on the effects of activated human cells on the growth of *M. leprae* in SCID mouse footpads.

EX5

MOUSE VACCINATION AGAINST LEPROSY WITH *M. leprae* SUBUNIT VACCINES ARE MORE EFFECTIVE THAN WITH WHOLE SONICATED *M. leprae*.

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Previously, we demonstrated that intradermal vaccination of mice with several progressively more purified and largely proteinaceous cell wall fractions of *M. leprae* diluted in Freund's incomplete adjuvant (FIA) conferred significant protection against footpad multiplication of live leprosy bacilli administered 1 month subsequently. It was noted in these studies that the most complex of the effective cell wall vaccines, the so-called cell wall insoluble fraction (CWIF), afforded protection when the amount of material utilized was as little as that derived from 10^5 *M. leprae*, while 10^7 or more killed *M. leprae* or furthert refined cell wall fractions derived from 10^7 or more *M. leprae* were required to provide protection.

In subsequent studies, we found that vaccination with a SDS-soluble fraction of CWIF, "soluble proteins", provides both unique and consistently (14 of 14 instances) prolonged mouse protection. While heat-killed *M. leprae* and progressively more refined cell wall fractions of *M. leprae* (CWP and PPC) generally protected when the interval between vaccination and challenge was 1-3 months, only soluble proteins protected when the interval between vaccination and challenge was extended to 6, 9, and 12 months.

Lastly, 10 density gradient subfractions of this material were eluted from a superose 12 column; certain of these subfractions in FIA were ineffective vaccines (fractions 11 and 12) while the others were effective (fraction 8, 9, 10, 13, 14, 15, 16, and 22), some at amounts of protein much lower than that in the whole killed *M. leprae* vaccine utilized herein (particularly fractions 8-10) and some significantly more protective (fractions 8, 13, 14, and 15). Analysis of SDS-PAGE of these soluble protein subfractions stained with $AgNO_3$ suggests that the likely critical protective *M. leprae* proteins therein are particularly the 10 kD protein and 1-3 kD proteins, and, to a lesser extent, the 65 kD protein.

EX6

BACILLARY PERSISTERS IN MURINE LEPROSY

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Studies on bacillary persisters were made in murine leprosy. Female mice were given a large inoculum of M. leproemurium in order to obtain a shorter survival time (SVT) of animals and to assure that an adequate number of bacillary persisters be included in the study. The SVT of normal animals was 535 days, and that of infected animals was 126 days. Dapsone was able to increase the SVT by 36 days, SM by 74 days, PZA by 126 days, INH by 154 days and kanamycin by 278 days. The average SVT of clofazimine (CLO)-treated animals was 519 days, approaching that of the normal mice. All animals revealed tremendous growth of murine leprosy throughout the visceral area at the time of their death except those treated with CLO, in which case there was no macroscopic growth at all. The last CLO-treated animal was sacrificed at 816 days and there were still a few organisms present in the pelvic fat. These organisms multiplied well in previously unused mice and CLO again showed

excellent suppressive activity (they were evidently not drug-resistant). Since nearly all inoculated organisms have been eliminated by CLO and drug-resistant organisms have never emerged under CLO treatment, it may be concluded that CLO is the first drug capable of killing the drug-sensitive organisms, preventing the emergence of drug-resistance and, more importantly, suppressing the growth of the persisters. In animals treated with a combination of INH and CLO for a period of 816 days the emergence of INH-resistant organisms was markedly delayed.

EX7

UV-B IRRADIATION OF MICE IMPAIRS THE PHAGOCYTIC ABILITY OF MACROPHAGES, DECREASES IMMUNITY TO MYCOBACTERIUM LEPRAEMURIUM, AND INCREASES DISEASE PATHOGENESIS.

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Ultraviolet (UV) radiation decreases immune responses to a variety of antigens introduced both locally and at distant, non-irradiated sites in experimental animals. In addition, exposure of humans to natural and artificial sources of UVB (280 - 320 nm) radiation can decrease immune function. These findings have raised concerns that increased environmental UV-B radiation, resulting from decreases in stratospheric ozone might affect the incidence or severity of infectious diseases. We are testing this hypothesis in a murine model of mycobacterial infection in which Mycobacterium lepraemurim (MLM) is injected into the hind footpad and disease progression is monitored by assessing the number of bacteria in the infected footpad and lymphoid organs. We demonstrated that exposure of BALB/c mice to a single dose of UV-B radiation, varying from 0.35 to 45 kJ/m^2, from FS-40 sunlamps suppressed the induction of a delayed type hypersensitivity (DTH) response to MLM in a dose-dependent manner. This was associated with an increase in the number of bacteria in the infected footpad and the lymphoid organs. Furthermore, UV-B radiation reduced the survival time of mice infected either in the footpad or intravenously with MLM. To determine whether the impaired clearance of bacteria seen after UV radiation was associated with altered macrophage function, we studied the uptake of MLM by macrophages collected from the peritoneal cavity of UV-B irradiated mice. Macrophages obtained from mice exposed to doses of UV-B radiation at or above $1.4kJ/m^2$ showed a significant reduction in their phagocytic ability when infected in vitro with MLM. These studies demonstrate that UVB radiation can alter the immune response to and increase the pathogenesis of a chronic mycobacterial infection in mice and suggest that impaired clearance of bacteria in vivo may result from an alteration in macrophage function.

EX8

MURINE STRAIN VARIATION IN M.LEPRAE INFECTED SCHWANN CELL FUNCTIONS AND THEIR MODULATION BY MACROPHAGES.

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Marophages (mφs) constitute the bulk of inflammatory cells in nerves of leprosy patients. Earlier studies indicate dysfunction in both ML infected human lepromatous as well as murine Swiss white (SW) mos. This dysfunction is important in processes of immunopathology, subsequent nerve damage and regeneration: this was assessed in Schwann cell tissue culture (DSC) in the 2 strains of mice (SW & C57Bl/6) that markedly differ in mφ response to ML infection. The parameters examined were a) Ability to support intracellular ML growth b) Expression of NGF & NgCAM c) Production of secretory proteins viz. fibronectin and collagen.

Constitutionally, DSC of the 2 strains responded differently to viable ML infection with respect to release of secretory proteins and NgCAM expression. However differences in mos of the 2 strains played no role in modulation of growth of ML or in their expression of NgCAM & NGF. Their role in modulating secretory proteins was at best temporary. Preliminary results of intraneural injections with supernatents of normal and patient mφs displayed diversity in the composition of intraneural granulomas that ensued.

EX9

THERAPEUTIC EFFICACY OF KRM-1648 IN COMBINATION WITH OTHER ANTIMICROBIALS AGAINST M.LEPRAE INFECTION INDUCED IN NUDE MICE

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A new benzoxazinorifamycin derivative, KRM-1648 (KANEKA Corporation), is known to have excellent in vitro and in vivo antimycobacterial activities, and is more potent than rifampicin (RMP). In this study, the therapeutic efficacy of KRM-1648, alone or in combination with DDS or clofazimine (CFZ), was evaluated against M.leprae infection induced in athymic nude mice. BALB/c nude mice infected sc with 1×10^6 of M.leprae Thai-53 strain were given test drugs by gavage, once daily six times per week, for up to 50 days from day 31 to day 80. The growth of organisms was observed in the hind footpad during the 12 months following infection, by counting the number of acid-fast bacilli in the tissue homogenate according to Shepard's method. In a dose-dependent manner, KRM-1648 markedly reduced the growth of leprosy bacilli at the site of infection (0.001~0.01 mg/mouse/day), and its therapeutic efficacy was greater than RMP. Furthermore, in vivo anti-M.leprae activity of KRM-1648 (0.001 mg/mouse) was enhanced when combined with other antimicrobial agents, such as DDS (0.2 mg/mouse) and CFZ (0.1 mg/mouse), as compared to the efficacy of either drug alone. From these findings, multi-drug regimens consisting of KRM-1648, instead of RMP, may be more efficacious for treatment of leprosy patients. Further studies on the therapeutic effect of KRM-1648 in combination with other antimicrobial drugs, such as clarithromycin, are now in progress.

EX10

COMBINATIONS OF RIFAMPICIN OR RIFABUTIN PLUS FLUOROQUINOLONES AGAINST MYCOBACTERIUM LEPRAE

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The treatment of leprosy worldwide is limited mainly to dapsone, clofazimine and rifampicin, either singly or in multiple drug therapy. Because of emergence of drug resistant M. leprae and toxicity of these drugs, there is an urgent need for new bactericidal drugs. The discovery of quinolones has given a new armamentarium in the fight against leprosy. The activities of several fluoroquinolones against several strains of armadillo-derived M. leprae were determined, both singly and in combination with rifampicin or rifabutin, in the in vitro system as well as in mouse foot pad system.

When incorporated singly into culture medium, ciprofloxacin, clinafloxacin, ofloxacin, sparfloxacin and temafloxacin were found to be most active against M. leprae, with MIC ranging from 0.75 to 1.5 μg/ml. In similar studies, it was determined that rifabutin was more active than rifampicin, both in the in vitro system and in mouse foot pad system. Excellent synergism was observed when either clinafloxacin, ofloxacin, sparfloxacin or temafloxacin was combined with rifabutin, but not with rifampicin. When ofloxacin was tested in mouse foot pad system, similar synergism was obtained with rifabutin, but not with rifampicin. Thus, it seems there are more effective candidates now available for incorporating into MDT regimens in leprosy.

EX11

STUDIES OF MACROPHAGE TRAFFIC INTO THE EXPERIMENTAL LEPROMATOUS LESION OF THE *MYCOBACTERIUM LEPRAE*-INFECTED NU/NU MOUSE FOOT PAD.

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In lepromatous leprosy (LL) the failure of the macrophage (MΦ) to cope with *M. leprae* (*ML*) is conspicuous; lepromatous granulomas consist of enormous numbers of MΦs packed with leprosy bacilli. They are not immortal cells but their half-life in the tissues is not known. Obviously there must be a continuous influx of new MΦs to support the growth of bacilli. In the athymic (nu/nu) mouse *ML* grows to enormous numbers producing a granuloma similar to that in human LL in man. In this experimental model for LL we have observed a high rate of turnover of *ML*-infected foot pad MΦs. Although newly arrived bone marrow-derived MΦ are heavily infected with *ML*, the fate of the initial granuloma MΦs and mechanisms by which they acquire their *ML* burden from the existing infected MΦs is not known. Our studies have explored the role of natural killer (NK) as well as normal and activated MΦs in the lysis of *ML*-infected MΦ target cells and the fate of the *ML*. Fresh NK cells and lymphokine (IL-2) activated killer cells (LAK) from popliteal lymph node (LN) draining the sites of foot pads inoculated with *ML* were cytotoxic for *ML*-infected target MΦs. NK and LAK activity was also detectable in LN from 14 month-old *ML*-infected nu/nu. The importance of dose and viability of *ML* in the target MΦs as well as the duration of their infection was examined. In an *in vitro* model for MΦ turnover, normal effector MΦs acquired the *ML* from target MΦs and continued to sustain their growth (oxidation of ^{14}C-palmitic acid to $^{14}CO_2$) but IFNγ-activated MΦs attacked infected target MΦs, acquired their load of bacilli and had a marked deleterious effect on these *ML*. These studies describe 2 mechanisms for maintenance of granulomas in LL that could underlie sustenance of *ML* viability in the absence of treatment. Chemotherapy and the eventual clearance of bacilli could depend heavily on acquisition of *ML* by a continuous turnover of new MΦs. Immunotherapy that activates MΦs could override the protection afforded to the bacilli by their normal host cell and lead to their subsequent destruction and clearance.

EX12

THE TRANSMISSION OF LEPROSY THROUGH THORN PRICKS IN NUDE MICE

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The mode and route of *Mycobacterium leprae* transmission is of continued interest. In our earlier studies we demonstrated the transmission of leprosy in nude mice through nasal mucosa, dekeratinized, unbroken skin, abraded skin and by subcutaneous and intravenous injection. Leprosy infection in feral nine-banded armadillos (Dasypus novemcinctus) is well documented. In an earlier study we observed thorns in the ears and nose of Louisiana armadillos infected with *M. leprae* in the wild. (Thorny bushes and briars are indigenous to the southern regions of the USA.) The study suggested that *M. leprae* may have entered the armadillo tissue by means of thorn pricks.

The present investigation was an attempt to simulate the transmission of leprosy through thorn pricks. The spines of the Bunny-Ear cactus were used to introduce *M. leprae* into the skin of nude mice. *M. leprae* (1×10^7) harvested from nude mouse footpad was placed on the dorsum of both hind feet of 10 anesthetized nude mice and allowed to partially air dry. A piece of cactus tissue was vapor sterilized with formaldehyde and the spiny portion of the cactus was immersed in suspension of *M. leprae* (1×10^9 AFB/ml). The plant tissue was then pressed against the mouse foot on the area containing *M. leprae*. The cactus spines detached from the plant and remained embedded in the skin. All of the mice developed swelling in the dorsum of the feet within six months. The infection progressed in a manner similar to that observed in nude mice experimentally infected with *M. leprae* by needle injections.

This study demonstrates that it is possible to transmit leprosy through contact with *M.leprae*-contaminated thorns. It is plausible that individuals living in endemic leprosy regions may encounter similar exposures to the leprosy bacillus, especially in those areas where going barefoot is common.

EX13

THE NEONATALLY THYMECTOMIZED LEWIS RAT AS A MODEL FOR THE ELIMINATION OF "PERSISTERS" BY CHEMOTHERAPY

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We have utilized the NTLR model to simulate chemotherapy of the "persister" state. In these studies we infected NTLR in the hind footpads with 5,000 *M. leprae*, and 1 year later, when the number of *M. leprae* per footpad was consistently $\geq 10^7$, these NTLR were treated with various regimens for 4 months; 2 or more months after discontinuing therapy, treated NTLR footpads were harvested so as to assess the presence of any surviving "persisters" by subpassage and assessment of viability in footpads both with small *M. leprae* inocula (5,000) in BALB/c mice and with larger inocula (generally 10^6 or more) in 2 NTLR. *M. leprae* from treated NTLR were judged viable if 1 year after subpassage either: (1) an increase of $\geq$ 5-fold *M. leprae* was found in any single NTLR supassage footpad, each footpad being harvested individually, or (2) the number of *M. leprae* per footpad in 4 foot mouse pools was found to be $\geq 10^5$. We found several regimens which do not regularly eliminate "persisters" (number of NTLR harboring persisters/number of NTLR treated) in this system: rifampin alone (7/11), 2 schedules of rifampin + dapsone (16/21), dapsone + ethionamide (5/11), minocycline alone (14/18), and rifampin + clofazimine (6/11). On the other hand, "persisters" were essentially entirely eliminated and the percentage of treated NTLR harboring "persisters" were statistically significantly less ($P < 0.02$) than with the previously described regimens when treatment consisted of: (1) rifampin + minocycline (0/13), (2) rifampin + ofloxacin (1/10), and (3) rifampin + ethionamide (0/14). This study of experimental chemotherapy suggests that these three combinations offer the most potential for effective short-course therapy of leprosy.

EX14

SURVEY OF MONOCLONAL ANTIBODIES AGAINST MYCOBACTERIUM LEPRAE FOR USE IN IMMUNOHISTOCHEMICAL AND IMMUNOULTRASTRUCTURAL LOCALIZATION STUDIES.

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Monoclonal antibodies (MAbs) against M. leprae components have become generally available for study through "libraries" maintained for the purpose. However, despite their specific characterization and use in a variety of immunologic studies, work on antigen localization by immunohistochemical methods or by immunoelectronmicroscopy has been sparse.

Antigenically characterized anti-M. leprae IgG MAbs were obtained from the Centers for Disease Control and Prevention (CDC), Atlanta, GA, and from active Hansen's disease workers. Lymph nodes and lepromas were obtained from heavily infected armadillos. For immunohistochemical studies, frozen sections were reacted with a variety of MAbs in an avidin/biotin-peroxidase/diazobenzidine system. For immuno-electronmicroscopy, embedded sections were exposed to MAbs, then to a gold-labelled ligand. In the immunohistochemical study, the best specific staining was obtained with mouse MAbs IIC8 (65 Kd protein), mc8026 (18 Kd protein), mc6225 (30-40 Kd glycolipid), mc2924 (broad 30-40 Kd carbohydrate), and a human polyclonal anti-lepromin A serum. However, although some ultra-structural localization of specific antibodies was obtained with the human polyclonal serum, gold labelling with MAbs has generally been poor, possibly reflecting degradation of antigenic sites by EM-preparative methods.

EX15

CHARACTERIZATION OF THE SPECIFIC RECOGNITION SITES OF MONOCLONAL ANTIBODIES TO THE PHENOLIC GLYCOLIPID I OF M. LEPRAE

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By the study using synthetic sugar-constructs of phenolic glycolipid I (PGL I) of M. leprae, we have revealed that the haptenic specificity of PGL I was on the sugar part of PGL-1. To

study the roles of each sugar-constructs, various kinds of sugar analog were synthesized. They included the outer monosaccharide (NM-P), outer disaccharide (ND-P), trisaccharide (NT-P) inner monosaccharide (IM-P), inner disaccharide (ID-P) and the trisaccharides with different anomeric configurations. They were coupled to BSA, methylated BSA (MBSA) or KLH, giving synthetic antigens.

Recognition sites of the various kinds of the monoclonal antibodies (MAb's) produced by immunizing mice with these synthetic antigens were determined with the set of synthetic sugar-constructs by ELISA and microHA. MAb recognizing outer monosaccharide (mAb (1-24), mAb (1-25)), outer disaccharide (PG2B8F, ml 6A12, ml 8A2, ml 8B2), trisaccharide (SF-1), inner monosaccharide (DZ1, A8) were characterized. Among these MAb's SF-1 had extremely high specificity. Namely, SF-1 required complete structure of three sugar residues and complete anomeric configurations of three glycosidic linkages. The set of MAb's could be very useful for the development of the sensitive method of quatitation of PGL I, immunohistochemistry and so on.

EX16

DENATURED MUSCLE AUTOGRAFTS IN PERIPHERAL NERVE REPAIR IN A MODEL OF LEPROSY

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The technique of denatured muscle autografting was used to examine nerve regeneration in a model of leprosy nerve damage. Granulomas were induced in the tibial nerve of guinea pigs, by the intraneural injection of cobalt - irradiated *Mycobacterium leprae* organisms. Peak granuloma formation and nerve damage occurred at 5 weeks. At this time, the granuloma was excised and the nerve gap was repaired with a denatured muscle autograft. Nerve regeneration was followed over 20 weeks, by assessment of return of sensation in the footpad and muscle function in the foot. The conduction velocities of the fastest fibres in the tibial nerve were measured by electrophysiology, and quantitative morphometric assessment of myelinated fibres in the tibial nerve, distal to the graft was carried out, at 8, 12, 16 and 20 weeks after grafting. The results were compared with nerve regeneration after muscle grafting of a normal, non-granulomatous nerve.

Nerve regeneration occurred in the grafted granulomatous nerve, where there was fibrosis, at a slightly slower rate than in the grafted normal nerve.

EX17

SUBPLASMALEMMAL LINEAR DENSITIES IN MONONUCLEAR CELLS INDUCED BY AN ANTIGEN IN HUMAN SENSORY PERIPHERAL NERVE.

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Subplasmalemmal linear densities(SPLDs) consist of electron dense deposits lying immediately under the plasma membrane of mononuclear cells occurring in the chronic inflammatory lesions of sarcoidosis and multiple sclerosis. We describe the presence of these mononuclear cells with SPLDs in an animal model of nonlepromatous leprosy.

Rabbits and Strain 13 guinea pigs develop skin lesions similar to those of nonlepromatous leprosy when injected with human sensory peripheral nerve suspension, or a non-myelin fraction derived from human dorsal roots. SPLDs were found in mononuclear cells in the dermis of these skin lesions in 3 out of 4 rabbits, and in 3 out of 4 Strain 13 guinea pigs. SPLDs were also found in mononuclear cells at skin test sites in 6 out of 10 rabbits displaying granulomatous hypersensitivity and were readily seen when a deoxycholate extracted fraction from sural nerve in doses of 1µg was used as skin test antigen.

Although mononuclear cells with SPLDs have not been reported in human leprosy, 'plasma like' cells surrounded by basal lamina have recently been described in sural nerves and may be similar to the plasmacytoid cells occurring in sarcoidosis, which have SPLDs and which are now considered to be precursors of epitheliod cells.

EX18

OBSERVATION ON PHAGOCYTOSIS TO M.LEPRAE BY CULTURED HUMAN SCHWANN CELLS

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Schwann cells from 25 cases(fetus 17, adult 8) of human peripheral nerves have been successfully cultured by means of tissue plantation merhod. Among these the Schwann cells of 3 fetus could be subcultured up to 10th generation covering more than 100 days. It was proved that the growing cells were Schwann cells through study by immunohistochemical reaction against S-100 protein and lysozymes, and also by electron microscopy which showed many microvilli on the surface along with plenty of lysosome and Golgi's complex in the cytoplasm. Even when fragments of peripheral nerve tissue or the cell suspension were stored in liquid nitrogen for serveral months, the nerve tissue or the cells were still able to survive and proliferate after rapid thawing.

The Schwann cells and M. Leprae were co-cultured by coverslip method, and the coverslips were stained(acid-fast stain) and the phagocytosis of M. Leprae by Shwann cells was observed under light microscopy in regular intervals. About 15% of Schwann cells phagocytosed M. Leprae 10 hours after infection. Later on the number of the cells phagocytosed M. Leprae steadily increased and reached the peak (95%) of phagocytic index 72 hours after co-culture. M. Leprae globi could asto be found in Schwann cells. By electron microscopy many M. Leprae could be observed among the microvilli as well as in the cytoplasm of the infected Schwann cells. Ninety six hours after infection the Schwann cells which phagoctosed many M. Leprae underwent degeneration and necrosis, but the M. Leprae in the cells still existed with their morphology unchanged.

EX19

EARLY CLINICAL AND PATHOLOGICAL RESULTS OF M. LEPRAE CHALLENGE OF MONKEYS AFTER ATTEMPTED PROTECTIVE IMMUNIZATION WITH LIVE BCG OR BCG + HEAT KILLED M. LEPRAE.

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Seventeen monkeys (10 rhesus and 7 sooty mangabeys) per group were challenged with live Mycobacterium leprae (ML) after vaccination and boosting with either live BCG or BCG + low dose (LD) heat-killed ML or BCG + high dose (HD) HKML. An additional 17 unvaccinated monkeys were also challenged. Biopsies of leprosy lesions were removed at intervals longitudinally and were studied histopathologically and clinical results were recorded concurrently.

The following histopathological criteria were observed in the biopsies: numbers of epithelioid cells, multinucleated giant cells and lymphocytes; numbers and viability (morphologic index) of acid-fast bacilli (AFB); necrosis and average lesion size at inoculation sites.

Some differences were noted between the 2 monkey species in the types and/or proportions of cells in the infiltrates. In both species, however, there were decreasing numbers and viability of AFB in unvaccinated > BCG only > BCG + LD HKML > BCG + HD

HKML groups. These observations together with clinical data and immunologic studies strongly indicate that anti-ML immunization has been achieved. Long-term observations are needed to verify these conclusions and to determine whether protective immunization against progressive clinical leprosy has occurred.

EX20

DETECTION OF Ig A ANTI-PGL-I IN MANGABEY MONKEY INOCULATED WITH MYCOBACTERIUM LEPRAE

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3- Neurology Institut,Wien Univ.-Austria.

M. leprae affects differents parts of the body but specially the peripheral nerve, skin and mucosae, where bacilli are found in large amount in lepromatous patients By infection with microorganisms through skin and mucosae predominantely Ig A class antibody is ilicited. however, the IgA antibody developement in leprosy patients has escaped the attention. The little knowledge about the developement of the immune response in leprosy patients is caused by the difficulty to make a longitudinal study in human leprosy, because of the unknow mode of transmission and the long incubation period.

The mangabey monkey has been reported to be a good model to study the immune respense in leprosy, since the course of the infection with M. leprae in this host is similar to human.

Using sera from 8 mangabey monkeys we could demonstrate that IgA antibodies against M. leprae specific PGL-I antigen were present in sera of some monkeys. These monkey sera were obtained in the course of 100 months before and after experimental infection with M. leprae suspensions, where by two monkeys each were inoculated with different numbers of bacilli.

Ig A antibidy levels to PGL-I in monkey sera were compared with Ig G and Ig M antibody levels and clinical course of infections

EX21

A NEW PATHOGENICITY MODEL OF LEPROSY : MUTILATION OF TOES IN MICE EXPERIMENTALLY INFECTED WITH M. LEPRAE/CAN BACTERIA.

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The leprosy bacillus had been shown to multiply outside the human body, chiefly in the mouse footpads, armadillos and some non-human primates, yet no animal mutilation model, comparable to the human disease, exists. We describe here such a model in mouse. Infant mice (white, 'Swiss' strain, inbred; 6-10 days old) were inoculated in both the (mouse) footpads (MFP) with 10^7/ 10^8/ 10^9 CFU of CAN/M. leprae bacteria in 0.05 ml volume containing 40 ug of sterile collagenase (Type VII, lyophilised, Sigma Labs., USA). Each batch consisted of 20 mice. Controls consisted of uninoculated mice of the same litters as well as those inoculated with collagenase alone. The animals were observed for 6 months. Mutilation developed in several animals belonging to different test batches after 3 months or later with or without being accompanied or followed with deformities or contractures. None of the control animals living in the same environment developed mutilations/deformities. Microbiological and histopathological studies of the lesions showed significant bacillary proliferation with disintegration/dissolution of the connective tissue and their replacement by fibrous tissues in the affected areas.

EX22

EVALUATION OF SODIUM STIBOGLUCONATE AND UREASTIBAMINE ON MOUSE, EXPERIMENTALLY INFECTED WITH MYCOBACTERIUM LEPRAE FROM HUMAN LEPROMA.

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The in vitro effects of any one of the currently used drugs in the treatment of leprosy are not well studied or understood, for which the present knowledge about the efficacy of these drugs on the in vivo or human systems is based on clinical trials or on the effects on mouse footpads. We have cultivated in vitro a large number of leprosy derived chemoautotrophic nocardioform (CAN) bacteria which appear to have a very close parallelism with the leprosy bacillus; these have been examined for in vitro susceptibility to Na-stibogluconate (a pentavalent arsenical), urea stibamine, ofloxacin, norfloxacin, rifampicin, DDS, as well as, for in vivo effects of these agents on the multiplication of the freshly harvested leprosy bacilli from human leproma and inoculated into the mouse footpads; pathological changes in the footpads as well as the internal organs were also studied.

We found that Na-stibogluconate most significantly reduced the bacterial multiplication and development of lesions in the internal organs compared with ureastibamine and all the other drugs, and also significantly with respect to the untreated but infected control mice.

EX23

UTILITY OF BEIGE MOUSE IN CHEMOTHERAPEUTIC STUDIES IN LEPROSY

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Animal models are very essential in the development of new drugs, a step between in vitro screening and clinical trials. Valid information is needed on the pharmacokinetics and toxicity of the drug and its effect on the in vivo multiplication of the organism. Animal models currently being used in leprosy — BALB/c mice, nude mice and armadillos — have their own drawbacks. The high susceptibility of Beige (C57BL/6/bg/bg) mice to M. avium complex (MAC) strains and its success to chemotherapeutic investigations for MAC infections led us to investigate its utility in leprosy.

Dissemination of M. leprae to visceral organs was seen within four months only in Beige mice, but not in BALB/c mice, following Iv or Ip inoculation. Bacilli harvested from Beige mice exhibited all the characteristics of M. leprae, including growth patterns in the foot pads of BALB/c mice. M. leprae inoculated into foot pads of Beige mice multiplied faster than those inoculated into foot pads of BALB/c mice. When Beige mice were fed ad libitum a diet containing 0.0005% dapsone, complete suppression in the multiplication of M. leprae in visceral organs as well as in foot pads was observed. Thus, Beige mouse has a potential usefulness in evaluating chemotherapeutic activities of new antileprosy drugs.

EX24

SIMULATION OF LEPROSY INFECTION IN MICE

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These investigations are an extension of the work of recent years devoted to studying

the peculiarities of mononuclear phagocyte system in leprosy. Models of leprosy infection in mice with previously affected macrophage compartment of their immunity were proposed and developed by Professor F.E.Vishnevetsky, now the deceased. Two novel approaches to leprosy simulation are presented. The first approach involves the formation of a defect of mononuclear phagocyte system by means of lavages of macrophages from peritoneal cavities of mice before their inoculation by Shepard's technique. The second way is to affect phagocytic activity of macrophages by means of introducing synthetic tetrapeptide tuftsin (Serva, Germany). Both approaches allow to shorten the experimental terms through stimulating M.leprae multiplication at the site of their inoculation. Furthermore, a generalized leprosy infection with the appearance of lepromatous granulomas in the internal organs has been observed in M.leprae-infected laboratory animals.

The data obtained suggest a value of the approaches described for leprosy simulation experiments and might be used for screening of the compounds with potential antileprosy activity and for elucidation of some aspects of leprosy pathogenesis.

EX25

PENETRATION OF DAPSONE, RIFAMPICIN AND CLOFAZIMINE INTO MACROPHAGES AND MYCOBACTERIA.

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The penetration and hence the presence of a drug inside the mycobacteria as well as the phagocytic cells macrophages is perhaps one of the key mechanism of drug mediated killing of invading organisms. We have examined the penetration of three antileprosy drugs-dapsone, rifampicin and clofazimine into M. lufu and M. smegmatis and mouse peritoneal and human macrophages.

M. lufu and M. smegmatis (10^8/ml) and cultured mouse peritoneal and human macrophages (10^6/ml) were incubated with 5-10 ug/ml of dapsone, rifampicin and clofazimine for varying periods and the levels of drugs inside the mycobacteria and macrophages were estimated by using spectrophotometry, TPLC and fluorimetry. The penetration of polylysine conjugated dapsone was compared with that of dapsone only. Other factors like temperature period of incubation and pH were also studied.

All three drugs penetrated into mycobacteria to an extent of 20-40% and the polylysine conjugation enhanced dapsone penetration by an additional 50%. Ionophores too enhanced the penetration of dapsone. The macrophage exhibited a permeability of 15-40% for the three drugs with moderate variation between the drugs. The process of drug penetration seems to be passive.

It may be possible to enhance the drug penetration through various methods of drug presentation such as conjugation of drugs to polyaminoacids, ionophores etc. Kinetic studies on drugs using macrophage as model need to be carried out.

EX26

THE ACTIVITY OF COMBINATIONS OF EFFECTIVE ANTIBIOTICS AGAINST *M. leprae*-INFECTED MICE

Robert H. Gelber, Lydia P. Murray, Mabel Tsang, and Patricia Siu.

Medical Research Institute of San Francisco, CA, USA.

Groups of female BALB/c mice were infected in both hind feet with 5,000 *M. leprae* and treated from day 60-150 afterwards with low but active schedules of the following 5 drugs singly and in all possible combinations of both 2 and 3 drug regimens: clarithromycin (C) 0.001% in diet, sparfloxacin (S) 5 mg/kg by gavage 5 times weekly, rifampin (R) 20 mg by gavage once monthly, minocycline (M) 0.004% in diet, and dapsone (D) 0.0001% in diet. At the completion of therapy and 4 & 7 months subsequently, the number of *M. leprae* in 2 mice (4 feet) was enumerated. Multiplication was considered to have occurred if the number of *M. leprae*/footpad in footpad pools of 2 mice (4 feet) was $\geq 10^5$. From the results of the first 2 harvest intervals all single agents were found to be active, but at the harvest 7 months after therapy was discontinued, *M. leprae* had multiplied in mice treated with each agent singly. At that time *M. leprae* had not multiplied in only 4 of 10 of the 2-drug regimens (S + R, S + M, S + D, R + D). The 10 3-drug combinations resulted in no *M. leprae* multiplication at all 3 harvest intervals, except for a single combination (C + M + D), which had demonstrated multiplication only at the last harvest.

These studies suggest additive or synergistic and certainly not antagonistic activity for combinations of antimicrobials effective against *M. leprae*. Furthermore, combinations of 3 active drugs were found to be generally superior to that of 2. Lastly, these studies confirm the previous work of Shepard on the activity of combinations of effective antibiotics against *M. leprae* in mice wherein more rapid bacterial killing usually resulted from the use of drug combinations. The implications of these findings to the combination therapy of leprosy will be discussed.

EX27

THE ACTIVITY OF CERTAIN NEWER QUINOLONE ANTIBIOTICS AGAINST *M. leprae*-INFECTED MICE

Robert Gelber, Ali Iranmanesh, Patricia Siu, Mabel Tsang, & Lydia Murray. Medical Research Institute, San Francisco, CA, USA.

Previously pefloxacin and ofloxacin were found to be active against *M. leprae in vitro*, in experimental animals, and in clinical trials of lepromatous leprosy patients. In this study we compared certain more recently developed fluoroquinolones (lomefloxacin, PD 124816, WIN 57273, temafloxacin, and sparfloxacin) with pefloxacin and ofloxacin in *M. leprae*-infected mice by the kinetic technique of Shepard (treatment day 60-154 after footpad infection), each by gavage at doses of 50, 150, & 300 mg/kg 5 times weekly. The number of *M. leprae* in footpads of 2 mice (4 feet) from untreated controls and all treatment groups was enumerated microscopically at the completion of therapy and at intervals of 2-3 months thereafter, generally up to 9-12 months subsequently. We judged drugs inactive (IA) if at the end of therapy the number of AFB was the same as in the untreated controls, bacteriostatic (BS) if at the end of therapy the number of AFB was less than in untreated controls but bacillary multiplication commenced immediately thereafter, partially bactericidal (PBC) if multiplication was further delayed, and fully bactericidal (FBC) if *M. leprae* did not grow for 9 or more months after therapy was completed:

	15	30	50	150	300 (all mg/kg)
pefloxacin	-	-	IA	BS	PBC
lomefloxacin	-	-	BS	BS	PBC
PD 124816	-	-	BS	BS	FBC
ofloxacin	-	-	BS	FBC	FBC
WIN 57273	-	-	PBC	FBC	FBC
temafloxacin	-	-	FBC	FBC	FBC
sparfloxacin	FBC	FBC	FBC	FBC	FBC

All 7 fluoroquinolones studied were active against *M. leprae*, temafloxacin and sparfloxacin being the most active, fully bactericidal at all 3 dosage schedules. Additionally, sparfloxacin was found fully bactericidal at 15 mg/kg and 30 mg/kg 5 times weekly. This study demonstrates that certain of the newer fluoroquinolones, particularly sparfloxacin, are more active than pefloxacin and ofloxacin against *M. leprae*-infected mice and merit clinical trial.

EX28

THE ACTIVITY OF MACROLIDE ANTIBIOTICS AGAINST *M. leprae*-INFECTED MICE

Robert H. Gelber, Lydia P. Murray, Patricia Siu, and Mabel Tsang.

Medical Research Institute of San Francisco, CA, USA.

Franzblau *et al.* first demonstrated in cell-free and macrophage culture, as well as in *M. leprae*-infected mice, that clarithromycin inhibited *M. leprae*. We tested a series of macrolide antibiotics at clinically achievable levels (0.06%-0.1% in diet) against *M. leprae*-infected mice by the kinetic method of Shepard (treatment day 60 to 150 after footpad infection) and found that while erythromycin and azithromycin were inactive, roxithromycin and clarithromycin were bactericidal, clarithromycin being found

more active than roxithromycin. Later we found by the proportional bactericidal test, wherein the actual killing of *M. leprae* is quantitated by using groups of mice infected with three serial 10-fold *M. leprae* dilutions, that azithromycin (0.1% in diet) resulted in no significant killing of *M. leprae* (11% ± 74%), while 0.1% in diet of both roxithromycin and particularly clarithromycin were found to be both bactericidal for *M. leprae* (82 ± 13% and 96% ± 2% respectively). Furthermore, we found that clarithromycin's minimal inhibitory dietary concentration for *M. leprae* in mice was exceedingly low, 0.001% (serum level < 25 mμg/ml and footpad level ≤ 0.7 μg/gm). We also found by the proportional bactericidal test that the minimal bactericidal dietary concentration was, however, somewhat higher, 0.05%. Lastly, clarithromycin (0.1% in diet) both 3 days weekly (M, W, F) and 1 day weekly entirely inhibited the growth of *M. leprae*, while administration only 1 day monthly was partially active. These studies demonstrate that clarithromycin inhibits *M. leprae*, is bactericidal, and is effective on intermittent administration, all encouraging for its application to the treatment of leprosy.

EX29

STUDIES ON THE ACTIVITY OF MINOCYCLINE AGAINST *M. LEPRAE*-INFECTED MICE.

Robert H. Gelber, Patricia Siu, Mabel Tsang, and Lydia P. Murray.

Medical Research Institute of San Francisco, CA, USA.

Previously we had demonstrated that minocycline treatment of *M. leprae*-infected mice inhibited the growth of *M. leprae* at serum levels (0.1-0.2 μg/ml) well below those achieved in man (2-4 μg/ml) by a standard daily adult dose of 100 mg, was consistently bactericidal (both by the kinetic method of Shepard and the proportional bactericidal technique), and additive in its activity when combined with other antimicrobials (dapsone, rifampin, & kanamycin).

We, also, evaluated the minimal concentrations of minocycline in the diet and in serum required to inhibit the growth of 7 *M. leprae* isolates in mice, including both a partially dapsone-resistant and fully dapsone-resistant isolate. Minocycline concentrations of 0.01% and 0.04% in the diet, which resulted in serum levels of ≤ 0.17 and 0.51 μg/ml, respectively, were consistently and completely inhibitory. Even 0.004% dietary minocycline (levels in serum, ≤ 0.08 μg/ml) partially inhibited 5 of these strains, while 0.001% minocycline was consistently inactive. We can now report that very low levels of dietary minocycline (0.01%) consistently inhibited the growth of all 18 *M. leprae* isolates studied. For 5 *M. leprae* isolates, minocycline at a concentration of 0.04% in the diet given 3 days weekly (M, W, F) and 1 day weekly completely inhibited the growth of *M. leprae*, and minocycline given even 1 day monthly was partially inhibitory for 3 of these 5 *M. leprae* isolates

Furthermore, dietary concentrations of minocycline 0.01%, 0.04%, 0.06%, & 0.1% were found bactericidal (P≤ 0.02) for *M. leprae* by the proportional bactericidal test, establishing that minocycline's minimal inhibitory concentration and minimal bactericidal concentration for *M. leprae* are similar.

EX30

LONG-TERM EFFECTS OF DAPSONE ON IMMUNE RESPONSES IN BALB/c MICE.

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Long-term exposure to Dapsone of BALB/c mice revealed a concentration dependent suppressive effect on humoral and cell-mediated immune responses with an initial enhancement at 4 weeks exposure. Adult mice were exposed to 0.01% and 0.001% dapsone concentrations in the diet for 24 weeks and the immune functions were assessed at the interval of every 4 weeks. Delayed type hypersensitivity reaction to SRBC, proliferation and IL-2 production to T-cell mitogen Con A by splenocytes was suppressed to both the concentrations of dapsone throughout the exposure period with a sharp initial increase at 4 weeks exposure. Lymphoproliferation to B-cell mitogen-LPS and PFC numbers to T-dependent (SRBC) and T-independent (LPS-SRBC) antigens were elevated at 4 weeks exposure and gradually declined to base level at 12 to 16 week exposures. Thereafter, proliferation to LPS and PFC profiles were suppressed in the subsequent exposures. Though dapsone at both concentrations showed similar effect on the above immune functions, the magnitude of the early stimulation and later suppression was higher at 0.01% dapsone concentration when compared to 0.001% concentration. This indicated a concentration-dependent response of identical nature. The implication of these results will be discussed.

EX31

STUDY ON NUDE MICE INOCULATED WITH MYCOBACTERIUM LAPRAE BY THE MULTIPLE ROUTES

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The immune-deficient nude mice were inoculated with nude mouse-derived mycobacterium leprae by multiple routes(intravenously, subcutaneously at the foot pads and ears). The results showed that these inoculated animals were capable of producing a great number of Mycobacterium leprae to the level of 10^{11-12} per gram of tissue, and much heavier lepromatous lesions were detectable histopathologically. The dessemination of the infection were particularly found in the sites with lower body temperature. The organisms are prone to proliferate in the striated muscles and peripheral nerves.

The authors suggest that the experimental leprosy in the nude mice is a very useful tool in leprosy research, especially in the countries without armadillos. Compared with the single-route inoculation reported previously, the multiple-route inoculation is of more practical value.

EX32

EXPERIMENTAL LEPROSY IN Dasypus hibridus IN ARGENTINA

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In Argentina leprosy bacilli could be obtained only from biopsy specimens of patients. To assure the continuous production of lepromin and other antigens used in serological assays, it was decided to focus the research on the armadillo. Appropriate facilities to breed and keep armadillos in captivity were built at the Sommer Hospital. In 1990 eigth animals Dasypus hibridus, which were sended by the Panamerican Zoonoses Center (PAHO/WHO), were inoculated with leprosy bacilli. A general examination was performed before the inoculation and each 60 days. The animals were weighed and the following laboratory tests were requested: blood count (red and white cells count, hemoglobin, leukocytary formula, hematocrit), sedimentation rate, prothrombin time, glycemia, uremia, alkaline phosphatasa, SGOT, SGPT, bilirrubin, serological and microbiological tests for the detection of leprosy, tuberculosis and blood parasitical diseases. The inoculum was injected with a tuberculin syringe in the external femoral vein under anaesthesia It was prepared with a human leproma obtained from an untreated patient. One mililiter of this inoculum adjusted to 10^8 b/ml was inoculated to each animal. One armadillo showed disseminated leprosy 26 month after inoculation. Abundant solid bacilli appeared in a skin ulcer (leproma), liver, spleen and lymph nodes. It was possible to purify bacilli from the infected tissues. The inoculation of bacilli into mouse foot pad and Piridin extraction were positive. The culture in diferent medium were negative.

EX33

NERVE CONDUCTION STUDY TECHNIQUE IN THE ARMADILLO

JOSÉ GARBINO, JORGE ALMEIDA, MARCOS VIRMOND

THE ARMADILLO (DASYPUS NOVEMCINCTUS) HAS BEEN ACCEPTED AS THE CHOICE ANIMAL FOR LEPROSY RESEARCH. IN ORDER TO STUDY THE POSSIBILITY OF ESTABLISHING THE ARMADILLO AS A MODEL FOR NEURAL LEPROSY INVOLVEMENT EXPERIMENTALLY, THIS REPORT DESCRIBES THE NERVE CONDUCTION STUDY TECHNIQUE IN THIS ANIMAL, PROVIDED THE LITERATURE ON THIS ISSUE IS SCARCE.

WE EXAMINED THE TIBIAL NERVE OF BOTH SIDES OF 10 ANIMALS FROM THE ARMADILLO FARM OF THE INSTITUTO LAURO SOUZA LIMA. THE TECHNIQUE PERFORMED WAS NERVE CONDUCTION STUDY, THE COMPOUND MUSCLE ACTION POTENTIAL WAS MADE FROM THE PLANTAR MUSCLES IN THE FOOT PAD OF THE LOWER LIMBS. THE STIMULATION SITES WERE DISTALLY, BELLOW THE ANKLE, AND PROXIMALLY JUST CLOSE TO THE KNEE IN THE MEDIAL ASPECT OF THE LIMB. THE DISTANCE BETWEEN THESE TWO POINTS WERE MEASURED WITH A TAPE MEASURE AND THE TEMPERATURE WAS MEASURED BY MEANS OF AN DIGITAL SKIN THERMOMETER WHICH ELECTRODES WERE PLACE HALF WAY OF THE ABOVE MENTIONED POINTS, IN BOOTH SIDES.

WE CONCLUDED THAT THE MOTOR NERVE CONDUCTION STUDY IN THE ARMADILLO IS A FEASIBLE AND EASY TECHNIQUE TO BE PERFORMED IN A STANDART LABORATORY AND COULD BE OF UTMOST IMPORTANCE TO BE USED IN EXPERIMENTAL LEPROSY NEURAL INVOLVEMENT. OUR DATA WITH STATISTICS STUDIES WILL BE PRESENTED.

EX34

THE ARMADILLO AS A MODEL FOR LEPROSY

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Leprosy is unique among human diseases in that the bacillus causing it does not grow in artificial culture media, and until 1971 would not produce disseminated disease in experimental animals. Research was at a standstill. Since then, leprosy bacilli grown in armadillos have been used to produce lepromin-A, a reagent used to predict the course of disease; and PGL-1, a reagent used for its diagnosis. Armadillo-derived vaccines for prevention of leprosy are under test on 470,000 people throughout the world. The biochemistry and genome of the leprosy bacillus, once complete mysteries, are slowly unraveling. As an animal model, the armadillo has led to a better understanding of the pathology, immunology and transmission of disease. The armadillo provides the ultimate answer to people who would like to ban use of animals in medical research. Without this model there would be no research on diagnostic reagents or vaccines. Leprosy would still linger in the shadows of medieval medicine.

EX35

LEPROSY IN WILD ARMADILLOS

Eleanor E. Storrs,
Florida Institute of Technology, Melbourne FL

Until the coming of AIDS, leprosy was the most feared of infectious diseases because the Bible linked it with corruption of both spirit and body. It was a punishment by God for transgression. Most physicians do not think that Biblical leprosy was the disease we know today, but these ancient fears lingered into modern times. In 1975, just four years after the discovery of the armadillo as an animal model, we found that some wild armadillos are naturally infected with leprosy. This was a remarkable coincidence that caused great consternation in the lay and scientific press. Since then, other workers have confirmed that leprosy occurs in many wild armadillos. A few years later, a mangabey monkey housed in our animal colonies at Gulf South Research Institute was found to have leprosy. Within a few years, leprosy was downgraded from its ancient status as a Biblical curse to just another disease common to humans and animals. This discovery opened up a vast natural laboratory for studies of transmission of leprosy in wild animal populations.

IMMUNOLOGY

IM1

THE 65 KDa PROTEIN OF MYOBACTERIUM HABANA AND ITS PUTATIVE ROLE IN IMMUNITY AGAINST M. TUBERCULOSIS.

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Mycobacterium habana (M. simiae serovar-1) an atypical mycobacterium has protective efficacy against M. tuberculosis $H_{37}Rv$ and M. leprae infections in mouse. It generates cell mediated immune responses and shares several immunodominant proteins with these mycobacteria.

The 65 KDa protein of this mycobacterium has been isolated in pure form by isotachophoresis. The isolated protein was run on SDS-PAGE gel, alongwith molecular weight marker, electro-transferred on nitrocellulose membrane and probed with two monoclonal antibodies (mab) IIC8 and IIH9. Both the mabs have identified a single band discrete protein at the same molecular mass. The yield from single dose of (1.5 mg weight = $6.27X10^8$ = 63.3 ug protein) M. habana vaccine is 3 ug. This dose has provided significant degree of protection in mice. The leucocytes/lymphocytes obtained from vaccinated animals and patients of T.B. & Leprosy had stoppage of migration and had shown strong lymphoproliferative response under antigenic influence. Strong CMI responses have been generated by this protein in animal against homo and hetrologous antigens.

IM2

A 25kDa PORTION OF 65kDa PROTEIN OF MYCOBACTERIUM LEPRAE HAS IMMUNO PROTECTIVE PROPERTIES.

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Rabbit antibodies to delipidified cell components (DCC) of M.leprae were used to screen the λgtll library of M.leprae genes and reactive colonies were picked out. One such colony had 1.6kb insert DNA and was expressing a 65kDa protein. This protein was identified in immunoblot using antibodies to DCC. This protein was not reactive with M.leprae 65kDa specific IIIE9 Mab. The DNA sequence showed that the insert started from 1.15kb portion of the classical 65kDa protein gene (Mehra et al,1986). This protein was reactive to another monoclonal antibody to DCC of M.leprae, but this monoclonal had no reactivity to 65kDa hsp of M.leprae. The DNA sequence and the antibody reactivity indicated this protein as a second 65kDa protein of M.leprae. The pUC19 lysate containing this 65kDa had good immunoreactivity listed below. However this 1.6kb insert on recloning in a modified pET vector expressed in BL21 De3 E.coli, a 25kDa protein. This was because of the restricted open reading frame available. This protein has reactivity with specific Mab IIIE9. The protein both in the crude lysate and as partially purified protein

showed (a) immunoprotectivity in vaccinated mice against M.leprae. (b) activation of peritoneal macrophage of vaccinated mice, to kill M.leprae in vitro. (c) ability to induce lymphocyte proliferation in PBMC of lepromatous leprosy patients with release of IL2 and IFN and lastly activation of the macrophages of lepromatous leprosy patients to phagocytose and kill M.leprae.

IM3

CLONING AND CHARACTERISATION OF A 42-kDA SERINE-RICH ANTIGEN FROM MYCOBACTERIUM LEPRAE.

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In order to identify and characterise protein antigens from Mycobacterium leprae which are relevant in the immunology of the disease, a screening strategy of a λgt11 library was carried out using pooled sera from lepromatous leprosy patients. Three positive plaques were identified which contained an identical 1.7kbp insert coding for an immunoreactive 145-kDa β -galactosidase fusion protein. The 1.7kbp insert was subcloned into the lacZ gene in pUR290 and sequence analysis of the end adjacent to lacZ revealed an ORF with no significant homology to sequences already reported. In order to isolate the gene for this protein, the 1.7kbp insert was used to screen an M.leprae cosmid library by hybridisation. Five overlapping cosmid clones were identified, and an M.leprae 1.8kbp HindIII fragment was subcloned from one of these to perform sequence analysis. A 1227bp ORF was found to code for a 408 amino acid protein with a predicted mass of 42,466-Da. The hydrophilic domain in the centre of this protein contains a high proportion of serine residues, and the hydrophobic amino terminal showed some homology to a 51-kDa hypothetical antigen of M.tuberculosis.

It was found that sera from multibacillary and paucibacillary patients (78 & 68% of cases respectively), had IgG antibodies directed against this molecule, whereas endemic control sera did not recognise a similar band in immunoblotting studies. We also demonstrated that this major M.leprae antigen carries cross reactive determinants since 26% of patients with active pulmonary tuberculosis had antibodies recognising this 42,466-Da protein.

IM4

HEAT SHOCK PROTEINS IN LEPROSY REVERSAL REACTIONS

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Heat shock proteins are synthesised by cells in response to cellular stresses. They have a wide distribution and have important roles in the immune, inflammatory and auto-immune responses. The immunodominant 70kDa M leprae protein has been shown to belong to the heat shock protein family 70. We have examined skin and nerve biopsies from reactional patients to determine whether heat shock proteins play a role in these acute inflammatory episodes.

39 skin biopsies and 10 nerve biopsies have been stained for constitutive and inducible heat shock proteins. Positive staining for HSP 70 was seen in macrophages in leprosy lesions. In reversal reactions there is a statistically significant, specific increase in the number of HSP 70 positive cells in both skin and nerve. It is possible that the elevated expression of host HSP70 in leprosy patients already primed to recognise *M leprae* 70 Kda results in the development of local auto-immunity with exacerbation of damage to nerve and skin.

IM5

CROSS-REACTIVE RECOGNITION OF HUMAN T CELL EPITOPES IN THE M.LEPRAE 18KDA ANTIGEN.

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The M.leprae 18kDa antigen was one of the first recombinant leprosy antigens to become available. It is strongly recognised by the T cells of healthy leprosy contacts who are presumed to have protective immunity (Dockrell et al. Infect. Immun. 57:1979(1989)), which might make it a candidate leprosy vaccine. However BCG-vaccinated donors, not previously exposed to leprosy, can also respond to this protein. We have used a panel of M.leprae 18kDa reactive human T cell clones, and a series of 15mer overlapping peptides which span the 18kDA sequence, to map the epitopes BCG vaccinated donors recognise in the M.leprae 18kDa antigen. One clone recognised the region amino acids 38-50, previously shown to be recognised by M.leprae-specific human T cell clones isolated from donors vaccinated with a killed M.leprae vaccine (Oftung et al, J.Immunol. 144: 1478(1990)). The region between amino acids 38 and 50 cannot therefore be considered to be M.leprae specific.Two further clones recognised the region 21-35, not previously described as a human T cell epitope. This region does not show striking homology with the M.tuberculosis 16kDa antigen (previously described as 14kDa (Verbon et al, J.Bact. 174:1352 (1992)).

IM6

A NOVEL PROTEIN ANTIGEN SECRETED BY *M.LEPRAE*: THE HOMOLOGUE OF *M.TUBERCULOSIS* MPT32

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Recent studies have indicated that secreted proteins are major targets in the immune response to mycobacteria, including *M.leprae*. To identify potential secreted *M.leprae* antigens we tested polyclonal rabbit antisera specific for culture filtrate proteins of *M.tuberculosis* against a panel of novel recombinant *M.leprae* antigens that were recently identified by leprosy patient sera. As expected secreted antigen 85 complex proteins specified by clones L7 and L44 were recognized by the rabbit antisera, but in addition three other clones designated L14, L24 and L2 were identified to express polypeptides that were recognized. Consecutive use of monospecific sera specific for distinct secreted proteins of *M.tuberculosis* indicated that L14 expressed an antigen similar to MPT32, a 41 kilodalton (kDa) secreted protein of *M.tuberculosis*. Sequence analysis of a cosmid clone homologous to L14 revealed the presence of an open reading frame (ORF) predicting an *M.leprae* protein of 287 amino acids. This ORF consists of a potential signal sequence of 39 amino acids followed by a mature protein of 248 amino acids. The 20 N-terminal amino acids of the mature protein show extensive homology with the N-terminal sequence of MPT32. We conclude from these findings that clone L14 expresses a homologue of MPT32, and is likely to be a secreted *M.leprae* protein. No significant homology was found with sequences in EMBL/Genbank databases. The C-terminal 230 amino acids expressed by L14 are extensively recognized by antibodies and T-cells from leprosy patients and healthy contacts. Together with the reported strong immune response to the secreted antigen 85 complex, these findings further indicate a major role for secreted antigens in the immune response to *M.leprae*.

IM7

NEW LEPROSY SKIN TEST ANTIGENS

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The dramatic reduction in the prevalence of global leprosy does not necessarily correspond to a fall in the incidence of disease. One of the most pressing needs of leprosy control programs is epidemiologically acceptable assays to measure incidence, reservoirs of infection, and transmission of disease. Yet our

options are limited. Serology has failed us. Gene amplification protocols may not be applicable. To address this immediate need, three new leprosy skin test antigens were developed: SP-, soluble proteins of M. leprae; SolPCW, soluble proteins extracted from the cell wall of M. leprae; and rMCP-I, recombinant major cytosolic protein of M. leprae of Mr 10.8 kDa. The SP- antigen is similar to the skin test antigens of Rees (STA, Lepromin, MLSA) and of Convit (STA, SPA, SA) except that cross-reactive "suppressive" carbohydrates and lipids were removed. SolPCW is composed of the SDS-extracted cell wall proteins which are known to be highly immunogenic. By separating cell wall proteins from the underlying peptidoglycan complex, it is thought that the undesirable feature, characteristic of lepromin A, of sensitization to a subsequent test, will be eliminated. The recombinant MCP-I protein is identical to its native counterpart and stimulates the proliferation of peripheral blood T-cells better than other native and recombinant products tested. Preliminary testing of each of these new skin test antigens in sensitized guinea pigs resulted in a strong DTH response. Based on these results, an investigational new drug (IND) application has been submitted to the Federal Drug Administration. Upon approval, phase 1 testing in humans will be conducted by Dr. G.P. Walsh in Cebu, Philippines. Work supported by NIH, NIAID Contract NO1 AI-05074.

IM8

B-CELL EPITOPES OF HSP65 IN THE AUTOIMMUNE DISEASES

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We describe B-cell epitopes of HSP65 of Kawasaki diseases (KD), Rheumatoid arthritis (RA) and leprosy patients, and will discuss the role of HSP65 in autoimmunity.

The sera from KD patients in convalescent but not acute phase cross-reacted with HSP65 of M. leprae. To determine whether the endogenous and/or exogenous 65kD protein are activated for B-cell epitopes in Kawasaki diseases, two kinds of chemically synthesized peptides were used. One is the epitope for MAb-IIIE9 for exogenous 65kD, and another is the corresponding site of a human homolog to the mycobacterial 65kD protein, P1 protein in human mitocondria, for endogenous epitope. The convalescent sera but not acute phase sera of KD reacted with both of these epitopes for endogenous and exogenous proteins. On the other hand, sera from mice immunized withM. leprae lysate or purified 65KD reacted with IIIE9 -epitope, but did not react with the P1 epitope.

In leprosy, 20% of lepromatous leprosy patients and 29% of tuberculoid leprosy patients show a significantly higher titer to HSP65 of M. leprae compared to the healthy controls. Since about 30% were sero-positive to RA factor in leprosy, the titer of sera from leprosy patients to HSP65 may be correlated to the RA factor. Sero-positivity to HSP65 was 20% in the group of RA positive sera, and 13% in RA negative sera.

IM9

RECOGNITION OF 21- AND 14- KILODALTONS ANTIGENS OF MYCOBACTERIUM ICRC BY ANTI-MYCOBACTERIUM LEPRAE ANTIBODIES

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ICRC, a cultivable mycobacterium isolated from human lepromata is undergoing clinical trials as an anti-leprosy vaccine in India. Antigens of ICRC share cross-reactive epitopes with antigens of Mycobacterium leprae. Radioimmunoprecipitation of 125-I labelled ICRC antigens with sera from lepromatous leprosy patients, borderline lepromatous leprosy patients, borderline tuberculoid leprosy patients, tuberculoid leprosy patients, healthy contacts, tuberculosis patients and healthy individuals, demonstrated that 21- kD antigen of ICRC was exclusively precipitated by sera from all lepromatous leprosy patients and those undergoing erythema nodosum leprosum reaction. The 14-kD antigen of ICRC was identified by sera from a few lepromatous leprosy patients (5 of 26) and all the contacts. However, using M.leprae antigens, it was not possible to distinguish between reactivities of sera from leprosy patients across the clinical spectrum. It was observed that polyclonal anti-ICRC and anti-M.leprae antibodies also showed predominant reactivity to 21-kD protein of ICRC. Furthermore, M.leprae-specific monoclonal antibody WML06 showed reactivity to 21- and 14-kD proteins of ICRC. Studies are in progress to map the relevant epitopes on the 21- and 14- kD antigens of ICRC showing reactivity with patients' sera and anti-M.leprae polyclonal and monoclonal antibodies.

IM10

T CELL RESPONSES TO SYNTHETIC PEPTIDES IN HUMAN LEPROSY

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12- 24mer peptides (kindly provided by M.E.Pattarayo, Institute de Immunologia, Bogota, Columbia and M.J. Colston, NIMR, Mill Hill, London, UK) were synthesised based on the sequence of the immunodominant protein LSR2, reported by us from the lambda gt 11 library of *M.leprae* (Laal et al PNAS, 88, 1054-58, 1991). They were screened in lymphoproliferation assay using peripheral blood of leprosy patients from three geographic regions comprising of Tamil Nadu (South India), New Delhi (North India), and Bogota (Colombia).

The pattern of recognition by T cells varied in different clinical types of leprosy as well as in different ethnic populations. Interestingly, peptide *CGAAIREWARRNGHVSTRGRIGC* was recognised by 60% of BL/LL patients who showed unresponsiveness to the total recombinant protein.

This peptide was recognised by all patients in Type I and II reactions. Studies using overlapping peptides indicated a preferential recognition of RGR and REW motifs.

PCR based mRNA cytokine profile of LSR2 and peptide stimulated lymphocytes of lepromatous and tuberculoid individuals showed discriminatory signals for IL-2, IFN-γ, GM-CSF, IL-4, IL-6 and IL-10.

IM11

DEMONSTRATION OF MYCOBACTERIAL ANTIGENS IN THE SKIN SMEARS OF TUBERCULOID PATIENTS OF LEPROSY

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Although many specific serological assays were developed for diagnosis of leprosy but none of these assays is able to detect more than 60 per cent of established cases of tuberculoid leprosy. It was noted that at any early stage of the disease the levels of both antibody (Ab) and antigen (Ag) were not above the level of the background level present in the endemic population. Hence Ag/Ab levels of many tuberculoid leprosy patients fell below the cut off point. The present study was, therefore, carried out to find out the level of Ag/Ab in in situ situations in the lesions. Using a cross reactive anti-BCG antibody about 80 per cent of tuberculoid leprosy cases could be identified in dot-blot immunoassay from routine slit and skin smear samples. It was interesting to note that many of these samples were positive for the presence of local antibodies also. The results will be presented in detail and discussed.

IM12

A 15-KILODALTON ANTIGEN OF *MYCOBACTERIUM LEPRAE* THAT IS RECOGNIZED BY BOTH HUMORAL AND CELLULAR IMMUNE SYSTEMS IN LEPROSY PATIENTS

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A colony immunoblot technique was used to screen the *Mycobacterium leprae* cosmid library with pooled sera from lepromatous (LL) leprosy patients. Four of the 100 clones that produced immunologically reactive proteins were found to specify a 15 kDa antigen (A15) that reacted strongly with LL patients' sera on a Western blot. This 15 kDa antigen also reacted with pooled sera from tuberculoid leprosy patients from the U.S. and Brazil. Each of these clones contained a common 1.2 kb *Pst*I fragment. Nucleotide sequence analysis of the 1.2 kb fragment revealed the presence of three open reading frames (ORFs), only one of which (ORF II) contains sufficient genetic information to code for A15. Sequences homologous to the A15 gene were also detected in chromosomal DNA from *Mycobacterium avium, Mycobacterium bovis* BCG, and *M. tuberculosis*. One of the γt11::*M. leprae* clones (L8) previously identified by us expresses a β-galactosidase fusion protein with 89 amino acids from the C terminus of A15. This fusion protein was clearly recognized by *M. tuberculosis*-stimulated T cells from both LL and BT leprosy patients.

IM13

ANTIBODY RESPONSE OF PATIENTS WITH BORDERLINE LEPROMATOUS AND BORDERLINE TUBERCULOID LEPROSY TO MYCOBACTERIAL 29/33 KDa DOUBLET AND 65 KDa SINGLET ANTIGENS.

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Using immunoblot assays (ImBA) and enzyme-linked immunosorbent assays (ELISA) for antibodies to mycobacterial immuno cross reactive antigenic components (Im-CRAC) we have already shown that sera of patients with lepromatous (L) and tuberculoid (T) leprosy reacts in significant manner to 29/33 (KDa) doublet and 65 KDa mycobacterial Im CRAC respectively (J Clin Microbiol 1990; 28: 379-382).
Furthermore, we proposed that measurement of antibodies to these antigens by an ELISA will be useful for distinguishing two polar types of leprosy. In this report we have extended our previous studies on a serological survey in which both EILISA and ImBA have been extensively used for diagnosis of different stages of leprosy, particularly those of borderline groups (borderline lepromatous (BL) and borderline tuberculoid (BT). The patient groups consisted of 32 LL, 26 BL, 22 BT and 37 TT patients. By making use of both serological methods we have been able to discriminate the four types of leprosy from each other with an average of sensitivities: 85 - 95 % and specificities: 80 - 95 %. We hypothesize that this presently described serology may be useful for diagnosis and follow-up.

IM14

IMMUNOGENICITY AND PROTECTION STUDIES WITH RECOMBINANT VACCINIA AND BCG EACH EXPRESSING THE 18kD ANTIGEN OF *Mycobacterium leprae*.

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The 18kD antigen is relatively specific to the leprosy bacillus and no homologue has been found in *M.bovis* BCG. T lymphocytes, which are essential for the control of mycobacterial infection in humans and mice, recognise a number of epitopes within this antigen following infection with *M.leprae* or immunisation with *M.leprae* sonicate. Whether immune responses to this particular antigen contribute to the control of *M.leprae* infection is uncertain. Since vaccination with recombinant vectors (rV) may enhance T cell responses to co-expressed antigens compared to adjuvant-based vaccination, rV using vaccinia virus (VV) and *M.bovis* BCG were prepared. The gene for the 18kD protein was inserted into the thymidine kinase region for the VV constructs under control of both the early and late promoter. The gene for the 18kD protein was inserted into BCG constructs under the control of either the 18kD promoter or the 65kD (heat shock) promoter. Different mouse strains were injected with viable VV (10^6 PFU) or BCG constructs (10^6 CFU) by various routes, and sera as well as lymphocytes from regional lymphoid tissue collected. IgM and IgG (including IgG1 and IgG2a) antibody responses to the 18kD antigen were detected by ELISA from all strains of mice, although the vaccinia constructs induced the highest specific antibody titres. T cell proliferative responses to the 18kD antigen, were maximal in B6-H2k mice after subcutaneous immunisation with either construct at 2 weeks. Recombinant BCG stimulated delayed type hypersensitivity responses to soluble 18kD antigen in guinea pigs. Prior vaccination with VV co-expressing the 18kD antigen conferred partial protection to BCG-18kD, as measured by a reduction in the number of CFUs of BCG in the spleens of mice challenged with recombinant BCG. This model system permits the comparison of the protective efficacy of recombinant viral and BCG vectors encoding the same *M.leprae* protein.

IM15

LYMPHOCYTE PROLIFERATION AND CYTOKINE SECRETION IN RESPONSE TO PURIFIED MYCOBACTERIAL HSP AND TO Ag85 DURING INFECTION WITH *MYCOBACTERIUM LEPRAE*.

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Peripheral blood leucocytes from 9 paucibacillary and 12 multibacillary leprosy patients, 18 healthy controls and 34 healthy leprosy contacts were stimulated with three mycobacterial heat shock proteins with respective m.w. of 70, 65 and 18 kDa and with the secreted 30-32 kDa protein, also called antigen 85. Ag85 was found to be the most powerful T cell antigen (as measured by lymphoproliferation and IFN-γ secretion), eliciting a response in 9/9 paucibacillary patients, in 10/10 lepromin positive controls and in 25/25 lepromin positive contacts. The three hsp were less active T cell stimuli. The 70 kDa hsp elicited responses in only 4/9 paucibacillary patients, in 8/10 lepromin positive controls and in 15/25 lepromin positive contacts. The 65 kDa hsp stimulated T cells of 8/9 paucibacillary patients, of 8/10 lepromin positive contacts and of 20/25 lepromin positive contacts. The 18 kDa hsp finally, elicited T cell responses in 7/9 paucibacillary patients, in 4/10 lepromin positive controls and in only 1/25 lepromin positive contacts. T cell reactivity of lepromin negative controls (n=8), lepromin negative contacts (n=9) and of multibacillary leprosy patients were low to all the antigens tested.

These data confirm our previous findings on the immunodominant character of Ag85 during *M. leprae* infection and suggest that this antigen is indeed a potentially protective T cell immunogen.

Secretion of the monokine IL-6 was also examined in this study. Elevated IL-6 levels were found, in response to all the antigens tested, in PBMC culture supernatants from paucibacillary and especially multibacillary leprosy patients. In lepromin negative healthy contacts, the 70 kDa hsp was the only antigen capable of inducing significant IL-6 production. In lepromin positive healthy contacts finally, Ag85, the 65 kDa and especially the 70 kDa hsp induced substantial IL-6 titers. The 18 kDa hsp did not induce any IL-6 in these healthy lepromin positive contacts.

IM16

LEVELS OF IL-6 AND TNF RECEPTORS IN ENL.

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ENL is an acute inflammatory complication of leprosy disease. it has been demonstrated that ENL patients present high TNFα levels in the serum and that the amount of TNF seems to correlate with the intensity of their clinical symptoms. Although high TNFα levels are associated to the fatal outcome in other syndromes, elevated TNF in ENL coexists with the benign course of the disease. Increased levels of other inflammatory cytokines in the serum and the presence of inhibitors seem to modulate the toxic systemic effects of TNFα in organs and tissues of the body. In this study, we investigated the levels of IL-6 and soluble TNF receptors by specific Elisa in the serum of 13 ENL patients previously found to be positive for TNFα. Nine patients were found to be positive for IL-6 in the sera with a mean ± SEM of 587 ± 286 pg/ml, ranging from 0 to 4,880 pg/ml. Although

IL-6 is also overproduced during the reactional state, IL-6 values were inversely related to those of TNFα. The amount of TNF-Rα (the 75 KD protein) was found to be elevated in all patients tested which correlated with the high TNF levels present in the circulation. The present data suggest that both presence of TNF-R and lack of simultaneous high levels of IL-6 in the circulation, during ENL, can justify at least in part the benign course of reactions in leprosy.

Supported by grants from TDR-WHO.

IM17

ASSOCIATION OF NK(CD16+) CELLS AND CYTOKINES WITH M.LEPRAE-SPECIFIC RESPONSES IN TYPE 1 REACTIONS

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During Type 1 reaction(TR1), a leprosy manifestation more frequent on borderline leprosy patients, and associated with neuritis, there is emergence of antigen-specific immune response to M.leprae, in previously unresponsive individuals. Enhancement of natural killer function was also observed during the course of TR1(PJ Converse & G Bjune, 1986). To further evaluate the participation of antigen-specific immunity and innate responses in TR1, we analyzed 18 patients(10 BL, 4 BB, and 4 LL; 12 male and 6 female). The 18 patients were previously negative for lepromin skin test and turned positive during TR1. The relative proportion of CD16+ on peripheral blood mononuclear cells(PBLs) had a 3x increase during TR1(13.0±0.4%, n=7) when compared with values post TR1(4.6±0.5%, n=10). T-lymphocyte *in vitro* proliferation to *M. leprae*, and production of IFN-γ were also present during TR1 but returned to absence of response after the end of the reaction(50.0±12.0 U/ml during TR1, n=5; and 3.5±3.2 U/ml after TR1, n=3). In the course of TR1, serum levels of IL-6 were higher than on normal volunteers(NV) and BT leprosy patients(340.0±58.5 pg/ml, TR1, n=5; and 79.5±20.1 pg/ml, BT+NV, n=5) but TNF-α serum levels were similar to BT and NV(10.6±0.4 pg/ml vs. 34.36±19.0 pg/ml. These observations are consistent with an enhancement of NK function during TR1 as a consequence of increment in NK cell number in the PBLs. It remains to be determined if the appearance of *M. leprae*-specific immune response during TR1, is a consequence of the transient increase in the level of NK activity, or if the specific immune response drives the innate functions during the reactional episode. Supported by grants from TDR-WHO and CNPq

IM18

PROBLEMS IN DETECTION OF SECRETORY ANTIGENS OF INTRACELLULAR MYCOBACTERIA IN MACROPHAGE AND SCHWANN CELL TISSUE CULTURE

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Identification of mycobacterial (ML and H37 Rv) antigens in supernatants of infected growth promoting host cells viz. Schwann cells (Sc) and mφs constitutes the first step in the development of an immunodiagnostic test that can be used ultimately to monitor efficacy of treatment in mycobacterial diseases such as tuberculosis and leprosy.

The well characterized BCG 85 antigen complex was used as a model detection indicator in a capture ELISA & 2-D electrophoresis for testing of supernatants derived from ML/H37 Rv infected murine Sc/mφs respectively. A significant problem was the establishment of BCG 85 as a true marker for viability as opposed to its release from lysed bacteria. This was attempted by co-detection of exclusively cytoplasmic antigens in the culture system. Approaches to enhance sensitivity of detection included physical concentration, minimization of serum content in the medium and use of protease inhibitors.

Future purposes for these observations will be outlined.

IM19

CYTOKINE PATTERNS IN LEPROSY

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Previous evidence from our laboratory indicated that T-suppressor (Ts) cells may be one mechanism of maintaining peripheral tolerance to *M.leprae* in lepromatous leprosy. To understand the cellular basis of Ts cell mediated suppression, we studied the lymphokine profile of the Ts clones and compared it with mycobacteria and tetanus toxoid reactive $CD4^+$ clones and allo-reactive $CD8^+$ cytotoxic clones. All of the mycobacteria reactive $CD4^+$ clones generated from tuberculoid lesions or healthy contacts produced γ-IFN and IL-2 but little or no IL-4 and IL-5, similar to the pattern of lymphokines characteristic of murine Th1 cells. These cells were designated "Type 1 cells". The $CD4^+$ tetanus toxoid clones produced little γ-IFN and high levels of IL-4, IL-5 and IL-10, a pattern similar to murine Th2 cells and were designated as "Type 2" cells. The clones making IL-4 also had helper activity for B-cells. The $CD8^+$ clones from lepromatous patients produced predominantly IL-4 but little or no IL-6, IL-5, IL-10 and γ-IFN. In contrast the $CD8^+$ cytotoxic clones secreted γ-IFN, IL-6 and IL-10 and made no detectable levels of IL-4 and IL-5. Although IL-4 and IL-5 production are highly associated in $CD4^+$ cells, IL-5 was not secreted by the IL-4 producing $CD8^+$ Ts cells. Our data suggest that the human $CD8^+$ population can also be divided into two subsets: Type 1 $CD8^+$ cytotoxic cells and Type 2 Ts cells. IL-4 production by the Ts cells was a necessary condition for suppression in this system because anti-IL-4 antibody was able to block the suppressor activity. Further the effect of IL-4 was at the level of IL-2 gene transcription of the Type 1 cells. Our findings suggest an explanation for the classical immunological dichotomy between the development of humoral immune responses and those of cell-mediated immunity. The observations of Type 1 and Type 2 T-cell functions in many infectious diseases can in part be explained by the action of IL-4, probably in conjunction with other cytokines, not only to enhance antibody formation but also to depress cell-mediated immunity required for protection.

IM20

CYTOKINES IN IMMUNOPATHOLOGY OF LEPRA REACTION

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Cytokines are involved in the immunopathological complications of several infectious conditions, but their role in leprosy has yet to be clearly defined. We have studied serum TNFα, IL-1β and IL-6 levels in 220 leprosy patients across the spectrum of the disease (lepromatous, borderline and tuberculoid types) and during lepra reaction. Dramatically elevated cytokine levels were observed: levels as high as 8,000 pg/ml of TNFα (382±176), 5,000 pg/ml of IL-1β (373±183) and 3,500 pg/ml of IL-6 (223±104) in lepromatous leprosy patients and also in patients during reaction, while cytokines remained within normal range in most of the patients with tuberculoid leprosy and in all clinically healthy individuals. At study entry, there was a significant correlation between serum levels of these cytokines. All these patients were followed up for 1-2 years. It was observed that 73% of patients having raised serum TNFα level >100 pg/ml and all patients with IL-1β level >200 pg/ml at admission time point manifest with severe episodes of lepra reaction following 2-4 months period in comparison to about 10% of patients having <100 pg/ml of TNFα and <200 pg/ml of IL-1β suggesting potential prognostic implications of these cytokines in predicting the onset of reaction, thereby helping to identify patients at risk. In the skin lesions of the patients, immunohistochemistry and *in situ* hybridization revealed elevated expression of TNFα in the epidermal layers and in granuloma areas implying the direct role of these cytokines in the immunopathology of leprosy. Localisation studies of different cytokines in the nerves of patients with reaction will be discussed.

IM21

DETERMINATION OF SUBCELLULAR LOCATION OF THE IMMUNOPROTECTIVE MOIETIES IN MYCOBACTERIUM HABANA

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M. habana, a nonpathogenic, cultivable mycobacterium offers protection against experimental infection with M. leprae and M. tuberculosis. Present study aims at subcellular localization of the protective moieties in this candidate vaccine.

The cell wall, cell membrane and cytosol fractions were prepared by sonication and differential centrifugati on of the bacilli grown in liquid shake cultures. Groups of mice were immunised with these fractions (dosages adjusted in relation to the dose of integral vaccine) in addition to the integral vaccine (killed M. habana) and placebo, and subsequently challenged with M. tuberculosis H_{37} Rv. The animals were examined for survival and associated parameters.

Preliminary results indicate that the protective moieties most probably are located in the cell membrane. Data on morphological, biochemical and immunological characterisation of M. habana membrane will also be presented.

IM22

M.leprae 10kD HEAT SHOCK PROTEIN IS A MAJOR T CELL ANTIGEN

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The development of reagents for prevention, control and early diagnosis of leprosy depends on identification of antigens relevant for eliciting T cell responsiveness. Several approaches to identify immuno-reactive determinants of mycobacteria have resulted in identification and characterization of many proteins that elicit T cell reactivity in small numbers of immunized donors. Our previous studies on the analysis of M. leprae antigens using T cell Western blots indicated that most M.leprae reactive T cell lines developed from lepromin positive individuals recognized an antigen of 7-10kD mol. wt. The gene encoding this antigen was isolated from lambda gtll library and sequenced. The deduced amino acid sequence of M.leprae 10kD protein was found to have 44% identity with hsp 10 (GroES) of E.coli. As native 10kD protein was found to be highly immunoreactive in inducing T cell proliferation in M.leprae immunized individuals, and DTH responses in guinea-pigs, we expressed it in E.coli using pMAL-c expression vector, to produce the recombinant 10kD protein in large quantitites for further evaluation. The immunological studies using recombinant protein show significant lymphoproliferation in vitro of PBL from leprosy contacts and TT patients to 10kD antigen. The magnitude of T cell proliferation to 10kD protein was similar to that with whole M. leprae throughout the spectrum of leprosy. Limiting-dilution analysis indicated that one third of M.leprae reactive T cell precursors responded to 10kD antigen. It evoked greater lymphoproliferation than other purified antigens tested. T cell lines derived from Mitsuda reaction showed marked proliferation to this antigen. Further, purified recombinant 10kD antigen elicited strong delayed hypersensitivity recactions in guinea-pigs sensitized to M.leprae. Strong T cell responses to M.leprae 10kD protein suggest a role for this protein in protection against leprosy.

IM23

STUDIES ON POTENTIAL USES OF MLPA IN LEPROSY

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Gelatin Particle Agglutination Test (GPAT or MLPA, MA) and NT-P-BSA-ELISA (NT-ELISA, NE) are two methods for detecting infection with M.leprae. In order to evaluate them, we conducted systematically comparison of MA with NE.Samples:Leprosy patients 158(LL 58,BL 55,BT 20,TT 20), Household contacts(HC) 155, random population(RP) 149, normal controls(NC) 40.

Results:1.MA at 1:32 serial dilution(MA 1:32),positivity rate(PR) was 73%, MA 1:16—91%;PR of NE1(OD=0.10) was 98%,PR of NE2 (OD=0.20)—91%. The individual agreement (IA) were more than 90% between MA 1:16 and NE,while the IA were more than 70% between MA 1:32 and NE. In multibacillary patients(MB), the IA were 96—100% between MA 1:16 and NE,and 83—96% between MA 1:32 and NE. Quantitative data support above results.These results suggested that NE could not be replaced with MA, and MA is suitable to detect MB.

2. Comparison of sera with dried sera and dried blood on filter paper: results indicated that: (1) the best results of them were those in sera in MA and NE, and in MA, the defferences were no significances between sera and dried blood (X^2 = 3.2, P>0.05), and the identical results were obtained in dried blood which were reconstituted by means of calculating sera content of dried blood. If the reconstitution does not consider the sera content of dried blood, the PR and IA were all to be decreased (<10%).

3. Comparison of U-bottom plate with V-bottom plate: the differences of results were of no significance between U-bottom and V-bottom plate (X^2=0, P>0.99, IA =93.3%). It is easier to judge the results using V-bottom plate.

IM24

PRODUCTION OF MONOCLONAL ANTIBODIES AGAINST MYCOBACTERIUM LEPRAE

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A series of hybridoma cell lines,which secrete monoclonal antibodies(McAbs),were produced by means of fusion between mouse myeloma cells SP2/0 and spleen cells from BALB/C mice immunized with whole M.leprae plus unique phenolic glycolipid I(PGL-I) of M.leprae and M.leprae sonicates supernatant fluid (MLSS) as immunogen.Primary identification indicated that H2 cell line can secrete McAb against the epitope of PGL-I; IIIE10 cell line can secrete McAb against PGL-I and MLSS and (5)24D6C8 cell line only against whole M.leprae. The uses of these McAbs in serodiagnosis of leprosy, identification of M.leprae, analysis and purification of M.leprae antigens, and key problems in technology for producing McAbs against M.leprae were also discussed.

IM25

REACTIVITY OF LEPROSY AND CONTROL SERA TO CRUDE AND RECOMBINANT MYCOBACTERIUM LEPRAE ANTIGENS.

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Immunoblotting studies were carried out in order to identify reactivity patterns of sera from leprosy patients and controls to crude and recombinant M.leprae antigens. Four armadillo-derived M.leprae sonic extracts and a 145-kDa M.leprae β-gal fusion protein were fractionated by SDS-PAGE and blotted onto nitrocellulose filters. Sera from leprosy patients across the disease spectrum, patients with active pulmonary tuberculosis, and healthy endemic controls were used to probe antigenic strips. The leprosy patients were from Mexico and Pakistan, whereas the patients with tuberculosis and endemic controls were from Mexico.

It was found that a total of 89 out of 116 (77%) individual leprosy sera contained IgG antibodies directed to antigens in the sonicates (90% of 75 multibacillary and 54% of 41 paucibacillary patients). Antigenic bands of 65, 33,

18, and 15-kDa were the most frequently identified. In particular, 83% of patients with a history of Erythema Nodosum Leprosum (ENL) had antibodies direct to the 33-kDa protein; a similar band was recognised by 16% of tuberculosis patients but not by sera from endemic controls.

A 42-kDa M.leprae recombinant antigen partially expressed as a 145-kDa β-gal fusion protein was recognised by 75% of 76 individual leprosy sera. Analysis of recognition patterns by different patient groups revealed that 78% multibacillary and 68% paucibacillary cases had antibodies directed to this molecule. The recombinant antigen was recognised by 94% of patients with a history of ENL, 26% of tuberculosis patients, and none of the control sera. Statistical analysis of recognition patterns among patients and controls suggested that the 42-kDa recombinant antigen has potential as a prognostic marker of leprosy reactions.

IM26

M.LEPRAE ANTIGENS CAN BE RECOGNISED BY BOTH TH1-LIKE AND TH2-LIKE HUMAN T CELLS

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Recent studies have suggested that tuberculoid leprosy may represent a Th1 form of the disease, while T cells with the properties of Th2 T cells predominate in lepromatous leprosy. A panel of human T cell clones have been obtained from BCG vaccinated donors who respond to M.leprae sonicate and to the M.leprae recombinant 18kDa antigen. Cloning was performed in the presence of antigen, IL-2 and autologous irradiated peripheral blood mononuclear cells as antigen presenting cells. Clones were selected by the ability to incorporate tritiated thymidine in a dose dependent fashion to the antigen used for cloning. Supernatants from antigen-stimulated cultures of clones were screened for the secretion of interferon-g by sandwich ELISA. On the basis of proliferation and interferon-g production, the clones could be separated into three groups. The majority of the clones showed a positive correlation between interferon-g production and proliferation resembling Th1 T cells. A smaller group showed much higher levels of interferon-g production relative to proliferation. A few clones gave proliferation without detectable interferon-g production. These clones, one of which recognised the 18KD antigen, produced IL-4, detected by ELISA. All the clones were CD4⁺ CD8⁻, αß⁺ and δ⁻. Thus even in donors with predominant Th1 T cell responses, a minority of Th-2-like T cells responsive to mycobacterial antigens are present, in the absence of any clear ongoing Th-2 response to allergens or worms. We are now investigating the role of other cytokines in the development of Th1 and Th2 CD4⁺ T cell response to M.leprae antigens.

IM27

MODULATION OF MHC CLASS-II ANTIGEN EXPRESSION ON ANTIGEN PRESENTING CELLS OF LEPROSY PATIENTS BY *MYCOBACTERIUM LEPRAE*.

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MHC antigens play an important role in antigen presentation to T cells. Down regulation of MHC class-II antigen by any pathogen would therefore hamper the full expression of T cell functions in the diseased host. The present study was undertaken to address whether aberrations in modulation of MHC class-II antigens on monocytes could explain the antigen specific T-cell anergy seen in lepromatous leprosy patients. Flow cytometric analysis using two colour fluorescence was used to analyse the expression of MHC class II antigens (HLA-DR, -DQ, -DP) and CD 14 as a marker for monocytes. MHC class-II antigen expression was induced with time in healthy individuals, tuberculoid (TT/BT) and lepromatous (BL/LL) leprosy patients. This was independent of antigenic stimuli. The expression of HLA-DR was 6-8 fold more than that of HLA-DQ and HLA-DP. Down regulation of class-II antigen expression was observed at 12 and 24 hours with live and heat killed *M.leprae*. However, this down regulation was not specific as it was also observed with live *M.tuberculosis* H37Ra.

IM28

IgG ACTIVITY TOWARDS PURIFIED HEAT SHOCK PROTEINS AND ANTIGEN 85 IN LEPROSY PATIENTS AND THEIR CONTACTS

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Sera from 9 paucibacillary and 12 multibacillary leprosy patients, 18 healthy controls and 34 healthy leprosy patients contacts were analysed towards three heat-shock-proteins with M.W. of 70, 65 and 18 kDa and towards the secreted antigen 85 in a dot blot assay.

High reactivity to the 70 kDa molecules was observed in all groups of subjects. Indeed, 10/12 of multibacillary patients, 7/9 of paucibacillary patients, 20/25 Mitsuda positive contacts and 6/9 of Mitsuda negative contacts recognized the 70 kDa protein.

IgG activity towards the hsp 65 was higher in patients with positive Mitsuda reaction -i-e paucibacillary patients and lepromin positive contacts - than in patients with negative Mitsuda reaction.

None of the serum samples tested showed binding to the 18 kDa molecules.

12/12 of multibacillary patients, 2/9 of paucibacillary patients, 7/25 Mitsuda positive contacts and 3/9 of Mitsuda negative contacts were positive with antigen 85.

In conclusion, multibacillary leprosy patients recognized preferentially the 70 kDa molecules and the antigen 85 and sera from paucibacillary patients exhibited reactivity to the 65 and 70 kDa molecules.

IM29

RECONOCIMIENTO DE ANTIGENOS DE *MYCOBACTERIUM LEPRAE* EN PACIENTES HANSENIANOS

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Las células mononucleares (linfocitos T) de pacientes con lepra tuberculoide, de sus contactos sanos y voluntarios no relacionados dieron una buena respuesta al estímulo con un extracto soluble de Mycobacterium leprae. En estudios preliminares realizados en el laboratorio, se aportaron evidencias experimentales, mediante T-cell blotting, de una respuesta positiva de células mononucleares de sangre periférica proveniente de dichos pacientes y familiares contactos Mitsuda positivos frente a antígenos proteicos separados por SDS-PAGE. Se encontró actividad en las fracciones con intervalos de peso molecular de 45-29, 22-18 y 14 kDa, principalmente. Estos hallazgos se han relacionado con ensayos posteriores de la respuesta humoral (inmunoblotting), utilizando sueros policlonales de 10 pacientes con lepra lepromatosa(LL). Se detectó actividad frente a algunos de estos mismos antígenos (30, 16 y 14 kDa) despues de la absorción de dichos sueros con M. bovis, evidenciándose en consecuencia una alta especificidad con respecto a M. leprae.

IM30

SEROLOGICAL RESPONSE AGAINST CROSS REACTIVE CELL-WALL ANTIGENS (65 kD PROTEIN & LAM-B) IN LEPROSY.

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Two hundred leprosy patients and one hundred and fifty six endemic controls were screened for IgG antibody response against 65 kDa proteins of M.leprae, M.bovis BCG, M.fortitum

M.lepraemurium and LAM-B by ELISA with the objective of discrimination of antibody response between leprosy patients and endemic controls against these antigens. The following observations were noticed:-

In cases: The lepromatous leprosy patients had significantly higher antibody level against M.leprae, M. bovis BCG and LAM-B and significantly low antibody level 65 kDa of M.fortitum. The other types of leprosy(Indeterminate,Borderline tuberculoid and Tuberculoid, Borderline leprosy) there is a significantly higher antibody response against 65 kDa of M.fortitum and M.lepraemurium with low antibody response against LAM-B but the Borderline lepromatous type alone showed higher antibody response against LAM-B.

In controls: The household contacts of treated LL(Adult and children) had significant antibody response against 65 kDa of M.bovis BCG and significantly very high response against LAM-B was noticed in adult contacts only. The occupational contacts elicited significantly higher response against all the antigens used in this study. This study of antibody response against cell wall antigens may help us to discriminate the leprosy patients with the endemic controls along with the subtyping of the subjects included in this study.

IM31

DETECTION OF 65 KILODALTON HEAT SHOCK PROTEIN FROM SERA OF LEPROSY PATIENTS - MYCOBACTERIAL OR AUTO ANTIGEN ORIGIN.

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Sera from 167 leprosy cases of 65 kilodalton heatshock protein antigen by Reverse Passive Heamagglutination(RPHA). The antigen positivity rates varied from 72-100 % along the clinical spectrum of leprosy. The same sera were also examined for the presence of IgG antibody to recombinant 65 kDa of M.leprae by ELISA. 72.6% of the patients found to be positive for antibody to 65 kDa protein in leprosy patients. There was no significant difference in the percentage of 65 kDa antigen positivity between the patients under treatment and patients released from treatment. The 65 kDa antigen detection by RPHA found to be more sensitive than the antibody detection by ELISA, and having a higher predictive value for the diagnosis of leprosy. The role played by this Heatshock 65 kDa protein and auto-immune response in leprosy will be discussed.

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IM32

MAJOR ANTIGENS OF *Mycobacterium habana* RECOGNIZED BY SERA OF PATIENTS WITH LEPROMATOUS LEPROSY

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Although *Mycobacterium leprae* infection of mice is self-limiting, it is possible to vaccinate mice such that they are protected against footpad infection. Intradermal immunization with killed *M.leprae* is the most effective means of vaccination. Of the cultivable mycobacteria which have been tested in this system, only *M.bovis* BCG has been found to give consistent cross-protection. Nevertheless, recently it was shown that *M.habana* may protect in a similar way to *M.leprae*, conferring 100% protection. Since immunization of mice with *M.habana* results in protection against infection with *M.leprae*, we have investigated, using a serological approach, the cross-reactive antigens shared by *M.habana* and *M.leprae*. By definition, the *in vivo* antibody (Ab) response to a given protein, where the response is preferentially of the IgG class, is an assay for Th cells. In this work we describe two *M.habana* proteins, with molecular masses of 30 and 28kDa. These doublet was recognized by all patients with lepromatous leprosy when their sera was diluted 1:100 and used in a Western blot analysis. The doublet was only recognized by IgG Ab and not by IgM. Neither the sera from tuberculosis patients nor from healthy people showed any antibodies against the doublet, when tested in a similar system. These proteins must have some cross-reactive epitopes with the *M.leprae* protein homologous, and since they are only recognized by IgG Abs we suggest they may play a role in protection. We also identified a similar doublet in *M.leprae*, BCG and *M.tuberculosis* with our LL sera. It is possible that the *M.habana* doublet is the simile of a doublet (33/29 KD) previously described in BCG and *M.tuberculosis*. The possibility of using a molecular genetic approach to investigate the role of these proteins in protective immunity is raised.

*Becarios de COFFA
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IM33

ANTIGENIC SIMILARITY MAY BE RESPONSIBLE FOR IMMUNE REACTIVITY IN LEPROSY.

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Antigenic similarity indicates that host and parasite share antigenic determinants that react with the same antibody or evoke cell-mediated immunity. It has been suggested that on one hand, such a similarity may fool the immune system and enable the parasite to avoid detection and destruction. This may occur in lepromatous leprosy. On the other hand, antigenic similarity may induce a state of enhanced immunity which is not only directed at parasites but also at the tissue of the host. Even when the parasite has been eliminated, damage to the tissue of the host may continue. This may occur in tuberculoid leprosy and during a reversal reaction.
For the human host, using an immunoperoxidase technique we demonstrated that skin and nerve had antigenic determinants that were in common with M.leprae. This was confirmed using Western Blot technique. It is interesting to note that macrophages also were able to express antigenic determinants that were similar to those expressed by M.leprae.
It has been shown that these antigenic determinants were often associated with heat shock proteins.

IM34

AN IMMUNODOMINANT .30KDa ANTIGEN(S) OF A CANDIDATE ANTI-LEPROSY VACCINE, *Mycobacterium w* SHARES T AND B CELL DETERMINANTS WITH *M.leprae & M.tuberculosis*.

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Peripheral T cell repertoire of *M.w* vaccinated leprosy patients was analysed using fractionated antigens of *Mycobacterium w*. Responses of unimmunised lepromatous patients, tuberculoid leprosy patients and healthy contacts (HC) were also analysed. All the subjects, except the unimmunised LL, recognized a number of low molecular weight antigens of *M.w in vitro*. One of these antigens, having a molecular weight of 30KDa, was recognized by a majority of the vaccinated subjects as well as the tuberculoid patients and HC. This antigen(s) mimicked *M.leprae* in the sense that the unimmunised LL showed a good antibody response to this antigen(s) but failed to show a T cell response, while the immunized LL, TT and HC showed a T as well as a B cell response to this antigen(s). Further studies on this antigen(s) using polyclonal antibodies against it revealed that it is associated with the cell surface. Immunofluorescence and Western blot studies demonstrate that it has homologues present in *M.leprae* as well as *M.tuberculosis*. DTH studies carried out in guinea

pigs immunized with this antigen(s) show that this immunodominant antigen(s) of *M.w* shares T as well as B cell determinants with *M.leprae* and *M.tubercuosis*.

IM35

IMMUNOCHEMICAL CHARACTERISATION OF 22 KD CYTOSOLIC PROTEIN OF MYCOBACTERIUM HABANA:A CANDIDE VACCINE

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The known adverse effects of certain constituents of integral mycobacterial vaccines have reemphasized the need for subunit vaccines based on immunodominant protein antigens. Present study aims at characterization of the major cytosolic protein antigen of M. habana, a candidate leprosy vaccine.

Cytosol was obtained as the supernatant (at 140,000 gx1 h) of the sonicate of logarithmic growth of M. habana. Pattern of cytosolic protein was analysed by SDS-PAGE. The major protein (Mr ~22 kd) was identified which almost exclusively got precip-itated at 80 to 95% ammonium sulfate concentration. Purity of the isolated protein was checked by silver staining, HPLC and isoelectric focussing. Initial immunological characterization was done by immunoblotting using homologous and heterologous polyclonal antibodies, LTT and DTH.

IM36

PGL-I LIKE ANTIGEN IN RENAL CARCINOMA

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Many methods for sero-diagnosis of leprosy have been established by using *M. leprae* specific phenolic glycolipid I(PGL-I) as an antigen. Gelatine agglutination tests by Izumi et al. and micro hemoagglutinin method by Minagawa et al. are two of most popular methods and used widely. By using Izumi's gelatin particle agglutinination test, we have examined sera from gravid women and obtained the conclusion that the sera from gravid women of gestation nine month especially had the anti PGL-I antibodies and would loose them after the labors. These results strongly suggest not only the relationship between anti-PGL-I antibody and fetus, but also existence of a new enbrionic antigen. In extensive studies, we examined sera from patients suffering from some kinds of cancer. We will discuss about the relationship between PGL-I like antigen and renal carcinoma.

RESULTS AND DISCUSSIONS

1) Anti-PGL-I antibody titer in serum: 200 times diluted sera from patients of renal carcinoma, L-type leprosy, and healthy control were examined with reactivity to sugar portion of PGL-I conjugated BSA as antigen by ELISA. Sera from 40 patients have been examined and about 70% of them showed high anti-PGL-I antibody titer. It was surprising that there existed a serum which is containing as high titer as those of L-type leprosy patient.

2) PGL-I like antigen in urine: PGL-I like antigen in urine was examined by dot blot detection. Urine from patient of renal carcinoma and healthy control have been serialy diluted with phosphate buffered saline and dotted on Nytran 13N nylon membrane filter. PGL-I like antigen was detected by anti-PGL-I monoclonal antibody SF1 and alkarine phosphatase conjugated anti-mouse immunoglobulins. Out of 10 tested urine from patients, PGL-I like antigen have been detected from 7 patients whereas all of 8 healthy controls were negative.

Wheather PGL-I like antigen might be usefull for the early diagnosis of renal carcinoma or not must be examined more.

IM37

IGG HUMORAL RESPONSE AGAINST THE ANTIGEN 85 COMPLEX HOMOLOGS IN LEPROSY

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Antigen 85 complex is the major protein component present in M. bovis BCG culture filtrate (CF) and consists of a family of 3 components 85A, 85B and 85C. Combining isoelectric focusing and Western blot analysis, we have identified different antigenically related proteins in CF from other mycobacteria (M.tuberculosis, M. kansasii, M. avium, M. gordonae and M. fortuitum) using monoclonal antibodies directed against the antigen 85 complex of M. bovis BCG. IgG antibodies directed against the antigen 85 cross reactive homologs from the 6 species were investigated in sera from 20 patients with multibacillary leprosy (BL/LL), from 20 patients with paucibacillary leprosy (BT/TT) and from 15 healthy leprosy contact subjects.

All the antigen 85 homologs identified with the monoclonal antibodies in these CF were recognized by the multibacillary leprosy patients sera but not by the paucibacillary leprosy patients sera nor by the healthy subjects sera.

The similarity in the recognition patterns of these different 85 homologs suggests that the epitopes inducing a significant humoral response in multibacillary leprosy are common to the 85 antigenically related proteins of all mycobacterial species.

IM38

MODULATION OF CITOTOXICITY AGAINST M.LEPRAE BY CYTOKINES IN LEPROSY PATIENTS.

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We studied the lack of cytotoxicity induced by M.leprae in multibacillary patients (MB), to determine whether it was due to a deficiency of activating factors. Peripheral blood mononuclear cells (PBMC) ($2x10^6$cell/ml) were cultured for 7 days in tissue culture medium (RPMI-FCS), in the presence or absence of whole M.leprae ($1.8x10^7$ bac/ml), and then used as effector cells (E) (19 MB(6 BL,1 BB,12 LL), 6 paucibacillary (PB) (2 BT, 4 TT) and 7 BCG vaccinated healthy individuals(N) Adherent cells were cultured in RPMI-FCS for 6 days, pulsed overnight with M.leprae and used as target cells(T). IL-2(50U/ml); IL-6(10U/ml) and IL 4(20U/ml) were added at the beginning of the PBMC incubation period, and IFN-γ(100U/ml) 18hr.before perfoming the cytotoxicity assay. ^{51}Cr release was measured after 4 hr incubation of E + radio-labelled T (E/T=40/1). Results were expresed as % cytotoxicity (Mean±SEM). Basal: MB:16±2, PB:33±4, N:29±2; +IL-2: MB:16±1, PB:33±4, N:28±1; +IFN-γ: MB:20±1, PB:43±4, N:36±2; +IL-6: MB:21±2, PB:38±5, N:33±2; +IL-6+IL-2: MB:26±2, PB:40±3, N:40±1; +IL-6 +IFN-γ: MB:26±3, PB:49±4, N:44±2; +IL-4: MB:2±1, PB:19±3, N:15±1; +IL-4+IFN-γ: MB:5±2, PB:24±4, N:26±2. Statistical differences were found for IFN-γ and IL-6 alone ($p<.05$) or when IL-2+IL-6 or IFN-γ +IL-6 ($p<.02$) were added to MB, PB and N. Addition of IL-4 diminished the cytotoxicity ($p<.05$) and IFN-γ antagonized the effect of IL-4 in a dose dependent fashion. Cytokines would be involved in the regulation of cytotoxicity against M.leprae.

IM39

RECEPTOR SELECTIVE ENKEPHALINS AS EFFECTIVE IMMUNOMODULATORS IN LEPROSY

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Enkephalins influence neuroendocrine and immune systems through receptors present on the cells. Of the four opiod receptors identified, δ receptor has immunostimulatory and μ receptor has immuno suppressive effects. Using Met enkephalins which binds to both receptors and δ selective (DPDPE), and μ selective (TOPA) peptides, *in vitro* immunomodulation was undertaken on lymphocytes derived from leprosy patients and healthy contacts.

Antigen specific lymphoproliferation and numbers of rosette forming T cells were significantly ($p < 0.05$) enhanced on *in vitro* treatment with Met enkephalins in both tuberculoid and lepromatous patients. This was further increased ($p < 0.001$) in the presence of the δ selective DPDPE. In contrast, treatment with μ selective TOPA inhibited lymphoproliferation substantially ($p < 0.01$) and rosette formation to a lesser extent.

These results indicate that 1) receptor selective enkephalin peptides have greater immunomodulatory effect than the total compound 2) DPDPE may have applications as immunoenhancing compound in lepromatous leprosy and 3) TOPA may be useful as an immunosuppressant agent in reactional leprosy.

IM40

SUPPRESSION OF HUMAN MONOCYTE CYTOKINE RELEASE BY PHENOLIC GLYCOLIPID I (PGL-1) OF *Mycobacterium leprae*.

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Defective macrophage activation is a prominent feature of lepromatous leprosy that depends on highly localized conditions occurring within macrophage-rich granulomas that contain numerous bacilli. It has been suggested that PGL-I play a role as protectors of resident **M. leprae** within phagosomes of phagocytic cells. Here we have measured monocyte activation by cytokine release in response to LPS in the presence or absence of PGL-1.

Peripheral blood mononuclear cells (PBMC) from healthy individuals were incubated in the presence of medium only or in the presence or absence of PGL-1 and LPS. After incubation for 24 h, culture medium was aspirated and TNF-alpha, IL-1 and IL-6 concentrations determined by using ELISA Kits.

Over a concentration range of 0.1-10 ug/ml PGL-1,no significant stimulation to produce IL-1, IL-6 or TNF was observed in cultured monocytes when compared to that observed for monocyte stimulated with LPS. The results were similar to that found for PBMC in the presence of medium alone. In contrast, a significantly increased ($p < 0.005$) levels of suppression of cytokine release was observed by the addition of PGL-1 (1 ug/ml) within the LPS-stimulated PBMC cultures. Thus, the percent suppression ranged from 35-74% for IL-1, 42-68% for TNF and 38-71% for IL-6 release (median of the experiment repeated 5 times).

These results might have a profound implication in the host response to **M. leprae**, once to our knowledge that acquired populations of specifically sensitized T cells and activated macrophages interact by means of cytokines to give rise to a state of protective immunity to this class of human pathogen.

IM41

EFFECTS OF GLUCOCORTICOIDS, DAPSONE AND THALIDOMIDE ON INTERLEUKIN-1 PRODUCTION

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Interleukin-1(IL-1) is a cytokine which has multiple biological effects on the immunity and inflammation.

Dapsone(DDS) has been used as an anti-leprosy drug for a long time. It has also been an effective treatment for neutrophilic dermatosis like dermatitis herpetiformis and erythema elevatum diutinum. Thalidomide was developed as a hypnotic and sedative since the 1950's, but use was discontinued due to teratogenicity. Recently, it has been reintroduced for limited use in the treatment of erythema nodosum leprosum. But, the mechanisms of the anti-inflammatory effect of these drugs are still controversial. On the other hand, glucocorticoids have been shown to suppress production of IL-1, which was used as a positive control in this experiment.

Therefore, we studied the effect of DDS, thalidomide on the IL-1β mRNA production in U937 cells measured by Northern blot method and IL-1 production in the supernatant of human adherent peripheral blood mononuclear cells which was measured by thymocyte comitogenic assay, in order to determine whether the anti-inflammatory activity derives from the suppression of IL-1. We found the following effects on IL-1 production after treatment with DDS, thalidomide and several glucocorticoids.

1. IL-1β mRNA production of U937 cells and IL-1 production of human adherent mononuclear leukocytes were not suppressed by either the treatment with DDS(1ug/ml, 10ug/ml, 100ug/ml) or thalidomide(1ug/ml, 10ug/ml).
2. IL-1β mRNA production of U937 cells was well suppressed by 10^{-7}M glucocorticoids(prednisolone, prednicarbate, dexamethasone acetate), of which dexamethasone acetate was the strongest, followed by prednicarbate and prednisolone.

In conclusion, neither DDS nor thalidomide suppress IL-1β mRNA production or IL-1 production. Therefore, their anti-inflammatory mechanism may be different from glucocorticoids.

IM42

COMPARATIVE EVALUATION OF ANTIBODIES IN THE SERUM AND URINE OF LEPROSY PATIENTS THROUGH DIVERSIFIED MYCOBACTERIAL ANTIGENS

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Approximately 1.5 billion people are globally exposed to the risk of contracting leprosy and the problem is expected to be exaggerated due to relentless prevalence of HIV incidence and as a resultant shift in the disease spectrum due to AIDS. Case detection and treatment are the principle methods currently used for control of leprosy but the former is inadequate in detecting early leprosy and contact cases. This study has been done with a view to increase the sensitivity of the assay and to replace the scarcely available M. leprae antigens.

We present here our latest efforts to detect M. leprae antibodies through Conventional ELISA test by using different antigens, namely PGL1, sonicates of M. leprae and M. habana, arabinomannan and 65 KDa protein derived from M. habana. A simultaneous detection of antibodies have been made from two different sample sources - the serum and urine of leprosy patients. The level of detection of M. leprae antibodies from both type of samples through antigens of M. habana (antileprosy vaccine candidate) showed superiority over M. leprae antigens. Antibodies levels were more in the serum than urine. Smear negative doubtful paucibacillary cases were also detectable and confirmed serologically for initiation of treatment. Significance of these findings has been discussed.

IM43

IgM SERUM ANTIBODIES TO PGL-I BY ELISA IN HEALTHY SUBJECTS AND LEPROSY PATIENTS

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Sera from 969 healthy subjects and 974 leprosy patients were tested for anti-PGL-I antibody (APGL-I) by ELISA with NT-P-BSA.

The results and discussion showed that,1)The mean OD($\overline{OD}$)and positivity rate of healthy females (0.090 and 6.9%)were significantly higher than those of healthy male(0.068 and 2.8%)(P>0.01), and there was a similar tendency between sex groups of leprosy patients. The female false positivity rate would be increased if calculated by overall positive criteria, thus the authors suggested that the positive criteria of $\overline{OD}$ of males and females must be calculated separately; 2) The levels of APGL-I were of skew distribution in all groups except the active MB patient group, suggesting it was not suitable to calculate cut-off point of $\overline{OD}$ according to $\overline{OD}$+2SD based on normal distribution. Therefore, the comparison of $\overline{OD}$ among various populations is more reliable than that of positivity; 3) From the epidemiological point of view, this detection can not reflect slight difference when leprosy prevalence is reduced to a lower level, but may reflect epidemiological dynamics in some focus with relatively higher incidence; 4) $\overline{OD}$ and positivity rate were still significantly higher in inactive MB and PB patients than those in healthy subjects. It remains to be proved what are their clinical and epidemiological significance and if t hey can serve as an applicable parameter in detecting relapses; 5)In order to have a good quality control of the detection at different times and in different laboratories, the procedures and reagents used, especially the control pool sera for correcting results, must be standarized.

IM44

LIPOARABINOMANNAN (LAM) BASED ENZYME-LINKED IMMUNOSORBENT ASSAY IN SERODIAGNOSIS OF LEPROSY

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To determine whether antibodies to mycobacterial cell wall carbohydrate would be valuable in serodiagnosis of leprosy, serum IgG antibodies to lipoarabinomannan (LAM) antigen were assayed, 40 leprosy patients, their household contacts which comprised of 31 individuals and 86 controls which included 46 apparently healthy individuals and 40 new-born babies, were recruited for this study. The serum samples from the study subjects were tested for anti-LAM IgG antibodies using an enzyme-linked innunosorbent assay. When results among leprosy cases were compared with control group and considering clinical diagnosis as gold standard, sensitivity and specificity of LAM based ELISA was 72.5% and 90.7% respectively. When ELISA results were compared with skin smear for AFB, the difference was significant by McNemar test for changes. A positive linear correlation was observed between Bacillary index and IgG anti-LAM antibody levels. The relevance of these findings to the serodiagnosis of leprosy and its importance in household contacts of leprosy patients is discussed.

IM45

THE ANTIBODY RESPONSES TO VARIOUS ANTIGENS OF M. Leprae IN BORDERLINE LEPROSY WITH OR IN REACTION

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The serological activities to various M. Leprae specific antigens (18KD, 65KD, WML, PGL, ND-O-BAS & NT-O-BSA) were assessed by ELISA against 365 sera from 95 patients classified Clinico Pathologically as BT(25), BTRR(17), BTRR-RFT(6), BT-RFT(9), BL(10), BLRR(10), BL-RR-RFT(5), BL-RFT(4), BTRR-RFT-RR(9) & 36 healthy volunteers. The sera from 71 patients were collected periodically at monthly invervals for 6-9 months during treatment and rest were collected only once.

A similar pattern of reduction of Antibody responses in both BT & BTRR groups suggests that steroids do not influence the antibody responses in the doses of 30-40mg of Prednisalone per day in both BT with nerve damage and BTRR patients.

On analysis of both the IgM & IgG response patterns during treatment to various antigens, it is quite likely that the IgM responses to any of these antigens may not play any significant role during reversal reactions, however by monitoring the IgG responses to WML alone it would be possible to differentiate early reaction from active disease alone and also from relapse, so that appropriate treatment can be given to the patients. The implications to clinicians of these results will be discussed in detail.

IM46

ANTIBODIES TO CEREBROSIDE-SULPHATE IN LEPROSY.

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A study was set up to investigate whether antibodies against cerebroside sulphate (sulphatide) may have pathological consequences in leprosy. Sulphatide is found on the surface of human cells including NK and notably Schwann cells. It was found that sera from leprosy patients contain antibodies to sulphatide and that anti-sulphatide IgM was higher in sera from lepromatous patients than tuberculoid patients (levels were
in 24/24 and 5/16, respectively, outside 95% confidence limits of levels in control sera). Anti-sulphatide IgG was also present in sera from lepromatous patients.

Lack of variation ($< \pm 20\%$ from mean values) of both anti-sulphatide IgM and IgG during ENL was noted; however, in 3 patients where sera were taken before ENL commenced, anti-sulphatide IgM fell 1.5 to 3 -fold at the onset of the reaction. Thus anti-sulphatide antibodies are present in leprosy but their role in the pathogenesis of nerve damage remains to be clarified.

IM47

AUTOANTIBODIES TO NEURAL ANTIGENS IN LEPROSY

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Neural lipids, namely galactocerebroside(Galc) and gangliosides(Gg) have been implicated in demyelinating diseases. In order to asses their role in leprosy, the humoral immune response to these lipid antigens as well as to ceramide, sulpholipids and human Myelin Basic Protein (MBP) was quantitated by microtitre enzyme linked immunosorbent assay. Sera from 219 leprosy patients, 18 neuritic patients and 43 normal healthy controls were screened. High titers of IgM antibodies directed to total nerve lipid (TNL), Galc and ceramide were present in patients across the spectrum while the antibodies to sulpholipids and gangliosides were present in low titers. Varying titers of IgG class of antibodies directed to MBP were detected in all categories of leprosy patients. No anti- lipid/ protein antibodies were detected in normals. Anti- TNL and anti-Galc antibodies were highest in TT patients with clinical evidence of nerve damage. A statistically significant positive corelation was observed between anti-TNL and anti-Galc antibodies in TT and neuritic patients. However anti-MBP antibodies were significantly high in LL-BL patients with evident nerve damage.These observations suggest that the neural pathology in these two forms of disease may be different.

IM48

COMPARISON OF A GELATIN PARTICLE AGGLUTINATION TEST AND ELISA FOR DETECTION OF ANTIBODY TO M.LEPRAE

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Two rapid diagnostic methods, Enzyme-linked Immunosorbant Assay(ELISA) and the Gelatin Particle Agglutination Test (GPAT), have been developed recently for epidemiological monitoring of the efficacy of chemotherapy and post-treatment follow-up of patients. Both these tests make use of semisynthetic analoques of the phenolic-glycolipid-I, the specific antigen of M.leprae, but differ in methodology. This report examined the two tests with 1059 sera collected at an endemic area in Manila, Philippines. ELISA and GPAT were compared in terms of the seropositivity, the concordant rates, the sensitivity and specificity.
The GPAT was found to be much simpler and easier to perform and generally more sensitive but less specific compared with ELISA. The sensitivity of GPAT in MB patients (83.04%) group was much higher than those in PB patients (41.86%). The concordant rates, ranged from 87% in normal populations and 57.89% in household contacts. Chi-square test of homogeneity indicated that the concordant rate between ELISA and GPAT in normal populations was significantly higher than that in patients and contacts populations. The concordant rate of MB untreated decreased after being treated by multi-drug therapy six months or longer. The seropositivity of GPAT was higher than that of ELISA in all study populations except the household contacts. The seropositivity of both GPAT and ELISA in MB patients were higher than the seropositivity of these two tests in PB patients. In conclusion, GPAT was found to be a sensitive but less specific test compared with ELISA. However, it is easy to perform and inexpensive. Therefore, it is considered as a screening test for detection of the M.leprae infection, especially of the multibacillary type.

IM49

A PROGNOSTIC VALUE OF SEROLOGICAL ASSAYS IN REGRESSED LEPROSY

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610 outpatients with different types of leprosy being under specific therapy over 10 years were examined with using enzyme immunoassay and counter electrophoresis. Native antigen from ultrasound-desrupted M.leprae (USD -ML) and a semi-synthetic analogue of PGL-1 (ND -O-BSA) (provided by WHO Bank) were used.Among the patients with inactive leprosy (BI=0) 182 cases (29,8%) were invariably seropositive for 1-3 years of the observational period. It was found out that the group above included the patients with chronic specific polyneurites, visceral and eye pathologies (hepatitis, orcho-epididimitis, iridocyclitis, uveitis, ètc). Only in 15% of the patients from this group antibody titers to ND-O-BSA were significantly higher as compared with the titers of antibodies to USD-ML.In other cases the ratios were inverse indicating the necessity of serological testing of regressed leprosy patients with either antigens. 26 patients relapsed, 80% out of them being seropositive 1 - 3 years before the occurrence of relapse. 23 (88,4%) cases out of them had high levels of antibodies to both antigens that is characteristic to active leprosy. In three paucibacillary patients anti-M.leprae antibodies were detected neither before nor at the moment of relapse. The investigation showed a value of serological assays in patients with regressing leprosy for assessment of the effectiveness of chemotherapy and early prognosis of relapses.

IM50

THE INFLUENCE OF BCG VACCINATION AND CLOSE CONTACT WITH LEPROSY PATIENTS ON THE RESULTS OF SKIN TESTS WITH 4 NEW TUBERCULINS

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Our study in Santa Fe Province of Argentina investigated the results of skin tests with Tuberculin, Leprosin A, Scrofulin and Vaccin on 672 young adults residing in a leprosy endemic area. Of them, 350 were in-house contacts, usually relatives, of MB patients, 87 were similar contacts of PB patients, and 235 were members of the leprosy service frequently exposed to patients. Within these groups distribution by sex, BCG scar and length of exposure were similar, but the leprosy workers tended to be the oldest group. The results were analysed individually for each reagent, and by responder categories (Category 1, +ve to all 4 reagents; category 2, -ve to all 4 reagents; category 3, +ve to some but not all reagents). Age made no difference to categorization, but the presence of a BCG scar significantly increased categories 1 and 3 at the expense of 2 ($p < 0.03$). A similar finding was recorded in leprosy workers when compared to MB and PB contacts ($p < 0.01$). BCG scars were also associated with increased positivity to Leprosin A ($p < 0.02$). These results emphasize the roles played by BCG vaccination and close contact with leprosy patients on the cellular immune response to mycobacterial antigens.

IM51

BCG VACCINATION AS A PROTECTION AGAINST LEPROSY. Maria Fernanda Sardella Alvim, Nadia Duppre, José Augusto Nery, Ana Maria Malta, Maria Lucia Penna e Euzenir Nunes Sarno. * Leprosy Department Fundação Oswaldo Cruz, Av. Brasil, 4365 - Manguinhos, 21.045-900 - Rio de Janeiro - RJ. ** Department of Epidemiology State University of Rio de Janeiro.

The role of BCG vaccination in protection against leprosy disease is not definitively clarified. Randomized controlled trials in four different populations demonstrated a range of efficacy against leprosy from 20% in Burma to 80% in Uganda. In Brazil BCG vaccination has been widely used since 1976 as a prophilatic measure against tuberculosis applied at birth. The official rules of the leprosy control program recommended since 1990, two BCG doses with a one year interval in contacts of multibacillary leprosy patients. The impact of this measures in leprosy control must be clarified in the future.In This study, 503 contacts of multibacillary patients with age 2 - 20 years were included to the trial with different periods of follow-up. These 55 leprosy cases and 448 controls were matched for age, close-association of index case, and BCG scar. Considering as control group those vaccinated, the unvaccinated contacts have a risk, estimated through the odds ratio, 4.3690 times greater than the control group. In the group without BCG scar, persons over 10 year old had an increased risk of developing leprosy (odds ratio = 9.0909). When compared to those under 10 years (odds ratio = 2.6556). Household contacts had to risk of contracting of disease 2,02 times greater than non-household. Among children under 10 years of age with BCG scar, 11 (50%) developed the Infantum Nodular Leprosy (Tuberculoid lesion). From the 55 new cases of leprosy multibacillary forms were diagnosed in 62% without BCG scar and 38% with BCG scar. This study strongly suggest a considerable value of BCG vaccination on protection of leprosy disease and protective efficacy against the more serious forms of leprosy

Supported by grants from TDR-WHO

IM52

INDUCTION OF LEPROMIN POSITIVITY BY A CANDIDATE ANTI-LEPROSY VACCINE MYCOBACTERIUM w AND ITS IMMUNO——PROPHYLACTIC EFFECT IN LEPROMIN NEGATIVE HEALTHY CONTACTS OF MULTIBACILLARY LEPROSY PATIENTS

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In a hospital based study, 362 household contacts of multibacillary leprosy patients under MDT were screened for evidence of leprosy and 54 (14.9%) were found to be having leprosy. The remaining 308 apparently healthy contacts were lepromin tested and 109 (35.4%) were observed to be negative to Mitsuda lepromin. M.w vaccine was administered intradermally to 95 of these 109 lepromin negative contacts. Sixty eight of them could be retested for lepromin A reactivity. Fifty six (82.35%) manifested lepromin conversion. The twelve subjects who did not show lepromin conversion, received a second dose of the vaccine, and eleven subsequently became lepromin positive. The overall lepromin conversion rate was thus 98.5% (67 out of 68). Follow-up of these contacts upto a period of 5 years did not demonstrate reversion of lepromin positivity back to negativity status. Among original lepromin positive contacts, so for four cases of Paucibacillary leprosy have been detected, but none from vacine induced lepromin converted contacts.

IM53

M.LEPRAE-RESPONSIVE T LYMPHOCYTES AND BLOOD MONOCYTES IN A RARE REACTIONAL FORM OF LEPROSY, THE LUCIO'S PHENOMENON.

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The Lucio's phenomenon(LP), a leprosy reaction with systemic manifestations, characterized by necrosis of the dermal capillaries and epidermal areas, was investigated in 3 polar lepromatous(LL) patients(LP1, LP2, LP3; male, 65 to 70 yr. old, 0 to 12 months of treatment), treated with thalidomide(LP1,LP3) or thalidomide plus glucocorticoid(LP2). Before treatment, patients had increased serum TNF-α(LP2), IL-6(LP1, LP2, LP3), and their peripheral blood mononuclearleukocytes(PBL) generated spontaneous TNF activity in vitro, as well as very high levels of oxidative metabolism intermediates(chemiluminescence; LP2,LP3). FACS analysis of PBL demonstrated absence or reduction of γδ+, CD8+ and CD14+ cells. On day 7, the lesions were healing. The parameters above with the exception of IL-6 serum levels were returned to normal or diminishing; and surprisingly the PBL(LP2,LP3) proliferated in vitro in response to *M. leprae*, but without IFN-γ production. The specific inhibition of TNF-α by thalidomide, and these observations support the hypothesis of a major function for TNF-α in LP, and suggest a role for *M. leprae*-specific T lymphocyte response in this leprosy reaction. Supported by grants from TDR-WHO and CNPq

IM54

LYMPHOCYTE SUBPOPULATIONS AND THEIR FUNCTIONAL PROPERTIES IN LEPROMATOUS LEPROSY

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Lymphocytes from LL patients were studied for their proliferative responses to PHA, ConA, PWM, and specific M.leprae antigen (lepronin). Besides,the functional activity of ConA-induced T suppressors and T cell subsets with CD2+, CD4+, CD8+ phenotypes were studied.It was shown that in active leprosy patients lymphoproliferation to mitogens, function of nonspecific T-suppressors and the relative percentage of CD2+ cells were significantly low as compared with cured patients and healthy donors ($p<0,01$). In long treated patients lymphoproliferation was also low, though at less degree than in untreated patients ($p<0,05$). LTT to lepronin was low in both groups of the patients. In leprosy patients irrespective of their disease status relative contents of CD4+ cells was lower while CD8+ content was higher as compared with normal values. CD4+/CD8+ ratio in both patient groups was significantly lower than in the control group. Increased level of CD8+ cells with simultaneous decrease in the functional activity of non-specific T-suppressors in leprosy patients seems to be a consequence of compensatory mobilization of suppressor/cytotoxic cells into circulation to replenish their functional deficiency. Thus, in LL patients there is a definite interrelationship between immune aberrations and their disease status. Prolonged specific therapy results only in partial recovery of disturbed functional activi*y and changed contents of lymphocyte subpopulations.

IM55

IMMUNOGENETIC ASPECTS OF SUSCEPTIBILITY TO LEPROSY

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According to literary data, an association between HLA antigens of the major histocompatibility complex and leprosy in different populations was extensively studied, but the patients belonging to Russian nationality were assessed only for HLA class I antigens. The investigation presented was aimed at studying a distribution of HLA class 1 and 2 antigens in lepromatous leprosy. 125 Russian patients who were admitted to the clinical department of our Institute were examined. For control 120 unrelated healthy individuals of the same ethnic group were randomly selected. HLA typing was carried out as described by Terasaki. It was stated that the frequency of HLA-DR3, DR2 and B7 antigens was significantly higher for LL patients than in the control group, whereas DR5 was absent. After the correction for the number of antigens tested statistically significant differences remained only for HLA B7 ($Pc=0,049$) and DR3 antigens ($Pc=0,00014$). The highest relative risk was to HLA-DR3 antigen ($RR=10,22$). Attributive risk, characterizing a strength of association with the disease, was also the highest for HLA-DR3 - carriers ($\sigma = 0,67$). Thus, based on these results it was concluded that HLA-B7 antigens (possibly, haplotype B7-DR2) and HLA-DR3 might be the markers of susceptibility to lepromatous leprosy in Russians that should be borne in mind when identifying risk groups among leprosy contacts.

IM56

ROLES OF LYMPHOCYTE SUBPOPULATIONS IN ERYTHEMA NODOSUM LEPROSUM AND ACUTE ANTERIOR UVEITIS

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One of the many sistemic complications of leprosy is a reactional state known as erythema nodosum leprosum (ENL). During ENL some patients develop acute anterior uveitis (AAU). It is still unknown why some patients develope AAU during ENL and others do not.

Considering that changes in lymphocyte subpopulations might be important in pathogenesis of ENL and AAU, we determined proportions of lymphocyte subpopulations, namely B cells (CD19+), T cells (CD3+), NK cells (CD56+), helper/inducer cells (CD4+), suppressor/cytotoxic cells (CD8+), CD4+ CD29+, CD4+ CD45RA+ and CD8+ CD11B+ cells, by flowcytometry. The study group consisted of patients with AAU, ENL, post reactional patients and patients who never suffered from these reactions.

Proportions of CD4+ cells and CD4+ CD29+ cells were significantly higher in AAU and ENL patients than post reactional and non reactional groups. In AAU patients CD4+ CD45RA+ cells were also high.

CD4/CD8 ratio was significantly high in ENL patients compared to non reactional group.

CD56+ (NK) cells were significantly lower in AAU and ENL group than other groups.

The importance of these results will be discussed.

IM57

IN VITRO LABELLING AND FUNCTION OF GRANULOMA MACROPHAGES FROM LEPROMATOUS LEPROSY

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Granuloma is an immunologic and pathologic unit of human lepromatous leprosy (LL), which is chiefly composed of macrophages (MACs) packed with *M. leprae* and lymphocytes. Until now little is known about the influx and turnover of these granuloma MACs in human LL, except high influx of bone marrow-derived MACs in experimental LL granuloma of nu/nu foot pad. We have been conducting autoradiography studies to evaluate influx of bone-marrow-derived MACs in Ll granuloma using [3H]TdR pulse *in vitro*. MACs are isolated by enzyme digestion and plated on LUX coverslips 1 x 10^6/ml with RPMI-10% AB serum, MACs with AFB bacilli and more than ten sliver grains on nucleus are counted to score Labelling Index (LI). LI are calculated labeled nucleus with AFB per on-thousand nucleus. In spite of major roles of suppressor lymphocytes in unresponsiveness of LL as reported, defective activation of LL MACs to exogenous gamma interferon (IFN-γ) is likely due to any cytokines or mediators such as prostaglandin E_2 (PGE_2) which inhibit gamma interferon in the microenvironment of LL granuloma. To find any difference following IFN-γ, BCG, IL-2 treatment *in vitro*, we have examined levels of PGE_2 production by radioimmunoassay and Toxoplasmacidal effect of MACs from LL granuloma.

IM58

KILLING OF MYCOBACTERIA-INFECTED MACROPHAGES BY LAK CELLS FROM LEPROSY PATIENTS

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Host resistance to bacteria is multifaceted with both specific and non-specific immune mechanisms playing important roles. In the present investigations, we have assessed the ability of lymphokine-activated killer (LAK) cells generated from lepromatous leprosy (LL) patients, tuberculoid leprosy (TT) patients and healthy individuals, to lyse targets (macrophages and T-24, bladder carcinoma cell line) infected with mycobacteria (Mycobacterium leprae/Mycobacterium ICRC). We observed that LAK cells generated from LL patients could preferentially lyse M.leprae or ICRC-pulsed macrophages and T-24 cells, compared to non-pulsed targets. However, LAK cells from TT patients failed to distinguish between non-pulsed and mycobacteria-pulsed target cells. The specificity of lysis of mycobacteria-pulsed targets by LAK cells was confirmed in a cold target competition assay. Furthermore, we have studied the killing of mycobacteria by LAK cells. ICRC bacilli incubated with LAK cells or bacilli obtained from infected macrophages incubated with LAK cells showed a significant reduction in the number of colonies of bacilli after plating on soft agar. Thus, our studies demonstrate that LAK cells may play a significant role in killing of intracellular bacteria and may serve as an immunotherapeutic modality in the treatment of leprosy.

IM59

MODULATION OF MONOCYTES/MACROPHAGES OF LEPROSY PATIENTS BY TUFTSIN FOR BIOCHEMICAL AND IMMUNOGENIC FUNCTIONS.

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Mycobacterium leprae is an obligate intracellular pathogen that is ingested by and proliferate within the cells of monocytes/macrophages (Mφ). Intracellular pathogens may escape killing mechanism either by inhibiting production of reactive oxygen intermediates (ROI) or by neutralizing these intermediates. We have investigated the effect of macrophage stimulant "tuftsin" on immunogenic functions of monocytes/Mo derived from leprosy patients as a function of in vitro culture age. Since we have earlier observed an aberrant phagocytic and microbicidal response in Lepromatous patients towards tuftsin pulsing, the present study was undertaken to correlate the microbicidal functions (by measuring O_2^- & H_2O_2) and maturation profile (by measuring adenosine deaminase activity) of monocytes/Mφ. Further the signals involve (by measuring $[Ca^{++}]$) in triggering the Mo membrane by tuftsin and tuftsin receptor expression (by radio receptor assay) on these Mφ were studied in detail. ROI production and $[Ca^{++}]$ release towards tuftsin pulsing showed a progressive increase with increasing in vitro culture age till day 3, than tapered off in older cultures of normal and BT/TT Mφ. BL/LL cultures were unable to undergo tuftsin mediated ROI production and $[Ca^{++}]$ release after day 1. ADA activity was found to be maximum in the early cultures of BL/LL Mφ. These results indicate that BL/LL Mφ has a differential maturation profile and there may be specific enzyme(s) defect associated with ROI production. From the study it can be also concluded that there is an altered signalling during Mφ activation and finally these defect may lie at the tuftsin receptor expression.

IM60

IS NERVE DAMAGE IN LEPROSY AN AUTO-IMMUNE PHENOMENON INVOLVING ANTI-PERIPHERAL NERVE ANTIBODIES

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The role of anti-peripheral nerve antibodies directed against the peripheral nervous system in leprosy patients in the pathogenesis of nerve damage is, till date, inconclusive and controversial. A study was therefore taken up to detect such antibodies in the sera of one hundred leprosy patients belonging to the entire spectrum of the disease, along with sera from normal individuals as controls. Using antigen derived from normal human nerve,

9% showed demonstrable levels of antineural antibodies of the IgG type and 11% of the IgM type. However, with antigen derived from nerve of a cured, bacteriologically negative leprosy patient, on testing twenty out of the above hundred sera, 40% tested positive for antineural antibody of the IgM type, and none tested positive for the IgG type. There was no correlation found in the present study between the presence of the antibodies and of neuropathy or of occurrence of active neuritis. There was also no correlation with the type or duration of the disease. The findings will be discussed.

IM61

ANTIBODIES TO A NERVE LIPID EXTRACT (NLE) IN SERA OF LEPROSY PATIENTS.

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Soluble serum factors have long been suspected to play an important role in the neuro-pathogenesis of leprosy. Humoral immune response to a Nerve Lipid Extract (NLE) was evaluated in patients of leprosy (n=131), patients with neuropathies other than leprosy (n=23) and normal healthy volunteers (n=51) using microtitre plate ELISA test. High titres of IgM class of anti-neural-antibodies directed to NLE were detected in 21% (29/131) sera of leprosy patients. The reactivity was minimal with normal healthy volunteers as only 2 out of 51 (4%) showed detectable anti-neural antibody titres. Interestingly, none of the sera from patients of neuropathies other than leprosy showed raised anti-neural antibody titres. All the twenty nine sera showing raised anti-neural antibody titres belonged to borderline or lepromatous type of leprosy conferring 30% positivity to the group whereas none of the 34 patients of BT/TT/P type of leprosy showed raised anti-neural antibody titres.

It also appears from this study that the anti-neural antibodies develop at a later stage of multidrug therapy as the majority of untreated LL patients(14/16) did not show reactivity against NLE. This suggests a possible role for cytoplasmic antigens of M.Leprae released during the period of treatment.

IM62

PREVALENCE OF ANTI-NEURAL ANTIBODIES AMONG LEPROSY PATIENTS

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Nerve damage is a major clinical manifestation in leprosy. As an effort to elucidate the pathogenic mechanisms of nerve damage in leprosy, this study was initiated to determine whether or not there is any association between anti-neural antibodies and nerve damage in leprosy. Lipid and glycolipid antigens including ceramide and galactocerebrodide (GC) were prepared, and the prevalence of antibodies to the antigens and asialo-GM$_1$ (AGM$_1$) was determined among leprosy patients and controls. The major immunoglobulin class to the nerve lipid antigens was IgM;therefore, only IgM class to the antigens was analyzed. Of 291 Korean controls who had no recent history of having traumatic injuries, 43 (14.8%) had elevated antibodies to ceramide, 54 (18.6%) to AGM$_1$, and 24 (8.2%) to GC, respectively, and 83 (28.5%) to at least one of the three antigens. In contrast, among 170 Philippine controls, 52 (33%) were seroreactive to ceramide, 38 (22.4%) to AGM$_1$ and 18 (10.6%) to GC, respectively, and 81 (47.6%) to at least one antigen, indicating that controls in Philippines have significantly greater opportunity to expose to neural antigens than in Korea. Of 105 untreated leprosy patients from Philippines, 57 (54.3%) were seropositive to ceramide, 40 (38.1%) to AGM$_1$, and 42 (40.0%) to GC, respectively, and 129 (58.9%) to at least one antigen, indicating that the prevalence of anti-neural antibodies in leprosy patients was significantly higher than controls. In addition, the prevalence of anti-neural antibodies was correlated with the extensiveness of anesthesia and nerve enlargement. The results suggest that anti-neural antibodies are closely associated with neurologic damage following *Mycobacterium leprae* infection.

IM63

MYCOBACTERIUM LEPRAE LAM AND PGL-I ANTIBODIES CROSS-REACT WITH HIV-1 ANTIBODIES IN SERA FROM HIV-1-SERONEGATIVE LEPROSY PATIENTS AND THEIR CONTACTS.

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Fifty seven leprosy patients (LP), 39 leprosy contacts (LC), and 500 pregnant women (PGW) were evaluated for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1), human T cell lymphotropic virus type 1 (HTLV-1), and type 2 (HTLV-2). Antibodies to mycobacterium leprae phenolic glycolipid 1 (PGL-I), and lipoarabinomannan (LAM) were analyzed to assess the association between leprosy and human retroviral infections. A low prevalence of HIV-1 infection occurred among LP (3.5%), LC (0%), and PGW (3.6%). LP and LC had a significantly higher prevalence of HTLV-1 infection compared with PGW (8.7% and 12.8% vs 0%, respectively). Sera from LP and LC were often false-positive by ELISA (64.7% and 23%, respectively), and indeterminate by Western Blot for HIV-1 (83.6% and 64.1%, respectively). In LP sera, both LAM IgM, and PGL-I IgM antibodies cross-reacted significantly with anti-HIV-1 Pol (p31, p61) and Gag antibodies (p24), respectively. Mycobacterial cell-wall antigens may share common epitopes with HIV. Caution should therefore be exercised when interpreting HIV-1 ELISA and western blot data from regions where leprosy or other mycobacterial diseases such as tuberculosis are endemic.

IM64

SEROPROFILE OF HBV, HIV and HTLV INFECTIONS IN ZAIRIAN LEPROSY PATIENTS AND THEIR CONTACTS.

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Objective : Preliminary study to determine the seroprevalence of HBV,HIV and HTLV infections in Zairian Leprosy patients and their contacts

Materiel & Methods : Patients with lepromatous (LL) and tuberculoid (TT) lepra and their contacts were serologically examined for HBV (HBS, AntiHBS seroconversion, AntiHBS titer, pre-S1 and Pre-S2), HIV (antiHIV), HTLV (anti HTLV1 and antiHTLV2) and for Antibodies to M.leprae specific antigens PGL-1 and LAM-B.

Results. HBs prevalence was significantly higher in LL (20%) than in TT (6,6%) patients and contacts. Anti HBs seroncoversion was significantly low in the 3 groups. Anti HBs was significantly higher in TT (4572,40 +/- 5234,61 UI/ml) than in both LL patients and contacts.Pre-S1 and Pre-S2 prevalence rates were higher in TT (26,6% and 30%) than in LL (12% and 20%).
HIV1 seroprevalence was 3,5% in leprosy patients, 0% in their contacts while it is known to be 3-8% in the general population. Unlike in this last group, high rates of HIV false + in Elisa (63,6%) and W-B indeterminate patterns (30,7%) were seen in the leprosy patients.
HTLV1 antibodies were detected in 8,7% of leprosy patients and in 12,8% of their contacts. No HTLV2 antibodies were seen in any group.
Antibodies to M leprae specific antigens were seen in 43.8 (antiPGL-1) and 42,1% (antiLAM-B) of patients.

Implications and Perspectives :
It is worth to extend such a study to the nuserous leprosomia in the country in order to asses the impact of these virus infections on the pathogenesis and the course of Leprosy. Furthermore one must be precautious in the interpretation of the HIV tests in people with leprosy.

IM65

ASSOCIATION OF HLA-A_1-B_1-C, AND DR ANTIGENS WITH LEPROSY

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The human major histocompatibility system (HLA) has been known to be associated with a variety of diseases. Various groups of workers have searched for HLA antigens and their associations with leprosy. However, except for the association of DR2 with tuberculoid type of leprosy, no other association could be related to any of the types of leprosy. As no strong association could be observed with single locus antigens, it was decided to find out if the combination of genes (haplotypes) have got any association with the types of leprosy. The present study was undertaken in families from an endemic area, Visakhapatnam (A.P.) In all 2009 individuals from 408 families were taken for the study. The normal healthy sibs were taken as controls. None of the HLA-A_1-B_1-C and DR antigen showed any significant correlation with the disease types except for BB group only. In this group HLA-A10 specificity showed a significant association (P=0.008) even after correction of the P value. Certain haplotypes also showed some significant associations which will be presented and discussed.

IM66

IN VITRO TEST SYSTEMS TO DETERMINE SUSCEPTIBILITY TO LEPROMATOUS LEPROSY.

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In vitro systems to demonstrate the level of superoxide produced by macrophages on exposure to live M.leprae and ability to kill the phagocytosed M.leprae, showed that lepromatous leprosy patients, before, during and after treatment had poor positive response in the two parameters. The normally leprosy resistant individuals in an endemic city like Bombay, showed these two potentialities in their macrophages. This has ben consistently found to be true in subjects analysed 30 patients 30 normal healthy. Extending this observation to families it was found that the index patient had the defects and the defects were shown by one or more of the children even though the male or female partner of the index patient was normal. Such progeny showing the defects in the macrophage were seen as either healthy or exhibited symptoms of leprosy infection. The complete analysis of the observations showed that in the normal population monitoring of macrophage interaction with live M.leprae by the in vitro systems could lead to indication of susceptibility. This along with lepromin negativity in skin test should help narrowing the susceptible population.

IM67

STUDIES OF LYMPHOCYTE PHYSIOLOGY-A STUDY OF MARKER ENZYMES OF METABOLIC PATHWAYS

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Infection with Mycobacterium leprae, the causative organism of leprosy is the result of defect in CMI. The abnormality has been correlated with defects both in number and functions of T-Lymphocytes. The changes that occur in the physiology of lymphocytes might be one of the reasons for their depressed functions, specially in the effector limb. We have studied a number of enzymes to elucidate different metabolic pathways like Arginase, Iso-enzymes of LDH and Aldolase, SOD and Peroxidase, Alkaline and Acid Phosphatases, beta-D-Glucuronidase, Adenosine deaminase and Amino Acyl t-RNA Synthetases besides rate of translation by labelled amino-acids, Lymphocyte Arginase showed an increase of activity in LL (5.48 units/mg), BB and BT (2.54 units/mg), TT (1.81 units/mg) in comparison to that in healthy controls (0.87 units/mg). Adenosine deaminase shows a reversal of this trend as in LL (265 units/mg), TT (375 units/mg), which is common in immunoproliferative disorders. Activities of all other enzymes also varied throughout the spectrum of the disease, which is well correlated with LTT and LMIT. Enzyme induction studies have been carried out to rectify the defects in lymphocytes which showed increasing response to different antigens including M. leprae.

IM68

OBEERVATION ON SUBCUTANEOUS IMMUNNE CELLS IN SITU IN LEPROUS NONREATIVE SLIN LESIONS

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This study attempts to evaluate changes in T-cell subsets, macrophages and natural-killer cells by using Leu-2a, Leu-3a, Mac718, Interleukin-2-receptors (IL-2R) and HLA-DR antingen in situ in leprous nonactive skin lesions of 24 leprosy patients and healthy normal controls(LL13, BL3, BB4, BT2,TT2, normal control 5).Cells were obtained from fluid aspirated from suction-induced blisters directly over nonreactive skin lesions. Significant differences were observed between LL/BL, TT/BT and normal control by HLADR, Leu-3a, Leu-2a. The LL/BL group had lower positive rate than the TT/BT group and normal controls. The T-helper/supressor ratio (Leu-3a+/Leu-2a+) was 0.39 in LL/BL and 2.39 in TT/BT. This indicated that even macrophages containing phagocytosed M. leprae could not react with T-helper cells. Macrophages due to HLA-DR antigen absence, and also T-helper cells are decreased in LL. The cell-mediated immunity defect is caused by lymphokines absence. IL-2R is also decreased in LL/BL. On the other hand, Leu-2a positive cells (supressor cells)were increased in LL/BL.They can supress cell-mediated immunity. The results can be interpretated as part of the reason for lymphokines absence in lepromatous leprosy. No significant difference was observed between LL/BL and TT/BT in Leu-7(NK cells). This indicates that perhaps NK cells are not importnant in cell-mediated immunity in leprosy. Macrophages had higher levels in LL/BL than TT/BT from nonactive skin blister. This is inadequately understood as yet.

IM69

BORDERLINE TUBERCULOID HANSENIASIS: PARAMETERS OF IMUNOLOGICAL ACTIVITY.

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Forty-eight patients with Borderline Tuberculoid Hanseniasis, according to Ridley & Jopling classification system, were studied in order to determine their capacity in circunscribing the disease in the skin (number of cutaneous lesions) and in the peripheral nerves (number of afected nerves). These clinical features were compared to each other, and to an humoral immunity test (ELISA test for PGL-I, phenolic glycolipid spe-

cific from Mycobacterium leprae) and to celular immunity tests "in vivo" (cutaneous Mitsuda test) and "in vitro" (lymphocyte proliferation stimulated by M. leprae and gama-interferon detection in lymphocyte culture stimulated by M. leprae supernatant). The celular immunity test that best related to the capacity of the patients in limiting their disease, with reference to the skin, was the gama-interferon detection test. BT form of Hanseniasis seems to be of systemic nature, though with tendency to circunscrile the manifestations in the skin and/or in the peripheral nerves, one feature not necessarily being accompanied by the other.

IM70

A POTENTIAL MARKER FOR THE PREDICTION OF ENL REACTIONS.

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A double blind study was conducted to identify a serological marker for the prediction of Erythema nodosum leprosum (ENL) reactions which occur in lepromatous patients. 538 sera samples {ENL,stable LL, LL with history of reactions (H/O REACTION), BT-TT,Familial contacts (FC), Non contacts (NC), Pulmonary Tuberculosis (TB)} obtained from endemic and non endemic areas of India were screened in an ELISA using Recombinant *M.leprae* antigen LSR, that was previously reported by us and 16 overlapping peptides(15-19 mer) based on its sequence. Significantly > 90% of the ENL and H/O reaction patients showed seroreactivity to the LSR antigen in comparison to only 68% of the stable LL patients. In contrast none of the NC individuals were seropositive to this antigen. On screening with the peptides,greater than 92% of the ENL patients recognised peptides 2 (GVTYEIDLTNKNAA), 3 (IDLTNKNAAKLRGD) and 13 (REWARRNGHNVSDRGRI) as compared to < 43% of the stable LL patients. The degree of seroreactivity based on the Optical Density (OD) values showed highly significant differences between stable and reactional patients (P value <0.01 to 0.001) for peptides 2,3,13 & LSR. Peptide 13 was found to be cross reactive with sera from TB patients (18%). It is proposed that peptides 2 and 3 are diagnostic markers for active ENL. They may also be useful for identifying lepromatous patients with a high risk of developing ENL.

IM71

HUMAN LEPROSY LESIONS IN SITU USING SUCTION-INDUCED BLISTERS: CELL CHANGES WITH IGM ANTIBODY TO PGL-1 AND INTERLEUKIN-2 RECEPTOR IN CLINICAL SUBGROUPS OF ERYTHEMA NODOSUM LEPROSUM.

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To examine the immunopathogenesis of type 2 erythema nodosum leprosum (ENL) reactions in leprosy, we studied cellular and soluble immunologic components of skin lesions in 57 patients with reactions (19 acute ENL and 38 chronic ENL), 61 active patients without reactions, and 33 control patients whose leprosy had been treated and cured. Cells, IgM antibody to PGL-1 and Tac peptide levels were obtained from fluid aspirated from blisters induced by suction directly over representative skin lesions. During ENL reactions: a) the lesions in chronic ENL showed a decreased number of $CD8^+$ (T-suppressor) cells and increased helper/suppressor ratio as compared to those in acute ENL and non-reactional leprosy; b) Tac peptide and IgM antibody to PGL-1 levels were elevated in the chronic ENL lesions; c) and systemic administration of corticosteroids appeared to cause a reduction in the intralesional $CD4^+$ cell population and IgM antibody to PGL-1 but did not change $CD8^+$ cell population and the levels of Tac peptide in the lesions. The elevated levels of Tac peptide were localized in the skin lesions while increased levels of IgM anti-PGL-1 seemed to be filtered from the peripheral blood. We conclude that spontaneous lymphocyte activation in situ, primarily of decreased $CD8^+$ and relatively increased $CD4^+$ cells, are important features of chronic, recurrent ENL reactions and may be an intermittent or cyclic phenomenon during the reaction. Understanding the mechanisms of these spontaneous changes in immunity in leprosy will enlarge our knowledge of reactions and of the underlying determinants of delayed type hypersensitivity and cell-mediated immunity in leprosy, which in turn will allow us to realize the potential for artificially manipulating these responses as proposed with vaccines or immunotherapy.

IM72

LEPROSY IN WOMEN: CLINICAL AND IMMUNOLOGICAL ASPECTS

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Renewed interest has been shown in the impact of tropical diseases in women. One of the basic areas of interest in the analysis of sex and gender differences is related to the relative contribution of biological and cultural factors. Disease characteristics and immunological reactivity in leprosy in Venezuela suggest a more effective immune response to *Mycobacterium leprae* in both healthy women and female patients. Among 64,559 contacts of patients, 48-hr skin test reactivity was higher to *M. leprae* soluble extract (MLSE) in females; the antibody response to PGL-I was significantly higher in females at every age level. Clinical leprosy of all forms was more frequent in males. The highest frequency in females occurred in the 15-24 year age group; the peak in males was 20 to 30 years later. A retrospective family study in Venezuela demonstrated a significantly higher incidence of leprosy in male offspring when the mother was infected, but multibacillary incidence was low in this group, suggesting maternal immunomodulation. Skin tests with PPD and MLSE were larger in females throughout a 5-yr follow-up after vaccination. Taken together, all of these data suggest a stronger immunological response to *M. leprae* in females which appears to reflect true physiological differences.

IM73

THE INFLUENCE OF THALIDOMIDE ON THE HISTOLOGICAL MANIFESTATIONS OF ENL. Miranda A, Sampaio EP, Miguel CF, Sarno EN. Leprosy Department, Oswaldo Cruz Foundation, Av. Brasil, 4365, Manguinhos, 21.045-900, Rio de Janeiro, Brazil.

Leprosy patients with various forms of the disease may develop reactional states, which are associated with changes in immunological reactivity. Biopsies from six multibacillary leprosy patients were collected at the time of developing ENL, during thalidomide therapy, or after thalidomide treatment was discontinued. In contrast to the lepromatous leprosy lesions, the ENL lesions demonstrated local changes identified as parameters of immune activation in situ. The overlying thickened epidermis exhibited pronounced keratinocyte ICAM-1 expression, increased number of Langerhan's cells and contained lymphocytes (mainly CD8+ cells) expressing the ICAM-1 ligand, LFA-1. HLA-DR staining was always present in ENL lesions from 50 to 100% of epidermal cells. The lesions showed recruitment of CD4+ cells into the dermal infiltrate. TNFα-positive cells in the dermis were increased in number as compared to the non reactional biopsies. Surprisingly biopsies taken from patients under different periods of thalidomide treatment showed complete remission of those manifestations. Treatment with thalidomide dramatically reduces the positivity in situ for ICAM-1, HLA-DR and TNFα protein in the tissue. Within 7 days of treatment, a decreased number of neutrophils and T cells in the dermis was noted. The histological changes seen in ENL biopsies, as well as the expression of activation molecules in in situ provide evidence for a cellular immune activation in this type of leprosy reaction.

Supported by grants from TDR-WHO.

IM74

LIPOARABINOMANNAN (LAM) - A POSSIBLE IMMUNOREGULATORY MOLECULE OF M.LEPRAE INFECTED SCHWANN CELLS?

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Despite bacterial killing by drugs, persistence of Mycobacterial antigen (LAM) in tissues may result in prolonged immunosuppression in and/or progressive damage to peripheral nerves. It is therefore important to define the nature of the immunoregulatory effects of LAM, if any, on the Schwann cell of peripheral nerves. Murine dissociated Schwann cells in tissue culture were tested for their ability to induce lymphoproliferation in the presence of purified LAM from H37Ra. This was studied in isolation and in conjunction with accessory cells viz. the endothelials and the fibroblasts. Simultaneously the functional competence of these tissue culture sensitized cells was examined in assays for M.leprae cytotoxicity, cytokine release, induction of nerve damage and granuloma formation.

Observations indicate LAM as a potent immunoregulatory antigen in all cell types albeit in different conditions. The findings indicate a novel mechanism for the precipitation of lepra reactions in peripheral nerves in leprosy.

IM75

SENSITIZATION TO MYCOBACTERIA IN TWO AREAS IN ZIMBABWE WITH DIFFERENT DISTRIBUTION OF LEPROSY TYPE AND LEPROSY INCIDENCE: ELISA.

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Antibody titers against eight mycobacterial antigenic preparations were determined using an Enzyme Linked Immunosorbent Assay (ELISA) in sera from individuals from two different areas in Zimbabwe. In the two areas that were selected, Chipinge (C) and Nenyunka (N), significant difference in the ratio of Paucibacillary and Multibacillary leprosy (C: 1:7, N: 6:1) and in the incidence of leprosy were observed. Leprosy patients (C: 13, N:24), their contacts (C:26, N:31), secondary school pupils (C:52, N:48) and healthy non-contact adults (C:10, N:10) were tested. The results of this study showed that sera of leprosy patients had higher antibody titers against all antigens than healthy controls from the same area. Significant differences in antibody titers in the sera of the leprosy patients from both areas were also observed for five antigenic preparations. These findings support the concept that humoral antibodies may not have any direct influence on the immunity against M. leprae and the pathogenesis of leprosy.

IM76

SENSITIZATION TO MYCOBACTERIA IN TWO AREAS IN ZIMBABWE WITH DIFFERENT DISTRIBUTION OF LEPROSY TYPE AND LEPROSY INCIDENCE: SKIN TESTS.

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Delayed type hypersensitivity (DTH) skin tests with eight mycobacterial antigenic preparations were performed to evaluate the relationship between cell-mediated immune response (CMI) and the type of leprosy in two different areas in Zimbabwe. In the two areas that were selected, Chipinge (C) and Nenyunka (N), significant difference in the ratio of Paucibacillary and Multibacillary leprosy (C: 1:7, N: 6:1) and in the incidence of leprosy were observed. Leprosy patients (C: 13, N:24), their contacts (C:26, N:31), secondary school pupils (C:52, N:48) and healthy non-contact adults (C:10, N:10) were tested.
Significant differences between the two areas and differences between leprosy patients and their contacts and between leprosy patients and controls were observed. These findings support the concept that sensitization by environmental microorganisms (mycobacteria) may influence the incidence and the pathogenesis of leprosy.

IM77

LEVELS AND COMPOSITION OF CIRCULATING IMMUNE COMPLEXES IN PATIENTS WITH ERYTHEMA NODOSUM LEPROSUM AND ACUTE ANTERIOR UVEITIS

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Acute Anterior Uveitis (AAU) is one of the ocular manifestations of type II reactions which leads to serious disabilities. Exact mechanism of development of AAU is still unknown. In the hope to determine the significance of specific factors manifested in AAU we determined the levels of circulating immune complexes (CIC), IgA, IgM, IgG, C4, C3c and CRP in patients with ENL, AAU, post reactional patients and patients who never suffered from these reactions.

There were no significant difference between levels of CIC of these groups. However, when reactional and post reactional levels of individual patients were compared, we found significant decrease in levels of CIC after reaction.

Considering these results we analysed composition of CIC by immunoblotting.

The results of these experiments will be discussed.

IM78

AN IMMUNOGENETIC STUDY OF DIFFERENTIAL MANIFESTATIONS OF LEPROSY IN NORTH INDIA

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Leprosy is a heterogeneous disease which presents in the form of multibacillary lepromatous (LL) type at one pole of the spectrum and paucibacillary tuberculoid (TT) type at the other end. To study the role of host factors in determining the immune response and the differential manifestations of the disease, the class II HLA alleles were studied by a PCR-oligotyping technique. DRB1, DRB3, DRB5, DQA1, DQB1 and DPB1 alleles were studied in 93 patients and 47 normal controls. DRB1*1501 and DRBI*1502 account for 83.1% of the multibacillary patients and 57.1% of the TT patients compared to 21.27% in controls. The much stronger association of DBR1*1501 and 1502 with the multibacillary form suggests a possible role of these alleles in the differential immune response to the M. leprae antigens. DQB1*0601 and DQA1*0103 was found significantly more often

than in controls throughout the leprosy spectrum. On the other hand, DQB1*0201 and DQA1*0201 were decreased in the LL patients as compared to TT patients and controls, suggesting a possible protective effect of these alleles against multibacillary leprosy.

IM79

GLUCOCORTICOIDES AND REGULATORY PEPTIDES IN LEPROSY PATHOGENESIS

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In LL patients the production of hydrocortisone and regulatory peptides (ACTH and beta-endorphine) was studied. Immunity status was assessed by lymphocyte blast transformation and by activity of non-specific T-suppressors. Mononuclear cell reactivity to glucocorticoides and interleukin-1 (IL-1) was assessed. It was found out that in active leprosy hydrocortisone levels were increased while glucocorticoide reserve was decreased. ACTH levels were in normal range in active leprosy and significantly increased when the disease regressed. Concentrations of beta-endorphine in leprosy patients were below the norm. A positive correlation between hydrocortisone levels and lymphocyte resistance to glucocorticoides and T-cell suppressing activity was found out. Lymphocytes from the patients with leprosy reaction responded to IL-1 while they were unresponsive to it in the patients with no leprosy reactions. The results suggest that marked neuro-endocrine disturbances in leprosy might be at hypothalamus-hypophysial and adrenal levels. Proliferative and regulatory potential of lymphocytes is dependent on the state of glucocorticoides production. These findings as well as the peculiarities of lymphocyte response to IL-1 in leprosy reaction represent the interrelationships between immune and neuroendocrine systems and might be used for prognosis of the course of leprosy and optimization of pathogenetic therapy with glucocorticoides and immune modulators.

IM80

EFECTO DEL IONOFORO A23187 Y 12,13-FORBOL MIRIACETATO SOBRE LA PROLIFERACION DE LINFOCITOS T DE PACIENTES CON LEPRA LEPROMATOSA.

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Los linfocitos T (LT) de pacientes con lepra lepromatosa (LL) son deficientes en proliferar adecuadamente ante estímulos antigénicos y/o mitogénicos (Bloom, Hastings), así como en la producción de IL-2 (Islas, Moghaghepour, Harege woin), por otro lado se ha demostrado que el receptor para IL-2 (IL-2R) está intacto (Fafutis). Cuando los eventos antes mencionados se llevan a cabo adecuadamente, el ciclo celular de LT humanos progresa. En LT de individuos sanos existen evidencias de que el Ca++ y la PKC son mensajeros secundarios importantes en la biosíntesis de IL-2, pero sólo PKC es necesaria para la expresión de RIL-2 (Mills). El ionóforo A23187 es una molécula que se disuelve en la bicapa lipídica de la membrana celular incrementando la permeabilidad al Ca++ (Alberts) y se le ha considerado un agente mitogénico de LT, así como cofactor de 12,13-forbol miriacetato (PMA) para activar PKC (Truneh, Akerman). En este trabajo el ionóforo A23187 y PMA se adicionaron a LT de sangre periférica para determinar su efecto sobre la proliferación y compararlo con el de fitohemaglutinina (PHA) en el cultivo celular.
Los resultados obtenidos sugieren que los LT de la mayoría de los pacientes con LL forman dos grandes grupos: los que requieren la presencia de ionóforo A23187 (incremento de Ca++) y los que requieren de PMA (activación de PKC) para mejorar su respuesta linfoproliferativa.

IM81

SERUM TRANSFERRIN (Tf) CONCENTRATION AND Tf RECEPTORS (R) ON THE SURFACE OF T LYMPHOCYTES IN LEPROMATOUS LEPROSY (LL) PATIENTS.

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The iron transport via systemic circulation is assured by Tf a serum globulin which binds iron and conveys it to high-affinity Tf-R on cell surfaces. It has been shown that the complex Tf/Tf-R plays an important role in the progression of the antigen and/or mitogen, that leads to the expression of interleukin-2 (IL-2) and its receptor. We have reported (Int.J.Leprosy 55:566. 1987,58;126. 1990) that the lymphocytes from LL patients have a deficient biosynthesis of IL-2, but express their IL-2 receptor. The present study concerns the serum concentration of Tf measured by radial immunodiffusion and the expression of Tf-R by flow cytometric analysis in PHA stimulated T lymphocytes from 25 LL patients.
In this work we found that T lymphocytes from LL patients under PHA stimulation, present a diminished percent of TfR positive cells and the serum Tf levels are not significattly different from those of normal subjets.

IM82

RECOMBINANT IL-2 IN UNTREATED AND TREATED LEPROMATOUS LEPROSY PATIENTS

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Interleukin 2 (IL-2), is a 15-kilodalton single chain protein produced by thymus-derived lymphocytes and is believed to stimulate T-cell proliferation after antigenic stimulation.

Ten lepromatous leprosy patients: 5 untreated, 3 currently receiving WnO-MDT regimen and 2 post-lepromatous patients were injected with interleukin 2 at specified dosage levels and intervals and administered as single and multiple injections.

In all IL-2 injected sites, early recruitment of cells: neutrophilic granulocytes, lymphocytes and mononuclear cells were noted to appear as early as 24 hours and which was more pronounced among the treated lepromatous patients as compared to the new untreated lepromatous patients. The migratory cells in the dermis noted after injection of IL-2 were identified as T-lymphocytes by surface phenotyping. There was an increase in both CD4 and CD8 cells and ratio of CD4 to CD8 was 2 to 3 times greater than in uninjected control sites.

These results suggest IL-2 may enhance cellular immune response among lepromatous leprosy patients. However, its clinical utility as a supplement to chemotherapy can only be determined by long term clinical studies in lepromatous leprosy.

IM83

TUMOR NECROSIS FACTOR (TNF) IN LEPROSY PATIENTS WITH TYPE II REACTION

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The broad spectrum of host responses of leprosy patients to antigens from *Mycobacterium leprae* provides a model for investigating the role of cytokines in the pathogenesis of the reactional state designed as "type II reaction", which includes ENL and Lucio's phenomenon. Of particular interest is TNF, a cytokine which may have both antimycobacterial and immunopathological effects. The production of one of the two types of TNF molecules, TNF-α, has been shown to be selectively inhibited by thalidomide, an anti-inflammatory drug, which is used to cure type II reactions. To evaluate the potential role of TNF in type II reactions and the effect of thalidomide upon the levels of TNF *in vivo*, we measured the levels of this cytokine in the sera of ten patients with type II reaction with no thalidomide treatment. After a first blood sample was taken, patients were put on thalidomide (100 mg/day). One month later, a second blood sample was taken from patients which had clinically recovered from the reaction (no clinical symptoms, one month on thalidomide). TNF levels in serum samples were measured by a bioassay with L929 cells. Levels of TNF in the first sample (reaction and no thalidomide) were high (x=235.7 U/ml). In the second sample (no reaction, thalidomide for 1 month), levels were similar (x=214.2 U/ml) to those of the first sample (not statistically significant). However, when four months later, a third blood sample from the same patients was obtained (no reaction, thalidomide for 4 months), levels of TNF were significantly lower (x=92.48 U/ml), compared with those obtained in the first and second samples ($p \leq 0.01$), and similar to those of a control group consisting of LL patients with no clinical history of reactions. Immunopathological damage in type II reaction can be trigger by immune complexes, TNF may also be responsible for some part of this pathology, a notion which could be supported by the fact that thalidomide accelerates the recovery from reaction. However, according to our results no correlation was observed between clinical recovery and serum levels of TNF. Since we used a bioassay, the TNF we measured was active, and no pathological conditions were observed (second sample), this suggest that type II reaction is accompanied by the production of TNF inhibitors.

*Becarios de COFFA.

The complex symptoms observed in lepromatous leprosy patients with reactive episodes of the erytema nodosum leprosum (ENL) type, is associated with different serum components actively participating in the acute inflammatory reaction. Among them are the tumor necrosis factor (TNF)and the acute-phase protein C-reactive protein (CRP). TNF and CRP were found at significantly more elevated concentrations in the serum of patients with ENL, with a positive correlation of about 95% when compared with patients with nonreactive LL or TT forms of the didiase or with control individuals. Furthermore, in another series of experiments, CRP had a specific and significant suppressive action on Con A-induced lymphoproliferation in culture from patients and controls, the reduction being more marked(75%) in patients with ENL. By extrapolation from its known actions, production of TNF may have a number of potential consequences for the immunobiology of ENL. Thus, TNF may cause direct injury to compromissed cells, facilitating mononuclear cell activation and production of cytokines such as IL-1 and IL-6, and upregulating hepatocyte expression of CRP. Both CRP and TNF in high serum concentration have the ability to enhance the acute inflammatory process in ENL; favoring increased macrophage activation and phagocytosis; contributing to the elimination of damaged cells and bacilli; as well as in the reduction of T suppressor cells, with a consequent improvement in the immunologic response of ENL patients.

IM84

CYTOKINE mRNA EXPRESSION IN LEPROMATOUS LEPROSY AND THE REACTIONAL STATES IN LEPROSY.

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Lepromatous leprosy patients expression of monocyte, NK and T cell cytokine mRNA was evaluated. Ten active LL/BL patients were compared to 5 normal controls and 3 patients who had completed therapy and did not have active disease. In addition 6 lepromatous patients in erythema nodosum leprosum (ENL) and 4 in reversal reaction (RR) were evaluated. Cytokines were evaluated directly after isolation from the blood, and in the absence of in vitro stimulation. Cytokine mRNA was not expressed in the PBMC of normal healthy individuals. However, mRNA for leukocyte cytokines was expressed in LL/BL patients. The majority of patients' PBMC constitutively express mRNA for TNFα and IL-8. The IL-2 receptor chain p55 mRNA expressed on NK and T cells and perforin mRNA expressed in cytotoxic cells were also observed. None of these patients demonstrated IL-2, IFNγ or GM-CSF mRNA. Lepromatous patients who were analyzed after having completed the therapy were negative for cytokine messages. A clear difference between ENL and RR patients was observed. All reactional patients expressed in addition to TNFα, IL-8, p55 and perforin, IL-1, IL-6 and GM-CSF mRNA. IFNγ mRNA was expressed only by patients with RR, not with ENL. Expression of IFNγ mRNA was associated with the release of IFNγ following in vitro stimulation of the PBMCs with M. leprae (mean IFNγ levels ± SD = 342 ± 146 pg/ml). Lepromatous patients without RR were unresponsive to the antigen, and cytokines such as IL-2 and IFNγ were not detected in these cultures (mean IFNγ levels ± SD = 11 ± 1.4 pg/ml).

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IM85

Correlation between TNF production, increase of CRP level and suppression of T lymphocyte during ENL reaction

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IM86

ANALYSIS OF CYTOKINE PRODUCTION BY MYCOBACTERIUM REACTIVE T CELLS: FAILURE TO EXPLAIN *MYCOBACTERIUM LEPRAE* SPECIFIC NONRESPONSIVENESS OF PERIPHERAL BLOOD T CELLS FROM LEPROMATOUS LEPROSY PATIENTS

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Recent analyses of antimycobacterial T cell clones indicate that mycobacteria preferentially induce helper T cells that produce high levels of IFN-γ and no or little IL-4 in *M.leprae* resistant TT patients and healthy subjects, whereas in one study *M.leprae* induced Ts clones from LL patients showed a reciprocal cytokine secretion profile and mediated their suppressive activity via the release of high levels of IL-4. We have evaluated these findings in peripheral blood T cells from a larger panel of TT and LL patients as well as healthy individuals. Mycobacterium reactive T cell lines generated from the PBMNC of these individuals were tested for cytokine secretion and proliferative capacity in response to *M.leprae*, *M.tuberculosis* and various individual mycobacterial antigens. The lepromatous pole of the leprosy spectrum was additionally investigated by analyzing the cytokine secretion profile of *M.leprae* induced (suppressor) T cell clones as well as primary ex-vivo PBMNC. Our results show that mycobacteria preferentially induce Th1 like cells across the whole leprosy spectrum. Although some T cells from lepromatous leprosy patients secrete IFN-γ as well as IL-4 and /or IL-10 neither IL-4 or IL-10 seem to play a pivotal role in the *M.leprae* specific T cell unresponsiveness observed in the peripheral blood of lepromatous leprosy patients.

IM87

RESPONSES OF CYTOKINE TREATED HUMAN MONOCYTE-DERIVED MACROPHAGES TO CHALLENGE WITH *MYCOBACTERIUM LEPRAE*

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An interesting dilemma in the study of anti-microbial effector mechanisms is the dichotomy between the ability of murine and human macrophages (MΦ) to inhibit, in vitro, an intracellular infection with mycobacteriae. While IFN-γ will prime murine MΦ to kill or restrict mycobacterial growth, primarily via an L-arginine-dependent pathway, this lymphokine will either have no effect on, or may actually augment, the growth of *M. tuberculosis* and *M. avium* in human MΦ. In the current study, human MΦ were evaluated for their ability to inhibit the metabolic activity of *M. leprae*. Peripheral blood was collected from nine different donors. The monocyte-derived MΦ were stimulated, for 24 hr, with IFN-γ alone, IFN-γ +

indomethacin, IFN-γ + LPS, IFN-γ + TNF-α, LPS alone or TNF-α alone. The MΦ were infected with 2 x 10^7 *M. leprae* per well for 4-5 hr and the culture fluid analyzed for TNF-α and PGE_2. The infected monolayers were reincubated, in the presence of the stimulants, for an additional 48 hr. The MΦ were lysed and the viability of the released *M. leprae* evaluated by measuring the oxidation of ^{14}C-palmitic acid to $^{14}CO_2$ in a modified Buddemeyer assay. As a control for antimicrobial activity, similarly treated MΦ were assessed for the ability to kill the intracellular protozoan, *Toxoplasma gondii*. Regardless of the stimulants employed, the human MΦ were incapable of consistently inhibiting the metabolism of *M. leprae*. In fact, in many cases the level of ^{14}C-palmitic acid oxidation was augmented in the bacilli recovered from IFN-γ-primed MΦ. In contrast, these same MΦ were quite capable of killing *T. gondii* if activated with IFN-γ + LPS. Interestingly, even though unable to inhibit *M. leprae*, infection of the MΦ with the bacilli induced TNF-α production in untreated MΦ, and these levels were greatly amplified if the MΦ were pretreated with IFN-γ alone, IFN-γ + indomethacin, or IFN-γ + TNF-α. Pretreatment with IFN-γ + LPS, TNF-α alone or LPS alone, however, reduced *M. leprae*-induced TNF-α production. In addition, pretreatment with IFN-γ + indomethacin or IFN-γ + LPS augmented *M. leprae*-induced PGE_2 production by MΦ. In summary, human monocyte-derived MΦ could not be activated in vitro with the stimulants employed to inhibit the metabolism of *M. leprae*. In contrast, great differences in TNF-α and PGE_2 synthesis were induced by challenge with the bacilli. This demonstrates that human MΦ are responsive to *M. leprae* and that these responses can be manipulated with cytokine treatment, even though they cannot, as yet, be activated to inhibit the bacilli in vitro.

IM88

POST-VACCINATION SENSITIZATION WITH ICRC VACCINE

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ICRC is one of the anti-leprosy vaccines tested in the multi-arm Leprosy Vaccine Trial being conducted by our Unit in Tamil Nadu, South India. A study was conducted in 368 individuals, from one village and a nearby school in Chingleput district, to obtain information on local reaction after ICRC vaccination and post-vaccination sensitization.

Each individual received either ICRC vaccine, in a dose of 10^9 bacilli, or normal saline by random allocation. They were tested and read for Rees' soluble skin test antigen (MLSA) and Lepromin-A tests 12 weeks after vaccination. Character and size of local response, at the vaccination site, were recorded.

Healing of vaccination lesions was uneventful. No vaccine related complications were observed. The mean size of lesion was 10 mm.

The mean sizes of post-vaccination sensitization to Rees' MLSA, Lepromin-A (early) and Lepromin-A (late) in the vaccine group were significantly larger than that in the normal saline group clearly demonstrating the ability of the vaccine to induce sensitization. The sensitizing effect attributable to vaccine was of the order of 3.5 mm, 1.7 mm and 2.2 mm respectively.

Thus ICRC vaccine was acceptable to the population and showed apparent potential for immunoprophylactic efficacy.

IM89

PROTECTION OF MICE BY VACCINATION WITH PURIFIED AND RECOMBINANT MAJOR *M. leprae* PROTEINS AND POLYPEPTIDES

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Groups of 10 mice were vaccinated intradermally in the right flank with in Freund's incomplete adjuvant (FIA, negative control), 10^7 killed *M. leprae* (positive control), and 10 μg of a number of purified and recombinant *M. leprae* proteins plus a single synthesized polypeptide diluted in FIA; 1 month later these mice were challenged in the right hind footpad with 5,000 mouse-derived viable *M. leprae*, and protection was assessed both at the peak of *M. leprae* multiplication of the mice vaccinated with FIA alone and 3 months subsequently utilizing the rank sum test and the Wilcoxon distribution. In these studies killed *M. leprae* was found generally, but not always, to be protective. The following proteins afforded no consistently significant mouse protection: a recombinant 35 kD *M. leprae* protein, a purified 16-17 kD *"M. leprae* protein", a recombinant 18 kD *M. leprae* protein (Watson), a purified 22 kD *M. leprae* protein, and a synthesized 27 amino acid N-terminal peptide of the 10 kD *M. leprae* protein. On the other hand, vaccination with the following *M. leprae* proteins resulted in consistent and significant protection: a purified 10 kD protein, a recombinant 10 kD protein (Mehra), a recombinant 65 kD protein (van Embden), and a purified 28 kD protein. It was noteworthy in these studies that when mice were vaccinated with each of the proteins found to be protective there was induction of significant splenic T cell responses *in vitro* to sonicated *M. leprae* (stimulation indices ≥ 4). These studies suggest which *M. leprae* protein epitopes are important to protective immunity and hence those which would best be included in a future-generation leprosy vaccine.

IM90

BCG VACCINATION PROTECTS AGAINST LEPROSY IN VENEZUELA

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The protective effect of BCG vaccination in the control of leprosy has been widely variable in trials carried out in different areas of the world. In Venezuela, repeated BCG vaccination of contacts of leprosy patients has been one of the components of the leprosy control program. Using the case-control approach, we have carried out a retrospective study of the efficacy of repeated BCG vaccination in reducing the occurrence of leprosy. The clinical examination of 63,878 contacts during the intake phase of a large vaccine trial revealed 91 previously undetected cases of leprosy. There appeared to be an inverse relation between the number of BCG scars and the prevalence of leprosy (no scar, crude rate 2.87/1000; 1 to 5 or more scars, 1.31 to 0.45/1000). In addition, multi-bacillary LL and BL cases were found only in the group with no BCG scar (18 cases) or one scar (3 cases). There was no evidence that the protective effect of BCG was different among household or non-household contacts nor that it was age-related. Both specific responses to shared antigens and non-specific activation of immunological mechanisms by BCG may be involved in the apparent BCG-induced protection observed in this study.

IM91

ANNUAL IMMUNOTHERAPY IN TREATED LEPROMATOUS LEPROSY WITH 3 DIFFERENT BCG-BASED VACCINES - A 6 YEAR ASSESSMENT.

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44 treated LL (37) and BL (7) patients were investigated clinically, bacteriologically and histologically and allocated to one of three annual vaccination regimens, either BCG alone (9 patients) or BCG plus 6 x 10^8 dead M leprae (18 patients) or BCG plus 1 x 10^9 dead M vaccae (17 patients). Patients were assessed by means of the rate of fall in the BI (in those still skin smear positive), by annual lymphocyte transformation tests and by skin testing with 5 different mycobacterial antigens,

including standard lepromin and sonicated M leprae (Rees skin-test antigen).

Although it was expected that lepromin conversion would constitute a major assessment, some very longstanding patients were found to be weakly lepromin positive on admission to the trial (Waters and Ridley, 1990); therefore lepromin conversion has be be interpreted with caution.

Results obtained with the various parameters over a 3 to 6 year follow-up will be described, and the value of immunotherapy discussed.

IM92

FIELD TRIALS WITH AN ANTI-LEPROSY VACCINE MYCOBACTERIUMw.

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A double blind field trial was started with an anti-leprosy vaccine, Mycobacterium w, as an immunotherapeutic and immunoprophylactic agent in a highly endemic region of Kanpur Dehat District in the Northern Indian State of Uttar Pradesh.
The study population, estimated to be around 400,000, has been divided into 4 groups, group I consists of multibacillary (MB) patients receiving a placebo (1/8th the dose of tetanus toxoid) and their healthy household contacts the vaccine, group II consists of MB patients receiving the vaccine and their contacts placebo while in groups III & IV the MB patients and their contacts receive placebo and vaccine respectively.
A total of eight vaccine doses are given at 3 monthly intervals together with multi-drug therapy to the MB patients,while the immunoprophylactic schedule consists of 2 doses at 6 months interval. Analysis regarding the immunotherapeutic effect of the vaccine is being assessed on the basis of clinical improvement, bacterial index, lepromin status & histopathology all of which are regularly monitored.
Upto the 31st of December 1992, about 350,000 people have been surveyed and 4045 patients have been resistered of which 1050 are multibacillary cases. A total of 21732 eligible contacts have been screened for disease of which 18131 have received the initial dose of vaccine /placebo showing a complaince rate of 83.4%. Booster dose for immunoprophylaxis has been given to 11533 healthy contacts. The vaccine has been well tolerated and there has not been any incidence of systemic reactions to the vaccine /placebo in any of the study groups.

IM93

T CELL RECEPTOR USAGE IN BLOOD AND SKIN LESIONS IN LEPROSY.

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Previous studies have shown a 100 fold enrichment of M.leprae reactive T cells in skin lesions compared to the peripheral blood in tuberculoid leprosy. We have used a panel of anti T cell receptor antibodies to quantitate the usage of various Vα and Vß genes in leprosy. In peripheral blood, positive cells were quantitated by FACScan, while immunochemistry was used to stain lesional T cells. T cells expressing Vα2, Vß2, Vß3, Vß5.1, Vß5.2 + 5.3, Vß6, Vß8 and Vß12 were analysed. There was no evidence for deletion of any family of T cell receptor genes in the leprosy patients. Comparing blood and lesional T cells, leprosy skin lesions contained more Vß2 and Vß5.1 positive T cells then the blood, although there was no connection with the clinical status of the patient. These results show that Vß2 and Vß5.1 positive T cells are attracted to or preferentially expanded in, leprosy skin lesions - perhaps stimulated by a leprosy superantigen.

IM94

Human T cell clones recognise mycobacterial specific and shared epitopes on *Mycobacterium leprae* 70kD protein.

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Centenary Institute of Cancer Medicine & Cell Biology and *Department of Medicine, University of Sydney. 2006. Australia

The 70kD protein of *Mycobacterium leprae* (hsp70) stimulates both cellular and humoral immune responses in leprosy patients and their contacts. We have previously demonstrated that the C-terminal region of the protein including the *M.leprae* specific C-terminal 70 residues is the major target for antibody responses of leprosy patients. Using peripheral blood lymphocytes from known responders to the protein and short synthetic peptides of 12 amino acids, we were able to identify two T cell epitopes in sequences 380-396 and 418-433. In order to characterise the fine specificity of T cell epitopes we screened a panel of human T cell clones generated against *M.leprae* sonicate with *M.leprae* hsp70 and synthetic peptides Two epitopes contain sequences specific to *M.leprae* and *M.tuberculosis*. One (71-90, restricted by HLA-DR3 or 4) spans a region containing a deletion restricted to the mycobacterial sequences. The second mycobacterial specific epitope (241-260) was DR7 restricted. A further two epitopes towards the C-terminal end show partial homology with human hsp70. The minimal epitope length of these to be 414-427 and 471-486. The key residues which determine the antigenicity of the mycobacterial peptides are being determined with sequential replacement of amino acids. The *M.leprae* hsp70 T cell clones produced IFN-γ and TNF-β, but one also released IL-4 in comparable amounts. Functionally each clone was cytolytic against autologous EBV targets pulsed with *M.leprae* sonicate, hsp70 or the specific peptide. Analysis of other CD4+ *M.leprae* reactive T cell clones confirmed that some recognising the *M.leprae* 65 and 18 kD proteins were also cytolytic, but others with undefined specificity were not cytolytic. Therefore there is a spectrum in cytolytic activity in anti-*M.leprae* CD4+ T cell clones.

In summary, the defined T cell epitopes are present in regions distant from major human antibody determinants of *M.leprae* hsp70.

IM95

FACS ANALYSIS OF CD4+ T-CELL SUBSETS IN REACTING AND NON-REACTING LEPROSY SKIN LESIONS.

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Increases in the number and percentage of CD4+ T-cells have been noted in lesions of leprosy patients with Type I (RR) and in some Type II (ENL) reactions. We therefore asked whether the so-called helper-inducer (HI) or suppressor-inducer (SI) subsets of CD4+ cells were preferentially increased in skin lesions in these reactions.

Cells were obtained in suspension from blisters induced by gentle suction directly over reacting or non-reacting lesions, 48 hours after induction. Control cells were obtained simultaneously from peripheral blood and, when possible, from blisters induced on non-lesional skin. A total cell count was followed by simultaneous labelling with FITC- and PE-conjugated Mabs Leu3 and Leu8, anti-γ,δ and other markers. Flow cytometry was performed using a FACScan, and results analyzed using Lysis software.

Twenty samples from active lesions from 14 patients were examined. Pairing of BB and BT lesions with and without RR indicated a definite increase in the Leu3+, 8- (HI) subset in RR lesions (without corticosteroid treatment). Although no consistent effect was observed in ENL, all ENL lesions studied were in patients receiving prednisolone. Cell subsets in non-lesional skin were generally similar to those in clinical lesions, but all cutaneous subsets were significantly different from those in the peripheral blood.

These results indicate that precise quantitation of T-cell subsets by multiple labelling and flow cytometry is possible with cells obtained from lesions using suction-induced blisters, and suggest that the previously observed increase in CD4+ cells in Type I reactions is accompanied by an increase in the Leu3+, 8- subset.

IM96

MYCOBACTERIUM LEPRAE INFECTION TRIGGERS SYNTHESIS OF STRESS INDUCIBLE hsp 70 IN SCHWANN CELLS AND ANTI hsp 70 ANTIBODIES IN SERA.

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Murine and monkey Schwann cells were exposed to elevated temperatures and the induction of heat shock protein synthesis was monitored. Synthesis of the stress-inducible 70-kDa heat shock protein (hsp 70) was detected in both murine and primate Schwann cells by metabolic labelling and by immunoblotting with a specific monoclonal antibody. Infection with Mycobacterium leprae caused induction of hsp 70 synthesis in Schwann cells which was detected within 24 hours and persisted upto one week post-infection. hsp 70 was purified from the Schwannoma cells and antibody response to it in leprosy was studied using Western blot technique. These antibodies were directed to both the constitutive and inducible members of hsp 70 family, as ascertained after 1D and 2D PAGE and Western blot of the purified protein. The presence of high levels of antibodies to self proteins suggests their possible role in nerve damage observed in leprosy.

IM97

THALIDOMIDE DOES NOT AFFECT SELECTED IMMUNOMODULATING SURFACE RECEPTOR MOLECULES ON CELLS WITH IMMUNE POTENTIAL.

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The uncertainties concerning the pathogenesis of ENL are underscored by the unknown mechanism of thalidomide's therapeutic effect in this condition.

Previous reports have described an increase in cells expressing CD4 molecules and an increase in Ia (HLA-DR) molecules on keratinocytes in reactive skin lesions of patient experiencing ENL.

As these manifestations are associated with parameters of CMI and were confined to the acute phase of ENL, it has been suggested that ENL is the consequence of a transient activation of the CMI cascade. If ENL is the consequence of an activated CMI response, an alteration of the existing or the density of immunomodulating surface receptor molecules would be expected.

In the present study, thalidomide did not alter the expression of immunoregulatory molecules such as CD4, CD8 and CD5 on lymphocytes from four healthy male donors; nor did it influence the expression of the interferon-γ induced cell surface molecules HLA-DR, HLA-DP, CR1, CD 14, CR2, N-CAM-1, FcR-γ, and CR3 on THP-1 monocytes.

IM98

SOLUBLE M.LEPRAE ANTIGEN SKIN TESTING AND LEPROMIN POSITIVITY IN CHILDREN OF MOTHERS WITH LEPROSY AND HEALTHY CONTROLS STUDIED PROSPECTIVELY FROM BIRTH TO PUBERTY

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149 children (K) of mothers with leprosy (MB and PB) and healthy mothers (NL) living in the same environment (80MBK, 40PBK, 29NLK) were studied from birth up to 2 years of age (Phase 1). Reassessments were made at age 3-4 years (Phase 2): 89 children (49MBK, 25PBK, 15NLK); at age 7-8 years (Phase 3): 86 children (48MBK, 23PBK, 15NLK); and at puberty aged 12-15 years (phase 4): 99 study children with an additional cohort of 79 healthy children (55MBK, 31PBK, 95NLK). Skin testing with soluble *M.leprae* antigen in Phases 1,2 and 3 readings at 48-72 hours (± = negative): Phase 1:- MBK: 1/47 (2%), PBK: 3/21 (14%), NLK: 1/11 (9%); Phase 2:- MBK: 16/37 (43%), PBK: 11/23 (48%), NLK: 8/14 (57%); Phase 3:- MBK: 10/43 (23%), PBK 11/22 (50%), NLK: 4/14 (33%). Phase 4 Mitsuda lepromin testing Fernandez readings: MBK: 38/55 (69%), PBK: 26/32 (81%), NLK: 78/95 (82%); Mitsuda readings (± (2mm) = negative): MBK:46/52 (88%), PBK: 28/29 (97%), NLK: 78/86 (91%). Lepromin reaction (Mitsuda) ++/+++ was seen in 35/52 (63%) MBK, 21/29 (72%) PBK and 54/86 (63%) NLK. Punch biopsies of Mitsuda reactions from 41 children (MBK23, PBK11, NLK7) all showed BT type/pattern of Mitsuda reaction. Stimulation index (SI) in LTT against intact *M.leprae* was: MBK 23.0±25.3 (n=54), PBK 28.0±34.9 (n=25), NLK 7.2±10.7 (n=80). SI › 4.0 *vs.* intact *M.leprae* was: MBK 27.8±25.7, PBK 28.0±34.9, NKL 14.1±13.3; numbers of SI ›4: MBK 44/54 (81/5%), PBK 24/25 (96%), NLK 35/80 (43.3%). Rank correlation test (Kendall) SI *vs.M.leprae* and size of Mitsuda gave r= 0.19, ($p<0.001$).

IM99

IMMUNOBIOLOGY OF MELANOCYTES IN RELATION TO HYPOPIGMENTATION IN LEPROSY.

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Hypopigmentation is a feature of all forms of leprosy and predilicts for neuronal involvement. However, it is strikingly more common in paucibacillary tuberculoid type of the disease. Although there is no strong correlation between cellular infiltrate and hypopigmentation in leprosy, it is assumed that destruction of melanocytes (MC: which originate from neural crest like Schwan cells) is a consequence of local T-cell mediated immune response. The potential importance of MC in the local immune response of human skin is being studied in our laboratory. Results of such studies have been recently reported by us (Arch.-Dermatol.Res.in press, 1993; Exptl.Cell Res.in press, 1993; Exptl.Dermatol. 1 p.95, 1992). Using immunohistological methods, we could demonstrate that MC can express MHC class I/II molecules, ICAM-1 and cytokines e.g. IL-1, IL-2 and IL-6. Interestingly, by using latex beads and applying confocal microscopy/electronmicroscopy and FACS analysis we could show that MC are capable of phagocytosis. These results are suggestive of an antigen processing and presenting ability for melanocytes. Indeed we could demonstrate that cultured human MC can process intact HSP-65 as well as whole M.leprae and can present processed antigenic peptides to CD4+ cytotoxic and proliferative Th1-like T-cell clones in a HLA-restricted manner. These T-cell clones were obtained from lesional skin biopsy material from tuberculoid leprosy patients. Such functions of MC can be involved in the pathogenesis of depigmentation in tuberculoid leprosy and can be extrapolated to the immunologic damage of these cells as "bystander targets" to some T-cell clones in the lesional infiltrates.

C.Le Poole and R.M.J.G.J.v.d.Wijngaard are recipients of subsidy from Stiefel.

IM100

NATURAL KILLERS IN LEPROMATOUS LEPROSY

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The present work is aimed at studying functional activity of natural killers (NK) in view of the distribution of HLA class I antigens in LL patients belonging to the Russian nationality. Cytotoxical activity of NK in leprosy patients and in healthy subjects was determined by their response to H3-uridine-labelled cells of myeloleucotic line K-562. HLA-typing by class I antigens was performed by standard microlymphocytotoxicity test.In active

leprosy functional activity of NK was decreased as compared to healthy donors and inactive patients ($p<0,05$), being higher in the last group ($p<0,01$). The decreased NK activity in active leprosy patients might be a consequence of NK-depletion due to massive antigenic load. Among possible causes of NK-activity in cured patients M.leprae persistence in body tissues might be supposed. In leprosy patients significantly increased frequency of HLA-B7 antigen was observed. Besides, the association between HLA-B7 antigen and low level of NK-cytotoxicity was found out suggesting a genetic determination of functional deficiency of NK in leprosy. NK-activity correlates with leprosy status and, alongside with other indices, might be used for assessment of immune state and effectiveness of therapeutic regimens.

MICROBIOLOGY

MI1

A MOLECULAR ANALYSIS OF MYCOBACTERIAL ANTIGENS WHICH STIMULATE γδ T CELLS

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Most T lymphocytes in human peripheral blood (hpb) express the αβ T cell receptor (TCR). T cells expressing the γδ TCR account for less than 10% of CD3+ hpb T cells. Several microorganisms, including mycobacteria, have been shown to produce a marked in vitro expansion of γδ T cells.

The nature of the γδ stimulatory molecule(s) is controversial. In this study we have used a variety of fractionation methods to identify these molecules, and to charactarise the γδ T cell response.

We find that virtually all individuals tested show a stimulation of Vγ9 γδ T cells when hpb are incubated in the presence of low molecular weight (<5kDa) fractions of mycobacteria, and that there are at least five low molecular weight molecules, all very close in molecular nature, involved in this stimulation.

The γδ T cell response to these molecules has been further charactarised in terms of the lymphokine profile, the involvement of the TCR, and the requirement for antigen processing.

MI2

N-TERMINAL AMINO ACID SEQUENCING OF Mycobacterium leprae PROTEINS: DEFINITION OF THE L12 RIBOSOMAL PROTEIN

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The high abundance of some specific polypeptides in armadillo-derived Mycobacterium leprae has permitted their purification in enough quantities to perform their complete amino acid sequence (see Pessolani et al., abstract this Congress). In anticipation of the conclusion of the biochemical definition of such proteins, the following approach has recently been undertaken in other to define the minor proteins of the leprosy bacillus: (1) fractionation of the bacterial proteins by SDS-PAGE or two-dimensional gel electrophoresis; (2) transference of proteins onto polyvinylidene difluoride (PVDF) membranes and subsequent N-terminal amino acid sequencing by automated Edman degradation; (3) cloning and sequencing of the genes that code for these proteins by using oligonucleotides derived from the amino acid sequences. The N-terminal amino acid sequences of two polypeptides present in extracts of whole cells and of four polypeptides present in the cytosolic fraction of the bacteria were obtained so far. A search in a protein sequence data bank indicated that a 15 kDa cytosolic protein shares 65% homology in a 17 amino acid stretch with the N-terminal region of the Streptomyces griseus L12 ribosomal protein, probably constituting the M. leprae L12 homolog. Two independent approaches are currently being undertaken in order to clone and sequence the gene that codes for the M. leprae L12 ribosomal protein: (1) amplification of the gene by using oligonucleotide primers derived from the N-terminal amino acid sequence, and from phylogenetically conserved amino acid sequences derived from the L12 protein of other bacterial species; (2) cloning of an approximately 4.0 kb EcoRI fragment from the M. leprae genomic DNA that hybridizes with a pool of degenerate oligonucleotides derived from the N-terminal amino acid sequence. In addition to contributing to the understanding of the physiology of mycobacterial ribosomes, the characterization of the M. leprae L12 ribosomal gene may favor the cloning of genes commonly arranged in the same operon, such as the gene that codes for the β subunit of RNA polymerase, the well-known target of the drug rifampicin.

(Work supported by NIH, NIAID Contract NO1 AI-05074.)

MI3

DETECTION OF MYCOBACTERIUM LEPRAE DNA BY PCR IN SKIN SCRAPINGS AND NASAL SECRETIONS FROM MULTIBACILLARY AND PAUCIBACILLARY LEPROSY PATIENTS.

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Detection and species identification of various difficult-to-grow mycobacteria have improved as a result of developments in DNA amplification tests. We have shown that M. leprae DNA can be detected by PCR amplification in extracts from human skin and that 99% of untreated, multibacillary (MB) patients and approximately 50% of AFB-negative, paucibacillary patients (PB) tested positive for M. leprae. Since routine diagnosis of leprosy does not rely on examination of skin biopsy material, but, is limited to clinical observation of the patient and microscopic examination of skin scrapings for acid-fast bacilli (AFB), we tested the utility of PCR to detect M. leprae in skin scrapings and compared these results with PCR reactivity of biopsies from the same patients. Another anatomical location, postulated as a site for initial entry and eventual dissemination of M. leprae in untreated patients, is the nasal mucosa. Nasal secretions were collected from leprosy patients and tested by PCR for M. leprae and compared with the results from skin scrapings and skin biopsies. Nasal secretions and skin scrapings were collected on cotton swabs and scalpel blades, respectively, and placed into 1.0 ml each of sputolysin containing Tween 20 (0.05%). The particulate fraction was recovered by centrifugation and resuspended in 100 ul of deionized water and frozen for subsequent analysis by PCR. Results of samples from 7 of 7 MB and 1 of 2 PB patients showed a direct correlation between PCR positivity of the skin biopsy and the skin scrapings taken from at least one site. Six of 7 (MB) and 1 of 2 (PB) nasal secretions tested positive by PCR. Preliminary results suggest that PCR testing of routine, clinically available samples may be useful in diagnosing and monitoring leprosy.

MI4

EVALUATION OF THE POLYMERASE CHAIN REACTION AS A TOOL FOR LEPROSY DIAGNOSIS

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The identification of ***M.leprae*** is difficult, partly due to the inability of the bacillus to grow *in vitro*.The current diagnosis of leprosy is

based on microscopic detection of acid fast bacilli in tissue smears, in combination with histopathology and clinical evaluation. Because of the large incubation period of leprosy, and the lack of a reliable test for detection of a subclinical infection, we aimed at the development of a sensitive and specific assay for the detection of *M.leprae* , based on the amplification of bacterial DNA through PCR and hybridization. Oligonucleotides for the amplification of a repetitive sequence, specific for *M.leprae*, were synthesized and PCR amplification was optimised. A hybridization assay augmented the sensitivity and specificity of the test. Different types of clinical samples such as blood, lymph, skin biopsy, nasal secretion and hair bulbs were collected from leprosy patients. Processing of these samples was optimized and inhibitors of the PCR reaction inactivated. A *M.leprae* specific DNA amplification was obtained for each of the samples and 79 patients with a defined clinical spectrum were analysed by gel electrophoresis and hybridization. Results assessed the possibility of using lymph, blood or hair bulb material for diagnosis of both multibacilary and paucibacilary patients in early stages of the disease and, additionally, use of nasal secretion for monitoring the therapeutic regimens.

This project was supported by UNDP/WHO Special Program for Research and Training on Tropical Diseases (TDR).

MI5

NUCLEIC ACID SEQUENCE-BASED AMPLIFICATION (NASBA) FOR IDENTIFICATION AND VIABILITY ASSESSMENT OF *M.LEPRAE* IN SKIN BIOPSY SPECIMENS

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NASBA is an isothermal amplification technique which does not depend on specialized equipment. We have selected a primerset in a highly conserved region of the 16S rRNA sequence allowing amplification of a 200 nt target which comprises a variable region. For identification of the amplified RNA of the mycobacteria, species-specific probes to this variable region were chosen and used in an Enzyme-Linked Gel Assay (ELGA). NASBA was shown to be sensitive and specific for identification of mycobacterial infections in biological samples. Identification of M.leprae in skin biopsy specimens could be performed in less than one day. An advantage of this in vitro RNA amplification technique is that it offers a tool for assessing viability of the mycobacteria. Using in vitro killed *M.smegmatis*, we found a correlation between viability of mycobacteria and the degradation of 16S rRNA. Detection of *M.leprae* DNA (PCR) and 16S rRNA (NASBA) in skin biopsy specimens of multibacillary patients showed that during treatment *M.leprae* rRNA disappears faster than DNA. Thus, detection of rRNA through NASBA might provide an objective means of assessing the bacterial load and efficacy of the therapy.

MI6

DETECTION OF *M. LEPRAE* BY THE POLYMERASE CHAIN REACTION IN NASAL SWABS OF PATIENTS AND THEIR CONTACTS

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Nose swabs from 4 PB and 8 MB patients and their contacts were tested for the presence of *M. leprae* by two PCR: one amplifying a gene coding for the species specific rRNA, and a second amplifying a specific repetitive sequence. Examinations were done monthly after the start of treatment, in PB cases during 4 months, in MB patients for periods of either 12 or 41 months. Sample preparation was by freeze-boiling. The inclusion of an internal control allowed the detection of inhibitors of the reaction, which were present in 30 % of the samples. Positive results were obtained in 1.9 % and 7.9 % of contacts of PB and MB respectively. Since this difference is not significant, these infections were probably community acquired.

MI7

COMPUTER RECOGNITION OF POSSIBLE FUNCTIONAL OR STRUCTURAL SITES ON MYCOBACTERIUM LEPRAE DNA

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Groups working on sequences of nucleic acids contributed a large amount of data stored in data banks. Several mycobacterial nucleotide sequences are also available through computer networks.

We applied a new computer methodology (1), able to recognize guanine and cytosine-rich zones on nucleotide sequences, to genomic DNA sequences obtained from MycDB (Mycobacterium Database).

The following M. leprae DNA sequences were analysed: 65 kDa, 36 kDa, 28 kDa and 18 kDa. Guanine and cytosine-rich regions were found on all genes within 500 bases from the start of the coding sequence.

The identified zones could be related to functional or structural features of the genes.

(1) Arrigo, P., et al., CABIOS, 7, 353 (1991).

MI18

DETERMINATION OF THE ADENYLATE ENERGY CHARGE (AEC)

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The adenylate energy charge (AEC) defines the proportion of energy-rich adenine nucleotides refered to the total amount of adenine nucleotides. The ratio is given by the equation AEC = (1/2 ATP + ADP)/(ATP + ADP + AMP). The determination of the AEC is - in contrast to the determination of the ATP content - independent of the number of bacterial organisms and well reproducible as shown in a variety of publications for different bacterial genera and also for eucaryotic cells. For mycobacterial species only a few data have been published so far. AEC data determined for several untreated mycobacterial species, including *M.leprae* derived from armadillo material, will be presented and compared with literature data. The influence of different drugs and drug concentrations on *M.tuberculosis* and *M.smegmatis* have been monitored via AEC measurements, demonstrating the general applicability of the method for the determination of drug effects and with that for drug screening. Furthermore, the AEC data derived in these experiments were compared with the results from the mass spectrometric determination of the medians of the intrabacterial Na^+,K^+-ratios of the same bacterial populations resulting in a linear correlation between these two parameters. Furthermore, a correlation between the AEC and the percentage of viable organisms was found. The latter will be shown to be dependent of the bacterial species but independent of the mode of drug action. We will discuss the technical details of the method with particular emphasis on the non-cultivable species *M.leprae* and the implications of the method for *in vitro* drug screening and *in vivo* therapy control.

MI9

A SIMPLE AND RAPID TECHNIQUE FOR THE DETECTION OF RIFAMPICIN RESISTANCE IN *Mycobacterium leprae*

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Rifampicin is the backbone of the current multidrug therapy used for the treatment of leprosy. It has been shown recently, in a study of lepromatous leprosy patients who had relapsed after rifampicin monotherapy, that drug resistance stems from missense mutations in the *rpoB* gene of *Mycobacterium leprae*, encoding the β-subunit of the essential enzyme, RNA polymerase. All of the mutations were found within a short region and similar mutations have been found in the *rpoB* gene of rifampicin-resistant *Mycobacterium tuberculosis*.

A rapid test for rifampicin-resistance would represent a valuable tool for leprosy control programmes. Such a test, based on the polymerase chain reaction and single stranded conformation polymorphism analysis, has been developed. Less than 48 hours are required to obtain the results directly from biopsies and this approach represents an attractive alternative to mouse footpad inoculation.

MI10

MOLECULAR CHARACTERIZATION OF RIFAMPIN RESISTANCE IN PATHOGENIC MYCOBACTERIA

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The majority of mutations which result in the rifampin-resistant phenotype in prokaryotes have been mapped to a 250 bp region of the rpoB gene encoding the B-subunit of the DNA-dependent RNA polymerase. Recently, the rpoB gene of *Mycobacterium leprae* has been sequenced (S. Cole, Pasteur Institute). Using the *M. leprae* rpoB sequence we have synthesized PCR primers which amplify a 644 bp fragment encoding region 4. Using nested sequencing primers and a direct DNA sequencing protocol, we have determined the nucleic acid sequence and deduced amino acid sequence of this region in several rifampin-sensitive (Rif-s) and one rifampin-resistant (Rif-r) strains of *M. leprae*. The DNA sequence of the Rif-s strains contain 100% homology with that reported by S. Cole. The sequence of the Rif-r strain was found to contain a point mutation at base number 1274 resulting in a change from a serine residue found in Rif-s strains to a leucine residue in the amino acid sequence of the Rif-r strain. Comparison of secondary structure predictions for deduced a.a. sequences from Rif-r and Rif-s rpoB polypeptides using the Chou-Fasman and Hopp-Woods algorithms showed that the serine to leucine substitution profoundly increased the hydrophobicity of this region, possibly contributing to the antibiotic resistance observed in this strain. A point mutation in the same codon in a *Salmonella typhimurium* changes the serine residue to a phenylalanine in the Rif-r mutant strain. This mutation has been characterized as the genetic basis of rifampin resistance in this mutant. Several other Rif-r strains of *M. leprae* are being sequenced to establish the potential number of mutations conferring resistance in this species. The sequence of the rpoB gene in region 4 of *M. tuberculosis* is also being obtained using a similar strategy.

MI11

CLONING AND CHARACTERIZATION OF THE GENES CODING FOR THE 85-COMPLEX ANTIGENS OF *MYCOBACTERIUM LEPRAE*

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The genes conding for antigens 85-A, 85-B and 85-C have been isolated from a λ-Dash::*M.leprae* genomic library screened with a labelled DNA fragment containing part of the *M.tuberculosis* 85-A coding sequence. This is the first report on the sequence of the full complement of 85-complex genes in *M.leprae*. The 85-A DNA coding sequence is 990bp long, the 85-B coding sequence 981bp long and the 85-C coding sequence 999bp long. The deduced amino acid sequences are 330, 327 and 333 residues long, respectively, with predicted molecular weights for the mature proteins of 31.0, 30.0 and 31.5 kDa. Comparison to other genes of the 85-complex and hydrophobicity analysis suggest the presence, in the protein sequences, of signal peptide regions. The *M.leprae* DNA coding sequences share 82.3% (85-A), 78.9% (85-B) and 84.4% (85-C) homology to the corresponding *M.tuberculosis* genes. These *M.leprae* proteins are now being expressed in *Escherichia coli* with the aim of obtaining large amounts of protein for functional and immunological studies.

This project received financial support from the UNDP/WHO Special Program for Research and Training in Tropical Diseases (TDR) and from the Conselho Nacional de Desenvolvimento Científico e Tecnológico, CNPq, Brasil.

MI12

STRAIN DIFFERENCES IDENTIFIED WITHIN *MYCOBACTERIUM LEPRAE*.

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Random amplified DNA (RAPD) was generated by the polymerase chain reaction (PCR) using an arbitrarily chosen 10-mer oligonucleotide. DNA patterns were also generated by PCR using primers based on the inverted sequences of enterobacterial repetitive intergeneric consensus (ERIC) and repetitve extragenic palindromic (REP) elements. The polymorphic patterns of *M. leprae* DNA shown by the three methods were clearly distinguishable from those of other (myco)bacteria. Thirteen isolates of *M.leprae* were investigated. The DNA patterns of these isolates were compared with that of DNA provided by the WHO, which served as a reference. Of the 13 isolates, one was from a naturally infected armadillo and 12 were from armadillos, experimentally infected with bacilli from multibacillary leprosy patients from different parts of the world. The isolates also differed in the number of passages made in armadillo. Distinct differences were observed in two isolates in both RAPD, ERIC- and REP-PCR; in one additional isolate only the RAPD-PCR pattern differed from the WHO-reference; different ERIC patterns were furthermore observed in two isolates and REP-PCR showed differences in two isolates.These preliminary results suggest that strain diffences do exist within *M.leprae*, but we did not find any relation with geographical origin.

MI13

POLYMERASE CHAIN REACTION FOR THE DETECTION OF MYCOBACTERIUM LEPRAE IN SKIN TISSUE

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We have tested several sets of primers for the amplication of a 530 bp and 372 bp fragment of genes specifically encoding for 36 kDa,18 kDa, and 65 kDa protein of M. leprae respectively. All were found to be very specific and sensitive for the detection of M.leprae organisms in suspensions. We have used the primers S 13, S62 which amplified a 530 bp fragment of the 36 kDa protein gene of M.leprae in PCR technique on fresh and paraffinized skin sections. The results

showed that PCR is much more powerful in specfic determination of M.leprae organisms in skin tissue as compared with conventional acid-fast staining method. Hybridization of the amplified fragments with digoxigenin-labelled 1 kb 36 kD gene probe increased the sensitivity of detection by 30% . A quantiative test to determine the proportion of viable bacilli in biopsy specimens by the PCR as compared with mouse footpad inoculation test is being carried out.

MI14

APPLICATION OF A POLYMERASE CHAIN REACTION FOR DETECTION OF MYCOBACTERIUM LEPRAE IN NASAL SWAB SPECIMENS

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Little is known about the scope and importance of subclinical infection or carriage of M.leprae. Given that multibacillary patients and nasal carriage of M.leprae are likely associated with transmission of leprosy and treated patients are not likely transmitters of the disease, as a first step developing a test, we decided to examine rates of nasal carriage in treated and untreatedmultibacillary patients by the polymerase chain reaction(PCR). In this study, PCR is based on the selective amplification of a 530-bp fragment of the gene encoding the proline-rich antigen of M.leprae was used to detect M.leprae in nasal secretions collected on swabs from 16 treated and 22 untreated multibacillary patients. To prevent false positive amplifications, dUTP and uracil-N-glycosylase were adopted. To minimize false negative results, due to inhibitory components from nasal mucosa, swabs were treated with quanidinium thiocyanate(GuSCN) or DMSO. It was found that the 59.1%(13/22) untreated MB patients were positive compared to 18.8%(3/16) treated MB patients. The reduced nasal carriage in treated patients is consistent with reports of decreased transmission in families of treated MB patients. These findings suggest that the PCR may be useful for studying transmission of M.leprae by comparing nasal carriage rates in families of treated and untreated MB patients

MI15

ENHANCED CHEMILUMINESCENT ASSAY (ECL) : A HIGHLY SENSITIVE METHOD FOR THE DETECTION OF M.LEPRAE INFECTION IN NASAL SECRETIONS

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The role of nasal carriage in the transmission of leprosy has always been considered in studies relating to the development of rapid and simple means of detecting M.leprae infection. Using non-invasive collection method, two test are available; the PCR method and a monoclonal test. The PCR has greater sensitivity but is very expensive, the monoclonal test is cheaper but is constrained by unstable color development thus making the interpretation of reactions difficult. In addition, data cannot be documented for the substrate fades with time. Recently, a non-radioactive labeling and detection system have been used to improve sensitivity of antigen detection in Western blot systems. For the first time, we have adapted the Enhanced Chemiluminescent Assay (ECL) and were able to detect M.leprae and its antigen, phenolic glycolipid-I (PGL-I) in nasal secretions of patients using our monoclonal antibody,DZ-1. Thirty one leprosy patients were tested, 24 were MBs and all were test positive; of the 6 PBs, three were test positive and three were negative and one Neural type was slightly positive. Thirty nine individuals free of leprosy were used a controls and all but 2 were test negative indicating the need to improve the specificity of the ECL which can easily be done without loss of sensitivity. Our data have shown that the ECL is highly sensitive. The most beneficial aspect of the test is the ability to keep a permanent record of the result on x-ray film. Therefore,the ECL has the potential use as a screening test to detect early leprosy, to study transmission, and disease reactivation.

MI16

UTILIZACIÓN DE 3 SISTEMAS DE PCR PARA LA DETECCION DE ADN DE M. LEPRAE EN MUESTRAS QUIMICAS.

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Se ensayaron 3 sistemas de PCR para la detección de ADN de M. leprae en muestras de suero y linfa de pacientes en los cuales se sospechaba la posibilidad de estar infectados con M. leprae porque tenian titulos elevados de anticuerpos en el suero contra este microorganismo.

En el suero no se detectó la presencia de las secuencias de ácidos nucléicos que estos sistemas amplifican mientras que en la linfa los resultados no permiten detectar bacilos cuando la baciloscopia es negativa.

MI17

MECHANISM OF ENERGY TRANSDUCTION IN MYCOBACTERIUM LEPRAE

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Adenosine triphosphate (ATP) constitutes the "molecular energy currency" in living cells. Energy released by the hydrolysis of the ATP drives life processes, including synthesis of nucleic acids and transport of metabolites across cell membranes. Most organisms synthesize their own ATP through the enzymatic degradation of utilizable substrates. Why Mycobacterium leprae is dependent on the host cells for its survival and proliferation has not yet been explained satisfactorily.

Free-living bacteria hydrolyze phosphorylated organic compounds extracellularly and transport the organic portion and the phosphate moiety in two separate steps; the compounds are resynthesized intracellularly. Obligate intracellular parasites generally transport high-energy molecules in the intact state from the host cells. M. leprae prepared from **FRESH** tissues of experimentally-infected armadillos or nude mice readily took up [2,8-^{3}H] ATP. Initially, there was a rapid electrostatic binding which is energy-independent. This ionic phase was followed by an energy dependent phase that was abolished by metabolic inhibitors. In a competition assay, unlabeled ATP or ADP inhibited transport of ^{3}H-ATP by M. leprae; adenosine or PO,had little effect. Evidently, the organism takes up unhydrolyzed ATP by an active transport process. The bacteria possessed an E_1 E_2 ATPase that creates a trans-membrane potential driving transport of solutes into cells, but not an F_0 F_1 ATPase that catalyzes ATP synthesis. This dependence of M. leprae on the host for high energy compounds may be a reason for its failure to grow in culture media.

MI8

CLONING AND SEQUENCING OF THE *TUF* GENE CODING FOR THE ELONGATION FACTOR TU OF *MYCOBACTERIUM LEPRAE*

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The *Tuf* gene encoding the elongation factor Tu (EF-Tu) of *Mycobacterium leprae* has been cloned and sequenced. Part of the gene fragment (-COOH terminal) was isolated from clone R7 obtained from the lambda gt11 library. The full gene was identified by colony hybridization of the *M. leprae* genomic DNA. Nucleotide sequence determination revealed that gene contains a coding region of 1188 bp with GUG as start codon. A putative Shine Dalgarno sequence is located 8 bp upstream. The deduced amino acid sequence has 396 residues with a molecular weight of 43.6 kDa. Computer analysis showed that the GDP or GTP binding sites are located at amino acid positions 19-26, 83-87, and 138-141.

Comparison of *M. leprae* EF-Tu amino acids with that of other species revealed 95.2%, 79.6%, 74.5%, and 74.7% homology with *M. tuberculosis*, *Micrococcus luteus*, *Escherichia coli*, and *Salmonella typhimurium*, respectively. Mitochondrial EF-Tu of *Saccharomyces cerevisiae* (62.7%) and chloroplast EF-Tu of *Arabidopsis thalina* (65.6%) are some of the eukaryotic EF-Tus' showing strong homology with that of *M. leprae*. Southern hybridization of *M. leprae Tuf* gene with genomic DNA of slow growing and fast growing mycobacteria and related species like *Corynebacterium fascians* and *Nocardia asteriodes* suggests that the gene is highly conserved among these species.

MI19

APPLICATION OF LASER MICROPROBE MASS ANALYSIS TO *IN VITRO* DRUG SCREENING

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The susceptibility of *M.leprae* to different anti-leprosy agents was assessed in a newly developed *in vitro* drug screening system. The drug effects on the physiological state of isolated *M.leprae* are monitored by the mass spectrometric analysis of the ratio of intrabacterial concentrations of sodium and potassium ions of single bacterial organisms (Na^+,K^+-ratio). The rational behind this approach is the ability of all living unimpaired cells, bacteria as well as eucaryotes, to accumulate K^+ and exclude Na^+ by energy-demanding processes and to use the transmembrane gradient as energy storage for several central metabolic processes, e.g. transport. We could show that the intrabacterial Na^+,K^+-ratio is a sensitive indicator for the physiological state -i.e., viability - of the bacteria and that changes of this value correlate with those observed by means of established microbiological techniques. For *in vitro* drug screening, armadillo-derived *M.leprae* were incubated at 32°C in modified - increase of malachite green content - Middlebrook 7H9 for 2-3 weeks in the presence of different drugs and their combinations. Changes in the distributions of the intrabacterial Na^+,K^+-ratios reflect time- and concentration-dependences of drug effects for those drugs which do not interfere with DNA-replication and multiplication. Moreover, it renders important information on the combined action of different drugs in terms of antagonism or synergism.

MI20

LABELING OF THE 65 KDA HEAT SHOCK PROTEIN IN *MYCOBACTERIUM LEPRAE* AND OTHER MYCOBACTERIAL SPECIES.

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We have used immungold ultracytochemistry to label *in situ* the 65 kDa heat shock protein on *Mycobacterium leprae* and other mycobacterial species (*M. tuberculosis*, *M. avium* and *M. smegmatis*). Leprosy bacilli were observed by thin section electron microscopy in liver samples of infected armadillo and in skin biopsy tissues of humans with Hansen's disease, both before and after strating chemotherapy.

We found that virtually all leprosy bacilli showed positive labeling by immunogold spheres coupled with polyclonal antibodies against the recombinant 65 kDa antigen of *M. bovis* BCG expressed in E. coli (the recombinant protein and thge specific antibodies were a gift of Dr. J D A van Embden, national Institute of Public Healthn and Environmental Protection, Bilthoven, The Netherlands). Interestingly, the immunocytochemical marking was still present in debris of dead *M. leprae* bacilli detected in the infected tissues. This indicates that the antigenicity of the 65 kDa heat shock protein of leprosy bacilli may persist well beyond the loss of viability of the mycobacteria. Since there is evidence that the 65 kDa mycobacterial antigen may be involved in autoreactive phenomena, which are often described in patients with mycobacteriosis, our results suggest that remnants of mycobacteria may be the cause of autoaggressive disorders in patients that have been "cured" from Hansen's disease.

We have also investigated the subcellular distribution of the 65 kDa antigen in cellular fractions of cultured *M. smegmatis* and *M. avium*. Our data, obtained by immunogold cytochemistry and immunoblotting, revealed that this heat shock element is present in all of the fractions studied (cytosol, membrane and cell wall) which may explain the *in situ* detection of the antigen in cell wall debris of mycobacteria.

MI21

EXTRACORPOREAL VIABILITY OF M.LEPRAE

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M.leprae available for laboratory research are very limited. Extracorporeal bacilli survive for a few days. However, while processing or handling tissues or bacteria for various experiments a good proportion of the organisms are often lost. At the same time viability of M.leprae may also be affected. Therefore studies were carried out to assess whether various methodological procedures adopted while conducting experiments or while maintaining bacilli under different conditions, affected the number of organisms made available or their viability.

M.leprae obtained from human or armadillo sources were subjected to several methodological procedures and also were maintained under various conditions of temperatures. Bacilli subjected to all these procedures were inoculated into hind foot-pads of Balb/c mice.

Results of mice foot-pad harvests showed that decontamination affected the viability whereas centrifugation and purification did not show any effect. Bacilli survived upto varying periods from 7 to 90 days under different conditions of maintenance and preservations. Thirty minutes of Ultra violet rays exposures killed all bacilli. Where as disinfectants took longer time to kill all bacilli. However, 70 per cent of alcohol was effective in killing bacilli within 15 minutes.

MI22

ULTRASTRUCTURAL PARAMETERS INDICATING VIABILITY OF M. leprae AFTER CHEMOTHERAPY.

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M. leprae causative organism for leprosy, can be identified by light microscope using, Fite-Faraco stain but it is not possible to clearly deliniate its morphology. Therefore, the ultrastructural characteristics of M. leprae obtained from lepromatous leprosy cases both untreated and treated with MDT (Rifampicin, Clofazimine and Dapsone, WHO Regimen) were studied and observations were compared with light microscopic findings. Skin biopsies of two untreated (BI=6$^+$) Ridley Scale and three treated (BI=3$^+$) lepromatous leprosy cases were examined. The treated patients had MDT (WHO regimen) for 6 months to 1 year. A uniform suspension was put on the collodion coated copper grid and examined under electron microscope (H-300) after carbon coating in vaccum under high pressure.

Ultrastructural studies of M. leprae in untreated cases revealed that bacilli were solid staining but of different length, thickness and some of these had banded structure. Under light microscope, bacilli in treated cases appeared to have irregularly fragmented cytoplasm with degenerated cell wall. However, under electron microscope these bacilli were found to be completely filled with cytoplasm like a solid bacillus but were of shorter length.

This is more so important because there is a need to define structural criteria and viability of the M. leprae organism, during the treatment of bactericidal and antimycobacterial drugs.

MI23

ASSESSING THE VIABILITY OF MYCOBACTERIUM LEPRAE ON 28 CASES ON MDT BY THE FDA/EB STAINING TECHNIQUE

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The authors evaluated the FDA/EB staining technique in assessing the viability of mycobacterium leprae in skin smears taken regularly from 28 previously untreated MB cases in the period of MDT. According to the theory of the FDA/EB staining technique, green cells were deemed to be viable, red as dead, and dual stained bacilli as viable. The results of this study showed that the average percentage of green cells was 42.75% (a range of 7.5% to 88%) before MDT, 20.46 %after 1 to 2 months' MDT, 14.79% after 3 months', 5.66% after 6 months ' 1.15% after 18 months' and 0.35% after 24 months' MDT. The authors believed that FDA/EB staining technique was accurate, simple, convenient, and feasible. The percentage of green cells could be used as one of valuable indicators in assessing the effectiveness of MDT and in predicting the possibility of relapse. The authors also observed that green cells were still found in 4 cases after 24 months' MDT, indicating they were in need of a certain period of continued intensive treatment. Compared with the findings of this mehtod, BI and MI values were not considered reliable in the assessment of the viability of Mycobacterium leprae.

MI24

DETECTION OF 16S rRNA FOR VIABILITY ASSESSMENT OF MYCOBACTERIA

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Previously we developed a specific polymerase chain reaction (PCR) for detection of *M.leprae* DNA in clinical specimens. Correlation between the amount of PCR product formed and the viability of bacilli in human skin biopsy specimens has been found. The amount of 16S rRNA in the bacteria may be a better indicator of the metabolic state of the mycobacteria, rather than the DNA content. Nucleic Acid Sequence Based Amplification (NASBA), an RNA-amplification technique, was used to test this hypothesis. An *in vitro* system for killing mycobacteria was developed to assess this hypothesis. Therefore, *M.smegmatis* was exposed to the antimycobacterial drugs rifampicin and ofloxacin. Growth and viability of the bacteria was determined by measuring respectively the optical density (OD) and the amount of colony forming units (CFU). Both parameters were compared to the presence of DNA (PCR) and rRNA (NASBA) in the bacilli. Exposure of *M.smegmatis* to rifampicin and ofloxacin showed that there was a loss of viability after 1 day. These resuts were compared to the DNA and RNA content of the mycobacteria. Although no decrease in the DNA content was seen, a slide decrease in 16S rRNA content was observed after 1 day and total clearance of the 16S rRNA was seen after 5 days. These results suggest that the 16S rRNA content reflects the viability of mycobacteria in an *in vitro* system.

MI25

THE EFFECT OF ELECTROCHEMICALLY ACTIVATED LIQUIDS ON MYCOBACTERIAL VIABILITY

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To stimulate the growth of some species of slow-growing mycobacteria, liquid media, modified with a cathode fraction of electrochemically activated salt solutions, were used. In addition, the effect of an anode fraction of the same solution on mycobacterial growth was studied. Standard Sauton's medium was taken for control. Slow growing species, such as M.avium, M.tuberculosis, M.01 and M.011 (growing strains isolated from LL patients), M.lufu and M.leprae (isolated from 3 LL patients and not growing on standard nutrient media). Viability of cultivable mycobacteria was checked by their growth on Loewenstein-Jensen medium, and M.leprae - by multiplication in mice foot-pads. Cultivable strains at a dose of $5x10^6$ microorganisms per ml were inoculated into test media, and 3, 5, 7 and 9 days later the material was transferred into a solid medium. The results of the experiment were judged by the amount of colony-forming units in a solid medium. M.leprae were introduced into cathode and anode fractions of salt solution at a dose of 10^6 - 10^7 microorganisms per ml and incubated at 20oC and 37oC. In 1, 2, 3 and 4 weeks of incubation M.leprae were inoculated into mice foot-pads. Cultivation of slow growing mycobacteria on cathode-containing media resulted in augmented mycobacterial growth. With anode fraction mycobacteria did not grow. M.leprae remained viable after their incubation in a cathode fraction of the salt solution as long as for 1-4 weeks, evidenced by the development of infection in mice.

MI26

A RAPID IN VITRO MICROASSAY FOR THE VIABILITY AND DRUG SENSITIVITY OF M. LEPRAE

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We have developed an in vitro assay for the viability of M. leprae based on the levels of mRNA detected by reverse transcription linked PCR amplification. The hypothesis is that because of the short halflife of procaryotic mRNA, dead or drug treated bacilli will have reduced levels or no mRNA and the measurement of mRNA levels can be used as an estimate of viability after drug treatment. mRNA is extracted from M. leprae bacilli by sonication in guanidinium thiocyanate and purification in CsCl gradients. cDNA is synthesised from total RNA with reverse transcriptase using a 3' gene specific primer for the 70kDa antigen (DnaK homolog) and PCR amplified after addition of a 5' primer. Bands of the correct size and restriction polymorphism patterns are obtained indicating that mRNA can be extracted from M. leprae and that it can be detected by RT-PCR. False positives due to contaminating genomic DNA were excluded by DNase 1 treatment. Using a recombinant truncated artificial mRNA template for the 70kDa gene mRNA, the RT-PCR assay can detect down to 1fg of mRNA: equivalent to 10^9 bacilli. Currently a two log fold killing can be detected from 10^9 armadillo derived M. leprae with a viability of $<0.1\%$. Three out of 6 M. leprae infected nude mouse footpad mRNA preparations give strong PCR bands which disappear after heat killing the bacilli, indicating that mRNA levels reflect viability. Correlation of mRNA levels with viability assessed in the nude mouse footpad after in vitro exposure of M. leprae bacilli to different drug regimens is underway. This technique combines the sensitivity of PCR based detection systems with the measurement of mRNA as a rapid and highly sensitive assay for the viability of M. leprae.

MI27

CULTIVATION OF MYCOBACTERIUM LEPRAE IN ARTIFICIAL CULTURE MEDIUM

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A novel procedure in the cultivation of M.leprae in combined Dubos-Lowenstein-Jensen medium after addition of thyroxine sodium is being reported. This has been found to be successful as the organisms,after multiplying vigorously in the thyroxine containing Dubos medium,have produced a visible colony on the surface of Lowenstein-Jensen medium during 8-16 wks of incubation at 37°C. The enhanced growth of this recalcitrant organism is due to stimulating effect of thyroxine as well as supply of ready-made basic nutrients in the synthetic Dubos medium. Intradermal inoculation of the bacterial suspension from the subculture into the foot pad of cortisone treated swiss mouse revealed an early appearance of specific histological lesion of leprosy with infiltration of nerve fibres by lepra cells.

The methodology,described here for in-vitro cultivation,may open out a new era in the preparation of purified vaccine,the study of in-vitro drug sensitivity,and as such ensure rapid eradication of leprosy.

MI28

EFFECTS OF PALMITATE ON THE GROWTH OF *MYCOBACTERIUM LEPRAE* UNDER DIFFERENT GASEOUS ENVIRONMENTS.

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Low oxygen tension has often been considered important for the growth of Mycobacterium leprae. Palmitate has been suggested as the oxidizable substrate for the growth of leprosy bacilli. Effects of palmitate on the growth of M. leprae under various gaseous environments were investigated. No multiplication of bacilli was observed in liquid or solid medium without palmitate when incubated under various gas mixtures or air. However, when palmitate was included in the media six to ten fold increase in the number of bacilli was obtained between 12 to 20 weeks of incubation under gas mixtures containing 2.5% O_2 and 5 or 10% CO_2 as well as under air. The use of different gas mixtures is tedious, laborious and time consuming. Since the cultures incubated under air gave the same cell yield as obtained when incubated under optimal gas mixtures, air alone can be used for the in vitro cultivation trials of M. leprae when palmitate is included in the culture media.

MI29

IN VITRO CULTIVATION OF *Mycobacterium leprae* WITH CYTOKINES

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Ever since its discovery, numerous investigators have tried to cultivate *M. leprae in vitro*, but in vain. However, this organism maintains its multiplication *in vivo*, with all the requirements for its growth.

It was hypothesized that the lack of nutritional factors may not have been the problem, instead, certain cytokines alone or in combination, may be the essential growth factor(s) for this organism. As a first step to test this hypothesis, the tissue homogenate of armadillo spleen infected with *M. leprae* was inoculated into Ogawa media with interleukin-2, interferon-α, or -γ, alone or in combination. Incubation temperature was 36°C, without CO_2. Gross and microscopic examination revealed the following results.

1. Round, oily, and white colonies were observed on the surface of the liquid in all the tubes with both *M. leprae* and interleukin-2, 3-6 months after the initiation of the cultivation. Above colonies could be observed 1-2 months earlier in the test tubes with *M. leprae*, interleukin-2, and interferon-γ. But no colonies could be seen in all the test tubes without *M. leprae* or interleukin-2.

2. The size of the colonies grew with time and they were the compact and solid collections of acid fast organisms under a microscope.

3. This experiment has been repeated 2 times, with the same results.

These data indicate the possibility that *M. leprae* can interact with interleukin-2, interferon-γ, and probably some other cytokines, which would turn out to be the essential growth factor(s) for this organism. Subcultivation, identification, and animal studies are under investigation. Furthermore, the effect of various cytokines on the growth of other microorganisms, including uncultivable ones, is also under investigation.

MI30

A COMPARISON OF DNA/RNA, MYCOLATES, PGL-I, ANTIGENICITY, ENZYMES, MORPHOLOGY AND STAINING CHARACTERISTICS OF THE LEPROSY BACILLUS WITH THE LEPROSY DERIVED CHEMOAUTOTROPHIC NOCARDIOFORM BACTERIA(IN VITRO).

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The chemoautotrophic nocardioform (CAN) bacteria had been isolated as single organisms from 90 different LL cases so far, as well as from the mouse footpads (MFP) and armadillo tissues experimentally infected with M.leprae. These CAN bacteria and M. leprae have been compared on the basis of their morphological, staining, metabolic and enzymological characteristics, and found to be extremely similar. Both the organisms also exhibited closely similar or identical patterns of lipid profiles, anergy and 'Mitsuda' responses to a large number of LL and TT cases respectively, PGL-I specificity, as well as, for DNA characteristics and resistances to γ - and UV - radiations. All were DOPA oxidase positive and lost acid-fastness due to pyridine extraction. The comparative study and an evaluation of all the above characters reveal an extreme closeness of the CAN bacteria to the leprosy bacillus to a point beyond which it may not be possible to distinguish them from each other any further.

MI31

DETECTION OF PGL-I IN THE CHEMOAUTOTROPHIC NOCARDIOFORM (CAN) BACTERIA

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PGL-I is a unique M.leprae antigen, detecting which may lead to identification of M.leprae. We have investigated the presence of PGL-I in the in vitro CAN-cultures derived from human, mouse-footpad and armadillo tissues infected with leprosy bacillus.

For this purpose, antisera were produced in rabbits against the 4 CAN bacterial suspensions. Microtitre gelatin particle agglutination test (Serodia M.leprae Fujirebio, Japan) had been used to detect and assay anti-PGL-I antibodies, if any, in such antisera. Use of synthetic antigens seemed to exclude possible artifacts.

The gelatin particle agglutination tests showed high titre anti-PGL-I antibodies to be present in

the immune sera. Biological controls, human serum (LL) and normal rabbit serum controls were used to exclude false positivity, and decide on reliability of the tests. The animals responded best by producing antibody when injected by the intramuscular route. Most of the animals initially developed immunologic paralysis towards the antigens, but showed gradually rising antibody titres.

In the light of other tests reported previously, e.g. chemoautotrophism, lipid profile, DNA(36K) specificity etc. the present test becomes significant with respect to the true identity of the CAN bacteria, viz-a-viz M.leprae. The close parallelism observed between lepromin and the CAN-AGs is thus explainable.

MI32

TOWARDS DEVELOPING A NEW SCHEME FOR RAPID CHARACTERIZATION OF MYCOBACTERIA WITH SPECIAL REFERENCE TO M.LEPRAE

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Difficult to grow and non-cultivable mycobacteria provide new challenges for the taxonomists, epidemiologists and immunologists all of whom have related interest in defining the degree of relatedness of mycobacteria. Data based on M.leprae gene probes reported so far supports the concept that M.leprae is a highly homogenous species in nature. However this may be because of the fact that only a small fraction of the genome could be examined by this type of analysis. Protein electrophorogram and multi-locus enzyme electrophoresis has advantage that large number of protein enzymes encoded by a sizeable proportion of mycobacterial genome can readily be compared. We have adapted and applied these techniques using nine enzymes and protein electrophorograms to 23 species of mycobacteria, many of which are related to M.leprae in one way or other so as to develop strategies to characterize strains of M.leprae or 'alleged isolates'. Our findings suggest that the approach can be helpful as adjunct to studies of rRNA genes and other molecules in strains of pathogenic mycobacteria specially M.leprae. Such investigations may possibly help to establish "Epigenetic Finger Prints". As a result, a simple and rapid identification scheme has been evolved which has potentiality to be used for several difficult to grow mycobacteria, armadillo derived mycobacteria, mycobacteria isolated from leprosy lesions as well as 'alleged isolates' of M.leprae.

MI33

ELECTRON MICROSCOPIC STUDY OF M.LEPRAE PASSED ON LABORATORY ANIMALS

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Ultrastructure of M.leprae (ML) taken from LL patients (original strain) and passed on laboratory animals (nine-banded armadillos and mice) were studied. ML of the 1st passage were characterized, as compared with the original strain, by a reduced microcapsule, thickened cell wall and condensed cytoplasmatic matrix with poorly differentiated ribosomes and nucleoide, that is typical for surviving bacterial forms. ML of the 2nd passage (mouse-to-mouse and armadillo-to-mouse) were identical and had fragmented microcapsule, normal cell wall with closely adjacent cytoplasmatic membrane and rare inclusions ("homogeneous bodies") in their cytoplasm. These strains differed from the 1st passage by the abundance of dividing cells, pronounced nucleoide and more developed mesosomes. For ML of the 3d passage the presence of numerous "homogeneous bodies" in their cytoplasm as well as the increased number of volutin granules were peculiar features suggesting ML adaptation to a new environment. In subsequent passages (4th-8th) no further changes in ML ultra-structure were observed. It was concluded that the changes in ultrastructure of ML passed from man to laboratory animals (within three passages) might be accounted for mycobacterial adaptation to the environmental conditions in a new host. These data should be taken into account when studying taxonomical properties of the adapted strains of M.leprae and in bio-technological developments as well.

MI34

PHAGOCYTIC MYELOPEROXIDASE AS A KILLING FACTOR FOR M.LEPRAE

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It is well known that functional activity of phagocytes depends on the state of their enzymes, in particular the activity of macro-phage myeloperoxidase. The present work is devoted to electron cytochemical study of myeloperoxidase (MPO) activity in active LL patients. Various activity and different lo-calization of MPO in macrophages correlated with the degree of completeness of M.leprae phagocytosis. In macrophages with a large number of peroxidase-active mitochondria alongside with the presence of MPO in phagosome membranes and electron-transparent zone around myco-bacterial cells intensive lysis of M.leprae was observed. On the contrary, in macrophages with low level of MPO M.leprae appeared mainly intact. Observation of MPO-activity in macrophages of leprosy granulomas in long-treated BL and LL patients showed that with low phagocytic activity of MPO the disease improved slowly and such patients were at risk of relapses. With a high level of phagocytic activity of MPO leprosy patients demonstrated a rapid improvement of their lesions and did not relapse throughout the observational period (up to 14 years). The results obtained were assumed as a basis for the development of our method for identification of patients at risk of leprosy relapses and could be used in improving experimental leprosy models available.

MI35

BIOLOGICAL PROPERTIES OF M.LEPRAE PASSED ON LABORATORY ANIMALS

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The alterations in some biological properties of the original strains (OS) of M.leprae, isolated from leprosy patients and passed (PS) to mice, rats and armadillos were studied. M.leprae from mouse and rat foot pads of the 3d-5th passages and M.leprae from armadillo spleen of the 1st passage were studied for the spectra of fatty acids (FA), antigenic structure and DOPA-oxidase activity with using gas-liquid chromatography, enzyme immunoassay and electron cytochemistry. It was shown that in FA spectrum in OS-M.leprae C22:0 > C24:0 ratio predominated. Being passed M.leprae showed FA spectrum similar to that in M.lepraemurium and M.avium, i.e. C24:0 >C26:0 ratio. M.leprae strains from the 1st passage to armadillo retained C22:0 > C24:0 ratio. DOPA-oxidase was present both in OS- and in PS-M.leprae while M.lepraemurium and cultivable mycobacteria had no such enzyme. With using a set of monoclonal antibodies (WHO Bank) protein epitopes 12, 18 and 65 kDa were demonstrated in the antigenic structure of OS-M.leprae while PGL-1, unique for OS-M.leprae and M.leprae from

the single passage on armadillos, was not discovered. The data obtained should be taken into account in taxonomical studies on M.leprae passed on laboratory animals, and when developing novel experimental leprosy models,specific diagnosticums and antileprosy vaccines.

MI36

OVEREXPRESSION OF *MYCOBACTERIUM LEPRAE* ANTIGENS IN *ESCHERICHIA COLI*

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Three genes encoding *Mycobacterium leprae* antigens selected with monoclonal antibodies were cloned in *Escherichia coli*. Nucleotide sequencing revealed that these genes are capable of encoding proteins of apparent molecular weights of 16, 26 and 45 kDa. The functions of these proteins in *M.leprae* are as yet unknown. However, the 45 kDa protein shows homology to a number of integral membrane proteins involved in the transport of compounds over the cellular membrane. We tried to overexpress these proteins in *E.coli* as native proteins using the T7 system. We found no overexpression despite efficient transcription, indicating that the lack of protein expression is due to inefficient translation. We were capable of overexpressing the proteins in *E.coli* as fusion proteins using a variety of expression systems (i.e. pUC8-2, pNGS21, pGEX1-3 and pVW500).In the present paper we will discuss the characterization, overexpression and purification of these proteins and their use in serology.

MI37

OVEREXPRESSION AND SEROREACTIVITY OF 15 KDA ANTIGEN OF *MYCOBACTERIUM LEPRAE*

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By screening lambda gt11 *Mycobacterium leprae* genomic DNA library with leprosy patient's sera, we isolated 16 clones of strong and weak reactivities. Sequence determination of these clones revealed that clone R9 has part of the gene coding for 15 kDa *M. leprae* antigen. The 4 kb insert DNA from this clone was sub cloned into pMal-c expression vector and expressed in *E.coli* HB101 as maltose binding fusion protein. The affinity purified fusion protein showed strong reactivity with leprosy patient's sera in western blot analysis. An ELISA developed using this protein showed 81.8%, 47.1%, 41.7%, 10% and 20% seropositivity to untreated LL, BL, BB, BT, and TT sera at 1:300 dilution. No significant reductions in the seropositivity rates were noticed on sera from treated patients as they showed 68.6%, 50%, 13%, and 25% to LL, BL, BT, and TT, respectively. This protein detected antibodies in contacts of leprosy patients as well as tuberculosis patients in which the seropositivity were 15.8% and 7.2%, respectively. This protein was also found to react with serum samples obtained from mice immunized with *M.* leprae.

MI38

CHARACTERIZATION OF M.LEPRAE STRAINS BY RFLP ANALYSIS OF AMPLIFIED rDNA

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Restriction Fragment Length Polymorphism (RFLP) analysis has emerged as a powerful tool to characterize various prokaryotic and eukaryotic organisms. These studies can not be easily done on M.leprae as sufficient amount of organisms can be isolated only from highly bacillated leprosy types. Earlier studies on strains grown in experimental animals showed very little divergence among such strains. In this study, nucleic acids from biopsies from leprosy patients across the spectrum belonging to different geographical locations in India, were extracted by a modified technique standardised at this laboratory. By using different sets of primers targetting variable regions towards the ends and flanking regions of ribosomal RNA genes, rDNA fragments were amplified. These were restricted with different restricted endonucleases and hybridized with ribosomal RNA probes by the techniques reported by us earlier. The origin of amplified rDNA was confirmed by using a set of oligonucleotide probes targetting specific sequences on rRNA genes of M.leprae. The combination of patterns obtained after restriction with different restriction enzymes revealed interesting findings. Overall, strong resemblence among the different strains was observed. However, some divergencies have also been observed. The relevance of these findings is being investigated further at sequence level and in larger number of strains. Amplified rRNA restriction analysis appears to be promising for rapid identification and characterizing of M.leprae directly from the lesions in leprosy cases.

MI39

DEVELOPMENT OF IMPROVED TECHNIQUES FOR EXTRACTION OF NUCLEIC ACIDS FROM LEPROSY LESIONS

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During the last 3-4 years, several probes and gene amplification techniques for detection/amplification of nucleic acid sequences of M.leprae have been developed. For the optimum application of these methods, the extraction of nucleic acids from leprosy tissue is an important step. Techniques reported for extraction of nucleic acids from tissue include physical as well as cnemical approaches. In this study, different techniques for lysis such as freeze--thawing, freeze-boiling, Proteinase K treatments for 1 to 16 hrs and a new modified lysozyme/SDS+Proteinase K method (followed by stepwise purification wherever necessary) based on optimised concentrations and duration have been compared and evaluated in the clinical specimens across the spectrum. The nucleic acids extracted were processed for detection of rRNA by oligonucleotide probes and for gene amplification by primers targetting 18kd, 36kd genes and reverse transcription-amplification of 16S rRNA sequences. All the extraction procedures appeared to be adequate for biopsies from multibacillary cases. However the freeze-thawing and freeze-boiling methods were found to be less efficient for biopsies from smear negative paucibacillary cases. The modified procedure standardised in this study is reasonably fast and appeared to be very efficient for all type of cases. The technique needs to be tried in a larger number of specimens.

MI40

STUDIES OF α ANTIGEN GENES IN *M. LEPRAE*

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Sero-diagnosis for leprosy has been performed mainly by two methods. One is agglutination test using gelatine particles coated with phenolic-glyco-lipid I(PGL- I). The other is ELISA method using bacterial cellular protein(s) as antigen(s). Among these methods cross reactivity with another *Mycobacteria* was one of the majour problems. To establish a new reliable method, antigen with high specificity is very important.

In this study, we planed the construction of recombinant antigen which contains *M. leprae* specific epitope(s). And we performed

molecular cloning and analysis of *M. leprae* α antigen gene family and constructed the overproduction system of *M. leprae* α antigen.

RESULTS AND DISCUSSIONS

1) We have cloned and characterized *Mycobacterium leprae* α antigen gene family. We obtained 2 kind of α antigen gene by screening 10000 plaques of *M. leprae* genomic library. Homology between *M. leprae* α antigen was lower than those between *M. leprae* α1 and α antigen of *M. bovis* BCG or 85 complex of *M. tuberculosis*.

2) Recombinant α1 antigen of *M. leprae* has been constructed and purified by amirose resin affinity chromatography. More than 20 mg of recombinant protein was obtained from 250 ml liquid culture.

3) Antibody titer against recombinant α antigen in the serum of leprosy patient was much higher than healthy control. Fusion protein produced in this study could be used as a new specific antigen for sero-diagnosis of lepromatous leprosy.

MI41

THE ABNORMAL STRUCTURE OF MYCOBACTERIAL recA GENES

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Mycobacteria are intracellular pathogens which are exposed to DNA-damaging agents as part of the host's defence against infection. In most bacteria the response to such agents involves the coordinated expression of over 20 genes through a common regulatory mechanism involving the RecA protein. We have previously reported the cloning and characterisation of the recA gene of M.tuberculosis. This gene is very unusual in that it contains a protein splicing element which is removed post-tranlationally.
We have now characterised the M.leprae recA and found that it too contains a protein splicing element. However the M.leprae and M.tuberculosis spliced sequences are inserted at different positions within the gene, are unrelated in sequence and differ in size, suggesting that their insertion into recA has occurred independently. Southern blotting with protein splicing element-encoded DNA indicates other mycobacteria do not possess these elements, suggesting that there has been positive selection for the abnormal recAs seen in M.tuberculosis and M.leprae.

MI42

BIOCHEMICAL CHARACTERIZATION OF TWO NEW MAJOR PROTEINS OF MYCOBACTERIUM LEPRAE

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Proteins synthesized in significant amounts by in vivo grown Mycobacterium leprae presumably play a key role in the host-parasite interface. In order to complete the definition of the major proteins present in armadillo-derived M. leprae, two polypeptides originally described as major membrane protein I (MMPI) and major membrane protein II (MMPII), with Mr of 35 kDa and 22 kDa, respectively (Hunter et al. 1990. J. Biol. Chem. 265: 14065-14068), were purified and subjected to amino acid sequencing. The sequencing strategy involved digestion of the polypeptides with different endoproteinases and purification of the generated peptides on a C18 reverse phase column. Peptides were then subjected to automated Edman degradation and their sequences were confirmed by fast atom bombardment mass spectrometry. Eleven peptides were isolated and sequenced from MMPI and eight peptides from MMPII, accounting for approximately 40 % of the total amino acid content of both proteins. The generation of the complete amino acid sequence of both proteins is in progress. In order to proceed with the immunological characterization of these proteins through use of their recombinant equivalents, the genes coding for MMPI and MMPII are under investigation (in conjunction with Drs. Brigitte Gicquel and Nathalie Winter). The C-terminus region of the gene coding for the 35 kDa protein has been sequenced. Fragments containing the N-terminus and internal region of the gene were identified using oligonucleotide probes derived from peptide sequence, and are presently being sequenced. A region from the 22 kDa gene coding for 50% of the protein was amplified from M. leprae DNA by using oligonucleotide primers derived from the amino acid sequence. We are currently sequencing this fragment and using it as a probe to clone the entire gene. Thus, the major cellular proteins of the leprosy bacillus are close to complete definition. (Work supported by NIH, NIAID Contract NO1 AI-05074.)

MI43

STRUCTURAL DEFINITION OF LIPOARABINOMANNAN: ITS BIOLOGICAL SIGNIFICANCE IN HOST-PARASITE INTERACTION

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All mycobacterial species are endowed with two dominant, highly complex polysaccharides, the mycolylarabinogalactan-peptidoglycan (mAGP) complex and lipoarabinomannan (LAM). Whereas the structure of mAGP is highly conserved, that of LAM varies among mycobacterial species. For instance, in a rapidly growing strain of Mycobacterium, the terminal arabinan ends are occupied with branched hexaarabinofuranosyl and linear tetraarabinofuranosyl arrangements, giving a product now designated as AraLAM. However, the same arrangements are capped extensively with mannose-containing oligosaccharides in strains of Mycobacterium tuberculosis, a product called ManLAM. Most importantly, LAM from Mycobacterium leprae demonstrates a hybrid structure, in that it shares the "naked" arabinofuranosyl arrangements of AraLAM as well as some of the mannose capping typical of ManLAM, and thus it is termed LepLAM.

Work by many collaborators has implicated LAM in a wide spectrum of immunoregulatory functions, such as inhibition of IFN-γ-mediated activation of macrophages, the scavenging of potentially cytotoxic oxygen-free radicals, inhibition of protein kinase C activity and evocation of a large array of those cytokines characteristically associated with macrophages. Thus, it appears that LAM may mediate production of macrophage-derived cytokines which, in turn, may evoke many of the clinical manifestations of leprosy. The relationship of structural features of LAM to these biological properties will be discussed. (This work has been supported by NIH/NIAID Contract No. AI-05074.)

MI44

SUBCELLULAR FRACTIONATION OF MYCOBACTERIUM LEPRAE AND THE SEARCH FOR NEW PROTEINS

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The availability of adequate quantities of armadillo-derived Mycobacterium leprae has allowed the complete characterization of many of its major constituents. However the subcellular location of these is largely a matter of speculation. Hitherto, subcellular fractionation of mycobacteria never did yield a subcellular fraction totally free of the components of another, possibly because sonication resulted in organelle fragmentation. To minimize wastage of M. leprae, pilot studies were conducted on M. smegmatis leading to the conclusion that microbead disruption and sucrose density centrifugation results in less cross contamination of subcellular fractions as determined by assays for membrane specific enzymes (NADH dehydrogenase and lactic dehydrogenase) and 2-D SDS-PAGE of proteins and carbohydrates. Application of the procedure to M. leprae resulted in two cell wall fractions of different specific gravity, cell membrane and cytosolic fractions. SDS-PAGE and Western blot analysis of the fractions revealed significant differences in terms of the various proteins and carbohydrates. The 10 kDa protein was significant only in the cytosolic fraction. The 71 kDa and 18 kDa HSPs and the 28 kDa (SOD) protein were seen in the cell wall and cytosolic fractions but were totally absent in the membrane. The 65 kDa HSP was mostly membrane-associated. LAM was predominant in the cytosolic and membrane fractions with only faint traces in the cell wall fractions. The goal of this work is to identify the major subcellular constituents (proteins, lipids and carbohydrates) of the various compartments of M. leprae towards a better understanding of its physiology and pathogenesis. (Work supported by NIH, NIAID Contract NO1 AI-05074.)

MI45

MYCOBACTERIUM LEPRAE METABOLISM: IN VITRO UTILIZATION OF GLUCOSE, URIDINE 5'-DIPHOSPHOGLUCOSE AND GLUTAMATE

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As a non-cultivable, intracellular parasite, a direct relationship between Mycobacterium leprae growth and specific cell nutrients has not been established. When maintained in vitro with a suitable axenic medium, limited metabolic patterns have been observed in M. leprae by measuring the utilization of radioactive substrates. In previous studies we observed the incorporation of ^{14}C-palmitate into the complex liquids of M. leprae. However, we were unable to detect any incorporation of ^{14}C-acetate into lipid. These results indicate that M. leprae does not synthesize lipids through the de novo, acetyl-CoA pathway, but must depend principally upon host metabolites.

We have recently shown that M. leprae does not readily utilize exogenous ^{14}C-glucose, as measured by the formation of ^{14}C-CO_2. These results suggest that the glycolytic and hexose monophosphate pathways may not be functioning in M. leprae. However, M. leprae must synthesize various bacterial polysaccharides such as those present in complex glycolipids. As an alternate source of glucose, we incubated M. leprae in the presence of uridine 5'-^{14}C-diphosphoglucose (UDPG). The results revealed that significant amounts of ^{14}C-CO_2 were released in the presence of labelled UDPG.

Organisms which do not glycolyze glucose, may use other pathways as energy sources, e.g. glutamate oxidation. When ^{14}C-glutamate was incubated in the presence of M. leprae, oxidation of glutamate was observed. Oxidation appeared to be enhanced by the presence of pyruvate, thus, indicating possible transaminase activity.

This study suggests that M. leprae has the potential to use host-derived UDPG as substrate for polysaccharide synthesis. Utilizing a high energy nucleotide would probably be metabolically advantageous for the organism. Further studies may also reveal any involvement of the Krebs cycle with glutamic acid oxidation in M. leprae.

MI46

RECENT RESULTS ON *IN VIVO* DRUG EFFICACIES FROM MASS ANALYSIS OF INDIVIDUAL *M.LEPRAE* ORGANISMS

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Laser microprobe mass analysis (LAMMA) of a limited number of individual *M.leprae* organisms allows the determination of the physiological state (viability) of a bacterial population and its changes upon the influence of drugs from the measurements of intrabacterial Na^+,K^+-ratios and the evaluation of mass fingerprint spectra. One of the applications of the method is *in vivo* therapy control. For this, *M.leprae* are isolated for mass analysis from patients' skin biopsies taken at different times during treatment. In principle, the results can be obtained already a few days after arrival of the biopsy specimens. Limitations of the method arise from the fact that not every biopsy contains sufficient numbers of bacteria and from difficulties in connection with the isolation procedure. For cultivable bacterial species a limiting value of the Na^+,K^+-ratio could be determined up to which the bacteria are viable ("limiting value"). Assuming that this limiting value is valid also for non-cultivable species, the degree of correspondence between intrabacterial cation ratios of *M.lepraemurium* treated *in vivo* with various drugs and the ability of the organisms to multiply in mice was examined. A linear relationship between the proportion of viable organisms, calculated from the Na^+,K^+-ratio and that calculated from the ID_{50} was found, suggesting that from measurements of the Na^+,K^+-ratio the effects of drugs can be predicted. The method is particularly useful for the early detection of drug resistance. Surprising results on the influence of certain drug regimens on the phagocytosis of *M.leprae* will be presented and discussed with respect to effectiveness and clearance.

MI47

THE EFFECTS OF RIFAMPICIN AND CIPROFLOXACIN ON MYCOLIC ACID LEVELS IN HUMAN TISSUE DERIVED M.LEPRAE AND ITS CORRELATION WITH VIABILITY

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Rifampicin is a potent anti-mycobacterial drug whereas Ciprofloxacin is a broad spectrum drug also posses anti-mycobacterial activity. The effect of these agents on mycolic acids was investigated and correlated with their killing mechanism(s) in M.leprae. Purified bacilli were incubated in a modified Dubos medium containing these drugs over 14 days. Biopsies without drug served as controls. Mycolates and ATP were analysed by HP-TLC and ATP photometry respectively. The results showed drastic reduction in the level of mycolates which was found directly proportional to decline in ATP level at 5 mcg/ml of Ciprofloxacin and 3 mcg/ml of Rifampicin, where the cells have poorly synthesized methoxy mycolate and other mycolate components. Though the ATP contents were markedly decreased at 5 mcg/ml of Rifampicin, mycolic acid contents were found to remain intact. The biosynthetic as well as catabolic processes are affected by Rifampicin at very high concentrations leading to preservation of cell wall skeleton. In case of Ciprofloxacin, catabolic process seems to be less affected thus leading to continuing degradation process. These observations have therapeutic implications.

MI48

INACTIVATION OF INTERLEUKIN-2 BY THE CULTURE ISOLATE FROM *Mycobacterium leprae* IN OGAWA MEDIA WITH CYTOKINES

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Round, oily, and white colonies were isolated in Ogawa media with interleukin-2 (IL-2) and interferon-γ, after the inoculation of the tissue homogenate of armadillo spleen infected with *M. leprae*. The size of the colonies grew with time and they were the compact and solid collections of acid fast organisms under a microscope (presented in a separate paper at this meeting).

To test whether or not the acid fast organisms forming these colonies inactivate IL-2, the microorganisms from a colony mentioned above were incubated with IL-2 in RPMI 1640 media, and the IL-2 activities were assayed on days 0, 5, 10, & 20 by measuring the CTLL-2 proliferation. Autoclaved microorganisms were used as control.

The results are:

1. The same levels of IL-2 activity were observed on days 0 & 5 in the media with autoclaved or nonautoclaved micororganisms.
2. The IL-2 activity in the media with the autoclaved was 4-8 times higher than that in the ones with the nonautoclaved on days 10 & 20.

These data strongly suggest the possibility that *M. leprae* may interact with and inactivate IL-2, which is essential for the activation of normal defense mechanisms. The immune defects associated with Hansen's disease may be explained partly based on this finding. Receptor assay, subcultivation, identification, and animal studies are under investigation. Furthermore, the effect of various cytokines on the growth of other microorganisms, including uncultivable ones, is also under investigation.

MI49

IN VITRO CULTIVATION OF MYCOBACTERIUM LEPRAE — EXISTENCE OF A GROWTH FACTOR.

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Inability of M. leprae to grow in culture medium in vitro has been a bottleneck in leprosy research. We had reported earlier about the limited growth of M. leprae in DH medium and our inability to achieve subcultures. One reason for this is the accumulation of oxygen radicals in the growth medium and the other is existence of a possible growth factor.

In our study, normal growth of M. leprae in DH medium was obtained when inocula were from livers and spleens of infected armadillos. However, M. leprae harvested from the foot pads of nude mice failed to multiply in the same medium. Even when the inocula were from armadillo lymph nodes or from human biopsy, the growth was much slower. Furthermore, using inocula from livers and spleens of armadillos, gradual decrease in inoculum size resulted in proportionally slower multiplication.

When the DH medium was supplemented with irradiated M. leprae from livers and spleens of armadillos, nude mouse-derived M. leprae exhibited growth in DH medium similar to that obtained with armadillo-derived M. leprae. Similar results were also obtained with cell-free extracts of non-irradiated M. leprae. All these findings point to the possibility of the existence of a growth factor in armadillo-derived M. leprae.

MI50

ANERGY AND MITSUDA RESPONSES TOWARDS CHEMOAUTOTROPHIC NOCARDIOFORM ANTIGENS RUN PARALLEL TO LEPROMIN ACROSS THE LEPROSY SPECTRUM

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Chemoautotrophic nocardioform (CAN) bacteria had been repeatedly isolated from infectious human, mouse-footpad and armadillo leprosy tissues which had been found to share similar/same metabolic, physiological, enzymological, 36K DNA, lipid profile, pathogenicity and other specificities with Mycobacterium leprae. For further studies on their homology with leprosy bacillus, anergy or contrarily, Mitsuda-type responses towards 4 of these CAN - AGs and a control lepromin were tested on 93 LL, TT and borderline cases of leprosy, categorised clinically and bacteriologically. Final results were obtained for 73 cases. The antigens injected per patient varied from a maximum of 5 to a minimum of 2. The suitability standard of the control lepromin was verified first in 4 TT cases where it produced nodules (+++) ⩾10 mm diameter. Complete anergy to CAN - AGs was seen in 92/92 instances tested on 24 LL cases, while the anergy was weakly modified or unmodified in 3 other LL cases which had been vaccinated before. Concurrent studies with the same antigens tested on 33 TT cases showed clearcut, dose-dependent, Mitsuda-type late responses in 80/81 instances which included 3 cases where the control lepromin was omitted. The CAN bacteria, therefore, despite their origin from different unrelated human, mouse footpad and armadillo tissues appeared to be identical with each other and also with the leprosy bacillus, on the basis of these and other parameters. Phenolic glycolipid-I could be demonstrated among these.

OPHTHALMOLOGY

OP1

A LONGITUDINAL FOLLOW-UP STUDY OF EYE IN 649 LEPROSY PATIENTS

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Periodic examination of eyes were done for leprosy patients attending this centre. The condition of eye in 649 patients for a period ranging from 3 to 20 years (mean 8.29) are discussed. Throughout this period, 458 (70.79%) eyes were normal while the rest 191 (29.21%) were affected and majority recovered with treatment. In tuberculoid and borderline patients, lagophthalmos was the only complication. In lepromatous patients, who had monotherapy, except for fleeting scleritis/iridocyclitis no complications occurred. In lepromatous patients of short duration on MDT, complications were few and subsided with treatment. In lepromatous patients of long duration and in M.B. relapses on MDT, eye complications were more and in some scleritis/iridocyclitis lasted for 4-6 years. Even in those who were normal at the beginning of treatment, some developed scleritis/iridocyclitis after 3-5 years. Blindness was mostly due to non-leprosy causes like cataract and corneal ulcer. Lagophthalmos and corneal hyposthesia were the only causes of blindness in tuberculoid and borderline cases. In lepromatous patients on treatment, blindness occurred only in those with severe pre-existing lesions. Steroid induced cataract led to blindness in a few. Early detection of disease, management of reactions and periodic eye examination prevent eye complications.

OP2

CONSENSUAL OPHTALMOTONIC REACTION IN LEPROSY PATIENTS

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The cosensual ophtalmotonic reaction (TOR) describes the phenomenon whereby alterations of the intraocular pressure in one eye is accompanied by a corresponding pressure change in the contralateral eye. It has been postulated that the COR is mediated via a nervous reflex mechanism. In this study the COR was determined in normals and in the leprosy patients with and without ocular involvement. The theory and the potential usage of the COR in the eye clinics will be discussed.

OP3

OCULAR PROBLEMS IN CASES RELEASED FROM TREATMENT

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Successful implementation of National Leprosy Eradication Programme through proper Anti-leprosy Treatment by MDT and Monotherapy has given rise to a large number of RFI cases in India. This study deals with the remaining ocular lesions in such RFT cases. This series of 6,000 RFT cases (and equal number of PB & MB) shows the involvement of eye in 52% of cases. 70% of them had ocular problems arising directly from the disease itself and the rest developed these as a coincidental phenomenon or ageing process. This study will critically high light the WHO declaration of a disease free state after completion of therapy, though the sufferers have got specific blinding lesions or high risk eyes resulting from leprosy.

OP4

OCULAR LEPROSY IN PATIENTS WITH FACIAL PATCHES

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Facial nerve is mostly involved in leprosy and gives rise to a number of complications following peresis or paralysis of orbicularis oculi with resultant lagophthalmos. Many of the patches over the face (Primary or following Type-1 reaction) are found to be the predisposing factors to develop facial nerve damage or the involvement of the trigeminal nerve- with resultant ocular lesions or keeping the eyes at risk. This is a study of 300 cases (both PB & MB) with facial patches in search of the co-existence of ocular leprosy. The pattern of ocular leprosy is discussed in relation to the different location of the patch on the face e.g. a. specific around the globe, b. on the parotid region over the facial nerve trunk and c. other non-specific areas of the face. About 30% of the patients with specific patch around the globe were found to have ocular leprosy without severe visual disability.

OP5

A CASE ANALYSIS OF THE PATTERN OF CATARACT AND POST OPERATIVE OUTCOME OF CATARACT EXTRACTION IN LEPROSY PATIENTS AS COMPARED TO NON-LEPROSY PATIENTS.

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The ocular status of one hundred leprosy patients and one hundred non-leprosy controls coming for cataract extraction in ALERT is assessed. The visual acuity, the intraocular pressure and the state of the anterior segment will be studied. Each group will be stratified by age, sex and type of leprosy.

All patients will undergo cataract extraction and their post operative visual acuity, intraocular pressure and state of the anterior segment will be assessed and compared. Level of inflammation will be assessed by assessing the anterior segment reaction /fare and cells/. The intra operative and post operative complications will also be assessed. This will be done at discharge and one month after discharge.

Cataract extraction will be done using a cryoprobe under retro bulbar anaesthesia. Visual acuity will be taken using a Snellen's chart. Intraocular pressure will be assessed using applanation tonometry. Assessment of ocular structures will be done by a slit-lamp biomicroscope. Post operative visual acuity will be taken after correction with a +10 sphere.

In the leprosy group classification will be made into the type of leprosy /Ridley Jopling/. The activity of the leprosy will be assessed by studying the Bacteriological and Morphological indices.

OP6

RISK FACTORS FOR CATARACT IN LEPROSY PATIENTS: RESULTS FROM A CROSS-SECTIONAL SURVEY IN THE P.R. OF CHINA

Susan Lewallen, Huan-Ying Li, Lu-Fang Hu, Paul Courtright

International Centre for Eye Health, London UK

Cataract has been shown to be associated with uveitis in leprosy but no study has controlled for the effects of age or other potential risk factors to determine the principal factors associated with cataract in leprosy.

We used data from the Liangshan Leprosy Eye Survey to assess the contribution of risk factors to cataract. Among 974 patients in the survey 69 (7.1%) had monocular or binocular sight impairing cataract. Univariate analysis showed that cataract was associated with a number of other clinical eye findings (lagophthalmos, corneal surface abnormalities, corneal hypesthesia, chronic uveitis), demographic characteristics (age), and leprosy-related clinical findings (other deformities, age at diagnosis, MDT status and history of dapsone monotherapy). Using logistic regression modelling we found that chronic uveitis, age, and history of dapsone monotherapy were the factors independently associated with cataract. Independent of age, about 45% of cataracts can be attributed to chronic uveitis. Implications of these findings will be presented.

OP7

THE CONTRIBUTION OF MDT TO THE PREVENTION OF EYE DISEASE IN LEPROSY: RESULTS FROM A CROSS-SECTIONAL SURVEY IN THE P.R. OF CHINA

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International Centre for Eye Health, London UK

The impact of MDT on the development of eye disease in leprosy remains unclear. We sought to assess the contribution of MDT on the prevention of eye disease and illustrate the hazards of pooling data from newly-diagnosed leprosy patients and patients who had a prior history of dapsone monotherapy. We used data from the Liangshan Leprosy Eye Survey to compare eye findings and other clinical characteristics in newly diagnosed MDT patients (n=292) and MDT patients on prior dapsone monotherapy (n=682).

Univariate analysis showed that newly diagnosed MDT patients were more likely to be Han Chinese, be of a younger age, be of MB disease type, have a shorter duration between onset and leprosy diagnosis, and to have a history of both reversal and ENL reactions than MDT patients with a prior history of dapsone monotherapy. Leprosy-related eye disease was recorded in 10.3% of newly diagnosed MDT patients and 23.0% of MDT patients with a prior history of dapsone monotherapy. The prevalence of eye disease remained constant in all MDT-start years (1986 through 1991), suggesting that most eye pathology found in these patients was probably present at diagnosis. Among the monotherapy/MDT patients eye pathology was most strongly associated with years on monotherapy prior to MDT. Implications of these findings will be presented.

OP8

EARLY DIAGNOSIS IRITIS IN LEPROSY PATIENTS

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Because of the redused or lack of sensations the diagnosis of iritis is very late in Leprosy patients. Quiet often this even reaches a stage where there are thick posterior synichae and complicated cataract. So the general physicians non-medical assistants should be able to diagnose at earliest to prevent complications.

Some guidelines for examination and detection of the disease will be discussed. This paper will be presented with help of slides

OP9

PUPIL CYCLE TIME IN LEPROSY

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Pupil cycle time (PCT) is an easily performed test which times the pupillary constriction and dilation stimulated by a beam of light at the pupillary edge with a slit-lamp. PCT is said to be stable in various testing conditions, repeatable to a high degree and considered to be a sensitive measure of the dysfunction of the parasympathetic efferent limb of the pupillary light reflex. Prolongation of PCT has been reported in various diseases, inferring ocular autonomic dysfunction.

Karacorlu and his colleagues reported prolongation of PCT in leprosy. They suggested that this could be an indicator of early ocular involvement, and might predict future uveitic reactions. However, the number of patients in their study was small, and many of them had pre-existing ocular complications.

We therefore recorded PCT in 361 unselected consecutive leprosy patients who had no visible pathology of the anterior and posterior segments and 173 healthy controls. The mean PCT of leprosy patients and that of healthy controls was well below those recorded by other investigators, denoting likely ethnic variation. Findings relating PCT to age, sex, type of leprosy, duration of the disease, occurrence of type I and type II reactions and the smear status of the patients will be presented and discussed.

OP10

INTRAOCULAR PRESSURE IN LEPROSY PATIENTS WITHOUT APPARENT ANTERIOR SEGMENT PATHOLOGY

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A widely prevalent notion is that intraocular pressures are generally lower in leprosy patients than in normal individuals.

Applanation intraocular pressures were recorded in 166 unselected, consecutive leprosy patients, without clinically visible anterior segment pathology, and in 111 healthy controls. The Mean(SD) intraocular pressure of the leprosy patients 13.1(2.9)mmHg was identical to that of controls 13.1(3.0)mmHg. Only 1.5% of the leprosy patient eyes had pressures of 7 mmHg or less. Correlation coefficient (r) between age, sex and intraocular pressures were not statistically significant either in leprosy patients or in the controls. No statistically significant difference in mean pressures were noted when patients were grouped according to the Ridley and Jopling classification. The duration of disease also did not alter the pressures significantly, neither did smear positivity and differing bacterial indices. Smear positive patients having the disease for more than ten years had a Mean(SD) pressure of 13.2(3.7) mmHg which was not statistically different from the pressure 13.0(2.9) mmHg of smear negative patients with the same duration of disease.

Low intraocular pressure is not that common a phenomenon in leprosy patients as is believed to be, and may not be a very useful indicator of early intraocular involvement.

OP11

VISIBLE CORNEAL NERVES IN LEPROSY

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Corneal nerve involvement is a well recognised feature in leprosy. Surveys on ocular leprosy make mention of prominent or thickened corneal nerves although these observations were likely to have been highly subjective, as no mention is made of the use of any measuring devise such as a graticule. Beading of corneal nerves, considered to be pathognomonic of ocular leprosy, has also been reported.

Corneal nerves, numbering about 70 to 80 in number, run towards the centre of the cornea from the limbus in the mid-stromal region, losing their myelin sheath within a distance of 1mm from the limbus. When viewed with a slit-lamp, they appear as thin lines which branch dichotomously. Although these nerves can be seen both in leprosy patients and in healthy individuals, the number of nerves visualized, even on careful and prolonged slit-lamp examination, varies. In order to find out whether this variation was of significance, we counted the number the visible corneal nerves, quadrant wise, in both eyes of 383 unselected, leprosy patients, who had no obvious pathology of the anterior segment, and in 213 healthy controls. Beading of nerves was also noted.

The results of the study will be presented and discussed, in relation to age, sex, type of leprosy, duration of the disease, occurrence of type I and type II reaction and smear status of the patient.

OP12

CORNEAL SENSITIVITY IN LEPROSY PATIENTS AND CONTROLS

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The corneal sensitivity (CS) of leprosy patiënts and controls has been determined. Leprosy patiënts were categorized into three groups; 1. patiënts without eye-pathology, 2. patiënts with lagophthalmos and 3. patiënts with signs of former iritis. Measurements were conducted with the corneal anaesthesiometer by Cochet & Bonnet. A correction for humidity changes during the measurements has been applied. The results showed that the CS of paucibacillary leprosy patiënts without eye-pathology is not significantly different from the control group. The CS of multibacillary patiënts, lagophthalmos patiënts and iritispatiënts

however differs significantly from the CS of both the control group and the paucibacillairy patiënts. The results support our hypothesis that a loss of corneal sensation in leprosy patiënts is mainly due to secundairy atrophy of corneal nerves or to multiple ocular pathology.

PATHOLOGY

PA1

HISTOLOGICAL AND IMMUNOHISTOCHEMICAL CHANGES OF ECCRINE SWEAT GLANDS IN LEPEOSY

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Histopathological and immunohistochemical changes of ecceine 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 immunochemical 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 TT sample and the LAM-B antigen, on all samples by the immunochemical staining technique. In addition, it is interesting to note that the immunochemical 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-(TGFβ) have been implicated in the progression of several inflammatory injury.This peptide is an importamt regulator of matrix formation, enhancing the syntesis of collagen, fibronectin an proteoglycans and has also been shown to be a chemoattractat 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 differents clinical forms of these disease using a polyclonal TGFβ1 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 ocurred in these infiltrate present on the skin biopsies from patients with tuberculoid leprosy TT. No reaction was observed in these biopsies when the TGFβ antibody was preincubate with TGF coupled to sepharose resin. These results suggest that TGFβ 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 perineuriums were proliferated. There are many bacterial blue particals 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

HISTOPHATOLOGICAL ANALYSES OF LEPROMIN TESTS PERFORMED AT BCG-IZED AND NON-BCG-IZED REGIONS OF MULTIBACILLARY LEPROSY PATIENTS UNDER MULTIDRUGTHERAPY.

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Ten lepromatous and two boderline-lepromatous patients were injected intradermically with o,1ml close 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 hipocromic rings surrouding 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

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

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

Three months after the sixth dose biopsy speciments were collected from three sites: A) Near the first B.C.G. injection; B) An hipocromic ring sorrouding 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-α+ 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 finantiated 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 occurence 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. Clinicohistological 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

CLINIAL AND HISTOPATHOLOGICAL CORRELATION IN THE CLASSIFICATION OF LEPROSY

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This 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 coincided 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%, corcordance 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 parhaps therapeutically irrelevent. 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 LEPROMA

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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. 7u thick sections were cut and stained with hematoxylin and eosin, toludine 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

MYCOBATERRIUM LEPRAE IN MAST CELLS IN HISTOID LEPROMA

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In this paper, a leprosy patient in relapse with widespread lesions of histoid leproma was presented. Histopathological examination confirmed the diagnosis of histoid leproma with high BI (6+). With Giemas 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 conjunctive 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/BRONCHIAL CHANGES

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A prospective study of liver involvement in leprosy was conducted in 30 patient (10 non lepromatous, 7 borderline 8 lepromatous, 4 erythema nodusum 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 nodusum 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 globulinsin 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: 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 Hansens, 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 occured, 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 colected. 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 sequels, irregularity of the treatment, high serum levels of billirrubin, leucocytosis and high erytrocyte sedimentation rate.

The anatomo-pathological findings related with severe forms were acute inflamatory 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 PERSISTANCE 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 persistant macrophage granuloma in 58% of cases. The macrophages were markedly vaculated with few giant vacules containing acid fast dust. Evidence of cellular or bacterial activity was absent. In PB cases epithelioid cell granluma persisted in 40% of cases. There was follicular pattern with dense collar of lymphocytes around the epithelioid cell nests.

The highest granulom a 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 cardio-vascular 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 nodusum 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 LEPROMIN 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

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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 egment, 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 infitration 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 leprous neuritis is unclear. We examined 25 dermal nerves of 15 early hypochromic, hypoesthetic cutaneous macules from leprous 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 oxons 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 cytoplamic processes devoid of oxons 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, Virchowiane 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

HISTOPHATOLOGICAL EVOLUTION OF PB PATIENTS UNDER WHO REGIMEN.

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Several published papers argue the eficcacy of paucibacillary regiment proposed by WHO in 1982. Some authors propose an addition of six months dapsone monotherapy. Histophatological 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 histophatological basis. Biopsies specimens were colected 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 histophatological healing of lesions, leading to the conclusion that WHO regiments 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 corelate 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 tc 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-REHABILITATED AND REHABILITATED 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 dehabilitation of persons afflicted with leprosy. (2) To find out the causes why certain patients were not dehabilitated 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 dehabilitation.

Fifty non-dehabilitated patients and 50 dehabilitated 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 findingsindicate 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.

The medium used to achieve this objective was the print medium. After due consultation with leprologists, educationalists, social scientists and development psychologists, appropriate story lines with the basic themes of positive and scientific facts about leprosy were developed, pretested and printed in the form of compact cartoon strips in two Indian languages. While developing the story lines, the socio-cultural and linguistic backgrounds of the client population were also taken into consideration.

The study tool employed was a pretested questionnaire. The cartoon strips were distributed to the respondents randomly selected, one week before the administration of the questionnaire through a network of volunteers and a post distribution evaluation was conducted.

The strategy was well responded to and the medium was acclaimed and accepted as effective by more than 98% of the respondents. 92% in urban and 87% in rural areas reproduced the cardinal message 'Leprosy is Curable'.

PS5

LEPROSY AND AIDS: BEYOND THE STIGMA

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References to AIDS as the "Leprosy of the 1990's" or to persons with AIDS as the "New Lepers" are frequent. Although it is the stigma that is usually compared, persons with leprosy and persons with AIDS share many experiences that go beyond the bonds of stigma. However, this is primarily true for persons who developed leprosy prior to the advent of sulfone therapy. Many of these individuals were in the prime of life when a diagnosis of leprosy robbed them of their plans and dreams for the future. They saw their friends die at an early age and faced the possibility of their own death daily. They learned to adapt to increasing disability at a young age and had to focus their energies on their illness rather than on work and a family.

In this era of outpatient therapy, it is easy to forget what those persons who contracted leprosy in the pre-sulfone era went through to get to where they are today. In many ways, people with AIDS can help us to understand the difficulties faced by these individuals. It is interesting to see that the insights of a 76-year-old woman with leprosy can help us better understand the feelings of a 32-year-old man with AIDS and, similarly, the experiences of a 32-year-old man with AIDS can help us to better understand the situation faced by a 76-year-old woman with leprosy when she was first diagnosed many years ago.

Through their experiences with disability, chronic illness, death, and the struggle to retain dignity and control in the face of increasing disability, persons with leprosy and persons with AIDS can also shed light on issues related to senior citizens and other persons with physical and social disabilities.

PS6

THE FUTURE OF LEPROSY STIGMA IN VIEW OF ITS PRESENT METAPHORS: A COMPARATIVE ANALYSIS

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Drawing on two anthropological studies conducted in Israel and Thailand, this paper focuses on a comparative analysis of the ways in which metaphorical uses of the word "leprosy" mold its image and reactions to it.

In Israel, with only 200 patients, leprosy exists in the public mind mainly as a metaphor for ostracism. Factual knowledge absent, erroneous perceptions of the disease derive from characteristics of other stigmatized phenomena with which it is habitually compared. Consequently, while individuals claim to be unafraid of leprosy, they paradoxically maintain that all others do indeed fear it.

In Thailand, successful MDT implementation led to a dramatic decline in leprosy prevalence, followed by changes in social reactions to it, which increasingly resemble those in Israel. Currently, public's knowledge of leprosy derives less and less from actual encounters with patients, whereas more and more from figurative uses of the name of the disease. This turns the study of leprosy metaphorization processes in countries like Israel into an enterprise relevant to understanding and predicting future developments in social trends presently occurring in countries like Thailand.

The analysis of leprosy stigma's future vis-à-vis its present-day references in common parlance raises doubts as to the effectiveness of prevailing destigmatization tactics. The discussion of those doubts aims both at the reevaluation of a wide spectrum of conventional views concerning leprosy stigma and at the synchronization of social remedies with current medical developments.

PS7

SOCIO-CULTURAL DIMENSIONS OF LEPROSY IN BOTSWANA

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A study to determine some socio-cultural factors influencing knowledge and attitudes of the community toward leprosy was done in northern Botswana, where cases of leprosy have been known to exist over the years. The study was largely qualitative, using ethnographic approaches. The research was tailored to capture the ethnic diversity of the region, in particular two ethnic groups, Bayei and Bambukushu.

The name or symptom complex associated with leprosy was "ngara" or "lepero" and this was associated with bad blood. Knowledge on disease causation was lacking which in turn influenced health seeking behaviour of patients. Patients were well integrated and accepted into the social structure of communities. The degree of rejection correlated with seriousness of disease and extent of disabilities and dysfunction. Women caring for these patients experienced some additional burden and identified time as their major constraint.

The present pattern of health seeking behaviour needs to be altered, so that an early diagnosis can be made at health facilities. This will aid appropriate management and prevent occurrence of deformities and disabilities, which in turn will reduce rejection and isolation of patients. Education of community, patients, traditional and religious healers on various aspects of the disease is essential to achieve a change in health seeking behaviour.

PS8

SOCIO-ECONOMIC REHABILITATION OF LEPROSY PATIENTS RELEASED FROM CONTROL THE KARIGIRI EXPERIENCE

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RFC patients are not reviewed routinely, in existing leprosy control activities. However, they continue to have various needs. From the time of inception of the control programme in 1962, about 20,000 patients have been Released From Control by the Leprosy Contol Programme of SLRTC Karigiri.

In 1987, in Karigiri, a project entitled "CARE AFTER CURE" was initiated, with the objectives of screening all RFC individuals and identifying their socio-economic needs. Detailed information could be obtained only for 16,601 patients, and out of these, 55.69% of patients were still living, who were then assessed in order to try and provide them their various requirements wherever feasible.

This study details our experiences in the area of socio-economic rehabilitation of patients from this group. It brings out a wide range of the various needs of leprosy patients. It highlights practical problems in identifying needy patients, and suggests ways and means of dealing with problems encountered. It also brings out the stages of social acceptance and other problems encountered by leprosy patients during the course of social rehabilitation. The significance of Care after Cure, and its usefulness and limitations are discussed.

PS9

SOCIAL INTERACTION AND THE DEVELOPMENT OF INTERPERSONAL RELATIONSHIPS OF THE HANDICAPPED IN INTEGRATED EDUCATIONAL ENVIRONMENT

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Taking the handicap as a socially constructed phenomenon and interpersonal relationships as the context where this construction occurs, this study was developed having as objectives: to identify whether the handicapped child, when living in an integrated context, develops stable interpersonal relationships; if so, what are their chracteristics and what kinds of hints are detected about their development's process; if not, what are the characteristics of the handicapped's contacts in the group.

Two integrated groups of pre-school children were video-taped during one academic year, in their free time at the school play-ground, trough scanning and focal taking techniques.

Data collected by scannings were treated by Cluster Analysis and by the construction of Minimal Generating Trees.

Data collected by focals originated a categories system, whose components were described by duration and frequency.

It was also developed a qualitative analysis of the interactional sequences of identified stable partnerships.

There were no qualitative differences in the process of development of stable relationships by the handicapped, when compared to the process of the non-handicapped. The observed differences relate to the rythm of the development and the intensity of relationships. The data also indicated that assymetrical relationships seem to maintain the dependency and passivity of the handicapped.

PS10

THE IMPACT OF SOCIAL MARKETING ON THE PERCEPTION OF LEPROSY IN SRI LANKA

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In low endemic countries, like Sri Lanka, the fact that leprosy can now be cured without deformities goes unnoticed by the general public. Consequently deep rooted prejudices still prevail, also among health care providers, and complicate case finding efforts.

This was revealed in a knowledge attitude and practice (KAP) survey conducted on a sample of 1,000 people by a market research agency in two districts in Sri Lanka in 1989. These prejudices were directly addressed in a highly attractive national social advertising campaign launched in 1990.

There campaign led to a 150% increase in new patients and every second patient seeks treatment on his/own accord. There is also a perceptible difference in the attitude of new patients.

In order to measure if changes could also be observed in the general public, the KAP was repeated in 1993 on a similar sample of 1,000 respondents. A deeper KAP study of 2,000 people on the entire island is being administered by the public health inspectors.

The paper will present changes in the knowledge, attitude and practice of the general public based on the pre and post intervention surveys. Areas where no/little progress has been made will also be highlighted and explained, if possible. Divergences in the results of the two post KAP studies will also be explored.

PS11

GENESIS AND PROFILE OF LEPROSY BEGGARS IN MADRAS CITY AND ITS LESSONS FOR REHABILITATION PROGRAMMES

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There a total of approximately 1000 leprosy beggars in Madras.

A Study through an interview with 200 leprosy beggars is presented, using among others the following information:

1. Interval between date of diagnosis and date of Social Displacement.
2. Response to the disease diagnosis - by the immediate family/by the village community or urban neighbourhood/by the Employer
3. Reasons for Social Displacement
4. Reasons for choosing Beggary as a Profession
5. Contact with original family/village
6. Attitude towards disease/treatment/cure
7. Attitude towards leprosy staff/services
8. Functional abilities versus individual disabilities
9. Income and Economics of Begging
10. Requirements to stop Begging

The information is utilised to suggest a MODEL Rehabilitation Programme for Leprosy Beggars.

PS12

SOCIAL MARKETING APPROACH TO LEPROSY

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Despite 100% coverage of all registered cases with MDT since 1982 in Sri Lanka, the transmission of leprosy was not interrupted. Active case finding efforts of the hidden cases were expensive and hampered due to a high rate of rejection of the diagnosis.

A social marketing campaign (i.e. the application of commercial marketing techniques to a social cause) was launched in 1990 in order to address these problems.

A national social advertising campaign was developed by a professional advertising agency in order to destigmatize leprosy, create an awareness of its early signs, and motivate patients to seek treatment. The entire primary health care staff, curative medical officers in hospital outpatient departments and other staff were trained in leprosy to enable them to make an initial diagnosis and to reduce their fear of the disease. Monthly meetings of the specialised leprosy staff are held to evaluate progress. More clinics were opened up to accommodate the increased demand for leprosy services. MDT blister packs are distributed for better patient compliance.

The impact has been dramatic. Every year around 2,500 new cases are detected compared to 1,000 in previous years. Moreover every second patient is self reporting (10% in 1989). This indicates

the increased awareness of the early signs of leprosy and reduced fear. If patients continue to seek treatment when they first suspect leprosy, Sri Lanka is well on the road to eliminating the disease.

PS13

PSYCHO SOCIAL PROBLEMS OF CURED LEPROSY PATIENTS AN INTERCONTINENTAL COMPARITIVE STUDY

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The traumas inflicted on victims by leprosy are irreparable, that even the hardest of humans too will undergo abnormal physical, psychological and social changes. This study attempts to compare the lives of two groups of cured leprosy patients inhabited in a village in Morogoro, in Tanzania, East Africa, with that in Anbunagar at Villivakkam, near Madras, in Tamil Nadu, India. All the inhabitants were interviewed for the purpose of this study.

Though situated in two continents, the colonies are identical in origin. In Morogoro the disabled are 50% of the inhabitants in contrast to 80% in Anbunagar. While the former depend on the nearby hospital for food, the latter earn their food through begging, illicit trading of arrack and ganja. The inhabitants of Morogoro are confined to their village, whereas the inhabitants of Anbunagar are wanderers, in pursuit of their occupations. As against 39% in Morogoro, 40% of the inhabitants in Anbunagar are economically better of than the remaining.

It was evident from the responses that the inhabitants in Morogoro and Anbunagar are not upset about their predicaments and ways of life.

As a striking contrast to their counterparts in Anbunagar, in Morogoro, the inhabitants are polygamous. Though socio cultural and moral standards of these two communities were found to be divergent, the impact of leprosy on the attitudes and life styles of them are similar. Human qualities, instincts and passions were found to be similar and universal, no matter colour, creed and geographical boundaries seperate them.

PS14

SOCIAL ACTION FOR LEPROSY CONTROL

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Social Action helps to empower the community or groups to identify, understand, analyse and solve its own problem. Social Action in leprosy control is possible if the community is taken into confidence through interactive communication and by addressing control activities to the concerns of the community such as disability and ulcer prevention and cure.

Different culture and area specific models are available and can evolve. Non-skilled roles of health workers are shared by the community groups and individual volunteers owning the responsibility for their actions. Blue print models cannot be designed for social action.

Sustained social action ensures internalisation of norms about leprosy control ultimately becoming a culture pattern. Social Scientists have a role to play in social action as facilitators in the beginning. Social Action refers to developing the partnership between health worker, patient and community for leprosy control. New role sets will have to be developed. Empirical examples are provided from India.

PS15

SOCIAL PROBLEMS OF WOMEN LEPROSY PATIENTS - A STUDY CONDUCTED AT DELHI URBAN LEPROSY CENTRES

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Leprosy is said to afflict women less commonly than men. Unfortunately, the effects are equally devastating if not more on the women than the men. This study carried out at the Urban Leprosy Centres of Safdarjung Hospital and Dr. Ram Manohar Lohia Hospital, New Delhi, showed that the impact of social stigma attached to leprosy was more on educated women belonging to higher socio-economic status. Despite many of the afflicted women getting support from their family, the disease had definite psychological effects. Fear of social ostracism prevented the women to disclose their disease to the community. Deformities and disabilities both deteriorated the functional capabilities and psychological state of mind. Pregnancy did not affect the patients treatment regularity.

PS16

SOCIAL ASPECTS OF DISABILITY AND REHABILITATION IN LEPROSY

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Leprosy is feared mainly because of the deformities and disabilities that it leads to in some patients. Hence this study intends to find out how some obviously deformed/disabled leprosy patients have managed to stay in the society and rehabilitate themselves in the society. The profile of these patients who are staying in the normal community was studied to bring out the factors responsible for absence of stigma and steps taken to overcome it.

A sample of 100 patients was drawn by stratified random sampling method from each of the following three groups: 1.Leprosy patients staying in Sivananda Rehabilitation Home. 2.Leprosy patients staying with their families. 3.Heads/responsible members of households of patients selected for study.

Three different types of schedules were devised corresponding to the three groups. Direct personal interview method using structured schedule complemented with observations was employed for data collection.

The study reveals the needs and requirements of different categories of leprosy patients in the background of the existing resources and facilities. The conclusions of the study would help to formulate rehabilitation programme basing on magnitude of the rehabilitation problem and will be discussed in detail at the time of presentation of this paper.

PS17

LEPROSY: A SOCIOLOGICAL OR MEDICAL PROBLEM ?

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Through time, due to the leading role of medical professionals in healthcare delivery, Health has become erroneously regarded as synonymous with Medicine. But in its real sense, Health is definitely a Social Science. This is evident in the various definitions of Health. The most universally acceptable and the most holistic definition of Health credited to the World Health Organisation describes Health as: "a state of complete mental, physical, social and economic well being, not merely the absence of illheath." This means that Health is primarily a condition of "complete ... social, economic well being."

What is more sociological than "health behaviour" (the activity undertaken by a person who is healthy for the purpose of preventing disease), and illness behaviour (activity undertaken by a sick person for the purpose of defining his condition and seeking relief from it); (Kasl & Cobb, 1966). In the case of leprosy we are faced with a chronic disease condition with multiple, complex, long-term sociological implications:

Why is leprosy so strongly stigmatised ? Why do people who find themselves with leprosy shy away from taking medical treatment even though it is provided free of change ? What explains the multiplicity of complications that are so common among people with leprosy ? Why has efficacious medicare failed to solve these problems? How did leprosy which used to be widespread in Europe up till the Middle Ages disappear from the region, long before the discovery of the first effective anti-leprotic drug ?

These and other questions unarguably concern the field of Sociology, rather than Medicine. The objectives of this thesis are therefore to:

- stimulate the interest of Social Scientists, especially Sociologists in the field of Leprosy Control;
- show the close relationship between Medicine/Health and Sociology;
- examine the causes of the strong, widespread stigma on leprosy and to suggest ways and means of combating it;
- explore the phenomenon of non-compliance among registered leprosy patients and propose solutions;
- identify the cause of the multiplicity of complications that are so common among leprosy patients and suggest possible solutions to these;
- seek an explanation for the failure of efficacious medicare and 'well-organised' drug delivery services as a solution to these problems.

PS18

ANALYSIS OF MENTAL HEALTH STATE OF LEPROSY PATIENTS

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The present study used SCL-90 to measure and analyse the psychological reaction on 71 leprosy patients of different sex, age, educational background, disease duration, disability and with or without relatives' care. The leprosy patients showed a higher total distress level, total mean score in psychological reactions (105.549±57.214)and a higher mean scores of 10 factors in SCL-90 as compared with those of the normal individuals. The SCL-90 factor scores in patients with disability grade II or III were significantly higher than in those with disability grade I. Mean scores of compulsion depression, phobic anxiety, paranoid idea and psychosis in patients without relatives' care and in hospitalized patients were higher than those of the outpatients. Disease duration was highly associated with total score of SCL-90. The longer the disease duration, the severier were the feeling of hopelessness, phobia and hostility. Among the illiterate patients, depression and phobic anxiety were more serious than those of The patients with educational background of primary level. There was no significant difference of SCL-90 scores among patients of different sexes and age groups. SCL-90 factors were analysed and significant difference among 10 factor scores was observed. Social relationship, depression and phobic anxiety were identified as the most sensitive factors, the next were compulsion, anxiety and hostility. The authors suggest that the solutions of the psychological problems in leprosy patients are: 1) to strive for support from people of all social strata, so as to improve treatment conditions; 2) to strengthen propaganda, so as to reduce the fear of leprosy; 3)to encourage patients with more positive suggestions frequently, so as to make patients relieved from the psychological disturbance; 4) to treat patients as early as possible, prevening disability and ensuring psychosomatic health.

PS19

PSYCHOLOGICAL ASPECTS OF LEPROSY PATIENTS IN ALTO AMAZONAS PROVINCE, LORETO REGION, PERU. OCTOBER 1987-SEPTEMBER 1990

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Thirty eigh patients with leprosy were studied in Alto Amazonas. The personality dimensions, introversion-extroversion and satbility-neurotism, were studied with Eysenck's Personality Inventory. Depression and anxiety were studied using Zung's scale. These aspects were also anlysed in the normal population. The following variables were considered: age, sex, place of residence (rural,urban) occupation, type of leprosy and duration of the disease.

Results do not show significant differences between patients and the normal population. However, among the patients studied it was found that:

- Introversion was directly proportional to age.
- Female patients had a greater tendency towards introversion, and an inclination towards depression.
- Urban residents had a greater tendency towards neuroticism.
- Laborers had a greater tendency towards anxiety.
- There were no significant differences among the other variables.

It was interesting to find that leprosy patients were integrated in the society, and segragation was almost nil.

(These paper was financially supported by Red Barnet - Denmark).

PS20

A STUDY OF DEHABILITATION PROCESS OF LEPROSY PATIENTS: INDIA

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The intoduction of multidrug therapy is fast bringing down the leprosy prevalence rate.This has necessited shift toward rehabilitation of patients declared as RFT(released from treatment).It is argued that to avert the problem of rehabilitation,it is better to arrest dehabilitation itself.Therefore,present study focuses on documenting the actual process of dehabilitation.

Data has been gathered using semi structured interview schedule,technique of observation and case study method for indepth understanding.The sample is composed of hundred leprosy afflicted patients around Pune City.

The study reveals that lack of education(43%),non-scientific notions regarding causation and spread of disease(81%) lead to the depression(93%).Further lack of support on part of family and community(64%)and feeling of helplessness by patients her/himself contribute to the process of dehabilitation.

The study further suggests that the role of health education will help ensuring self reporting,taking regular treatment and reduction in stigma,to arrest dehabilitation.

The entire process has been presented diagramatically.

PS21

MEASUREMENT OF DEHABILITATION IN PATIENTS OF LEPROSY - A SCALE

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Leprosy interferes with the psychological and social life of the patient thus bringing about debilitation or 'dehabilitation'. Therefore it becomes essential to assess the extent and direction of dehabilitation inorder to make the treatment plan holistic and effective. The objective of this work was to: a. construct a scale for measuring dehabilitation and b. to standardize it. The methodology included preparation of 52 statements (in English) spread over four sub areas of life viz, family relations, vocational condition, social interaction and self esteem. It was administered to 122 randomly selected respondents. Scores were given to them by summing up the weights of each statement. A high score indicated low dehabilitation. Statistical tests were applied for standardizing the scale. To establish reliability, split-half reliability test and item discrimnant analysis were used. Factor analysis

was used to test the validity. The results show that the split half reliability coefficient ranged high (from 0.64 to 0.83) in all four sub areas. The item discrimnant analysis had a level of significance of 0.001 for 42 statements while the factor analysis explains variance covered over 70 percent. Hence the scale can be an useful instrument in pointing to specific directions while planning intervention strategy for the total person by way of counselling, case work or rehabilitation.

PS22

REHABILITATION: RESTORING TO USEFULNESS

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This paper addresses the psychodynamics of transition , by an adult male patient, from twenty-five years at the leprosy settlement of Kalaupapa to his reassimilation in the city of Honolulu.

In the absence of a mentor, an established support system,and with no analogs on which to build, the presentor will speak of his process; from initial motivation, to fear, shame, trust, despair and crisis, involvement and triumph. Psychosocial developmental milestones are achieved as this ex-patient's journey takes him first to a rehabilitation center for the blind, then to dormitory life on the campus of a major university (at age 37, alone, blind, with hands reshaped by Hansen's disease leaving him unable to use braille, where he would earn two degrees), to marriage and a successful career in the performing arts.

PS23

INTEGRATED APPROACH IN HEALTH EDUCATION OF LEPROSY TO CREATE MASS AWARENESS

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Health Education is very important to prevent and eradicate any disease, so also leprosy, especially in the field. To achieve this, we have tried our best to make the message as simple, specific and clear as possible. Two way communication and interaction was encouraged.

This paper deals with the Health Education given to the School Children, Teachers, and others during the period 1986 to 1992. Film shows and Essay writing competitions on Health Education in Leprosy were held simultaneously during the School Survey every year. MEDEX-91, a Medical and Health Exhibition was organized for the general public in Dec.'91, involving a medical college, various departments of medicine, UNICEF, National Society for Prevention of Blindness, Indian Health Organisation & Others, wherein the cause of leprosy was highlighted. Orientation courses in Health Education for School Teachers were held in 1992. The study was conducted with the help of 'HELP US', a Society involving an Eye Specialist a Psychiatrist, a Dermatologist, a School Teacher, a Bank Employee & others.

Further details will be discussed at the time of presentation of this paper.

PS24

HEALTH EDUCATION HAS CHANGED THE ATTITUDE OF SOCIETY TOWARDS LEPROSY

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Effective Health Education Programme is playing an important role in breaking the long established stigma in the society towards leprosy. This stigma against leprosy will be completely wiped out during this century.

Before the Dapsone Era, patients were uprooted from their homes and the various ways of helping these patients changed as per the attitude of the community.

The outcome of a study conducted in the control area allotted to the Leprosy Mission Hospital, Naini proved that effective Health Education had changed the tide and it seems we have come to the end of the road of stigma. The result shows that out of 1504 cases, only 20 cases are not coming in open for treatment due to STIGMA. This number is only 1.32% which is very negligible. The number of deformed cases are as follows - Grade I = 175 (11.6%), Grade II = 127 (8.4%), Grade III = 36 (2.39%).

Rehabilitation will not be relevant in the field of leprosy any more since patients are not being uprooted. That does not mean these patients will not require any help they will definitely need assistance for Socio/Economic Development.

PS25

ASSESSMENT OF SOCIAL ACTIONS AND HEALTH EDUCATIN IN THE CARE DELIVERY TO LEPROSY PATIENTS

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The aim of the paper is to discuss the procedures of evaluation of the social actions in the care delivery to leprosy patients.

It is noteworthy the hardness to ascertain the quantity of the social actions,the reason why it was choose to adopt the methodology of qualitative research.

The main tool used was a "questionnaire" to be adopted by the Health Care network.This structured document includes all significant data coceming the leprosy patient life: -maintennance of day life activities,taking into account all psycho-social aspects.

The assessment wil be fulfilled in a continuous and cumulative frame.

The expected results could help to implement the integral care to he patient and so to lessen the prejudice against the disease.

PS26

TOWARDS AN UNDERSTANDING OF THE STIGMATIZATION OF LEPROSY

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Brazil is one of the few countries where leprosy is increasing and yet adherence to treatment is under 50%. Interviews with health professionals

corroborated by a survey of the media and scientific publications indicate a total lack of concern with this illness.

Many factors contribute to turn leprosy into a forgotten disease: the decline of leprosy cases worldwide; the changes in local health policy with emphasis on primary care and the lack of emotional impact due to lack of information and the adoption of a new terminology obscuring the understanding among the general public.

The analysis suggest that the strategies employed to overcome leprosy stigma, such as the substitution of the word leprosy by Hansen's Disease, ended up by masking the disease. The results lend support to the relevance of using social representation theory for a better understanding of this masking phenomena and its implications for health care.

PS27

SOCIAL AND CULTURAL ASPECTS OF THE STIGMA OF LEPROSY IN NORTHEAST RURAL THAILAND

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A nine-month anthropological study was performed in a village in northeast Thailand, which was reported to have the nation's highest leprosy case rate. The main purpose was to investigate how the stigma of leprosy was created and maintained, and its effects on patients' adaptation to the disease. The study shows that stigma ideology of leprosy is culturally and socially constructed with its association to states of uncleanliness, impurity, pollution, immorality, and sin. Although community members views patients with bodily disfigurement as persons who should be shunned, they tolerate these patients without any attempt to expel patients from the village, and even maintain some social contacts. I discuss factors responsible for the production of the stigma of leprosy (e.g. religion, everyday use of the languge, health worker activities). I also show how the stigma of leprosy is understood in relation to a person's position in the Thai social structure (such as class, age, and gender). A diagnosis of leprosy brought severe psychological suffering. Patients have feeling of shame, as well as fear of ostracism, debilitation and the possibility they may spread the disease to family members. Ex-patients, especially those with bodily disfigurement, live with the fear of being ostracized and diseased all their lives

PS28

INFORMACION,CONOCIMIENTO Y ESTIGMA EN LA ENFERMEDAD DE HANSEN.

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Programa de Prevención y Control de la Enfermedad de Hansen.Conselleria deSanitat.Generalitat de Catalunya.Hospital de Sant Pau.Barcelona.España.

Se presentan los resultados de las encuestas realizadas a población escolar de distinto estatus social y diferentes edades,antes y despues de recibir información sobre la Enfermedad de Hansen.

El -esconocimiento sobre la misma condiciona el rechazo y el estigma sobre la misma.

PS29

PROYECTO DE EDUCACION EN SALUD PARA EL COMBATE AL ESTIGMA DE LA LEPRA

Dora Martins Cypreste

Este proyecto tiene su objetivo nel combate del estigma de la lepra aun muy presente en nostro pais.

A falta de investimentos cientificos en tiempos passados posibilito el tratamiento inadecuado y como consecuencia las incapacidades fisicas, el mayor temor de la sociedad.

Por lo tanto se hace necesario un trabajo social que alcance todos los seguimientos sociales nel sentido de dismistificar la lepra y posibilitar la reincorporacion social de los pacientes y ex-pacientes ahora alijados de la sociedad.

Areas de actuacion: Servicios de salud, educacion, grupos familiares, movimientos populares organizados, organiciones en general, utilizandose todos los medios de comunicacion de masa.

Alcanzandose a populacion en general estaremos contribuindo para minimizar el estigma asociado al portador de lepra haciendo con que los resultados sociales acompanen lado a lado los tan eficientes resultados clinicos que tenemos alcanzado.

PS30

PROYECTO PARA EL ATENDIMIENTO A LOS PACIENTES IDOZOS DEL SANATORIO DR. PEDRO FONTES

Dora Martins Cypreste

El presente proyecto tiene como objetivo prestar atendimiento clinico y psico-social a los pacientes idozos del Hospital Dr. Pedro Fontes. Estos pacientes cuando acometidos de la lepra fueron abandonados por sus familias y hospitalizados compulsoriamente.

Sin oportunidad para un tratamiento eficaz tuvieron como consecuencia las secuelas tales como ceguera, perturbaciones psico-sociales y otros.

Este trabajo viene presentando notables resultados en la recuperacion de los pacientes idozos portadores de la enfermidad, siendo nel momento el unico implantado en Brasil.

Aunguq abandonados por la familia hoy estos pacientes se sienten como seres humanos recuperando sus derechos de ciudadania.

PS31

INTEGRACION SOCIAL Y ECONOMICA DE UN GRUPO DE PACIENTES DE LEPRA EN LA ZONA RURAL DE DOMINICANA CON GRAN PARTICIPACION DE LA COMUNIDAD

Rafael Isa Isa, Huberto Bogaert, Sócrates Canario.

Instituto Dermatologico Dominicano,Santo Domingo,Rep. Dom.

Se presenta la información básica sobre un Programa de Asistencia Directa para la Integración Social y Econó-

mica en pacientes de lepra en la Región Sur y Sur-Oeste de la República Dominicana, regiones consideradas por Organismos Nacionales e Internacionales con los niveles más bajos de pobreza en el país.

Se trata de un proyecto de Infraestructura Física y Social que involucra a los pacientes en la Educación, Organización y Participación Comunitaria en colaboración con instituciones de apoyo no gubernamentales y Asociaciones de Desarrollo Locales y Regionales.

PS32

EVOLUCION DE LA ENDEMIA LEPROSA
EN REPUBLICA DOMINICANA
1966-1992

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Se hace una revisión del comportamiento de la endemia examinando la incidencia (tasa anual de detección de casos) y prevalencia desde el inicio de la aplicación de las medidas de control hasta el 31 de diciembre de 1992. Se observa una caída contínua de la incidencia desde el año 1976 acompañada de un descenso de la prevalencia a partir del año 1980. Se hace una distribución de los casos por forma clínica, sexo y edad además de su localización en medio urbano o rural.

Los datos revelan una razón prevalente del sexo femenino sobre el total de enfermos con mayoría de varones en las formas multibacilares. El porcentaje de menores de 15 años se mantiene elevado a pesar del esfuerzo realizado, año tras año, para disminuir la endemia.

La situación así encontrada, se atribuye a la existencia de condiciones socio-económicas-culturales que se mantienen en un nivel muy crítico.

PS33

SOCIAL ADVERTISING FOR LEPROSY

Sandya Salgado[1], Upali Herath[1], Rohan Piyadasa[1], Dayamal Dewapura[2], Penny Grewal[3], Padmini Gunawardena[2], Sunil Settinayake[2]

[1]Grants Bozell, Colombo, Sri Lanka; [2]Anti-Leprosy Campaign Ministry of Health, Colombo, Sri Lanka, [3]Ciba-Geigy Leprosy Fund, Basle, Switzerland;

Leprosy continues to be one of the most maligned diseases in the world. In order to change its perception a social advertising campaign was developed by a professional advertising agency in Sri Lanka. The campaign stimulates spontaneous demand for diagnosis and treatment by making people aware of the early signs of leprosy, able to spot them in themselves and others, fearless of the consequences.

The emphasis throughout is on physical beauty and how early, regular treatment would leave it unimpaired. It combines nation-wide advertising with popular radio and TV serials in which the hero or heroine suffers from leprosy, but always has a happy ending. All the available mass media are used: TV, radio, bill boards, posters, stickers, direct mailings, newspaper advertisements, etc. The campaign logo, a flower held sensitively by fingers, is a poignant reference to a point where the disease often strikes.

A poster exhibition will display samples of the advertising material used in the campaign as well as summarise the main experience made with social advertising.

PS34

SOCIAL MARKETING: A NEW STRATEGY TO ELIMINATE LEPROSY

Penny Grewal[1], Dayamal Dewapura[2], Padmini Gunawardena[2], Sunil Settinayake[2], Francisco Castellanos[3], Alberto. Barocio[4]

[1]Ciba-Geigy Leprosy Fund, Basle, Switzerland; [2]Anti-Leprosy Campaign, Ministry of Health, Colombo, Sri Lanka; [3]Anti-Leprosy Campaign, Ministry of Health, Mexico; [4]Ciba-Geigy, Mexico

Poor awareness of the early signs of leprosy and/or fear of social rejection have led to a high hidden case load in all countries. Unless these problems are effectively addressed on a national scale leprosy cannot be eliminated.

Social marketing is being successfully applied in Sri Lanka and Mexico to dispel the fear of leprosy, encourage patients to seek treatment and to provide easy access to treatment.

Social marketing involves the application of the philosophy, concepts, and techniques of commercial marketing to socially beneficial practices. It is built around the knowledge gained from business practices and involves organising the services to suit the convenience of patients. Social marketing also requires the careful co-ordination of the marketing mix of promotion (social advertising), place (treatment points), price (costs for seeking treatment), and product/ packaging to achieve the desired impact.

The paper will elaborate on the concept of social marketing, the key factors for its success and how it differs from traditional approaches of health education. It will also explore the advantages and limitations of the approach as well as the lessons learnt through its application in Sri Lanka and Mexico.

PS35

THE SOCIAL IDENTITY OF THE PHYSICALLY HANDICAPPED

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This study had as its goals: 1.to identify personal aspects of the handicapped's identity, as well as its value attribution 2.to identify the handicapped's perception of the existing stereotypes in the in and in the outgroup, with its correspondent value 3.to identify signs of collective action for social change. 12 physically disabled, 12 to 36 years old, were submitted to an adaptation of Zavalloni's (1973) Psycho - Social Identity Inventory. Data analysis indicated that most of the attibutes designated by the handicapped to itself is positive. Now, when characterizing the other handicapped, the attributes are mostly negative. In relation to what the handicapped think about how he is perceived by the non-handicapped (outgroup), the representation is characterized mainly by negative attributes. Such results are consistent with the ones obtained by Zavalloni-positive attributes seem to be, more frequently, related to "WE", while the negative ones to "THEY". The answers obtained to the SELF were exclusively of personal nature, differing from the ones obtained by Kuhn & McPortland (1954)who verified that initial answers reproduced social characteristics and only later ones had a personal connotation. The data indicates, yet, that most of the subjects are in search of social mobility and not of collective action for social change.

PS36

PSYCHO-SOCIAL TREATMENT FOR LEPROSY PATIENTS: METHODOLOGY FOR INDIVIDUALIZED APPROACH IN ROUTINE TREATMENT.

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Though there has been an awareness among the program scientists about the effectiveness of the psycho-social interventions in leprosy control work, the application of such techniques has not yet been achieved, due to lack of standardized methods with in the reach of the Paramedical Workers' comprehension.

To evolve a standardized methodology for the use of paramedical staff out-patients of the referral hospital of Gandhi Memorial Leprosy Foundation have been systematically diagnosed and treated by a group of counselors comprising of a Trained Social Worker, a Paramedical worker and a Psychologist, from psychosocial point of view.

The inferences drawn based on the exercise, presented in the paper, show that psychosoc' l treatment in leprosy involves a systematic procedure comprising of 3 steps a) psychosocial diagnosis, b) prescription of needs and c) treatment. The paper also presents a tentatively standardized methodology of treatment,which could be easily modified as per the local needs, in the above mentioned 3 steps and the achieved results of application of the evolved methodology in terms of reducing the non-compliance of the patients and preventing dehabilitation of the patients.

PS37

IMPORTANCE OF SOCIAL REHABILITATION OF THE PATIENTS IN LEPROSY CONTROL

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In the recent years it has been understood that to reach the goal "to control leprosy" or "to eradicate leprosy" one has to take leprosy patient "as a whole" and take in to consideration all the different aspects of disease and conditions related to disease.

Because of leprosy people with deformities can not earn their living and go on begging or living in very bad conditions as outcasts will continue giving the image that "leprosy is a dangereous disease" which cripples and although they say that it is treatable they end up in very bad conditions.

We realized that if we were able to rehabilitate leprosy patient socially in other words if we can create a new way of living and earning money for the treated patient we could prove the society and ourselves that leprosy could be really controlled in the near future.

With this judgement and reason we put on emphasis on the social rehabilitation of the patient together with the medical, physical and protective treatment.

In this study we planned to give 22 case reports about the social rehabilitation of 34 patients. Their previous and present situation and efforts made to realize each project are given in short with the aim of being an example of managing the patient "as a whole" and by this way serving for the real "eradication of leprosy".

PS38

FOLLOWING THE REHABILITATION OF HANSEN'S DISEASE PATIENTS UNDER SOCIAL ASPECTS

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University Hospital (UFF)/Social Worker Service

In the metropolitan areas and in the midle size cities of Brazil the health system network usually has social workes in its staff not only to assist doctors in difficult situations but also to divise some solutions for those patients whose difficulties are not always been identified by other staff members. Although health service does not take full advantage of all this professional's skills their initiatives regarding leprosy patients have been increasing as the MDT schemes allow a better relationship between patients and health professionals. Theese experiences have shown some difficulty to make patients come for group discussion specially in urban areas where the treatment is through health centres located in the patient's residencial area. One of the patient's reason for not coming is the fear of meet friends or neighbours.

Taking into account that the society prejudice as well as cultural factors is responsible for such attitude the social service of the UFF has been developing an "action-research" project focousing the level of participation of 2 kinds of patients:

Those from a slum area, treated in Primary Health Care Centre through community-based program and those refered from different areas of Rio de Janeiro city, treated in the University Hospital.

Considering the illness stages from a social point of view, this video documentary shows through the cases studies problematic situations demanding a social diagnosis. It also shows that the "role of the patients from both institutions in urban area are quite different".

PS39

COPING STYLE IN LEPROSY

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Leprosy is more a social problem rather than simple medical problem. Therefore there is need to know the impact of coping style in leprosy. Here coping is defined any response to leprosy that serves to prevent or control the emotional distress.

100 cases of Hansens disease were selected randomly. Questionnaire was distributed. On analysis, it was found that coping response depends upon severity of the disease and various coping resources. 22% cases where severity of disease was less,accept the situation but redefine it and find something favourable like hypopigmented patch. They were regular in treatment but they do not want to know about leprosy. 9% feel that the leprosy is curse from God,doing nothing to maintain the situational demand.They were irregular in treatment. 60% were using problem and emotion focused coping together. Emotion focused coping maintain hope and optimism while problem focused coping is responsible for collection of information and action.Positive belief, problem solving skills, social and material resources are important coping resources, which are helpful for early detection regular treatment, and prevention of deformities.

Study of coping gives better insight of each leprosy patient,which can be a great help to select appropriate and effective medical interventions.

PS40

RESPONSE OF NEWLY DIAGNOSED PATIENTS TO LEPROSY IN KERALA (S. 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 Leprosy Mission has recently instituted Leprosy Control Programmes in the Manjeri Sub-district and Kollam Urban Area in Kerala.

The study among newly diagnosed patients is aimed at understanding the acceptance or otherwise of the label of a leprosy patient and the resultant behaviour in terms of patient's perception about the disease causation, treatment and cure. This will help to design appropriate leprosy control strategies to ensure voluntary reporting and regularity of treatment and decreased stigma. Both quantitative survey method of interview schedule and qualitative case studies have been used for data collection.

Preliminary observations indicate a spectrum of total ignorance of leprosy, fear of social rejection and stigma about diangosis and treatment.

The results of this study are being used to design intervention measures to combat this problem.

PS41

SUMMARY AND RESEARCH OF LEPROSY ACCOUNTS IN THE BIBLE

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This paper systematically and briefly quoted the accounts about leprosy in all chapters of the Bible, providing important reference materials for research of the history of leprosy and social medicine.

In the discussion the author suggested,

1)The term "tsaraath"used in the OLD TESTAMENT did not refer to leprosy alone nor to diseases other than leprosy, but to all kinds of skin diseases including leprosy.

2) Citing some references of the Bible scholars, historians and archaeologists, theauthor believed that there might have been leprosy patients in the Palestine area at the12th century B.C., and by the 7th century B.C., leprosy was definitely endemic.

3) From the 7th century B.C. to the 1st century B.C., there were strong fear of and prejudice against leprosy patients in the society of the Palestine area. But Jesus,(whose actual exisitence is still being debated among scholars, the author mentions him according to the Bible story) untike the others , showed sympathy and love for the leprosy patients; he dared to contact them and was willing to help them. Such an attitude and behavior were noble and praiseworthy both at that time and at the present.

PS42

THE ACTION OF THE SOCIAL ASSISTANT AND THE IMPROVEMENT OF THE LEPROSY PATIENTS TREATMENT REGULARITY - DUQUE DE CAXIAS PROJECT - RIO DE JANEIRO - BRAZIL

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CERPHA, Rio de Janeiro, Brazil

The study assesses the patients regularity regarding the MDT/WHO leprosy treatment regimen.

The patients clinical records were compared in two different periods: one in the years 1989-1990 when no social assistant was assigned to the program, and other in the years 1991-1992 after the appointment of these personnel.

The results point out to the hypothesis that the treatment regularity is directly proportional to the action of the social assistant working in the health team. The same results can be can be reached with other kind of personnel (Sociologists, Psychologist, graduate Nurses).

PS43

A SURVEY OF JOB SATISFACTION AMONG LEPROSY PERSONNEL *

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A survey was conducted among the health personnel working in leprosy in two Multidrug therapy (MDT) districts in India to study their levels of job satisfaction. The following four variables were taken into consideration for determining job satisfaction.

1) Self-image of the staff.
2) Promotional satisfaction.
3) Satisfaction towards the introduction of MDT
4) The role of pay as a satisfier.

There were 356 respondents in the study, an overall response rate of 96%. The results show that the overall self image of the health staff working in leprosy has improved in the MDT era as compared to what it was in the monotherapy era of the 60's. The dissatisfaction with chemotherapy which was a significant observation before the introduction of MDT has virtually disappeared and it has been replaced by a moderate-level of satisfaction. In comparing satisfaction due to Promotion with that due to Pay, the latter was found to rank higher.

In a few instances, physicians, paramedics and personnel from different geographical and administrative structure had significant differences in their levels of job satisfaction. This study analyses these findings in the light of existing psycho-social theories.

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* A part of the thesis for a privately undertaken PhD by the First author

PS44

DETERMINANT ABOUT IRREGULARITY ON AMBULATORIAL TREATMENT OF LEPROSY IN AN UNIVERSITY HOSPITAL

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We studied 305 patients with leprosy on ADS-HUPE-UERJ between 1985 and 1990. The socio-epidemiological characteristics were identified with 35,5% of patients on irregular treatment. We also concluded that clinical form presentation, acessibility and principal occupation seems not to be an infuence in therapeutic non adhesion rate, while ethnical group and ins - truction level suggest important association with the subject.

PS45

IN-FACTORY MDT

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Many leprosy patients find it very difficult to do regular multidrug therapy whilst working in the factories of Manaus's industrial district. The social work department of the **"Alfredo da Matta"** Institute of Tropical Dermatology sought alternative ways around this problem.

From 1988 onwards, the team started educational work with the factory managers, the staff medical services in the indurstrial district and with the patients themselves. The result can be seen in the fact that working patients are doing MDT at work in 94 of Manaus's 217 factories.

PS46

HOW THE MEDIA AFFECTS LEPROSY PATIENTS

Bill Malo, Valerie Monson

Kalaupapa settlement, Hawaii, USA

Bill Malo, who was a Hansen's disease patient at Kalaupapa for 25 years before leaving as a healthy man in 1965, still cringes when he sees fund-raising materials distributed by some leprosy organizations. The close-ups of deformed faces and partial limbs make Malo think that leprosy patients are being "exploited in order to raise money" for their care.

Valerie Monson, a reporter for The Maui News, remembers her first visit to Kalaupapa when many patients refused to talk to her because they worried about being exploited to sell newspapers.

Throughout history, leprosy patients have not only suffered physically, but they have been forced to endure mental anguish due, in part, to an insensitive media.

From popular television shows such as "M*A*S*H" and "The Simpsons" to the rock music of "Was (Not Was)" to Vanity Fair magazine, the word "leper" has been used to conjur up images of fear, shame, pity or disgust.

What can we do?

Malo believes that leprosy organizations can help by showing healthy patients -- those who have been treated with sulfone drugs -- along with sick ones to raise money. By presenting "the other side of Hansen's disease," the public would realize there is hope and that patients can have full and happy lives.

Monson, who has managed to gain the trust of the patients at Kalaupapa and has been writing about the community for four years, believes a serious effort must be made to inform the professional media that the word "leper" is considered repugnant and that Hansen's disease is no longer a death sentence.

The media can make an enormous difference not only in how the public views people with leprosy, but how people with leprosy feel about themselves.

PS47

PUBLIC PRECONCEPTIONS OF LEPROSY. A LINGUISTIC APPROACH.

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Preconceptions of stigma and segregation have played a dominant role in the discussion of public education on leprosy. All too often health workers, representing the values of educated middle class, have taken it for granted that segregation was practiced among ordinary people.

We have found as a common pattern is the co-existance in society of two parallel sets of terms for the disease, one with cultic associations, where the disease connotes "uncleaness" or "pollution", leading to ostracism; the other, secular set of terms has no such connotions or implications.

In the Bible, the cultic concept in Hebrew is tsa'rat, initially was not compatible with leprosy. In the Septuagint Greek translation of the Old Testament, lepra was used, and this became also the term in the New Testament. Only during Renaissance did it became the medical term for leprosy. Local equivalents like spetelsk existed in northern Europe, and this became the root of the word hospital (house, spetal). Independent secular terms, such as spillsjuke in Norway, did not connote uncleaness and caused no segregation among lay people. Segregation was introduced on "scientific" basis, and the medical establishment used the term spedalsk. In Ethiopia the biblical term tsa'rat was translated into the ancient church language Geez by lemts in both testaments, a word is used also in contemporary Amharic, connoting a skin disease. Other words(gumtinna/däwe siga/ bis äla/dill) are used in daily speech to depict the progressive symptomatology of leprosy. None of these terms connotes "uncleanness" or carry association to stigma or segregation.

In the Koran, juzam is conceptually the same as tsa'rat in biblical Hebrew. Again a number of symptom-related terms replace juzam in daily reference to leprosy, and these do not imply segregation.

In an ancient Sanskrit text, Charaka Sanhita, sexual excesses are given as one possible cause of kushtha, leprosy. This association has certainly caused some stigmatization among educated Indians. Still, a leprosy patient retain his caste, and does not become an "untouchable". In most contemporary Indian languages, the term for leprosy is not related to kushtha. The idea of segregation is correlated to higher classes and urban life.

Leprosy workers should carefully study the lingusitics of leprosy in the society to make sure that public education does not contribute to sigmatization of leprosy where no stigma in relation to the disease is observed in the society.

PS48

LA LEPRE VUE PAR LE LEPREUX AFRICAIN

Kongawi Kinda
Zaire/Africa

L'idée que le lepreux africain a sur l'origine de sa maladie est tout à fait différente de celle des scientifiques.

Malgre l'explication scientifique,le lepreux africain croit que sa maladie provient d'une malediction, d'un mauvais esprit,d'une sorcellerie ou des ancêtres mécontents.
Le traitement médicamenteux ne suffit pas à convaincre ce lepreux africain.

La prise en charge d'un lepreux africain doit tenir compte de deux aspects importants:

1. L'aspect technique qui consiste à soigner et à suivre le malade mais aussi
2. L'aspect psychologique qui consiste à préparer spirituellement le malade en lui expliquant que même si sa maladie est envoyée par un mauvais esprit, il existe un Etre suprême capable de neutraliser tous ces esprits.. Si l'on suit bien ses traitements et l'on croit en ce Etre qui est DIEU, on sera guéri et aucun mauvais esprit ne pourra s'approcher de celui qui croit en Dieu

PS49

SOCIOECONOMIC AND PSYCHOSOCIAL DIMENSIONS OF LEPROSY: A CASE STUDY ON TREATMENT TYPES AND PATIENTS COMPLIANCE

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Leprosy is a social disease and the social stigma attached to leprosy is universal in all directions in all societies. The lower socioeconomic groups are more prone to experience in view of the lower socioeconomic status. One of the social factors favour the spread of the disease is low standard of living. Tamilnadu is one of the leading states in India to witness a high prevalence rate of leprosy. The status of deformities caused a great concern in view of the disfigurement of of the patient due to the disease which leads to serious psychological, economic and social difficulties. The study is based on the analysis of socio-economic and psychosocial dimensions of leprosy patients in relation to their preference towards the treatment types and their compliance to express their satisfaction and willingness to continue to follow the regular treatment. The present study also made an attempt to identify the major socioeconomic and psychosocial dimensions with reference to monotherapy and multidrug therapies (MDT). The study was based on questionnaire survey by direct observation methods conducted among 300 respondents chosen in various endemic areas of the districts of Tamilnadu. The data were analysed with the help of Factor analysis, a multivariate statistical technique to decipher the major dimensions. Twenty major dimensions were emerged with an eigen value ranging from 13.54 to 1.00 with a total variance of 69.64%. The dimensions worthmention -ing are: Infrastructure facilities, Treatment considerations, Family Response in view of Deformity, Status of Patients, Environmental Effect, Social effects of disease, Regularity of Treatment,Accessibi -lity and Treatment efficiency, Efficiency of Treatment, Treatment Adoption and Treatment Efficiency

PS50

STUDY OF PSYCHIATRIC MORBIDITY IN HANSEN'S DISEASE AT A REHABILITATION CENTER

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The number of Hansen's patients in India is about 3.2 millions out of 11 millions of patients throughout the world.The present study is on psychiatric morbidity in Hansen's patients at a rehabilitation center, among out-patients and in-patients. Fifty out-patients and fifty in-patients were administered General Health Ques-

tionnaire and screening questions from Indian Psychiatric Survey Schedule. Sociodemographic data was also collected. Analysis of results shows that out-patients out number in-patients in having psychiatric illness with a 19:5 ratio which is statistically significant. The predominant diagnosis is Dysthymia,of Secondary type, according to DSM_III R. There are no observed differences in different types of Hansen's disease, different durations and presence or absence of Lepra reactions. The results are discussed:

PS51

PROBLEMS AND COPING STRATEGY OF FAMILIES WITH DEFORMED AND NORMAL LEPROSY PATIENTS

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Disease status in leprosy is an important determinant of the kind of non-medical problems the patient and his family have to face in the society. Though several epidemiological studies were conducted to understand deformities and disabilities, sociological understanding about them is meagre. This paper attempts to understand the magnitude of the problems and the coping strategy adopted by the affected families of both deformed and non-deformed (normal) leprosy patients.

This investigation, as part of a larger study "Acceptance level of leprosy patients in the family" conducted by the CSSRL, GMLF, Wardha covered a sample of 500 leprosy patients and their families spread over in four leprosy control units in Tamil Nadu.

A large number of medical, demographic and other variables had differential impact on families facing problems with deformed and non-deformed leprosy patients. The extent of the problems faced by these families and the coping strategy adopted were analysed. Implications of the results for the control programme are discussed.

PS52

HUMAN RELATIONS RESEARCH AMONG LEPROSY PERSONNEL AND STRATEGIES FOR BEHAVIOUR MODIFICATION *

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This study was conceived to understand the behaviour of health personnel working in leprosy in India, towards patients and fellow health-workers. The latter was studied in three areas:
1) Interaction with supervisors.
2) Inter-group behaviour, between paramedics and doctors.
3) Inter-departmental relationships.

The data was collected using a perception-attitude-behaviour (PAB) scale developed specifically for this purpose. The scale consisted of four independent test instruments, each of which measured five factors, reflecting five aspects of behaviour towards the group concerned.

The results indicated that a significant number of health personnel did not possess the minimum desirable behavioural standards towards their patients. The quality of relationships was unsatisfactory with supervisory figures and also between paramedics and doctors. However, inter-departmental relationships in the existing infrastructure of leprosy control programmes were found to be satisfactory.

Behaviour modification methods tried at Karigiri, to improve working relationships in both of these areas, are presented.

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* A part of the thesis for a privately undertaken PhD by the First author

PS53

LIFE AFTER MDT

Emanuel Faria

Executive Editor, THE STAR, Carville, LA, USA

Hansen's Disease is not like any other illness in the sense that effective treatment is all that matters to the sufferer. For those who have it, Hansen's Disease is a life-long problem. Effective therapy is not the end of the story. People with HD worry, and rightly so, about the possibility of becoming disabled and thus being unable to support themselves and their families. Even after being "cured", this anxiety remains.

There is also the possibility of ocular and other medical complications. Completing MDT and being considered "cured" does not guarantee the absence of eye problems and other medical problems later on. Regular eye examination is necessary even for the "cured" in order to detect possible incipient sight-threatening conditions.

In addition, being considered clinically "cured" does not necessarily mean that one is automatically accepted in the community or the work place.

Here in the U.S., we have state-of-the-art treatment, but I anguish at the plight of those who live in regions where care is distant if non-existent. We at Carville have so much, yet it can still be a very lonely place. Rejection experienced in earlier times can result in a permanent inferiority complex if one isn't careful. MDT alone cannot restore one's dignity. The restoration of dignity and a sense of pride in being able to provide for one's family are an imperative part of any cure.

PS54

THE COMPREHENSIVE CARE OF CAMBODIANS WITH HANSEN'S DISEASE IN A LARGE AMERICAN CITY.

Alec Style

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This paper will describe a constellation of physical, psychological and social problems in 39 Cambodian patients with Hansen's disease treated at the USPHS Hansen's Disease Center in Boston. Many of these patients have major hand and foot deformities, caused by lepromatous leprosy. Before coming to the United States as refugees nearly all of these patients suffered major psychological and physical traumas in Cambodia and/or refugee camps. Many contracted infectious diseases such as tuberculosis and hepatitis B. After arriving in the United States they had problems adjusting to their new country, because of cultural and language barriers. These problems continue as their children become Americanized and lose many traditional values. These patients have a high incidence of depression and post-traumatic stress disorder because of their previous suffering. In addition, they face the stigma of Hansen's disease within the Cambodian community. These case histories will show that Hansen's disease cannot be treated effectively without addressing other major medical and social problems. These and similar patients are best served by a medical system that provides comprehensive primary medical care and by providers who are sensitive to their history and culture. A Hansen's disease program should either offer this level of care or work closely with health providers who can.

PS55

THE PARTICIPATION OF HANSEN'S DISEASE PATIENTS IN THE GOVERNMENTAL HANSEN'S DISEASE CONTROL POLICY-"HANSEN'S DISEASE AND THE CONSTITUTIONAL ASSEMBLY" - A BRAZILIAN MINISTRY OF HEALTH'S EXPERIENCE

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The national movement "Hansen's Disease and the Constitutional Assembly" started and coordinated by the Brazilian Ministry of Health's Sanitary Dermatology Division, in 1988, with decentralized seminars from the local and regional levels, had the participation of the government and sectors of the society at large (Movement for the Reitegration of Hansen's Disease Patients - (MORHAN), popular health movements, the scientific community.

This paper discuss the methodology used, which allowed the majoritary participation of patients in the decentralized seminars, covering 22 federated units and five macroregions and leading to the reformulation of guidelines and strategies for the endemy's control activities in the country and a backgroud document of subsidies for the 1988 Constitutional Assembly, regarding the chapter on the universal rights of man.

It also discusses the results of the deepening debate about ensuring the exercise of citizenship in relation to the discrimination and restrictions to patients with Hansen's Disease; the right to a job; the restructuring of the colony hospitals; the patients integral and integrated assistance in the service network and the revoking of discriminatory Legislation.

MORHAN'S presentparticipation in the Brazilian Ministry of Health's Chamber of the National Health Council is analysed under the focus of the unfolgind of this movement.

PS56

RESTRUCTURING THE COLONY-ASYLUM HOSPITAL, A SHARED ACTIVITY OF THE GOVERNMENT, PATIENTS AND SOCIETY AT LARGE

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The process of restructuring the colony-asylum hospitals in Brazil is an ongoing reality.

Between 1987 and 1989, the Brazilian Ministry of Health began restructuring the 333 colony-asylum hospitals housing Hansen's Disease patients and thoses that, though cured, had difficulties in their social integration and restrictions to exercise their citizenship rights.

The specially formed Tecnical Social Committee, made up by technical and legal MoH staff and by participants from the representative organization of HD patients (Movimento de Reintegração do Hanseniano - MORHAN) created local restructuring groups, supported by the state administration level, moving towards changing the colony hospitals into general or sanitary dermatology hospitals, integrated into the health services network for the entire population and hospital network open to the local community.

The initial survey carried out by a questionnaire filled by the 33 hospital allowed to identify the living situation of HD patients and to define strategies for in loco action.

The participation of HD patients, local groups and the federal administration ensured the effectiveness of this change, and in some places made possible the right to land, jobs, housing, and whole and integrated care of the patient and his family.

PS57

THE MEDIEVAL LEPROSARIUM: ITS PLACE IN MEDICAL HISTORY

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This study is based on the examination charters and operational documents of medieval leprosy hospitals. Such hospitals began to proliferate in Europe in the eleventh century and reached peak numbers of beds in the thirteenth century. These hospitals represented part of an increase in building in general and hospitals in particular. As institutions, however, they differed significantly from modern hospitals. First, their primary intent was not medical. As the name hospital suggests, hospitality was their function and most medieval hospitals housed pilgrims, widows, and orphans. Leprosaria filled this function for those who held the legal status of those diagnosed with leprosy. Therapy and intent to cure did not exist. Leprosy patients were legally dead in medieval Europe and had no access to ordinary necessities. The leprosy hospital offered hospitality to this group, but, in nearly all cases, imposed a semi-monastic lifestyle on the patients, requiring special clothing and diet. The ideal of their custodians was based on hagiography and behavior such as kissing the patients' sores and sleeping in their beds, actions considered likely to infect the person so acting, were highly applauded. A curious feature of many charters of leprosy hospitals was the stipulation that the hospital serve as the retirement home for the persons founding it. Thus, in intent, function, ideal, and even the medieval leprosarium bears essentially no relation to the modern hospital. The medieval leprosy hospital was profoundly different from its modern equivalent, only the name suggesting a continuity, which crumbles under scrutiny.

PS58

THE PARTICIPATION OF THE "MOVIMENTO DE REINTEGRAÇÃO DE HANSENIANOS" - MORHAN - IN THE LEPROSY CONTROL PROGRAM IN BRAZIL

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The paper is a analysis of the contribution of a lay association of patients and professionals engaged in their care - the MORHAN -. This entity start its activities in the eighties and have as aim to contribu te to the control/elimination of the leprosy endemy.

The "MORHAN" believes that the fight against the disease is not only to treat the cases but, also, the real and organized participation of the patients and professionals to achieve the betterment of life conditions.

The "MORHAN", while a popular movement, tries to cope with the prejudices associated with the disease and the attitude of charity. The main objective of the "MORHAN" is to favor a position of defense of the citizenship like others popular movements.

It was used the method of qualitative research reporting the history of the Association, its political importance and posing a question to the those concerned with the social aspects of leprosy and/or he health problems in general.

PS59

BEHAVIOR HEALTH CHANGE INTERVENTION ON LEPROSY CONTROL IN SOUTH SULAWESI, INDONESIA

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Leprosy control has been done for years in South Sulawesi. Using MDT system in the last 5 years has a great effects to decrease the leprosy prevalence. Unfortunately the decrease of prevelence can help the occurance of new cases. In 1992, there was about 2,000 new cases was found and 10% has a serious disability.

Having a traditional health concept on leprosy and practicing **leprophobia** to hate to the victims is a real obstacles on leprosy control in this area. Back to the leprosy transmitted is "man to man", the intervention of behavioral health change on health promotion, early diagnosis and prompt treatment and rehabilitation can be chosen as an alternative. Supported by a couple of experiences based on two researches by using health behavior change in qualitative and quantitative researches in South Sulawesi, Ngatimin offers a model to support leprosy control include to take care to subclinic patients which were caught by serologic or microbiologic detection.

PS60

NUTRITION, GROWTH AND MENTAL DEVELOPMENT OF CHILDREN OF URBAN LEPROSY PATIENTS

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This paper describes a cross-sectional study of physical and mental development of a high-risk group of 182 socially deprived healthy children of leprosy patients in their pre-school age to early teens. They were rescued at the age of 4 years from the distress of leprosy colony where they were born, and brought up in government after-care homes,under better environmental and messing facilities. Of them, 135 children could be followed clinically for the development of childhood leprosy. Another 94 children of leprosy patients,but living with their parents in the colony were included for comparison.A group of 150 normal children of similar economic status and age group were included as another control group. It was observed that although better environment,food and training were provided in the after-care-homes, so that the children could be brought into the national mainstream, nevertheless 5 children developed indeterminate type of leprosy during the course of 10 years. This is the first report describing the growth and mental development of children of leprosy patients from the Indian subcontinent.

REHABILITATION

RE1

INTEGRATION OF LEPROSY INTO GENERAL REHABILITATION SCHEMES - AN EXPERIMENT IN BOMBAY.

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In Bombay city, there are 6 institutes which are working for rehabilitation of persons disabled due to causes other than leprosy and 8 institutes in voluntary and Government sectors doing antileprosy work through their 153 leprosy clinics. In 1985, a combined workshop was organised for representatives of these organisations to acquaint them with leprosy and discuss possibilities for including leprosy patients in general rehabilitation programmes. Periodic follow up meetings were organised to review progress and resolve difficulties in implementation. Visits of the staff of leprosy institutes to vocational centres and workshops of non leprosy agencies were organised which acquainted them about facilities available at these centres. A booklet giving these details was printed and made available at 153 leprosy clinics in Bombay for ready reference. Since 1987, 206 referrals have been made by leprosy agencies of which 97 were accepted by non-leprosy agencies for the training programme and 95 patients got job placement and loan facilities.

Such an integrated rehabilitation programme for leprosy patients can be practised in cities and district towns where non-leprosy rehabilitation organisations exist.

RE2

A MODEL FOR THE HEALING OF LEPROSY IN KOREA

Joon Lew, M.D., Ph.D., Lew Institute for Biomedical Research, Seoul, Korea

Leprosy patients in Korea, regardless of their socioeconomic status, had been roaming around near villages to beg the food for their survival, and they were the symbol of fear, rejection, prejudice, hatred, and segregation, until 30 years ago. Since, drastic changes have been noted. For example, a. According to the WHO definition, leprosy as a public problem has already been eliminated since 1983 (before MDT), but the prevalence of tuberculosis is still one of the highest among southeast Asian countries. b. the living standard of the HEALED, once beggars on the street, is now better than that of the ordinary population.These are the results of the unique Korean way of approach. Of course, the chemotherapy, physiotherapy, and corrective surgery played one of the major roles --Physical Rehabilitation. But, the focus should be on the unique Korean way to implement spiritual & socioeconomic rehabilitation. It was not emphasized to the patients that they were the ones to get help from others, insteads, it was emphasized that they themselves should do their own best to support themselves with whatever ability they had and furthermore they should seek the opportunities of helping others -- Spiritual Rehabilitation.

The patients themselves gathered together and settled at resettlement villages. They started with the scratches donated from various resources, raising pigs or chicken. The business at the resettlement villages was not run by the government or charitable organizations, but by themselves. The poultry product from the resettlement villages, now, occupies about 1/4 of that in Korea. And, furthermore, they are now the managers of the industry and the general public provides the labor -- Resettlement Village Movement -- Socioeconomic Rehabilitation. It is roughly estimated that this Resettlement Village Project in Korea has conferred a benefit of about 12 billion US Dollars. Over 70-80% of the residents at Resettlement Villages are not patients. And all of the patients have left, in some Resettlement Villages, which have become ordinary villages.

The victims of Hansen's disease in Korea are now happy, prosperous and are no longer the symbol of fear. They are healed and have become a man with all rights and dignity. Even an active case of this disease is considered as a patient with a disease called leprosy. They restored their MANSHIP fully.

I propose that my experience in Korea, Resettlement Village Project run by the patients themselves not by others, be extended to other parts of the World, and my colleagues here be my partners of this campaign.

RE3

COMMUNITY BASED REHABILITATION PROGRAMME OF THE LEPROSY MISSION, INDIA.

Dr. P. D. Samson, Dr. Paul Jayaraj,
Mr. P. K. Roy, Mr. Shirish Shegaokar.

The community based rehabilitation programme was launched in 1990 at 27 different leprosy hospitals of The Leprosy Mission, India. This programme was planned in a systematic way with in build training programmes for the P. M. W. with emphases on proper selection of leprosy patients, trades and market research.

Six hundred nineteen leprosy patients received the benefits of this programme Following are the observations:

64.45% leprosy patients had a deformity, 47% patients were staying in thatched houses. 78% leprosy patients do not have agricultural land, 82% patients were rehabilitated in rural areas, 78% were male and 22% were female. Twenty different trades were selected to rehabilitate these patients. 8% patient showed failure in this programme.

This study shows that deformity is one of the important factor of dehabilitation of the leprosy patient. But at the proper time, if the community extends the financial help and encouragement, patients can be rehabilitated in their own society.

RE4

FREQUENCY OF LEPROSY NEUROPATHY IN HYPERENDEMIC AREAS OF MEXICO AND ITS CORRELATION WITH CLINICAL, EPIDEMIOLOGICAL AND STRUCTURAL FINDINGS.

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Disability from leprosy neuropathy is a major problem for Mexican patients. According to the National Register of the Programme for Leprosy Control up to 30% of cases present nerve damage at the time of diagnosis. In many cases, morbidity due to peripheral neuropathy increases after diagnosis due to complex logistic problems in the availability of MDT and following withdrawal of patients who live in isolated rural areas. Moreover, multibacillary patients suffering Type 2 reactions receive treatment with thalidomide, a drug known to produce peripheral neuropathy in a proportion of patients. The purpose of this study was to investigate distinct patterns of neuropathy among patients across the leprosy spectrum from different endemic regions in Mexico.

It was found that 70% of all known leprosy patients are multibacillary, and different endemic areas present characteristic patterns of frequency by disease type. In particular, diffuse lepromatous leprosy was found in the Northwest of the country, and patients with this type of polar disease present characteristic nerve damage. Particular disease types were found to determine specific patterns of nerve involvement and correlation of findings was carried out using the following variables: age, sex, type of disease, history of reactions, treatment, electromyography, BCG status, involvement of nerve trunks, nerve biopsy, and biopsy of skin lesions.

Actions to prevent progressive nerve damage and a rehabilitation programme were drawn from our findings to be included in the National Programme for Leprosy Control.

RE5

IMPROVEMENT OF HAND IMPAIRMENT AND LIFE QUALITY BY FIELD DELIVERED SPLINTS AND GRIP AIDS IN DEFORMED LEPROSY PATIENTS

Atul Shah, Neela Shah, S Kingsley & R Ganapati

Comprehensive Leprosy Care Project, Leprosy Management Training Centre, Ciba Compound, Diana Cinema Lane, Tardeo, Bombay 400 034,India

In view of less number of institutions available for comprehensive leprosy care and considering the success of MDT programmes it has become imperative that field programmes should concentrate on related aspects of leprosy deformity, its prevention and correction by such techniques that patient benefits from existing services. In our experience over the last few years, we visualise two important advances made in the deformity care by a new type of simple splints devised by Atul Shah and the Modulan grip aid concept pioneered in India by Ganapati. The presenting author standardised the technique of prefabrication of splints and tested in urban situation for its benefits. The hand impairment particularly claw hand was not only improved but was completely corrected in many instances. In those patients who are beyond reconstructive surgery, modulan grip aids prepared by Kingsley enabled them to carry out activities of daily living and occupational functions in a better ergonomic way thereby improving the quality of life. The principles, techniques, statistical and functional analysis of data of 168 patients receiving these modality of deformity care will be presented.

RE6

INTEGRATION OF CARE OF THE HIGHLY DISABLED IN MDT PROGRAMME -A FIELD EXPERIMENT ON REHABILITATION IN DISTRICTS HYPER ENDEMIC FOR LEPROSY.

R Ganapati, Atul Shah, Rukmini Rao, S Kingsley, Neela Shah, Nagi Reddy and P Sankariah

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No field technology aiming at reasonable care of leprosy patients with high degree of mutilations is still available. Experience gained in a low endemic area by "Borsad Model" (reported elswhere) in offering comprehensive leprosy management, integrating care of all categories of disabled with an ongoing MDT programme emboldened us to extend studies =to two hyper-endemic districts, Ongole and Kurnool in Andhra Pradesh, contributing to a pool of over 3000 disabled patients. Care of the highly disabled at the field level using 'Modulan' grip-aids (Ganapati et al 1983) formed a special subject for training of the government staff of the National Leprosy Eradication Programme. The integrated package of training imparted included usage of pre-fabricated splints (Atul Shah 1991). 332 patients with grade III disability received 473 grip-aids in both the districts, coverage of deformed patients reaching 100% in Ongole. 75% of the patients found the grip-aids useful for daily activities. Patients belonging to the monotherapy era would never have received any care, had it not been for this field intervention. Many deformed patients have been rehabilitated at the community level entirely due to the initiative shown by the government staff.

This experiment has shown that integration of deformity care with MDT programme is feasible in high endemic areas.

RE7

AN IMPROVED METHOD OF ASSESSING 'WORK' AND 'HAND FUNCTION' IN LEPROSY

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The term 'WORK' is used in relation to the physical and psychosocial capabilities of an individual. Many testing systems have been evolved in the past to assess this. Similarly, there are atleast 15 well known tests to assess another closely related activity, namely 'HAND FUNCTION'.

At Karigiri, assessment procedures of these two vital parameters of patient management have been used regularly for some years. However, in the process of continuous improvement of all such activities, these too have undergone a major revision recently, to enable more effective monitoring of both WORK ABILITY, and HAND FUNCTION. Additions that were incorporated, were from similar standard tests used in other neuromuscular diseases.

1) WORK ASSESSMENT is now carried out under (a) Physical Capacity, where actual capabilities related to the use of eyes, hands, and feet are recorded; and (b) Work behaviour, where a sample evaluation of a specific task is carried out. Additionally, psycho-social aspects, such as attitude towards work, trainability, stigma etc., are evaluated.

2) HAND FUNCTION ASSESSMENT includes tests of grasp, grip, pinch strength and fine manipulation, are now standardised and graded into three ranges Normal/Poor/Unable, along with Normal values, to assist the clinician in making a better evaluation of functional ability.

This presentation specifically deals with test procedures for these two assessment areas, including rationale of each sub-test, scoring techniques and interpretation of such scores.

Portions of this work include information presented by the First Author, in the yet un-published "Manual on Rehabilitation, for Primary care Rehabilation workers", Ed. Dr V P Macaden, Hubli, India

RE8

LEPROSY AND REHABILITATION - A PRIMARY HEALTH CARE APPROACH.

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The disease of leprosy is dreaded because it produces deformities. It is in the context of leprosy as a deformity - producing disease that the concept of Rehabilitation comes in.

Due to the low cost effectiveness of institutionlised rehabilitation centres on one hand, and the unsuccessful efforts to combine case detection and chemotherapy with Rehabilitation on the other, the desirability of a new approach that addresses the shortcomings of the aforementioned rehabilitation strategies obviously suggests itself.

The primary Health Care based Rehabilitation programme, currently in operation in Kaduna State of Nigeria, is suggested in view of it's acceptability, afordability adaptability and accessibility.

The programme involves active participation by patients PHC workers and especially the district level governments who contribute a minimum of 150 dollars each, and provide farmlands for use by leprosy patients both on treatment and RFT. The funds are used in provision of farming and cooking equipments, ulcer care materials, subsidy on protective footwear, and surgical operations and health education posters on Rehabilitation.

This method provides a holistic approach to rehabilitation and makes it practicable for rehabilitation and efficient leprosy control programmes to complement one another.

RE9

MODIFIED DISABILITY GRADINGS - A NEW CLASSIFICATION FOR DISABILITY EVALUATION

Atul Shah and S Kingsley

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The disability grading to be adopted for the field programme had undergone innumerable changes from 1970 to date. The WHO technical report 1969 classified the hand, feet and face into 5 grades. In 1980, the WHO suggested the 3 grade classification for hand, feet and eyes and in 1988 it suggested 3 grades but essentially it is 2 grade if one disregards grade '0' and it has combined hands and feet primarily for collection of general data on disabilities and impairments. With increasing importance being given to deformity care programme, it cannot be naturally used as guide to deformity care service (or) a reflection of improvement by physical, medical and rehabilitative intervention. Therefore, a patient who has recovered from sensory motor peresis may still continue in visible deformity data or a patient with visible deformity, who has progressed into contractures may still be in the same grade. Therefore it is imperative that a working classification be designed which can reflect the extent of deformity and disability, the need of the patient for deformity care services, health education, or rehabilitation as well as improvement recorded through deformity care services. A new classifiction is proposed which reflects the above mentioned needs.

RE10

ANALYSIS OF STRESSES IN TWO DIMENSIONAL MODEL OF LEPROTIC FOOT

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The internal stresses developed in the foot skeleton cannot be measured directly in vivo or post mortem. However, using a modelling procedure such stresses can be calculated. A two dimensional articulated model of the foot skeleton, which include cartilages and ligaments, is used in this study and the stress analysis is done by using the GIFTS finite element program. The model is used to analyse stresses in leprosy subjects with deformed feet combined with partial or complete paralysis of certain muscles. Stress patterns in the feet of 3 patients (in different stages of tarsel disintegration) are analysed. The analyses shows that in one patient (where the bone in the mid-foot region has collapsed, leading to plantarward protrusion), the maximum principal stresses are the highest at the protrusions during push off. The clinical data for this patient shows an ulcer at the same spot. The stress analysis for the second patient shows very high stress in the portion where cartilage has become thinner due to a strong local compression and possibly causing the navicular bone to become ejected out (as observed from the X-ray). The third patient analysis shows highest stresses at the forefoot support (where the foot is shortened due to disintegration of the forefoot metatarsal bone, as seen in the X-ray). It is found, from the analyses, that the shape of the foot and the paralysis of muscles are factors which contribute to the development of high stresses in different regions of the foot. It could be stated (from the analyses) that these high stresses developed in certain regions of the foot could be one of the important factors contributing to the process of tarsal disintegration in leprosy.

RE11

ANALYSIS OF STATIC AND DYNAMIC FOOT PRESSURE IN LEPROSY PATIENTS

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Static and dynamic foot pressure measurements are carried out for normals and leprosy subjects using image processing technique. In this method, light images of the foot are obtained by scattering of light (at areas of contact of the foot) on a device called barograph. A software package is developed on an IBM PC-AT to present on-line variations of foot pressures and the path of centres of pressure during walking. Some procedures that are developed for representing the standing and walking foot images are: depiction of centres of pressures, perspective view of pressures, pseudo colouring and half toning. Pressure distributions under normal feet while standing are even and symmetrical. The range of normal average pressures are 2 to 4 N/Sq.cm. In leprosy patients while standing the pressures are uneven, localized and unsymmetrical. The average pressures are higher and the peak pressure is found to increase with deformity. A normal walking pattern is characterised by low mid-stance pressure and high pressures at heel strike and push off phases; the push off pressure being the highest coinciding with high instantaneous centre of foot pressure velocity (CFPV). The normal walking pressures are 3-4 times the

standing pressures. In leprosy subjects, the high pressures are found to coincide with the scars or ulcers. Separate localized peaking of pressures is found to occur in case of early tarsal disintegration (TD) and peaking of pressures in larger area and shortening of foot, in later stages of TD. In the advanced stages of TD, the highest foot pressures are observed during mid-stance compared to heel strike and push off phases. The magnitude of impulse during mid-stance is also found to be the highest for the advanced TD leprosy patients as compared to the normals and it is about 3-4 times the normal value.

RE12

DEVELOPMENT OF PLASTIC FOOTWEAR FOR ANAESTHETIC FEET IN LEPROSY

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The requirements of protective footwear in leprosy are a) It should provide sufficient rigidity to prevent excess pressure under weight-bearing areas of foot and yet have controlled flexibility b) Footwear appearance should not carry stigma of disease c) Acceptable cost. The first can be achieved by inclusion of a spring steel shank between the sponge insole and the plastic sole.

A number of models have been developed for 4 different sizes of footwear. These are currently being evaluated. Changes in material and design are being considered to optimize the life of the footwear and reducing cost. More accurate information is being sought about foot pressure distribution before and after use of this footwear. Trials demonstrate acceptability of the footwear and its protective effects in leprosy and in diabetic patients who exhibit anaesthesia of the feet.

RE13

RISK FACTORS FOR DEVELOPING DISABILITY BEFORE THE DIAGNOSIS OF HANSEN'S DISEASE

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A set of 3302 Hansen's disease pacients diagnosed between January 1970 and April 1991 in Rio Grande do Sul State, Brazil, had their grade of disability evaluated at the moment of the diagnosis. Out of these 3302 pacients, 689 (20.8%) had disabilities of grade 2 or 3. The multivariate analysis has shown that the time elapsed between the beginning of the disease (referred by the pacient himself) and the moment when Leprosy is identified by a physician is an important risk factor for developing disability before the diagnosis: risk of having disability duplicates each three years that Leprosy remains without diagnosis. Other variables identified as significant risk factors by multivariate analysis were: sex (higher risk for males); age (higher risk for older pacients); bacteriological status (higher risk for pacients bacteriologically positive); clinical form (lepromatous cases had the highest risk) and mode of detection (cases detected by active methods had the lowest risk). These results show the importance of early diagnosis to prevent disabilities in Hansen's disease.

RE14

IMPAIRMENTS AND DISABILITIES. THE DIFFERENCE AND IMPLICATIONS FOR LEPROSY CONTROL.

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Leprosy workers are very familiar with the term disability and the compound terms in which the word disability is used e.g. disability prevention and disability grading. Yet, what is usually meant and understood by disabilities in leprosy control projects are impairments as defined by the World Health Organization (WHO). In 1980 the WHO published the International Classification of Impairments, Disabilities, and Handicaps (ICIDH) as a classification for trial purposes to enable health workers to classify health related problems at three different levels:

impairment; organ level, dysfunctioning or changes of an organ or organ system;
disability; the personal level, the possible effect(s) of impairment(s) on the functioning of the person in areas such as locomotion, personal hygiene and household activities;
handicap; social level, the consequences of disease, impairments and disabilities in maintaining or attaining a normal role in the community/society.

In order to be able to describe the health status of a patient and to evaluate the effect of treatment policies on the individual patient or control programs as a whole, it is essential that use is made of a common language and a uniform terminology. The ICIDH offers a conceptual framework to describe and evaluate the overall health status of a patient. Use of the ICIDH concept and terminology will also facilitate the gathering of epidemiological data in order to asses and evaluate the impact of health policy and treatment approaches on the incidence and prevalence of sequelae of leprosy and leprosy neuropathy.

A common language will also facilitate communication. The ICIDH has been widely used in the field of rehabilitation medicine by various disciplines for many purposes. There has been much criticism also. A formal revision procedure of the ICIDH will soon be initiated and WHO collaborating Centres on the ICIDH have already made proposals for a better structured and more practical ICIDH. 'Impairment' and 'disability' are defined and it will be explained how the ICIDH can contribute to a common language regarding the health status of patients and thereby will facilitate registration and research in leprosy control programs.

Brandsma JW, Heerkens YF et al. The International classification of impairments, disabilities and handicaps in leprosy control projects. Lepr Rev 1992;63:337-344.
World Health Organization. The International Classification of Impairments, disabilities, and handicaps. Geneva, 1980.

RE15

A SYSTEMATIC PROGRAMME FOR DISABILITY PREVENTION AT KARIGIRI ("DISLEP") A PRELIMINARY REPORT

Samuel Solomon and Vijayakumaran P

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The feasibility of vigorous Disability Prevention being included into routine leprosy control activities was considered at the SCHIEFFELIN LEPROSY RESEARCH AND TRAINING CENTRE, KARIGIRI. It was noted that in the last few years, all over the world, major fundings had been accorded to the implementation of MDT. It was felt that with minimum additional resources, a systematic disability prevention programme could easily be added on to the existing activities, with good results anticipated.

A comprehensive DISABILITY PREVENTION & LIMITATION PROGRAMME IN LEPROSY was therefore initiated, in 1990, aimed at "preventing/limiting the progression of disabilities among patients, (by the application of existing knowledge and methods), as part of a leprosy control programme"

This programme has inducted about 3000 patients, including those who are Newly-Added, Under-Treatment, and Released-from-Treatment-but-still-under-surveillance. On induction, patients are assessed in detail to identify (1) those who are at a higher risk of developing disabilities; (2) risk factors that are likely to cause initial or recurrent disability; and (3) their need for disability prevention aids, which are provided if necessary. Patient intake was completed in December 1992. They are scheduled for reassessment at 6-monthly intervals for a period of three years after RFT. The study is about half way through the total period of investigation.

Patients and their families are given intensive education to help them identify possible areas of danger and causes of disability, especially in the earliest stages. Our experiences in the implementation of the project, new methods of Health Education, and problems and pitfalls, are presented. A preliminary analysis of baseline disability levels, and periodic changes in the profile, is also presented, as an index of the efficacy of the various intervention activities undertaken.

This project was funded by the IMPACT Foundation, UK.

RE16

PLAN PARA PREVENCION DE INCAPACIDADES EN MEXICO

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El compromiso en México de eliminar la lepra con el uso de PQT, ha permitido curar al 47% de los casos y el 17%

ya está en vigilancia postratamiento, lo que obliga a intensificar las acciones de rehabilitación y prevención de incapacidades con técnicas sencillas, como una estrategia para lograr la curación más integral de los casos. Para ello se aplicó una encuesta que determinara la frecuencia y tipo de incapacidades en los enfermos y su distribución geográfica para ubicar "Módulos de prevención de incapacidades en lepra".

El 1er. módulo piloto se instaló en 1990 para iniciar la capacitación del personal.

Las funciones de estos módulos ubicados en unidades de atención primaria comprenden:

- Capacitación del personal sobre educación a enfermos para prevención de incapacidades.
- Atención de pacientes para la práctica de medidas sencillas como: aplicación de férulas, curación de úlceras, modificaciones al calzado para cambiar puntos de apoyo viciados y a los utensilios de trabajo para evitar quemaduras y traumatismos.
- Referencia de pacientes que requieran atención en unidades de rehabilitación de 3er. nivel.

Resultados de la Encuesta justifican la instalación de estos módulos que han sido bien aceptados por personal de salud y población.

RE17

INFLUENCE OF MDT ON THE INCIDENCE OF DISABILITIES IN HANSEN'S DISEASE

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85 cases who had not disabilities before MDT were investigated. 13 cases have occurred disabilities during 5 years after start of MDT. The incidence of disabilities was 13.68%. Among the 13 cases, 61.58% cases (8/13) of disabilities occurred during the first year after start of MDT. 53.85% cases (7/13) of disabilities were occurred associated with leprosy reaction. Leprosy reaction is still the most common facter associated with disabilities. 46.15% of disabilities occurred without any leprosy reaction. Among them there were 4 disabled patients were found during the first year of MDT. In addition, the incidence of disabilities was also associated with sex and leprosy type, but not associated with the duration of disease and the age of patients. The incidence of disabilities in male (17.19%) was much higher than female's (6.45%), and multibacillary's (MB) was much higher than pacibacillary's (PB). All of the 13 cases were MB patients. None of PB patients in this group had occurred disabilities. Finally, the authors note that although MDT can reduce leprosy reaction, there are still some of the patients could occur disability during or after MDT. Therefore, it's very important to prevent deformities and carry out rehabilitation, when we are widely implementing MDT. It's quite necessary to carry out a more detailed investigation to make clear the association between MDT and disability.

RE18

A STUDY ON THE EFFECTS OF PREVENTION OF PHYSICAL DISABILITIES IN HANSEN'S DISEASE AND TREATMENT BY SIMPLE TECHNIQUES AT A CONTROL PROGRAM ON THE STIGMA

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Hansen's Disease (HD) is a peripheral neurologic disease with high incapacity risk. The surveillance of precocius disabilities can prevent deformities and interrupt the misuse syndrome. It is only possible when prevention and treatment by simple techniques are part of the specific treatment of HD. This study is based on 2122 records collected during the last ten years (1983-93) at the Metropolitan Health Center in Curitiba, Brazil, and it intends to evaluate efficacy of Simple Techniques at the HS Control program. The hypothesis is that the adoption of routine procedures avoid disabilities, or their progression, and favours the normal activities. The present situation of the patients will be known through a questionaire applied to 90 persons (a random sample from the file), in home visits. The sample include 61% men and 39% women, between 15 and 70 years old, living in the metropolitan area of Curitiba. The initial and final degree of disability will be compared, and related to the amount of preventive measures adopted. The data will be submitted to basic statistic treatment, including association test, besides qualitative analysis of significant answers.

RE19

THE DANGERS OF UNDERESTIMATING PERMANENT LOSS OF SENSATION

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It is generally accepted that the WHO disability grading is useful only as a measure of how effectively the programme is detecting cases early. It cannot be used for individual patient follow-up.

This being so, is the WHO causing leprosy workers to underestimate the importance of permanent loss of sensation by calling it Grade 1, compared with, for example, a mobile claw hand which is Grade 2?

In order to determine what happens to patients with Grade 1 disability, 200 patients who were diagnosed in 1987 and 1988 (before the 10gm filament was used) are being followed up by the ALERT Leprosy Control Programme on a 'one-off' visit. The condition of the feet and the hands and any history of ulcers are noted.

The hypothesis being tested is that a two grade disability scale would be more useful. "Presence of Disability" means loss of pressure sensation or any visible disability. "Absence of disability" means no disability or loss of light touch sensation only.

The results of the study will be discussed.

RE20

THE DEVELOPMENT AND ADAPTATION OF THE SEMMES-WEINSTEIN LIGHT TOUCH/DEEP PRESSURE SENSORY TEST IN BRAZIL

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The purpose of this paper is to demonstrate the complexities of adapting technology and developing the sensory testing technique of the Semmes-Weinstein (S-W) monofilaments in Brazil to enable early detection and monitoring of peripheral nerve function in Hansen's disease(Hd). The adoption and diffusion of this innovation involves: identifying and understanding attitudes, knowledge, and beliefs about sensory testing; developing the ability and skills of the testers using the sensory testing instruments; making access to materials and equipment available for sensory testing; and gaining support of governmental and non-governmental agencies and local professionals and experts in decisions to adopt, produce, and teach new sensory testing techniques.

This history of adoption and implementation of the use of the S-W monofilaments in Brazil follows the sequence described in adoption and diffusion theory of innovations. This theory shows how behavior changes

over time and the stages through which new innovations are adopted by individuals and society.

In conclusion, the authors note the sensory testing instrument produced in Brazil facilitated the utilization of the S-W sensory testing technic. It proved to be more accessible, durable, portable and practical in meeting the local needs. Its availability increased health care worker awareness and desire to want and use better sensory testing technology to prevent disability. As a result sensory testing techniques improved, facilitating patient evaluation and treatment and lessening disability.

RE21

COMPARISON OF SENSORY RESULTS OF THE THERMAL TESTER AND THE SEMMES-WEINSTEIN LIGHT TOUCH/PRESSURE IN PERSONS WITH HANSEN'S DISEASE AND WITHOUT KNOWN DISEASE

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Two sensory modalities tested in Hansen's disease have been heat/temperature and light touch/pressure sensation. Results of test using these modalities have been discredited because instrumentation or methods used in field testing have been shown to be variable and not repeatable in the hands of different testers. Two instruments which have been developed that are simple, consistent and repeatable by others are the Thermal Tester sponsored by WHO and the Semmes-Weinstein (S-W) monofilaments. The eletric heat tester and the monofilaments were used in field trials to compare the ability of the two systems to detect early sensory loss and to determine which single sensory modality would be most effective for use in the field.

Ninety persons with Hansen's disease were tested in pre-selected sites on both hands and feet and skin patches with both instruments. Sixty-one persons with no known disease were tested with both instruments in the same pre-selected sites on both hands and feet. Both groups were analized separately.

The results demonstrate a significant difference between the findings of both sensory tests. The S-W monofilaments were more sensitive in detecting and quantifying early sensory loss related to peripheral nerve involvement. The Thermal Tester detected a more gross loss of sensation and was influenced by increased skin keratin layer and battery power.

RE22

RELIABILITY OF MANUAL MUSCLE STRENGTH TESTING IN THE EVALUATION OF PERIPHERAL NERVE DYSFUNCTION IN LEPROSY PATIENTS.

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Manual muscle strength testing is one of the most commonly practiced evaluation techniques in the assessment and evaluation of peripheral nerve dysfunction in leprosy patients. The results of manual muscle strength testing often determine and guide decisions regarding pharmaco-therapeutical treatment (e.g. cortico-steroids and other anti-inflammatory drugs), change of anti-leprosy drug therapy, or surgical interventions (neurolysis and tendon transfers). It is therefore important to have knowledge about the reliability of manual muscle strength testing (MMST). Little is known about the reliability of MMST in general and nothing about the reliability of MMST of the intrinsic muscles of the hand.

In 28 leprosy patients with complete or partial damage of the ulnar or median nerve or ulnar and median nerve the strength of nine intrinsic finger muscles was assessed manually. Muscle strength testing was assessed for one hand only and the testing was performed by two examiners.

The following strength tests were performed:

- Abduction and adduction of the little finger;
- Abduction of the index finger;
- Abduction and opposition of the thumb;
- "Intrinsic" strength test for the four radial fingers.

Testing was performed according to a standardized protocol and grades were given independently by the examiners using the Medical Research Council Scale (grades 0-5). One examiner performed the strength tests again on the third day following the first examination. The reliability coefficients ranged from .84-.99 for both the inter- and intratester reliability. In the presentation it will be explained why the strength testing, testing positions and point of application of resistance, deviate from the 'classical' strength tests of the intrinsic muscles of the hand. Guidelines and suggestions for further research into manual muscle strength testing of the intrinsic muscles of the hand will be given.

RE23

INTER-OBSERVER VARIABILITY IN THE ASSESSMENT OF NERVE FUNCTION IN LEPROSY PATIENTS IN ETHIOPIA AND NEPAL

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One of the major problems in leprosy is to detect early enough changes in nerve function so as to increase chances of recovery and prevent disability. Several tests have been developed to evaluate and measure nerve function and it is extremely important that their results are comparable, especially when performed by different workers on different occasions. We studied inter-observer variability of sensory testing (ST), using a set of nylon monofilaments (NF) and a ball-point pen (BP), of voluntary motor testing (VMT) and also of the assessment of clinical signs of neuritis in leprosy patients, in Ethiopia and Nepal. Duplicate measurements were performed in random order on 50 leprosy patients by two physio-technicians (PT) and recorded using pre-determined scoring scales. In addition, duplicate measurements were performed on 50 similar patients by two para-medical workers (PMW) in Ethiopia.

Observers are compared by plotting for each test the differences in measurements against their mean and calculating the limits of agreement. Proportions of agreement are examined with various criteria. Systematic bias between observers is estimated with matched paired t test. Repeatability and reliability are calculated for each test.

Although comparability depends upon measurement scale, it is found that VMT (MRC scale) is the least variable between observers for all tested nerves except the facial nerve, when performed either by physio technicians or by para-medical workers (72% to 98% complete agreement). The assessment of neuritis signs is extremely variable between observers (complete agreement: 14% to 41%), with a systematic bias and a large spread of values around the mean. For nylon filaments and ball-point pen, inter-observer variability depends upon the type of observer (PT or PMW), the site of test and the status of the patients. When performed by PMWs, agreement between observers appears better for BP (73% to 92% complete agreement) than for NF (35% to 53%), partly explained by the use of a different scale. When tests are performed by PTs, the pattern is less clear, with 32% to 58% complete agreement for NF and 71% to 80% complete agreement for BP. The mean difference in scores vary according to the site of the test, and there is a systematic bias in either direction depending upon the observer. Implications of these findings are discussed with the view to improve comparability for an early detection of nerve damage.

RE24

RELATIVE SIGNIFICANCE OF ABD.DIG.MIN. PALM. INTER, AND 1ST DOR.INTER, WITH REGARD TO DETECTION FOLLOWUP, EVALUATION OF ULNAR NERVE DAMAGE

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In patients with ulnar nerve damage instead of testing all the muscles in the hand for convenience, simplicity and feild use it is commonly agreed to test the muscles ADM, Ist D.I. In most cases these muscles are sufficient for detection and follow up. We have studied an additional muscle in 50 cases, Palmar interrosei of the little finger - adductor of the little finger. This was found to be involved earlier than the other muscles and better suited for detection but has certain disadvantageous for follow up. Whereas the other two muscles were suitable for detection and evaluation, provided the trick movements are avoided. Necessary precaution taken be mentioned in this regard. We feel that this additional muscle testing may be helpful in the field for early detection and hence be recommended since it is simple.

This muscle belly is small and cannot be seen as compared to Ist dorsal interrosei. Hence the gradient of the muscle on MRC scale is not possible for grading.

RE25

LATE RESPONSES IN TUBERCULOID LEPROSY

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A study of late responses (F-wave and H-Reflex) of posterior tibial nerve was done in 25 patients of freshly diagnosed tuberculoid leprosy and data were compared with 15 normal persons which served as control.

F-wave latency was delayed in 18 patients (72%, mean±3SD = 54.34±16.04 msec, t=7.21, p= $<$.001) and F-wave conduction was prolonged in 20 patients (80%, mean±3SD = 38.72±12.84 m/sec., t=7.66, p= $<$ .001) showing significant involvement of alpha motor axons as F-wave is produced by centrifugal discharges from individual neurons each of which is initiated by antidromic axonal volley.

H-Reflex latency was delayed in 12 patients (48%, mean±3SD = 31.93±4.44 msec, t=5.54, p= $<$.001) and H-Reflex conduction was prolonged in 4 patients (16%, mean ±3SD = 49.33±7.35 m/sec., t=4.46, p= $<$.001) showing involvement of H-Reflex arc which is a monosynaptic reflex depending on group Ia afferent fibers from muscle spindles and alpha motor axons.

Late responses were deranged regardless of clinical involvement of posterior tibial nerve, thus study of late responses is an important tool in evaluating nerve damage in early stages of tuberculoid leprosy.

RE26

MONITORING OF PERIPHERAL NERVE INVOLVEMENT UNDERLYING DISABILITY OF THE HAND IN HD: A SEVEN YEAR FOLLOW-UP IN A U.S. POPULATION

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This study expands upon traditional disability measurement to include, as simply as possible, direct measures of peripheral nerve involvement of the hand in a U.S. patient population. Patients treated in the National Ambulatory Hansen's Disease Program, and the Gillis W. Long Hansen's Disease Center were given standard hand screens based on that developed in the Hand and OT Department at the Center beginning in 1984. 4,000 evaluations are reviewed. Patient data is reviewed in two-year intervals for frequency and severity of peripheral nerve involvement as compared with disability, and for progression/regression in function of patients on subsequent exams. Particular attention is given to patients who had zero disability at the time of beginning antileprosy medication treatment. Results show a number of patients continue to have peripheral nerve changes during treatment, that patients who change in peripheral nerve status more often become worse than improve, that peripheral nerve involvement and disability of the hand continue to occur across the disease spectrum, that the frequency of peripheral nerve involvement in the U.S. although slightly less than in patients seen at the GWLHDC is as high as over half of the patients measured, and that some patients who were normal by monitoring measures on initial treatment later develop peripheral nerve complications. These findings underline the need for such measures in HD populations, and for continued research into treatment capable of reducing the peripheral nerve involvement common in the disease, in particular loss of sensory and motor function of hands.

RE27

SEMMES-WEINSTEIN MONOFILAMENT DETECTION THRESHOLDS: A COMPARATIVE STUDY

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Semmes-Weinstein monofilaments have been found to be repeatable within a small standard deviation relative to other sensory testing instruments, making this test an optimum choice for an objective sensory test. Normal sensory detection thresholds for the entire body have been established by Weinstein for the test. The stimuli force produced by the filaments was originally tested by Weinstein. He found a nylon filament of .005 inch diameter, 38 mm in length, produces a mean force of 68 milligrams, and is predictive of normal for the hands and most of the body. However, manufacturers of the nylon filament material accept an 8-10% tolerance in diameter when making filaments. This small change in diameter results in a small variation in force among filaments of a given size. It has not been previously determined what effect this small variance in force makes on accuracy of the .005 inch filament to detect normal thresholds. This study compares the 2.83 (index number) filament available through the Gillis W. Long Hansen's Disease Center (mean of 60 mg) with those from North Coast Medical (mean of 95 mg). These along with heavier and lighter filaments of measured force are used in a standard testing protocol for hands, arms, face, legs, and feet in 100 subjects by 6 examiners. Results show little difference in the two 2.83 filaments, and confirm this filament a good predictor of normal for most of the body. It is suprathreshold for the face, making use of a lighter filament possible, and subthreshold for the plantar surface of the foot which requires a slightly heavier filament for normal threshold detection.

RE28

MONITORING PERIPHERAL NERVE INVOLVEMENT DURING REACTIONS

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Reduced sensibility and muscle function is common in Hansen's disease especially in patients experiencing reactions. Monitoring sensory and motor status is important in establishing a baseline and for monitoring worsening or improvement in patients under treatment. The Semmes-Weinstein Monofilaments are an objective measurement device used to map sensation in the hands and feet. The resulting map provides a visual diagram of the level of sensation. Mapping is combined with the manual muscle test of intrinsic hand musculature. Repeating sensory and motor evaluations at regular intervals during the treatment of reactions provides feedback on the effectiveness of treatment including anti-inflammatory medications etc. in reducing the changes in function. Three case studies are presented. The first shows a patient experiencing reaction with normal sensation that remains normal throughout treatment. The second is a patient who has a loss of sensation in the ulnar nerve distribution without improvement under drug therapy. The third patient demonstrates varying levels of sensation as prednisone and thalidomide dosages are increased and tapered. This paper discusses the use of an objective repeatable technique to track improvement and degradation of sensory and motor function which can be directly compared with treatment during reactions in Hansen's disease.

RE29

NYLON FILAMENT MEASUREMENTS IN LEPROSY PATIENTS AND NORMAL SUBJECTS IN THAILAND

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Semmes Weinstein filament measurements were made on the hands and feet of 112 normal subjects and 25 leprosy patients at the McKean Rehabilitation Center, Chiangmai, Thailand to determine reliability and normal thresholds. In 64 normal subjects occupation was rated on a 3 point scale for degree of physical activity. Testing was also made on 34 patients with a known history of ulceration to obtain hand and foot injury thresholds. Between tester and between session reliability was found to be

high (ICC = .88 - .93) for all sites tested. Statistical analysis showed normal filament thresholds were significantly related to age ($p < 0.002$) and occupation ($p < 0.001$). Subjects who performed heavy and medium work had significantly higher sensory thresholds than subjects engaged in light work. Normal filament thresholds are presented for five sites in the hand and foot, for subjects under 50, and over 50 years of age. Injury thresholds based on a history of ulcerations in 30 feet and 24 hands are also presented.

Results demonstrate the reliability of nylon filament testing in a field setting. In this study age and the physical nature of occupations significantly increased normal threshold values. Care should be taken in interpreting sensibility tests based on normative data.

RE30

IDENTIFICATION OF PERIPHERAL NERVE DAMAGE IN HANSEN'S DISEASE AND ITS IMPLICATIONS FOR CONTROL PROGRAM MANAGEMENT

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Peripheral nerve(PN) damage is the primary cause of disability and deformity in Hansen's disease. Disability and deformity are the visual reminders to society that the individual has had the disease.

This study included 85 patients on MDT at Citrolandia Health Center in Betim, Minas Gerais-Brazil from February 1987 to May 1990. The study analized all patients with more than 2 exams by February 1992. The study analized the first and last upper extremity exams of peripheral nerve(PN) involvement and compared them with the World Health Organization(WHO) Disability Grade.

Results demonstrated that 91% had PN involvement in the beginning compared to 26% with WHO disability. Of those with no WHO disability, 88% had peripheral nerve involvement in the beginning which significantly decreased to 51% with PN involvement at the last evaluation. The authors concluded that individuals with PN involvement were at high risk of permanent disability if nerves were not monitored and if adequate treatment was not provided for neuritis and reactions. Adequate abbreviated base-line neurological exams and periodic monitoring demonstrated that permanent disability and PN damage could be avoided or lessened. In this study the WHO disability grading showed an inadequate ability to identify and monitor persons at risk. It also underestimated resources needed for prevention of disability control programs.

RE31

ASSESSMENT FOR QUIET NERVE PARALYSIS IN FIELD

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A seven grade scale for nerve damage status (grade-0 indicating no evidence of damage and grade-6 indicating complete sensorimotor paralysis) was developed and tested in the field. Reproducibility of the technique could be improved to 82% with experience and training.

12 contiguous villages, with a population of 25,000 was the study area, and 246 patients needing treatment were identified. 64 (26%) of them were found to have thickening of one or more nerve trunks.

Nerve thickening was found to be primarily a male gender related problem. Multiple nerve trunk thickening was primarily an adult male problem. 58 (91%) of the 64 patients with nerve trunk thickening had some evidence of nerve trunk damage. Most of the thickened nerve trunks (95% or 144/152) showed evidence of damage. About half of the 238 non-thickened nerve trunks also showed evidence of damage.

In leprosy patients having one or more thickened nerve trunks, other nerve trunks also must be assessed for evidence of nerve damage. Our studies also show that in patients without any thickened nerve trunks, risk of nerve damage is extremely low.

RE32

QUIET NERVE PARALYSIS ASSESSMENT WITH RESPECT TO MDT AND CORTICOSTEROID THERAPY

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Observations reported here are based on prospective field studies for evaluating the seven grade Quiet Nerve Paralysis (QNP) assessment scale. Nerve damage status was assessed in 187 nerve trunks of 24 patients before putting them on Multi Drug Therapy (MDT), and again 3 months later. Variability data on the status of nerve damage was obtained through a parallel study on comparable 272 nerve trunks. After MDT, in most cases there was no change in nerve damage status while there was deterioration in a small though statistically significant number of nerve trunks.

From another group of 64 patients with thickened nerve trunks, from 12 villages with 25,000 population, 31 patients were allotted for MDT along with oral corticosteroids for three months; and another comparable group of 25 patients was given only MDT. All patients were reassessed for nerve damage at the end of three months. Of the 31 patients belonging to the first group, steroids could not be administered in 13 because of contra-indications, and 6 patients were irregular. Observations on the remaining 12 regular patients did not suggest any role for steroids in preventing or correcting quiet nerve paralysis.

RE33

A STUDY ON FACTORS INFLUENCING THE RECOVERY OF MOTOR NERVE FUNCTION WITH STEROID THERAPY

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This Non concurrent prospective study was conducted on leprosy patients receiving steroid therapy for motor nerve paralysis during the period 1988-91. Patients received 30 mg prednisolone daily during the period 1988-89. Due to a policy change, patients received 45 mg daily during the period 1990-91.

Of the 61 patients, 36 received 30 mg and 25 received 45 mg. 44 were males and 17 were females.

In both groups the dosage was reduced by 5 mg. once in 2 weeks. The patients were assessed by voluntary muscle testing once in 2 weeks. The effect of the duration of muscle paralysis at diagnosis and muscle power at the first visit, on recovery rate were also studied.

There was a significantly higher recovery rate in those who had been administered 30 mg prednisolone daily. The recovery rate was significantly higher when the muscle power at the first visit was greater than grade 3. There was a

greater chance of recovery if the duration of paralysis was less than 3 months. The preliminary findings suggest that higher dosage of sterioids do not increase the recovery from muscle paralysis among leprosy patients.

RE34

THE NATURE AND THE LOCATION OF PERMANENT DAMAGE TO PERIPHERAL NERVES IN ADVANCED TREATED LEPROSY

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Neuropathological observations in leprosy are usually confined to cutaneous sensory branches. The few reports on nerve trunks in leprosy, of invariably active cases, give little or no account of nerve regeneration. However, in treated leprosy, we had previously observed large-scale nerve regeneration at the 'predilective damage sites' of nerve trunks. The regeneration, which followed the decrease of inflammation, was functionally ineffective.

In order to characterize the permanent damage to and the regeneration in peripheral nerves of advanced treated leprosy nine full-length nerves dissected from amputated legs of leprosy patients were studied. All patients (2 BT, 3 BL and 4 LL cases) had lost sensation 10-40 years ago and they were released from antileprosy treatment. The main histological findings included: 1. The resection line in the posterior tibial nerve showed numerous regeneration clusters. 2. The regenerating axons persisted for decades. 3. The numbers of Schwann cell processes and regenerating axons decreased centrifugally and were inversely proportional to the endoneurial fibrosis. 4. The dermal nerves and superficial sensory endings were destroyed beyond recognition. 5. The sural nerve was transformed into a fibrotic cord.

Conclusions: 1. Irrespective of the original classification, the leprous nerve damage was most severe at the dermal level and decreased centripetally. 2. The total destruction of the distal neural elements was responsible for the ineffectiveness of the nerve regeneration observed proximally. 3. The sural nerve was not representative in advanced leprosy. 4. The present study also contributed to the understanding of the spreading of leprosy in peripheral nerves.

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RE35

CLINICAL ASSESSMENT OF EARLY LEPROUS NEUROPATHY WITH ELECTROPHYSIOLOGIC CORRELATION

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This report describes the neurological and electrophysiological examination of 35 subjects with early leprosy (average duration of symptoms 3.4 years, average time since diagnosis 6 months). Clinical examination in the distribution of bilateral median, radial and ulnar nerves was performed with the following clinical modalities: Nerve palpation (NP), manual motor testing (MMT), pressure sensation with 0.05 gm. monofilaments (PS) and thermal sensation with a thermal sensitivity device (TS). 59% of ulnar nerves had abnormality of at least one of the four tests versus 53% of radial nerves and 31% of median nerves. NP was the most frequent clinical abnormality for all nerves. Leprosy cases were grouped into minimal, moderate and severe neuropathy categories based on the number of abnormal nerves, and the number of abnormal modalities for each nerve. Thirteen (37%) had minimal neuropathy, 16 (46%) moderate and 6 (17%) severe neuropathy.

Unilateral electrophysiologic studies were performed on the leprosy subjects and 32 age matched normal subjects. Abnormal or absent responses were found in 54% of ulnar sensory, 37% ulnar motor, 37% radial sensory, 29% median sensory and 20% of median motor responses among the leprosy subjects. Low sensory amplitudes and drops in amplitude and NCV over the across-elbow segment of the ulnar nerve were the most important findings. Both clinical and electrophysiologic abnormalities were positively associated with duration of symptoms, but not with age or type of leprosy. The four clinical modalities were compared by crosstabulation with the electrophysiologic data. This yielded the following overall positive predictive values: TS= 95%, PS= 92%, MMT= 84% and NP= 70%. Overall negative predictive values were: NP= 75%, PS= 71%, TS= 69%, MMT= 66%. An index for rating diagnostic tests showed the thermal sensitivity device and monofilament pressure sensation testing to have nearly equivalent accuracy in predicting electrophysiologic abnormalities. Both were superior to NP and MMT as tools to identify neurofunctional deficits in leprosy.

RE36

A LONG-TERM OBSERVATION ON THE EFFECT OF TENDON TRANSPLANT OF THE POSTERIOR TIBIAL MUSCLE IN THE CORRECTION OF FOOT DROP OF LEPROSY

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A 4-15 year observation on the effect of tendon transplant of the posterior tibial muscle through the subcutaneous tube or through the interosseus membrane in correcting 37 foot-drops of 35 leprosy patients was reported. The recent results of the above mentioned two kinds of surgical procedures were satisfactory. The long-term effect of 30 footdrops which were corrected by transplanting tendons ended and fixed at the foraman of the intermediate or lateral cuneiform bone remained satisfactory("excellant"in 15, "good" in 13, "improved" in 2) for a stronger contractility of the transplanted tendons, as regards the results of those corrected by transplanting tendons which were ended and fixed at the tendon of the anterior tibial muscle, the results of the first 4-10 year observation were "good" in all 7 foot drops corrected, but their results changed to "improved"in 3 and"no effect"in 4 cases 9-15 years after the correction due to the relaxation of the tendons transplanted. The longer the post-operation time, the more serious were the complications. In the 37 feet treated, there were 4 feet with plantar ulcers, 5 with shortened toes, 1 with arch reversed, 1 with joint problem and 6 with claw toes during the period of the first 4-10 year observation, but there were 14 feet with plantar ulcers, 10 with shortened toes, 4 with arch reversed, 2 with joint problem and 9 with claw toes during the 9-15 year observation. Some cases of them suffered from a combination of several kinds of deformities.

The importance of regular follw-up, health education of self care for patients and implementation in self care through out the life time was emphasized. The author suggested that the method of tendon transplant of the posterior tibial muscle ending and fixing at the tendon of the anterior tibial muscle was only suitable for patients of old age with low labour ntensity.

RE37

TENDO-ACHILES LENGTHENING ALONG WITH TIBIALIS POSTERIOR TRANSFER FOR CORRECTION OF FOOT-DROP - A FIVE-YEAR FOLLOW UP

Lobo D, Chellam P, Arulprakasam P, Kamala.

Tibialis Posterior Transfer is the routine procedure for the correction of FOOT-DROP due to common peroneal nerve damage in Leprosy. If done, correctly, it gives good results with a good range of movement and satisfactory gait.

However, we have observed that in due course, the action of the transfer tendon weakens and the foot reverts to plantar-flexion because of the powerful Tendo-Achiles muscles acting against the transferred Tibialis Posterior.

In order to avoid this problem, we have routinely performed a Subcutaneous Lengthening of Tendo-Achiles simultaneously with Tibialis Posterior Transfer. It facilitates additional range of dorsi-flexion and weakens Tendo-Achiles, thus preventing its counter-action.

A follow-up of SEVENTY ONE (71) patients who underwent the combined procedures in our Centre from 1984-1988 is presented using the following parameters:

- Range of dorsi-flexion
- Gait

The advantages/disadvantages of the procedure are discussed.

RE38

"TRAC OPERATION" - A NEW TECHNIQUE FOR RECONSTRUCTION OF TRANSVERSE METACARPAL ARCH ALONG WITH CORRECTION OF ULNAR CLAW HAND

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The lesions of leprosy in the ulnar nerve at elbow level tend to paralyse the intrinsic musculature and produce characteristic deformity in ring and little finger which is called ulnar claw hand. The procedures aimed at correction of such claw disregard the movement of transverse metacarpal arch which is essential for pulp to pulp pinch action of thumb and litle finger as well as cupping of the hand required for eating rice or making a bolus of food. More often it is not possible to attain these functions by tendon transfer because of its straight line of action. Some surgeons have attempted to correct this anomaly with varying results. The author has devised a new technique by modifying "lasso" procedure using ulnar slip of flexor superficials to attach it to the Abductor Digiti Minimi at the base of the proximal phalanx. Thus the flattened transverse metacarpal arch is corrected and protraction movement occurs as in normal hand.

The technique in detail and results will be presented.

RE39

EXTERNAL FIXATORS & DISTRACTORS IN LEPROSY.

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Soft tissue contractures in the hand are usually overcome with POP casts,skin grafts,flaps,dynamic spl+ints.However contracture of volar capsule is not easily corrected by these methods.
For the last two years we are using the external fixators and distractors deviced by Dr.B.B.Joshi (used in cases of fractures)in:1)Fixed flexion deformity of PIP joints:to release soft tissue, including capsule,contracture.2)Thumb paralysis with fibrotic adductor.(3)After sequestrectomy of fingers or toes,to keep-temporary-the normal length,till further surgery is done.4)In wrist drop correction,after bone grafting,to keep the wrist in extension.The advantages are:1)Lengthening of all tissues,including neurovascular bundle,is achieved gradually over a period of 3-4 weeks.(2)The volar capsule resistance is easily overcome without surgery & risks of joint damage. (3)In cases of first web contracture the distractor keeps the thumb in the desired position while preventing the split adductor from re-uniting.(4)The fixators can be inserted under local anaesthesia,with minimal or no trauma.(5)As the distractor completes a full rotation a 1mm lengthening is obtained and the desired results are achieved in 3-4 weeks,as against the usual 2-3 months required by POP casts or physiotherapy.
Results:out of 36 fingers/thumbs operated so far,29 had excellent results (i.e.PIP at 180 , thumb in full opposition),3 had good results;2 fingers had pin-track infection:in 2 cases the fixators came out after 2 weeks,however good results were achieved by that time.We feel that external fixators and distractors can and should be used more frequently in leprosy.

RE40

CORRECTION OF CLAW HAND AND RESTORATION OF METACARPAL ARCH BY INTRINSIC REACTIVATION

LONG TERM FOLLOW-UP STUDY IN 158 HANDS

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Clawing of fingers due to ulnar paralysis in leprosy patients is often associated with either flattening or reversal of distal transverse metacarpal arch. Restoration of this arch is necessary to facilitate cupping of palm. In order to correct both these deformities, intrinsic reactivation procedure with insertion of five tails of the motor into interossei and hypothenar tendons was performed in 238 hands at this centre since 1977. 158 of these hands were followed up for periods ranging from 1 year to 13.5 years (mean 4.5 years). The results were as follows: Appearance was good in 60.4%, fair in 18.2% and poor in 21.4%. Function was good in 70.4%, fair in 23.4% and poor in 6.2%. Fist closure was good in 81.9%, fair in 14.1% and poor in 4%. Restoration of distal transverse metacarpal arch was good in 78.5%, fair in 13.4% and poor in 8.1%. The reasons for poor results were analysed and suggestions for better results recommended.

RE41

CORRECTION OF CLAW FINGERS BY LASSO PROCEDURE IN HANSEN'S DISEASE

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Lasso procedure(Zancolli) is a combination of dynamic and static principle.In this technique the transfered tendon is attached to proximal pulley(A_1) under proper tension.This transfer helps in preventing hyper extension of metacarpophalangeal joint and initiates flexion of proximal phalanx during flexion of fingers.From March 1987 to June 1992, 135 hands were corrected by this procedure at Central Leprosy Teaching and Research Institute, Chengalpattu, India.Out of which 113 patients came for post operative follow up varying from 6 months to 5 years.Left hand in 53 and Right hand is 60.Age of the patient varied from 11 to 60 years.Deformity and function of the hand was assessed pre and post operatively. Correction of deformity was good in 99, fair in 12 and poor in 4.Functional improvement was good in 64, fair in 45 and poor in 4.Direct Lasso was done on 109 hands and Indirect Lasso on 4 hands. The complications were Swan neck deformity in 5 hands and infection in 5 hands.The correction failed in four hands.One due to severe infection and the other three may be due to streching of the transfered tendon.The results of the procedure were better(97% satisfactory) compared to other tendon transfers(70%).The procedure is simple, complications are less and reeducation is easy.

RE42

INTRA OCULAR LENS IN LEPROSY

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Intra Ocular Lens has been accepted as the best method of rehabilitation for aphakia. Though it is known that simple cataract extraction is well tolerated in Leprosy, one is not sure whether the same is true with Intra Ocular Lens. There is no specific report in the literature about this aspect. This paper describes our experience with 20 Leprosy cases. Both Lepromatous and Tuberculoid type were included in the study. Out of the 20 cases 9 were active cases with Bacillary Index ranging from 0.7+ to 3.3+. In Lepromatous Leprosy 7 patients had Erythema Nodosum Leprosum reaction at the time of surgery. Five of these were treated with Thalidomide. Patients were followed up for a maximum period of 5 years. Visual recovery, Post-operative complications and their management are discussed.

RE43

1.DENATURED MUSCLE AUTOGRAFTS IN PERIPHERAL NERVE REPAIR - SURGICAL TECHNIQUE

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Denatured muscle autografts for peripheral nerve reconstruction is a novel technique, that has proved useful in the repair of traumatised nerves, and has now been adapted for use in leprosy nerve trunk damage. Localized lesions in the median nerve, at the wrist, and the posterior tibial nerve, at the ankle, were excised in carefully selected patients, and the nerve gap repaired with a muscle graft. The details of the surgical technique will be described.

Results of clinical trials in South India and at ALERT will described in the accompanying papers.

RE44

2.DENATURED MUSCLE AUTOGRAFTS IN PERIPHERAL NERVE REPAIR - RESULTS ON LEPROSY PATIENTS

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DD Palande, A Subramanian and TS Narayanakumar
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Autologous muscle grafts were used to repair 41 mixed peripheral nerves (8 median, at the wrist, and 33 posterior tibial, at the ankle) in 32 leprosy patients, who had total anaesthesia and analgesia of the area supplied by the nerve. The aim was to assess the effectiveness of this technique in restoring protective sensation to such patients. The study has been in progress since November 1989, and the current clinical results will be presented. Follow - ups of 3 to 36 months indicate that the progress in sensory recovery, after grafting, is slow, but encouraging, particularly in the recipients of grafts in the median nerves.

RE45

REPLACEMENT OF THE MAIN SENSORY NERVES QF HANDS AND FEET IN LEPROSY PATIENTS WITH FREEZE-THAWED MUSCLE AS GRAFT MATERIAL.

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Autologous nerve graft material for leprosy patients has previously not been available since conventional graft material in most cases has been affected by the disease. A method of using autologous freeze thawed muscle is now available.

To study the possibility of restoring sensation of the palm of the hand and the sole of the foot of treated leprosy patients with total loss of sensation, 13 patients had 19 nerves (18 Post. Tibial and 1 Median) resected and replaced with freeze thawed autologous muscle grafts. The myelinated axon population at the upper and lower resection line was assessed per-operatively on frozen sections.

Pre-operative assessments and 3 monthly reviews, including tests for Tinel's sign, pain, light touch, 2-point discrimination (static and moving), temperature, vibration, joint position, sweat, texture discrimination and NCV, were made. Longest observation time was 28 months. Graft length between 45 and 90 mm.

In all grafted nerves the Tinel's sign has migrated past the distal end of the graft. Return of sensation for vibration, weighted pins and sweat function have been observed. Subjective remarks such as 'beginning to feel the ground' and 'getting less ulcers' have been observed.

The results are displayed and discussed.

RE46

NEUROLYSES ET DECOMPRESSIONS NERVEUSES

Raymond Bernardin, Thomas Berman

Institut Cardinal Leger contre la lepre (HAITI)

Etude de 162 cas de decompression et neurolyse pratiques a l'Hopital Cardinal Leger de Sigueneau Haiti.

Essai de classification anatomoclinique.

RE47

RESULTS OF ULNAR NERVE DECOMPRESSION IN LEPROSY PATIENTS

Marcos Virmond, Lucia Camargo, Stella Almeida and Frank Duerksen

The ulnar nerve is the most commonly involved nerve in leprosy leading to clawing of the fingers, instability of the thumb pinch and lack of sensation in the hand. Although clinical treatment of ulnar nerve neuritis with steroids is of some help, the peculiar anatomical condition of this nerve in the elbow calls for surgical release to achieve full management of this condition.

Tirty leprosy patients with ulnar nerve involvement previously treated with steroids were submitted to ulnar nerve decompression at the elbow, including opening of the Osborne's ligament and epireurotomy. The results were assessed by means of progressive Semmes-Weinstein monofilaments test and VMT. The conclusion is that surgical decompression of the ulnar nerve is valuable in most cases of ulnar nerve neuritis.

RE48

RECOVERY OF SENSATION BY NERVE DECOMPRESSION USING SELECTIVE MESHING OF THE EPINEURIUM.

Kentaro Hatano, Aprue Mong, Philomena Commons,

Christian Leprosy Centre Chandraghona, CTG. Bangladesh

Following the presentation by W.J.Theuvenet et.al. at the 13th International Leprosy Congress on nerve decompression by selective meshing of the epineurium, 125 cases of Posterior Tibial nerve decompression have been performed.

Recovery of sensation of the plantar surface of the foot was observed as follows :

24% : Good improvement

43% : Moderate improvement

32% : No improvement

We also noted a decrease in the frequency of hospital admission for ulcer care in many of these cases.

We believe that this operation should be considered a standard procedure for the anesthetic foot.

RE49

NEWER TECHNIQUES FOR RESURFACING THE PLANTAR ULCERS

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With the advances in plastic surgery the plantar ulcer defects in leprosy no longer should remain an enigma to surgeons dealing with the same. The newer techniques applied by author are (a) reconstruction of heel defect by flexor digitorum brevis myocutaneous flap (1985), (b) neurovascular island pedicle flap for 1st and 2nd matatarsal head ulcers (1990). (c) retrograde medial plantar artery island flap (unpublished) for ulcers on 3rd, 4th, 5th matatarsal head or the lateral aspect of the sole of the foot.

From a series of 53 cases operated 15 for (a) 35 for (b) and 3 for (c). The inference of benefits and drawbacks of each technique is derived. The details of surgical techniques and results will be presented.

RE50

A TEN-YEAR OBSERVATION ON THE CURATIVE EFFECT OF SURGICAL OPERATIONS FOR CORRECTION OF LEPROSY DEFORMITIES --- A REPORT OF 86 CASES

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△ Shanghai Zunyi Hospital, China

★ Jiashan County Sishancun Hospital, Anhui Province, China

Several kinds of surgical operation for correction of leprosy deformities performed on 86 cases are reported. The indications and the criteria for curative effect assessment are also discussed. The long-term effect are satisfactory. The authors emphasize the importance of restoration of the function of adductor muscle for the correction of thumb deformities and they believe that the corrections of foot and ankle deformities are important in the treatment of plantar ulcer.

RE51

SURGICAL REHABILITATIVE NEEDS OF LEPROSY PATIENTS RELEASED FROM CONTROL THE KARIGIRI EXPERIENCE

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The Karigiri Leprosy Control Project, in Tamilnadu, South India, has, since the early 70's, Released From Control (RFC), as cured, about 20,000 leprosy patients. A study was undertaken to evaluate the surgical rehabilitative needs of such patients, and the magnitude of the problem.

Information could be obtained only for 16,601 patients. 56% who were alive, were assessed for their surgical needs, based on a three-tier referral system. The first screening was undertaken by Para-Medical Workers, who then referred 13% for more comprehensive assessment by a physiotherapist, specially trained in line with the objectives of the study. The final review was by a Surgeon, who then decided the type of surgical intervention, if required.

To our surprise, only about 15% of these patients actually required surgical assistance. Again, of those who were identified as requiring surgery, only a small proportion actually felt they needed it, since they had adapted themselves fairly satisfactorily, to living with the disability. Cured leprosy patients do not come under the purview of routine leprosy control activities. It would be best to provide for their needs in the regular programme itself. However, since the magnitude of the problem is actually fairly small, one must aim for an equitable distribution of available resources.

RE52

CORRECTION OF MILD AND MODERATE SADDLE NOSE DEFORMITY IN LEPROSY BY ONE STAGE PROCEDURE

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Leprosy sometimes causes deformities of nose in certain groups of patients where nasal ulcerations and destruction is substantial. One such deformity is saddlenose deformity. The conventional procedures involving acrylic processes are not only cumbersome but the result of correction does not correctly match the nose of facial features. A single stage correction procedure to restore nasal shape for moderately deformed noses involving bone graft has been in practice at Central JALMA Institute for Leprosy,Agra for almost a decade. The results are gratifying with fewer donar site problems. The Osteo-Periosteal grafts from second metatarsal have been used to restore the dorsal crest. These grafts not only ensure better take-up but also a satisfactory moulding and insitu survival for long time.

Over-ridding of toe is a post-operative problem which has been tackled by correcting the surgical syndactyly. Plantar ulceration in the donar foot has not been observed. Technical details,clinical results will be discussed supplemented with post operative radiological findings.

RE53

EYEBROW RECONSTRUCTION BY MEANS OF A FREE GRAFT TAKEN FROM THE HAIR BEARING SCALP OF LEPROMATOUS PATIENTS

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30 missing eyebrows were reconstructed by means of a free graft taken from the scalp. This method appeared to be relatively simple to perform and safe. It was completed in a single stage and didn't require hospitalization. Eight months after each operation we could evaluate the appearance of the patients, the growth of each eyebrow and also the relation between the mode in which the hair bearing skin grafts took to their recipient bed and further growth of the hair.

RE54

EVALUATION OF COMMUNITY BASED REHABILITATION FOR LEPROSY PATIENTS IN SOUTH INDIAN EXPERIENCE

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THE LEPROSY MISSION
PHILADELPHIA LEPROSY HOSPITAL, SALUR,
ANDHRA PRADESH, INDIA.

59 Leprosy patients were chosen for community based rehabilitation over a period of four years. These patients are from the Leprosy Control Unit, Philadelphia Leprosy Hospital, Salur, of South India.

The following were the trades:

Vegetable, Flower & Tanning business, Tea Stall, Petty shop, Cycle shop, Cart & Bullock, Buffalo and Caster Oil production.

The data was collected by interviewing the patients. The interview schedules were prepared after pretesting on ten rehabilitated patients of other Leprosy Control Unit.

The parameters taken for evaluation were marital status, family size, educational level, caste, presence of deformity, income, community acceptance and repayment of loan.

The results of the study will be discussed.

RE55

ELIMINATION OF LEPROSY AND ITS COMPLICATIONS: THE CASE OF HAND NEUROPATHY.

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Ulnar, radial, and median nerve involvement clinically manifest as sensory loss, autonomic and motor dysfunction of the hands are common findings in a high proportion of Mexican patients with leprosy. In specialised centres, up to 70% of the total of cases present symptoms and signs of peripheral neuropathy involving one of both hands. This study was carried out in 100 patients in order to provide early diagnosis, and therefore, to prevent complications leading to disability and deformity of the hands.

The diagnosis of leprosy was carried out by dermatologists using the Ridley and Jopling criteria. A detailed anatomical map of clinically normal and damaged nerves was used and patients were classified accordingly. Nerve biopsy was taken in a proportion of patients included in this study, and correlation with electromyography and other clinical data was performed. The role of secondary amyloidosis in hand neuropathy was investigated and surgical procedures for hand rehabilitation were performed in cases expected to recover 30% or more by established functional criteria.

Strategies to prevent and treat leprosy complications secondary to neuropathy of the hands, were included in the National Programme aiming at the elimination of leprosy.

RE56

REHABILITATION OF LEPROSY HANDICAP BY MODULAN GRIP-AIDS AN EVALUATION

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Rehabilitation of advanced deformed patients who are beyond the scope of reconstructive surgery is a challenge to scientists and social welfare workers. One of the modality recently employed in "Borsad Model" was 'Modulan' grip aids. The grip aids were provided to 34 patients on 59 articles used for daily living and occupational activities. Detailed evaluation study by a special questionnaire was carried out on 21 patients within the follow-up period of 6 months to 3 years after using the articles with grip aid. The important observations were 90% patient regularly used Modulan grip aids. It not only facilitated the normal grip with crippled hands but also provided protection from pressure, abrasions and heat. The patients could perform activities of daily living and job comfortably and personally without dependance on others. Thus Modulan grip aids improve the quality of life of handicapped leprosy patients by making them not only psychological, physical and economic independence but also help the patients to get fresh grip on life. The grip aids were prepared by leprosy workers trained by physio technician under special deformity care programme of the project. The format of questionnaire and detailed evaluation of the results will be presented with case studies.

RE57

INK IMPRESSION TECHNIQUE - A NEW METHOD FOR RECORDING THE IMPROVEMENT IN CLAW HAND

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The common problem encountered in the field area deformity care service programme is the unavailability of any simple technique to record the deformity and improvement in claw hand. The improvement in the deformity before and after by any type of intervention whether medical, physiotherapeutic or by reconstructive surgery needs to be assessed by field workers.

The method of measurement of proximal interphalangeal joint angle ie, unassisted,

assisted, contractural angles cannot be taught to leprosy workers in the field area. As well as patient himself may not remember subjectively the partial improvement brought out by any intervention, unless the deformity is completely corrected. It is equally important that leprosy worker is able to gain confidence of the patient by demonstrating that there is gradual but definite improvement.

This technique designed and published by the first author in training series booklet on splintage has been field tested. It was found to be simple and reasonably accurate. Its applicability in field area, advantages, disadvantages and results of field testing will be presented.

RE58

COMPREHENSIVE PROTECTION EFFECTS ON LEPROSY SOLE ULCER AND SIMPLE SOLE SENSORY LOSS

Xu, Shaomei and Jean M. Watson

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Comprehensive protection measures were taken according to the unitary guidelines of ILEP Sole Wound Study Project. Here is the result of a three-year observation of 47 patients having sole ulcers (64 ulcers in total) and 48 patients having simple sole sensory loss.

Among the 64 ulcers, 54 healed; 1 improved markedly; 4 improved; 2 remained unchanged; 1 worsened; and 2 recurred. The total effective rate is 92.2%; healing rate 84.4%. Of total ulcers, the effective rate and healing rate of 56 simple sole ulcers were 96.4% and 92.9% respectively; the effective rate and healing rate of 8 cases of complicated ulcers were 62.5% and 25% respectively.

Among the 48 cases of simple sole sensory loss, 2 cases of ulcers occurred during the first-year observation with an incidence of 4.2% and in the second and third year, no new case was found, the incidence being zero.

We analysed causes for the unhealing, recurring and new occurring of ulcers and put forward the concrete proposals of fulfilling comprehensive protective measures enhancing protective effect further.

RE59

DEVELOPMENT AND APPLICATION OF PROTECTIVE SHOES FOR LEPROSY PATIENTS

Xu, Shaomei and Jean M. Watson

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From Dec. 1989 to Dec. 1992, we started to develop protective shoes for leprosy patients We designed and manufactured five kinds of shoes - Cloth Shoes, Army Shoes, Travel Shoes, Sports Shoes and Basketball Shoes and two kinds of microcellular rubber (MCR) insoles. We also provided the patients in four pilot units of rehabilitation in China with shoes (five kinds) and insoles for field use. Moreover, we sent 140 pairs of sample shoes to TLMI, ALERT, DAMIEN FOUNDATION and 11 leprosy hospitals in 9 countries, and also provided 10,000 pairs of Army Shoes with high uppers to ALERT (ALL AFRICA LEPROSY & REHABILITATION TRAINING CENTRE).

After application of three kinds of shoes in Hubei Province, our observations show the differences of the shoes: Among 5 kinds of protective shoes, Army Shoes are well accepted by patients because of their good appearance, comfort, cleanliness, long-wear, good ventilation, cheap price and use all the year round. The percentage of patients satisfied with the hardness of sole, softness of insole and comfort is over 95% after they used Army Shoes.

A two-year observation of the experimental use of Army Shoes shows the result: healing rate in 130 cases of sole ulcers is 60%; ulcer occurrence rate in 236 cases sole insensation 2.1%; protective effective rate 97.9%.

RE60

CAN SELF CARE PREVENT ULCERS IN ANAESTHETIC LIMBS?

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In the control program run by CHAD hospital Bagayam Vellore, all patients at risk of ulcers are taught self care activities to reduce ulcers.

This study was done to measure whether patients without ulcers showed increased self care activities as compared with patients who developed ulcers. The study group consisted of 30 patients with ulcers and 30 similar patients without ulcers. Self care activities were measured in the 2 groups for the use of protective aids during work, foot care activities, regularity of use of MCR chappals, distances walked to the work spot and distances walked during the day.

Analysis of the results showed that the group of patients without ulcers, demonstrated increased self care activities such as inspection & frequency of inspection, more regular use of MCR foot wear and foot care as compared with patients who had developed ulcers.

This study demonstrated that getting patients to increase their self care activities helps in the reduction of ulcers.

RE61

IMPACT OF HEALTH EDUCATION IN THE PREVENTION OF PLANTAR ULCERS IN A LEPROSY CONTROL PROJECT - PRELIMINARY FINDINGS -

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Plantar Ulcers are a major cause for admission to the hospital. During 1990 & 1992, 245 patients from the Leprosy control project area were admitted for inpatient management of ulcers. A significant proportion of the inpatient costs of the hospital were directed to managing these patients.

An intensive health education program was launched for patients at risk of developing plantar ulcers and with plantar ulcers. Health Education measures included drama, printed material and practical demonstration in self care in the control area. The methods are described in detail.

Preliminary analysis of the impact of health education suggests that these measures are contributing to a decrease in the prevalence of plantar ulcers. The full analysis of the data is being done.

As MDT treatment effectively cures patients, the care of disabilities and prevention of plantar ulcers becomes a greater priority. This study design demonstrates practical methods of patient self care and ulcer prevention.

RE62

FREQUENCE ET EVOLUTION DES MAUX PERFORANTS PLANTAIRES: EXPERIENCE HAITIENNE.

Nicole Beliard, Raymond Bernadin, Gysette Blanc, Marlene Dambreville, Florence Desvarieux, Florence Foucauld, Claude A. Leveille, Claude Pean

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1) La frequence et le pourcentage des maux perforants plantaires, suivant l'age, le sexe et la forme clinique de la maladie.

2) L' avantage de la mise en platre sur les techniques traditionnelles de traitement.

3) Les moyens de prevention.

This paper outlines lessons regarding the management of prevention of disability that were learnt through the study. For example:

- The importance of the commitment of senior management. This need not be time-consuming.
- How critical is the development of record forms that are designed to show change in impairment over time and used to monitor change and guide activity.
- The importance of ongoing monitoring of change in level of impairment, in patients having peripheral nerve impairment, after discharge from chemotherapy control.
- The disruption of activity that can be caused by lack of small amounts of funding, for example to visit a patient at home.
- The motivating influence on grass root staff members of actively involving them in planning through team discussions.
- The motivating effect of adopting an Action Learning Management Component that encourages staff to interact with one another and to learn from the experience of change ... where feasible together with other,nearby teams struggling to attain similar targets.

RE63

THE EFFECT OF THE ILEP JOINT STUDY PROJECT ON SOLE WOUND PREVALENCE

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The objective of this presentation is to demonstrate that improved management of disability prevention activites can in many cases result in a reduction in the prevalence of impairments.

Projects participating in the ILEP Study were invited to make a concerted effort to reduce sole wound prevalence in a selected group of patients having sole sensory loss, through systematically improving foot-care and footwear. 30 projects in 9 countries took part.

The aims of the study are:

- to see if it is feasible to reduce the wound prevalence year by year in the selected group,
- to see what useful lessons in disability management can be learnt in the process and
- to encourage project staff to adopt continuing habits of monitoring change in levels of impairment and of improving the efficiency of activities where indicated by findings.

Almost all of the projects which persevered in their efforts succeeded in obtaining a year to year reduction in sole wound prevalence. Results are given and some useful lessons relating to activities are described, for example lessons relating to use of protective footwear. The main problems encourtered by projects which either did not complete the study or did not succeed are outlined in the hope that awareness of them may encourage others to avoid similar problems.

RE64

MANAGEMENT STEPS NEEDED TO IMPLEMENT A SYSTEMATIC APPROACH TO PREVENTION OF SOLE WOUNDS

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Participants in this ILEP study were required to endeavour to obtain a year to year reduction in sole wounds in a selected group of present and former patients having sole sensory loss, 50% initially having sole wounds or cracks. Results are encouraging in those who persevered.

RE65

MANAGEMENT OF COMMON PERONEAL NERVE DAMAGE (FOOT DROP) IN HANSENS DISEASES DHOOPET LEPROSY RESEARCH CENTRE APPROACH

Dr.Solomon V.K.
Mr.Muzaffer, Dr.Uday Kiran,

During 1982-1992 early diagnosis and treatment of type I Reactions with recent Nerve damage are reversible, with regard to foot drop, due to reasons which will be dealt, we have treated these patients on an out patient basis. Without any special foot wear for the foot drop and without POP. They were given instructions with regard to care of the foot, on weak muscles, anaesthesia and exercises. All cases with Recent Nerve damage were treated with steroids and most cases showed improvement. ALthough management of Nerve damage with steroids is an established phenomenon, our work shows that in the field set up, where facilities are not available for admission/transportation/special foot wear/for such patients it may still be possible to give acceptable good results in cases of foot drop. Since our approach is simple and acceptable, the same can be applied in fields set up, without Institutional way of management.

The essential feature related to foot drop will be discussed in details. (Volume of Muscle, Weight, gravity).

Dhoolpet Leprosy Research Centre (DLRC) Hyd.

RE66

EFFECTIVENESS OF PROTECTIVE ORTHOPAEDIC SHOES IN NEUROPATHIC AND DEFORMED FEET IN LEPROSY

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The orthopaedic shoe workshop was initiated in our hospital in Bakırköy, İstanbul in 1980. The objective of this workshop is to help prevent foot injuries as a result of loss of protective sensation, also to provide protective and corrective footwear and orthoses to patients with deformities.

410 leprosy patients were studied in this survey and they were evaluated according to their age,sex, level of education the regions they live, as well as the condition of their feet and the type of shoes they required. 74 % of these patients were male and 26 % were female; the average age was 52.62. 56 % of these cases came from rural areas, 56 % were illeterate, 37 % of them were unemployed and 80 % of them were seen to have

insensitive feet, 66 % to have claw toes and 11 % to suffer from drop-foot.

57 % of them had healed ulcers on their feet and 56 % of these ulcers were on the first metatarsal head. 39 % of these 410 patients were seen to have ulcers at the present and 51 % of these ulcers were on the first metatarsal head. 5 % of the patients with ulcers had orthopaedic shoes and 95 % did not have orthopaedic shoes. 6.5 % of the patients have charcot joint and 81 % have plantar ulcers.

All the other results will be analyzed and the advantages of orthopaedic shoes will be discussed at the congress.

RE67

REHABILITATION OF PEOPLE WITH LEPROSY

In many diseases, rehabilitation is an after thought. When a patient is cured, then think about getting him back to work, to his home e.t.c.

In Leprosy, rehabilitation is an intergral part of the programme of prevention as well as of treatment and of final restoration to National Social relationships.

Being a Crippling and disabling disease, it (Leprosy) is second to Poliomylitis - in developing Countries. Affected persons are disturbed and find it difficult to live in communities like those not afflicted by the disease.

Without effective rehabilitation leprosy control is a failure because patients are not willing to expose themselves for treatment unless they can see that others who have done so have been able to return to a meaningful existence.

Without effective rehabilitation measures medical treatment may also be a failure because patients who are rendered free from mycobacterium Leprae can never be called cured if they are left with blindness and Crippling deformities as a sequel of the disease.

To realise the dream of eliminating Leprosy by the year 2000 AD will be possible if, and only if the problem of (social and economic) rehabilitation of leprosy persons is effectively addressed.

RE68

WLEREC PROTECTIVE FOOTWEAR

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World Leprosy Rehabilitative Engineering & Training Centre

Loss of sensory perception in the feet is a major handicap, often leading to secondary ulceration and deformity. It is estimated that at least 1,000,000 leprosy patients and former leprosy patients have insensitive feet and need protective footwear. Over the years a score of shoes has been developed, ranging from simple sandals made of local materials to highly sophisticated orthopedic boots. However, none of these solutions was generally applicable, particularly since leather was often the major material used. Leather under "poverty conditions" has been found unsuitable for protective footwear, because it becomes hard, dry, inflexible and therefore deformed, causing ulcers instead of preventing them. Therefore, polyurethane was chosen as the material to manufacture the WLEREC shoe. The final shape of the shoe was determined by extensive research in both the laboratory and the field. This report will focus on the final test results based on 375 test reports from 5 leprosy centers located as far apart as Brazil, Nigeria, Turkey and Pakistan. The results showed that the shoe satisfied 77.5% of the patients. Moreover, of the initial 69 ulcers only 8 were still present after six months. The rest had healed. The importance of unmended socks must be emphasized. Data on the durability of the material will also be presented. It suggests that at last acceptable, durable and affordable leprosy footwear has been developed.

RE69

PREVENTION OF FUNCTIONAL IMPAIRMENT, DISABILITIES AND DIFFORMITIES

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The tardy detection of any neurological alteration may result in irreversible disability. The prevention of functional impairment and disabilities should be based on continuous surveillance of leprosy patients.

Therefore at the moment of diagnosis, as well as during MDT and during follow-up, basic preventive measures should be taken such as : regular nerve function assessment, information on the possible onset of nerve alteration and health education.

This strategy should result in early treatment of neuritis and in a decrease of the number of disabled patients. In order to prevent the functional degradation of disabled patients, a supportive program of care and cure should be included in public health activities.

The authors present a poster showing all measures to be taken according to different clinical situations.

RE70

AN EPIDEMIOLOGICAL SURVEY OF DEFORMITIES AND DISABILITIES AMONG 14,257 CASES OF LEPROSY

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This study was planned and conducted in Yangzhou Prefecture covering 11 counties. Out of 14,257 leprosy patients, 8,122 (56.97%) cases with deformities and disabilities were found. The disability rate was much higher in patients with MB leprosy (81.15%) than in PB (53.04%). Males were more often disabled than females (58.21% for males, 53.68% for females). The disabilities became more common and more serious with the increase of age. The disabled rate increased with increasing duration of disease. Out of 8,122 cases disabled, 62.04% belonged to Grade 3. Among 14,257 cases of leprosy, 3,656 (25.64%) lost sensation of the hand, 4,762 (33.40%) and 2,064 (14.48%) had hand deformities as claw hand and thumb paralysis respectively, 3,327(23.34%)lost sensation of the foot, 2,237 (15.69%) with foot drop needing surgical treatment, 1,882 (13.2%) had plantar ulcers (608 simple ulcers, 1,274 complicated ulcers), 2,114 (14.13%) had a deformity of lagophthalmos and 1,587(11.13%) had vision loss or blindness, 3,485 (24.4%) had different kinds of facial deformities such as lateral/bilateral facial paralysis, loss of eyebrow, or collapsed nose.

In this study, 10-25% of 8,122 disabled cases were suitable for reconstructive or plastic surgery. However, according to patients' attitude during the survey, the majority of them (58.54%) refused surgical treatment. Analysis of disability in this study showed that health education in the self-care of hand, foot and eyes, and protective shoes, etc., had a greater potential in reducing disability than reconstructive surgery in leprosy.

RE71

SURGICAL TREATMENT FOR THE BILATERAL FACIAL PALSY IN LEPROSY

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Facial deformity in leprosy, particularly bilateral facial palsy with ectropion of lower lip, is the most markable sign of leprosy, which can prevent patients' being accepted in society. The bilateral static slings used to be taken for the correction of this deformity, but the long-term result was not good. Since

1970's, a bilateral dynamic slings have been used for the correction of lower lip. Eighteen cases who had this operation have been followed up for 3 years averagely (the longest for 6 years) whose results are excellent. The procedure of the dynamic slings: A strip of fascia lata is taken from the thigh. this should be about 20-25cm and under 0.5cm in width. The slip of fascia is passed from one side of the face to the other side of the face through the lip tunnels using the middle incision on the center of the lip as a step. The end of the slip goes around a bundle of each side of masseter and is attached to each side of masseter. Or the end of the slip is attached to a more vertical bundle of temporal muscle of each side.

RE72

"DISCAPACIDADES EN EL ENFERMO DE LEPRA"
REPUBLICA DOMINICANA
1979-1992

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Se hace un análisis de las discapacidades producidas por la enfermedad de Hansen en un grupo de 4,236 enfermos diagnosticados en el período 1979-1992. Los afectados se dividieron por grado de discapacidad, forma clínica,sexo y lugar de localización de la lesión (manos,pies y ojos). Se observa que de un 20% de discapacitados, el grado II alcanza el 8.48 y que la forma lepromatosa es la que produce más discapacidades. En cuanto al sexo el masculino es el más afectado, encontrando la misma situación en el grupo menor de 15 años.

La localización de las manifestaciones, por orden de frecuencia, se observa en manos, pies y ojos.

RE73

IMPACT OF MDT ON DISABILITY PROFILE:
CULES EXPERIENCE IN AN URBAN CUM RURAL PROJECT

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Deformity rate (Grade I and II) among 5655 Urban and 6104 Rural patients who were selected to receive Chemotherapy was 13.6% and 19.6% respectively. The rate was higher among MB patients; a slightly higher rate was encountered in rural patients.

During the course of therapy, deformity sttus downgraded in 1.8% of Urban and 2% of Rural patients. 25.9% of Urban and 19.4% of Rural patients manifested some recovery of sensation.

Deformity rate in neuly detected patients has declined to 1.3%

This paper will seek to identify and present the determinants of these varying deformity profile in the two situations. It will also focus on disability prevention and limitation as critical components of leprosy eradication strategy.

RE74

PREVALENCE OF DEFORMITIES IN THE LEPROSY PATIENTS IN MOZAMBIQUE.

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Mozambique is one of the African countries with the highest prevalence of leprosy (L) (1.3‰; Africa 0.68‰). It is generally known that among the L pts there is a high prevalence of deformities (Def) and disabilities, with considerable variations between different areas. No data were available for Mozambique.

So, during 1992, all active pts in two different areas were observed and the presence, kind, grade (WHO criteria) of Def were registered along with sex, age and clinical classification (PB or MB):
1- a rural area (Nampula town, NPL) with a high prevalence of L (4.7‰) and less organized health services: 550 pts, 307 males, 243 females; 166 PB and 384 MB;
2- an urban area (Maputo town, MPT) with low prevalence (0.1‰) and better organized services: 101 pts, 52 males, 49 females; 20 PB and 81 MB.
Statistical analysis: Epi-Info 5.1 computer programme.

A preoccupantly high rate of Def was encountered:

	Deformities	Grade		M	F	PB	MB
NPL	218 (39.6%)	I	55 (10%)	41	14	8	47
		II	163 (29.6%)	98	65	36	127
MPT	54 (53%)	I	16 (15.4%)	7	9	2	14
		II	38 (37.6%)	25	13	7	31

Male pts presented higher prevalence and higher grade of Def both in NPL and MPT ($P < 0.05$) (kind of work, less self-care, less familiarity with health facilities). A more prolonged natural history and a greater number of involved nerves may explain the higher prevalence of Def in MB pts, if they are associated with other factors (e.g. low level of knowledges, low level of health services, access problems; only for NPL: $P < 0.001$). Only for the pts in NPL, a correlation was found between age and Def grade ($P < 0.001$). No difference was found between the prevalence of Def on the right and those on the left side of the body.

In conclusion, the high prevalence of Def encountered indicates:
1- the problem has a relevant social impact,
2- a high percentage of pts delay many years before contacting the health services, thus indicating the of improving early diagnosis,
3- there is an urgent need of reorganizing the health system in order to extend primary prevention and treatment of the L complications.

RE75

THE APPLICATION OF CIRCULAR DISTRIBUTION METHOD TO ANALYSES OF 14258 LEPROSY CASES FOR DEFORMITIES SURVEY IN YANGZHOU, CHINA

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** Yangzhou Institute of Dermatology,P.R.China

The purpose of this study is to analyse the regularity of time distribution for onset, detection and occurrence of deformities in 14 258 leprosy cases. In this paper the author applies a circular distribution method to analyse the data collected in a survey of leprosy deformities in Yangzhou, China. The results indicate that the peaks (15% of the total cases) of onset, detection and deformities in these cases have occurred in March, June and April respectively.The periods of peak (about 4 months) of onset, detection and deformities are observed in March-June, May-August and March-June respectively, it includes nearly 50% cases in each period of the peak ($p<0.01$).The results suggest that leprosy control should have more resources to deal with case-finding and case-holding in order to detect the cases as early as possible and therefore reducing the deformities, in order to little cost to get great benefit in the months of peak and periods of peak.

RE76

COMPARATIVE STUDY OF A HERBAL OIL PREPARATION WITH AN OIL MASSAGE WITH PLAIN EXERCISES IN WASTING OF MUSCLES.

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An oil based Herbal Oil preparation was used in wasting of muscles in a set of patients. In another set of patients, a different vegetable oil was used for massage and exercises were advocated. In the third set

of patients, no application was advised. Massage and exercises were advocated in all the three sets of patients included in the study. The results were documented and analysed.

It has been observed that in most cases exercises improved wasting of muscles. The improvement was more and time taken was less in case of herbal oil preparation. It also revealed few other findings in the course of the study.

RE77

FIELD BASED DEFORMITY CARE SERVICES IN SRI LANKA

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Until recently leprosy control efforts in Sri Lanka focused on detecting and treating patients with MDT. Little attention was paid to the care or correction of deformities. Due to the personnel constraints in the anti-leprosy campaign a highly pragmatic and cost-effective approach to deformity care was adopted, based on the experience of the Comprehensive Leprosy Care project in Borsad Taluka, India.

Deformity care services are provided by the leprosy public health inspectors after training in basic physiotherapy measures and in the application of pre-fabricated splints for patients with deformed hands. The collection and analysis of data on the extent and type of deformities enabled drawing up a clear strategy and priorities.

Ink impressions of the hands were taken before and 3 months after the application of splints to measure the progress. 50 of the 63 patients who received splints during the first six months and were followed-up and showed moderate to good improvement. This often increased patients' earnings. It also prevents the progression of deformities and reduces the case load requiring surgery.

This approach clearly demonstrates that deformity care services can be provided through the leprosy field workers on a national level with adequate supervision and motivation.

RE78

CUSTOMIZED LATEX FINGER CAPS FOR INSENSITIVE HAND

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A need continues for increased knowledge and understanding in the care of the insensitive hand. An important aspect of treatment is providing protective devices that are also functional in activities of daily living performance. One such device is a custom made finger cap. Customized latex caps are form fitted to the individual finger regardless of the degree of deformity. Each cap is individually made from the positive plaster mold of the finger.

Latex caps decrease the risk of shear stress and provide a protective barrier. Latex is softer than thermoplastic and other materials, and there is less chance of injury from the device itself. Injuries are a concern when using harder materials. The latex caps provide some padding, do not restrict range of motion of each joint of the finger, and reduce callus formation. Thermoplastic materials can be quickly fabricated, however, do not allow as close a fit. Thermoplastic and other materials also inhibit fine motor manipulation on hand grasp of an object because of absence of flexibility.

These and other advantages and disadvantages will be discussed, including enhanced patient compliance, improveddurability, and enhanced gripping properties of the latex.

RE79

PHYSIOTHERAPY AND HEALTH EDUCATION - A DHOOLPET APPROACH

Mr.MUZAFFARULLAH, Dr.SOLOMON, Dr.UDAY KIRAN

DHOOLPET LEPROSY RESEARCH CENTRE (D.L.R.C.) is situated in Hyderabad City, India. It is an out patient clinic. It has no admission (in patient) facility, except in its parent Hospital, Victoria Leprosy Hospital, Dichpalli situated at 150 Kms.from Hyderabad.

Being a reputed institution, more number of problem cases, self selected patients come to DLRC. During the year 1982-1992 more than 500 cases of recent nerve damage were treated completely on an outpatient basis.

Ideally, a case of recent Nerve damage can be given maximum care/physio/H.E., if admitted in the Hospital. So when we treated these cases due to lack of admission facility on an out patient basis we had to develop appropriate methods of HE/Physio which were applicable on an out patient basis and whose patient acceptability was good.

The simple exercises we advised, lhow we educated our patients, why each exercise is useful and required, how we made the use of double steel cups, protective utensils available in Market, and protective glasses, and how we transferred the responsibility to the patient to achieve good results and also how we planned our available resources in providing them (Where they could not get immediately) will be discussed.

Colour transperencies depicting the whole process and items used will be presented. We hope that these methods will be found useful for field conditions.

RE80

COMPARABILITY OF BALL PEN AND NYLON FILAMENTS IN TESTING SENSORY FUNCTION OF PATIENTS WITH LEPROSY IN NEPAL AND ETHIOPIA

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Various methods have been developed to assess sensory function in leprosy patients under field conditions. The most in use are the nylon filaments (NF) and the ball-point pen (BP). Each method has its own advantages and disadvantages, but their comparison is complicated by the absence of a "golden standard". In an attempt to compare these two methods, randomly selected leprosy patients have been tested with BP and NF in Nepal (ANANDABAN) and in Ethiopia (ALERT). In each centre, the 2 tests were performed on the same patients by the same observer on two different occasions in a random order. Each test was performed on specific sites of both hands and feet and the results were reported on a pre-determined scale. Fifty two patients have been tested in Nepal and fifty in Ethiopia.

The two methods are compared by plotting the differences in measurements against their means and calculating the limit of agreement. Percent agreement is evaluated with various criteria. Matched paired t test is applied to estimate systematic bias between tests. Kappa statistics are calculated to determine whether the agreement is better than would be expected by chance alone.

It is found that both methods compare reasonably well for ulnar and median nerves, when applied on similar conditions by a trained observer (70% to 90% complete agreement). Kappa statistics lie between 0.54 and 0.74, showing moderate to good agreement. Comparability is less good for the posterior tibial nerves (44% to 54% complete agreement) with a wider spread of values. Overall, there is no statistical evidence of a systematic bias, but a consistent tendency for BP to measure in excess compared to NF. For all nerves, agreement is optimal at the extremes of the scale, when there is full sensation or complete anaesthesia. Reasons for these discrepancies are examined in relation with the practicality of each test, the nerve status of the patients and their treatment.

RE81

THE TEST-TRACK. A USEFUL TOOL IN TESTING SENSITIVITY OF FEET?

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Leprosy patients with impaired sensation of their foot soles and undergoing treatment for neuritis, sometimes report a returning awareness of the ground on which they are stepping. As an alternative to conventional testing of texture discrimination a test track has been constructed consisting of a board with 5 slots into which different trays with various, standardized surfaces are fitted in a random fashion. Two additional surfaces are neutral but one is warmed up and one cooled down to check sensation for temperature.

20 cases undergoing neuritis treatment, 20 with LOS (for 10 g filament) with no ulcer for at least 2 years, 20 with recently healed ulcers, and some that have undergone nerve resection and grafting of the Post. Tibial nerve with freeze-thawed muscle have been investigated. 20 non-leprosy cases without any nerve damage were tested for control.

All patients were assessed with standard methods such as VMT-ST(graded), vibrometry, test for texture discrimination, joint position sensation, temperature sensation with test tubes, NCV, as well as questioned about their subjective sensation.

The findings are discussed.

RE82

FOOTSOLE SENSATION IN NORMAL SUBJECTS IN ETHIOPIA

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Finding a reliable instrument to measure sensation is still a problem in most control programmes. In ALERT, we use 10gm filaments for both the hands and the feet. Many health workers complain that they are registering false findings of anaesthesia on footsoles. Therefore 200 normal subjects were tested using 5, 10, 20, 35 and 50gm filaments. 100 were from highland and 100 from lowland areas. The skin was described as hard, soft or cracked. The occupation and use of footwear were also noted. The lowest filament felt was recorded at 8 sites on the footsole.

The results show a difference between highland and lowland, and call into question the use of 10gm filaments to detect sensory loss, especially in the heel.

RE83

THE EVOLUTION OF SENSORY LOSS IN SKIN PATCHES OF HANSEN'S DISEASE AT THE TIME OF DIAGNOSIS AND DURING TREATMENT USING THE SEMMES-WEINSTEIN MONOFILAMENTS

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The authors observed in daily practice that sensory loss in skin patches of newly diagnosed patients with Hansen's disease improved with treatment specific to the disease and with the use of steroids.

Frequently this improvement was noted within the first month of treatment. Conflicts arose among some patients who sought second opinions to confirm diagnosis after several months of treatment. The consulting doctor frequently did not detect sensory changes in skin patches due to either recovery of sensation with treatment or lack of detection of sensory loss due to gross sensory testing instrumentation of the consulting doctor.

This prospective study started in January 1993. All newly diagnosed patients in 1993, virgin to treatment have their skin patches mapped using the Semmes-Weinstein monofilaments. These mappings are done at diagnosis time followed by monthly mappings until discharge.

The preliminary results of approximately 20-30 cases are anticipated by July 1993. These results will be discussed and their implications on second opinions to confirm disease.

RE84

DISABILITY IN NEW CASES IN HANSEN'S DISEASE IN THE STATE OF MINAS GERAIS, BRAZIL, FROM 1988 TO 1992 BY REGIONS OF EPIDEMIOLOGICAL PRIORITY AND TRAINING

Linda Lehman, Aparecida Grossi, Maria Ana Leboeuf

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The authors discuss the disability in new cases of Hansen's disease detected in the state of Minas Gerais, Brazil, from 1988 to 1992. Disabilities are compared in the 23 regional areas by regions of epidemiological priority and by the number of training courses and persons trained in each region.

The classification of regions of priority was based on prevalence and new case detection data. Disability classification utilized the WHO disability grades 2 and 3.

The results of the preliminary findings demonstrate that deformity in newly detected cases has decreased in the state from 13.9% in 1988 to 7.6% in 1992.Regions of high priority and increased participation in training demonstrate fewer disabilities as compared with less participation in training. There was an increase in new cases detected with a decrease in disabilities suggesting that training has improved early diagnosis and adequate treatment and improved program management.

RE85

SOMATOSENSORY EVOKED POTENTIALS IN LEPROSY

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A study of somatosensory evoked potentials (SSEP)of posterior tibial nerve was done in 25 patients of various types of freshly diagnosed leprosy and data were compared with 15 normal persons which served as control.

Significant alteration (more than mean ± 3SD) in various latencies of SSEPs were observed in 20 patients(80%). It was because conventional sensory nerve conduction studies deal with more distal portion of the peripheral nerve as the proximal segments are not easily accessible to stimulating electrodes while SSEP allow assessment of the entire somatosensory pathways and secondly nerve imvolvement in leprosy is segmental in nature.

Interpeak latency N7-N18 (Proximal Conduction Time) was prolonged in 3 patients while Interpeak latency N18-N35 (Central Conduction Time) remained unaltered denoting peripheral involvement of nervous system in leprosy.

Thus study of SSEP is an important diagnostic tool in evaluating nerve damage in leprosy neuropathy.

RE86

SPECIFICATIONS FOR THE SEMMES-WEINSTEIN MONOFILAMENTS FOR SENSIBILITY TESTING, AND CONSIDERATIONS FOR FIELD FILAMENTS

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Semmes-Weinstein Monofilaments are being increasingly used for testing sensibility in Hansen's Disease due to their advantages in improved objectivity, and usefulness in establishing an absolute baseline sensory detection threshold that can be compared with treatment. However, limited availability of the test and costs have in the past made the test out of reach of many field clinics. Various versions of the test have emerged, and with these increasing variability of the filament forces.

In order for the test to be used as a standard, the filaments must be as identical as possible in their stimuli, and in particular, the force they produce. This paper reports on research into the physical properties of the nylon material, the repeatability of the filament stimuli, and factors which are important in making them more or less accurate. The relative comparison of the force control of this instrument which varies in milligrams from one application to the next, versus other hand held instruments which vary by many grams, is shown by measurement made on testing equipment designed by a biomedical engineer specifically to measure the dynamic stimulus force. The obtaining of the filament material in bulk for making field filaments, and factors important in their force measurement in the field are discussed.

RE87

SEMMES-WEINSTEIN MONOFILAMENT TESTING TO DETERMINE NORMAL SENSORY THRESHOLDS IN THE FOOT AND HAND: A COMPARATIVE STUDY IN INDIA

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This study was undertaken in order to enable the PMW, therapist, and physician to utilize this integral tool for measuring peripheral nerve involvement underlying disability of the hand in HD. This tool, unlike other tools for touch-pressure testing, boasts several assets: repeatability of stimulus, identification of progression or regression of neuropathy, and practicality in the field. In order for this tool to be of optimal utility, thresholds for feet and hands need to be corroborated in an Indian population. This is crucial in India, where over 50% of the HD population may reside, and where footwear can be minimal or nil. Once normal thresholds have been corroborated, application of such a paradigm to HD patients can lend valuable insight into peripheral nerve involvement.

600 hands and feet were tested in 600 subjects, males and females of ages 7 years and up. 500 subjects were tested by one tester, 100 by 3 testers. Right and left extremities were selected on a random basis to avoid bias. 50% of subjects live and work in urban India; 50% in rural India. Three categories of hands and feet were devised according to occupation and footwear. Hands were identified in terms of light, moderate, and heavy use. Feet were identified according to degree of footwear: shoe/enclosed sandal, light/open sandal, and none.

This paper discusses minimum threshold of each of the categories, and compares them. The interrater reliability and presence of callus are also discussed.

RE88

THE WRINKLING TEST IN LEPROSY PATIENTS

Marcos Virmond, Lucia Camargo and Rosemarie Baccarelli

Wrinkling of the skin of the distal finger after immersion in warm water has been proposed as a test for peripheral nerve function. It is related to the integrity of the autonomous fibers and not to the motor or sensory fibers. Twenty-four leprosy patients were submitted to this test consisting in the immersion of the hand in water at 40°C for 30 minutes. Before and after the tested hand was photographed. The results reveal that in leprosy this test is suitable to detect nerve damage in the hand since in most cases there was no wrinkling of the skin in areas where further examination with Semmes-Weinstein monofilaments revealed altered sensation. Although it seems to be no correlation with motor or sensory recovery, this test is easy, simple and cheap to carry out for initial nerve function evaluation and is particularly suitable to be used in non-cooperative patients.

RE89

TRANSLATING THEORY INTO PRACTICE: THE CHOICE OF SENSORY TESTING METHODS IN DIFFERENT FIELD SITUATIONS

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Prevention of Disability (POD) should have high priority in every leprosy control programme since disability still causes stigma amongst leprosy patients. A control programme cannot be called successful if it does not control disability.

Some actions required to control disability are inspection of eyes, hands and feet, nerve palpation, sensory testing, and voluntary muscle testing. These tests enable the field worker to recognise nerve damage as early as possible and to take proper action.

"The ball-point test" is the most common method used in the field to test sensation and regularly leads to wrong diagnosis. The accurate Carville (Bell) method tends to be too expensive and too complicated for field use. Hence the need to look for methods which combine simplicity and accuracy.

Points to consider while choosing a suitable testing method in specific circumstances will be presented in the poster.

The poster will show experiences from 3 POD projects in Africa and South East Asia where local circumstances have led to different choices of tools and methods.

RE90

PAN-SENSORY LOSS IN LEPROSY-CASE REPORTS.

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We report the clinical and investigative features of seven patients (3males, 4 females, age 28yr-6lyr) with polyneuritic leprosy (BT or BL) who developed a remarkable and disabling sensory ataxia in one or more limbs, in addition to the usual loss of cutaneous sensations.

The motor system was not severely affected. Tendon reflexes were absent in the affected limb/s. Detailed investigation for other causes of this type of proprioceptive loss were negative in all (one patient had borderline diabetes). Electrophysiological studies of the thenar muscles confirmed involvement of muscle (and cutaneous) afferents.

More widespread muscle afferent involvement in leprosy is difficult to explain. From an analysis of the clinical picture we suggest that the site of pathology in the patients described is probably not the mixed nerve trunks or the muscle spindles but more rostrally in the ganglion or sensory roots. Alterations in a spinal ganglion which was biopsied in one patient are described, and the literature reviewed. Even this explanation appears less than satisfactory and it is suggested that further elucidation of spinal ganglion or root involvement be obtained by exploiting a primate experimental model for polyneuritic leprosy. (Baskin et al. Amer.J.Trop.Med.Hyg.37:385,1987; Int.J.Lepr.59:618,1991).

RE91

CLAW-TOES CORRECTION. PERSONAL TECHNIQUE

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Claw-toes are common deformities in leprosy.Fritschi has identified 3 degrees.Degree I & II are the most common in our clinical experience. We propose,for grade I & II a very simple procedure which can be performed in 20 minutes and it is usully done along with foot-drop correction. TECHNIQUE.With a tenotomy knife a stab incision is made midway between the PIP and MP joints of each toe on the plantar aspect.In grade I a stab incision is sufficient.In cases of grade II,we prefer a star-shaped incision.The knife is pushed down to the bone and both flexor tendons are cut. All the while the toe is forcibly kept in dorsiflexion.As the tendons are cut the toe,usually "gives in".Often the volar capsules of PIP and/or MP joint act as contracting forces.By moving the knife a few mms.both capsules can be reached and incised.Now the toe can be dorsiflexed maximally and it will remain straight.Minor resistances can be broken manually.If small skin grafts are required,the plantar skin is readily available as donor.No sutures.6 weeks POP with toes in maximal extension.STATISTICS.76 feet for a total of 324 toes:53 of grade I & 271 of grade II.Excellent results(=toes straight and functional)in 289 toes(89.2%);i.e.all the 53 of grade I and 236 of grade II.Good results in 25 (grade II).Poor in 10(grade 2).Poor results at the time when technique was not refined,and/or when the capsule was not totally excised.Clawing of toes & fingers is due to palsy of intrinsics.It is proved that if flexors are cut,the clawing disappears.This cannot do for the hand,but in the foot it flattens the toes & partly the foot which is an advantage because it broadens the weight-bearing area.

RE92

FINGER DYNAMOGRAPHY- BEDSIDE METHOD FOR EVALUATION OF PARALYTIC FINGER DEFORMITIES BEFORE AND AFTER CORRECTION

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Finger dynamography is a new concept to study the movements of fingers at its various joints. During routine activities the fingers can acquire different postures for various purposes. Four extreme postures are possible at MCP and PIP joints. The MCP and PIP joint angles at these extreme positions,if plotted and joined together result in a rectangle,corners of which are represented by one of these positions. Any point within the rectangle will depict a posture and any line a movement.

If intrinsic muscles of the hand are paralysed the motor capability of the hand changes and to acquire these extreme posture becomes impossible. The movement of paralysed hands when plotted,therefore,will result in a rectangle of different shape which is characterstic for the type of paralysis. After surgical correction all the activities of the fingers are not restored, hence the movement pattern of corrected fingers is different from normal. The different corrective procedure restore different set of functional capabilities therefore the movement patterns are different. This difference is obvious when the plots are examined.

The technique of finger dynamography is simple,requires minimal tools and can be performed at the bed side.

RE93

A MODIFICATION OF SURGICAL PROCEDURE TO PREVENT POST-OPERATIVE SUBLIMIS MINUS DEFORMITY AT THE DONOR FINGER.

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In surgical reconstruction in leprosy the Sublimis Minus Deformity is frequently developing at the donor finger when its Sublimis tendon has been used as motor tendon for correction of clawed fingers in case of Sublimis Transfer (Stiles-Bunnel) or for Opponens Replacement of the Thumb.

A simple modification of the surgical procedure at the donor site, which prevents the ugly post-operative Sublimis Minus Deformity, and the pull-out-wire suture technique used is described.

The modification consists in joining one distal stump portion of the Sublimis tendon with the Flexor profundus tendon of the donor finger.

During the past two and half years 72 cases were studied, who either underwent Opponens Replacement or Sublimis Transfer.

In most of the cases a considerable degree of passive hyperextension of the proximal interphalangeal joint was present at the donor finger and the modification indicated.

In no case, where the modified surgical procedure was used, signs of post-operative Sublimis Minus Deformity developed.

The results are discussed.

RE94

FOLLOW-UP OF POSTERIOR CHAMBER INTRAOCULAR LENSES IN FIVE LEPROMATOUS PATIENTS

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Intraocular lens implantation obviates the need to wear cumbersome thick glasses after cataract surgery. In leprosy patients with deformed hands and noses this advantage is of great significance. Despite this and other optical benefits, intraocular lens implantation has been undertaken very cautiously in leprosy patients, especially lepromatous ones, since they are prone for uveitic inflammatory reactions. As a result, scant information exists on the long term effectiveness of intraocular lens implantation in lepromatous leprosy patients.

We report the ocular status of two lepromatous leprosy patients and three borderline leprosy patients who had posterior chamber intraocular lenses implanted in seven eyes, between one and five years ago. At the time of lens implantation, all patients had had the disease for over twenty five years, were smear negative, and had no signs of uveitic reactions.

At the time of follow-up, they did not show any ocular complications, other than slight degrees of (1) posterior capsular opacities, (2) pupillary irregularities, (3) pigment deposition on the anterior surface of the intraocular lens, and (4) astigmatism, none of which reduced corrected visual acuity below 6/12.

RE95

RESULTS OF SURGICAL CORRECTION OF LAGOPHTHALMOS (GILLIES TECHNIQUE) IN LEPROSY PATIENTS

ROSEMARI BACCARELLI, MARCOS VIRMOND, FRANK DUERKSEN

THE RESULTS OF THE TEMPORALIS MUSCLE TRANSFER (GILLIES TECHNIQUE) IN 51 EYES (34 PATIENTS) HAVE BEEN ANALYSED. THE MAIN OBJECTIVE WAS TO EVALUATE THE DEGREE AND TIME NEEDED TO RECOVER VOLUNTARY AND INVOLUNTARY EYELID OCCLUSION AND STATIC EFFECT OF THE TRANSFER ON THE LOWER EYELID IN CASES OF PARCIAL ECTROPIUM AND EPIPHORA.

ALTHOUGH THERE WAS NO RETURN OF INVOLUNTARY BLINKING IN ANY OF THE OPERATED CASES, IN 34 (66,67%) THERE WAS COMPLETE AND LASTING VOLUNTARY EYELID OCCLUSION. THE MEDIAN OF TIME TO OBTAIN COMPLETE EYELID CLOSURE WHILE BITING, WAS 8 DAYS (1-120) IN THE EXCELLENT GROUP AND 14 (1-120) DAYS IN THE GOOD GROUP. THE CORRECTION OF ECTROPION AND EPIPHORA WAS SEEN IN 15 (83,33%) EYES.

THE RECUPERATION OF VOLUNTARY EYELID CLOSURE AND REPOSITIONING OF THE LOWER EYELID AS OBSERVED IN THE MAJORITY OF OUR CASES CONFIRM THE EFFECTIVENNES OF THE GILLIES TECHNIQUE FOR CORRECTION OF LAGOPHTHALMOS.

RE96

CHRONIC PLANTAR ULCERS OF LEPROSY PATIENTS TREATED BY MUSCULO-CUTANEOUS INSTEP FLAP TRANSFER

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Amputation for nonhealing chronic/malignant plantar ulcers in leprosy patients is one of the commonest surgical operations performed in leprosy control programme. The social and economic impact of this on the patients, the society and the programme itself is devastating.
Where convetional methods of healing fail, this method has proved effective in preserving the limbs of patients and therefore rendering them far more independent than they will be with the loss of a limb.
The poster shows each ulcer pre-operatively, some 14 days post-operatively and finally at certain periods after discharge from hospital.
It takes an average of 45 days to completely heal such an ulcer. Compared to the convetional method which takes about 150 days (if ever it heals).
However, convetional methods have to be tried before embarking on this procedure.
The modified foot wear of the patient is further modified to prevent recurrences - posters of modified foot wear also shown.

RE97

NURSING CARE FOR LEPROUS PLANTAR ULCERS CURED WITH DORSO-PEDIS VESSEL PEDICLE FLAP

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Plantar ulcers of 10 leprosy patients were succesfully managed by transplantation of dorso-pedis vessel pedicle flap in combination with the implementation of comprehensive nursing care. Among these patients, there were 8 males and 2 females, 2 MB and 8 PB. The age and duration ranged 18-25 years and 8-23 years respectively. The duration of ulcers ranged from 4 to 20 years with a size varying from 2×3 cmxcm to 4×4 cmxcm. Excluding one case of failure resulted from necrosis of flat for infection three days after the operation, no recurrence of plantar ulcers was found in the other 9 cases after an annual follow-up for 5 years. The authors emphasize following points 1) Health education together with psychological nursing care should be strengthened at the beginning in order to make the patients realize of that " plantar ulcer is curable" as long as they cooperate well with the nurses during the whole period of treatment; 2) Keep wards cleaned and sterilize the related facilities to prevent cross infection, and the room temperature should be regulated at 20-25° C; 3) Monitor the status of flaps trnasplanted, including their temperature, color and elasticity closely; 4) Guide patients to exercise step by step two weeks after transplantation; 5) Train patients how to practice self care; 6) Patients should be followed up once a year after discharge from the hospital.

RE98

A LONG-TERM OBSERVATION ON THE EFFECT OF SURGICAL TREATMENT OF LEPROUS PLANTAR ULCERS

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In the past 10 years, the recurrence rate of plantar ulcers was markedly reduced after the implementation of surgical treatment.

The results of surgical operations on 52 leprosy patients with 55 plantar ulcers were reported. The duration of the ulcers ranged from 7 months to 20 years with a size of 4 cmxcm to 80 cmxcm . The locations of ulcers were: heel 9; lateral border of the foot, 10; neutral area of the sole, 3; head of the first metatarsal bone, 7; and head of the 2nd-5th metatarsal bones. 26. As for the status of deformities, 7 cases with talipes equinovarus, 41 with claw toes, 3 with boat-shaped foot(arch reversed) and 6 with talipes planus.

Surgical operations were performed in three ways: 1) correction of the original deformities (30 cases) (group 1); 2) skin grafting, particularly with vessel pedicle flaps (group 2); 3) debridement and skin transplantation, used only for those ulcers not suitable for skin grafting (group 3).

All patients wore protective shoes and were trained in self care of foot. After an observation for more than 5 years, the overall recurrence rate of ulcer was 35%(19/55). The recurrence rates of group 1, 2 and 3 were 43%(13/30), 10% (2/20, the lowest) and 80% (4/5, the highest) respectively. The authors suggested that the success of the treatment of plantar ulcers, including the possibility of their occurrence rates, depended not only on the method of surgical operation used, but was also closely related to the degree of deformities, location of ulcers and the practice of self care.

RE99

TREATMENT OF NEUROPATHIC ULCERS WITH FULL-THICKNESS SKIN GRAFTS

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When venous ulcers are treated with full-thickness skin grafts, healing takes place with a median time of 15 days (Mol et al. J Am Acad Dermatol 1991; 24: 77-82).
As this is a simple method, which requires only little equipment, this technique was applied in the treatment of neuropathic ulcers in 10 leprosy patients. The ulcers were

localized at the plantar side of the feet or the lower legs. If necessary destructed bone and necrotic-inflamed tissue were removed surgically. In case of infection, proven by bacterial cultures, systemic antibiotic therapy was be given. Preoperative preparation consisted of three times daily changing of gauze pads moistened in fysiologic saline untill the wound was clean and granulating. Five or 6 mm full-thickness punchgrafts were taken from the upper leg and laid approximately 5 mm apart on the ulcer bed and were fixed by a parafine gauze and bandaged. The first dressing change was performed after 5 days.
In superficial wounds reëpithelialization took place within three weeks; in deeper ulcers this period was longer.
Bedrest was continued till the ulcer was completely healed; in the meantime adequate support was provided for the foot deformity.
With this method in 8 of the patients complete healing was obtained.

RE100

THE VASCULAR COMPONENT IN POSTERIOR TIBIAL COMPARTMENT SURGERY FOR PLANTAR ULCERS

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Traditional surgical decompression of the posterior tibial nerve yields equivocal results. The authors postulate that the posterior tibial artery is the most compromised structure in the neurovascular compartment. The best surgical results in healing of plantar ulcers is achieved by rechannelising of the blood flow in the posterior tibial artery during posterior tibial neurovascular compartment surgery.

This procedure has been of benefit to patients with plantar ulcers of greater than 7-10 years duration in whom all other modes of healing had failed. It has been undertaken as an outpatient procedure under local anaesthesia, supported by vasodilator drugs. The use of tourniquet, antibiotics and surgical interference with the ulcer per se was eschewed. A report of over 200 patients is presented with follow-up of up to 5 years in the earlier cases.

RE101

A 20 YEAR REVIEW OF AMPUTATIONS IN THE NATIONAL LEPROSY CONTROL PROGRAM IN PARAGUAY

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A review of all amputations done on patients with Hansen's Disease in Paraguay from 1972 - 1992 is presented. Our hospital is the only Referral Center for surgery and prosthesis for Hansen's Diseased patients in the country. The total patient population during this period varied between four and five thousand. A total of 43 amputations were done on 36 patients. The most common level were below knee (23) and transmetatarsal (13) and the average age was 62 years (29-87). Thirty patients were classified as Lepromatous, 2 Borderline and 4 Tuberculoid. The indications for amputation were: Foot ulcers (14) - malignancy (7) - leg stasis ulcers (6) and Charcot, rigid equinovarus, P.V.D., (3) each. Average time of follow-up was 6 years (1-20). Most patients with below knee and transmetatarsal amputations had recurrent problems. Through knee and Boyd had the least problems. We conclude that amputation is not very common in our patient population, but that it is a major disabling event, even at the TM. level. Although we have a good prosthetic service available, only 50% of the patients became regular prosthesis users and most of these had recurrent problems.

RE102

PRE/POST OPERATIVE REHABILITATION FOR TENDON TRANSFERS

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Current objectives of the World Health Organization target the elimination of Hansen's disease as a public health problem by the year 2000 A.D. Peripheral nerve damage, however, remains a glaring reality among the present Hansen's disease population underlining the need for continued attention to prevention and correction of deformity. In the Hand and Occupational Therapy Department of the Gillis W. Long Hansen's Disease Center, hand therapy is a primary focus with pre/post-operative rehabilitation a significant aspect. Tendon transfer surgery and rehabilitation is an effective option for many patients suffering from the typical "claw hand" deformity resulting from Hansen's disease.

Presented will be a case study of a tendon transfer HD patient. A suggested protocol will be discussed for pre/post operative rehabilitation including information regarding: pre-operative evaluation and preparation, post-operative treatment program based on biomechanical principles, and a time frame sequence, all of which serve to maximize surgery results producing a more balanced hand and therefore a more functionally independent person.

RE103

THE OBSERVATION ON THE EFFECT OF EYEBROW TRANSPLANTATION BY SINGLE AUTOLOGOUS HAIR---A REPORT OF 274 CASES

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Eyebrows are not able to regrow in MB patients with madarosis. Eyebrow transplantations with single autologous hair were performed for 274 MB patients in Hanzhong Leprosy Hospital since 1980. A long-term observation showed satisfactory results, giving a total effective rate of 100%.

The method used was as follows. After a 3-month regular anti-leprosy treatment, whatever the results of smear examination followed, a split thickness skin graft (with hairs, of course,) was taken from the auditory post superior area and was processed according to principles and methods for transplantation, separating each hair carefully to avoid the injury of hair follicles. Separated hairs were counted and placed in order on the wet compress macerated with antibiotic liquids.The shape of transplanted eyebrow was designed as "sabre-shaped" for males and "lancet-shaped" for females in majority cases. Holes were made by slantingly stick with 8# needle in the region to be transplanted with hairs and in these holes completely separated single hairs were implanted in regular order. Usually more than 350 hairs were implanted on each side for males, while more than 300 hairs on each side for females. The region implanted was tied upwithpressure dressing. The patients were given some analgesics and/or antibiotics after transplantation.

TRAINING

TR1

THE DEVELOPMENT OF MULTIPROFESSIONAL PREVENTION AND CONTROL OF DISABILITY COURSES IN MINAS GERAIS, BRAZIL, FROM 1988 TO 1992

Linda Lehman, Aparecida Grossi, Beatriz Orsini

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Limited resources have made it necessary to prioritize programs and services. In Hansen's disease the priority has been given to early diagnosis and treatment of the disease with the belief that this would prevent the majority of disability and deformity. However, inadequate neurological exams and lack of early treatment of neuritis and reactions have contributed to permanent nerve damage leading to stigmatizing deformities.

The need to integrate both disease control with programs to prevent and control disability made it necessary to develop a practical course to develop skills of local health care workers.

This presentation is to demonstrate how the course was developed based on needs identification from field work experience and control program supervision and evaluation. The key component of the course is the selected teaching methodology adopted to teached the needed skills. The course objective is to develop basic skills to solve problems specific to each local area using simple evaluation and treatment techniques.

The authors note the importance of course and program evaluation to update and modify future courses. This evaluation is critical in evaluating change in health care workers skills and needs for continuing education and field supervision. Evaluation technics and results will be demonstrated.

TR2

ACTION KIT: A MEANS OF PROMOTING LEPROSY AWARENESS

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There must be increased efforts to identify leprosy cases in population groups not yet covered by medical centres. If new cases are identified early enough and treated before disabilities can appear, fear of the disease and the stigma under which leprosy victims suffer will be broken down.

Increased leprosy awareness will play a vital role in early identification. Youth groups can help doctors and health workers promote this.

The Action Kit is a leprosy awareness tool. The information on the new MDT it contains shows people that the disease can be cured, thereby stimulating a desire to actively help fight leprosy.

TR3

DEMYSTIFYING VIDEO - TRAINING HEALTH WORKERS IN ELEMENTARY VIDEO PRODUCTION

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The possibilities of using video as an educational aid are many. There is a need to use Video in a more immediate way apart from producing "well made, slick, professional" programmes. Indeed the intrinsic quality of video is that it can be used in a malleable form. An ideal variation to the conventional well made programme is by using a simple VHS camcorder. If trainers themselves are able to competently handle the camcorder then they would be independent, this would also open out the possibility of using the medium to many more trainers. With these intentions a series of lectures on various cinematographic aspects was conducted at Karigiri. Now after 3 workshops that vague format has evolved into a well structured model. The body of this paper deals with the structure of this workshop, which comprises of 13 modules - Introduction, The Educational Video - A perspective, Camera, Camcorder Hands on - Introduction, Sound, Editing, Direction, Script Writing, Connections and Adjustments, Screening of Prior Exercises, Shooting of Individual Exercises, Analysis of Educational Videos & Evaluation. Objectives, lesson plans, educational aids & assessment methods were identified for each module. The conclusion of the paper will be a discussion on the experiences encountered while conducting these workshops here in Karigiri and also the different ways in which the camcorder is currently being used by teaching staff.

TR4

ARTISTIC INNOVATIONS IN LEPROSY EDUCATION

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Leprosy to this day arouses fear and dread in most people. Although much has been done to educate the public, new methods need to be found to dispel this fear.

The "Our Own Vision" project was designed to educate the public about the facts of Leprosy in an extremely dramatic manner.

"Our Own Vision" project worked with a group of children from the Adivasi colony in Goregaon, a suburb of Bombay, who were aware of Leprosy and they were encouraged to express their feelings in the form of drawings.

These drawings were painted on the outside of a Western Railway commuter train in Bombay. Commuter trains are the primary vehicles that thousands of middle and low income people use to travel from the suburbs to the city and vice versa.

This paper describes the project, the process of educating the children, encouraging them to express their views of leprosy, and the results of a study that measured the effectiveness of this project.

TR5

ALERT IN THE 1990s: EVOLVING TO MEET NEW NEEDS IN LEPROSY TRAINING

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Almost 28 years after being founded to "train men and women for leprosy work in Africa". the All Africa Leprosy and Rehabilitation Training Centre (ALERT) has had to undergo a major restructuring and reorganisation. in order to adapt to the changing circumstances of Africa.

The changing epidemiology of leprosy in the post-MDT world, the important change of perception of the problems of disability and the need for rehabilitation, the non-medical needs of leprosy patients, recent advances in teaching methods and learning materials, and changing social and economic circumstances in Africa - all of these have had to be considered in developing new and appropriate courses for new categories of health workers in leprosy.

Along with a changing pedagogy, ALERT is successfully introducing reforms and innovations in its organisational structures and managerial functions.

This paper describes some of these changes and argues that ALERT is a leaner and more efficient training tool, of greater relevance to the new circumstances of Africa in the 1990s.

TR6

DIFFERENTIAL EFFECTIVENESS OF INDIVIDUAL COMMUNICATION METHODS IN SOCIAL EDUCATION

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Health Education in leprosy involves educating the people by communicating scientific facts towards adopting a rational attitude and practices. This action-research has the objectives of: 1.Measuring the level of awareness about leprosy among high school students. 2.Promoting their awareness through social education and 3. Evaluating the relative merits of different communication methods employed.

The study respondents were 9th class students from 25 randomly selected schools in the city (n=2000). Firstly the awareness level of the respondents was assessed using a questionnaire. It contained 24 items and scores were given to each respondent (S1).

Secondly the schools were divided into clusters of five and in each cluster, one of the five methods namely lecture, exhibition of posters, distribution of pamphlets, comics and screening of film was used. English and one vernacular media was chosen as the media for communication.

Lastly the same questionnaire was re-administered and scores were computed (S2) which indicated the present level of awareness.

Statistical analysis was done. Results pertain to the significance of differece between the pre and post scores(S1&S2)* and among the different methods. The reliability of the questionnaire was also tested and the relavance of results are discussed.

* Tests of variance.

TR7

MANAGEMENT STRATEGIES IN THE CONTROL OF HANSEN'S DISEASE IN THE STATE OF MIANS GERAIS-BRAZIL FROM 1988 TO 1992

Aparecida Grossi, Maria Ana Leboeuf, Eni Magalhães, Sonia Parreiras, Linda Lehman

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The authors discuss some of the epidemiological and operational aspects of Hansen's disease control in the state of Minas Gerais, Brazil, from 1988 to 1992. In 1988 the state of Minas Gerais had 37,102 cases on the active registry with a prevalence of 2.45 which included 1,835 new cases. Deformity among new cases was 13.9%. In 1992 the authors observed a decrease in prevalence, an increase in new cases detected, and a decrease in deformities among new cases. The principal management strategy adopted for improving disease and disability control was the development of training courses. The objective of these courses were to develop human resource capabalities to implement a decentralized control program, to expand the use of multidrug therapy, to implement disability control, and to organize effective actions of control at local health facilities.

Strategies for training priorities were based on epidemiological studies identifying key regional areas which would impact the disease.

The impact of training, was measured by the change in the indicators of new cases detected, prevalence, disability and deformity in new cases, and the number of persons discharge as cured, and the number of services treating the disease with MDT.

TR8

MEASURES AND EFFECTS OF LEPROSY PROPAGANDA IN SICHUAN PROVINCE

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Leprosy propaganda is associated closely with realizng the goal of basic elimination of leprosy in Sichuan province. In order to make local officials change their traditional views on leprosy, intensified propaganda about the knowledge of leprosy has been made especially to government officials at different levels. The programme of leprosy propaganda has been integrated into chronic disease control programme of local government at different levels. Responsible contract for leprosy propaganda is signed annually. Rewards and punishments have been implemented according to the outcome of regular evaluations. Through the above mentioned activities, local officials in Sichuan province are no longer frightened of leprosy and have paid more attention to leprosy control. Leading cadres at prefectural and provincial levels have given lectures on the knowledge of leprosy to the public for about 200 person times per year, making people get rid of their fears of leprosy. A sample social survey showed that 82% of the population surveyed recognized that the infectivity of leprosy is not strong, 74% considered leprosy is curable and 96% have a view that leprosy patients should have a right of work after cure. As a result of contineous and intensified propaganda activities about the know-ledge of leprosy, leprosy control programme in Sichuan province has been implemented more successfully, about 500 new cases were detected and about 1,500 patients were cured annually from 1984 to 1991, and the prevalence rate decreased from 0.1‰ (1984) to 0.04‰(1991).

TR9

PARTICIPANTS' EVALUATION OF A TRAINING PROGRAMME

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The Schieffelin Leprosy Research and Training Centre holds various courses related to leprosy, round the year, with periods ranging from one week to nine months.

The six weeks Medical Officers' Course is one of its more important Training Courses and is held twice a year. An integral part of the Course is its evaluation by the participants. Various methods of evaluation have been tried out and the advantages and disadvantages of each have been utilised in modifying the evaluation in subsequent courses.

During the past four courses, we have used a modified method of evaluation based on that suggested by Abbatt.

We discuss and present here the various aspects involved in this evaluatory method.

TR10

ACTION LEARNING: ITS VALUE FOR LEPROSY PROJECTS

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Action Learning (AL) is an approach to change based on the idea that effective learning occurs when it is: a) focused on the experience of resolving real, not simulated, problems and b) reinforced by the critical but mutual support of fellows, "comrades in adversity", facing similar experiences.

From 1990 AL was used in the ILEP Prevention of Sole Wounds Study (SWS) where 30 leprosy projects were facing the same change experience: introduction of a systematic approach to wounds in insensitive feet. AL was introduced through a) one-week workshops to develop mutual support skills, and increase understanding of the management of sole care; and b) Continuing 1-2 day meetings between participating projects that were close enough to each other to meet at least once every three months until the end of the SWS.

Three workshops (East Africa, India, South-East Asia) took place, all positively evaluated by participants. Organisation of continuing meetings was patchy. Two groups (three projects each) have managed to meet regularly; and interaction traceable to the workshops has continued between several other projects.

Useful organisational initiatives as well as individual learning have resulted: Team enthusiasm for disability prevention; generation and exchange of practical tools; stimulation of short-term action targets; and commitment at project level to action in response to SWS findings.

Our experience suggests that frequent contact, and therefore geographical proximity is very important. Where intensity of mutual support was generated, significant change occurred.

TR11

AN EVALUATION INSTRUMENT FOR LEPROSY TRAINING CENTERS

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This paper describes an effort to provide a valid and reliable evaluation instrument for use in leprosy training centers. An instrument was developed by a panel of leprosy experts and was administered to students (N=163) at the National Training Centre, Ujung Pandang, Indonesia.

Indices of reliability were analyzed by Cronbach's alpha for internal consistency and by a correlation of individual items to total test items. Other psychometric properties of the instrument were evaluated including a difficulty index.

Students consisted of two populations--physicians and paramedical personnel. Responses from these groups were compared by a t-test for independent samples.

Results yielded a reliability coefficient of .58, primarily because many questions could not be included in the analysis, since they had to be translated from the Indonesian language. However, with additional items, the reliability of this instrument could be increased, and could be used in other training centers.

TR12

RESEARCH IN LEPROSY HEALTH EDUCATION - EMERGING TRENDS AND CHALLENGES

C.S. Cheriyan, Dr. Thomas Abraham, Health Education Materials Unit, GLRA, 4, Gajapathy Street, Shenoy Nagar, Madras 30.

Health Education as an essential component of the service delivery system for the management and eradication of leprosy has been emphasised time and again in almost all forums for several decades. It is as imperative as the supply of drugs and a vital area of activity.

Research to improve the practice of health education has to be innovative and the first step for promoting it is documentation of existing knowledge derived through research and field experiences.

In leprosy health education the problem 'of drop-outs' is a major one. Research on this will throw light on the significance of social science models for explaining behaviour in epidemiological terms such as the host, the environment and the agent factors.

We may characterise the main challenges to research in leprosy health education in terms of two major axes namely, 'The degree of meaning' and 'The degree of effort' The factors influencing evaluation of health education methods and programmes, inter personal communication among field workers, their skills and the benefits of preventive health practices have to be investigated in the light of three fundamental elements of evaluation; a)object of interest b)comparison and c)the selection of a standard; the first a conceptual, the second a methodological and the third an administrative problem.

Health education as a new discipline, has to develop its own fund of knowledge through applied research without which the quality of health education will deteriorate. Do we not have sufficient manpower to promote research in this important area? We better take up this challenge in the interest of posterity.

TR13

TRAINING AND EDUCATION STRATEGY IN LEPROSY CONTROL PROGRAM IN SENEGAL

Jean-Claude Naudin, Pape Malick Sylla, Grégoire Detoeuf and Willy Wéry

DAHW, Dakar, Sénégal

In a leprosy control program, strategies to promote the use of MDT and the prevention of disabilities will be fully effective only if the strategy includes training of health service staff and education of the public at large.

Therefore, in the National Leprosy Control Program in Senegal, a health education strategy has been seen up with 4 main components : 1) training for health service staff ; 2) community social mobilization campaign ; 3) information dissemination to primary school teachers in rural areas ; 4) occasional actions with special target groups.

Health education and training materials adapted to each component have been produced in Dakar : flip-book, posters, comic strips, slide show, booklets, etc...

The authors present the general training and education strategy developed in Senegal as well as the educational and training materials produced. A demonstration is given of the battery-operated slide show.

TR14

EDUCATIVE ACTIONS AND HANSEN'S DISEASE CONTROL PROGRAM IN THE STATE OF SÃO PAULO - BRAZIL

Zenaide L. Lessa, Otilia S.J. Gonçalves, Heleida N. Metello, Wagner Nogueira, Marcia Buzzar

Since the State Secretary of Health created the Special Program Group for Hansen's Disease and the Education Group, in 1987, were established the basic guidelines for implanting educative actions for Hansen's Disease Control Program, developed by the Health Teams in the 65 Regional Health Offices of the State of São Paulo.

Its major objective is socialization of scientific knowledge on Hansen's Disease and its interfaces, starting from a holistic vision of the human being, including the biologic.

From 1987 to now, the major option was to give instruments to professionals of health teams to work with pedagogical and ludopedagogical techniques, regarding a problem raisingpedagogical option. Until the year of 1992,

professinals were prepared to develop these actions including local planning of educative actions.

Pedagogical advisory and educative material complement conditions to ensue that educative actions will reach the impact previewed by the Hansen's Disease Control Program for the State of São Paulo.

TR15

THE IMPACT OF PERSONNEL TRAINING ON THE EPIDEMIOLOGICAL AND OPERATIONAL INDICATORS - BRAZIL, 1986 TO 1997

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Between 1986 and 1991, the Dermatology Division developed a broad proposal for personnel training nationwide, targeted to the implementation of activities required for the control of a rising endemy, in a service network with a quantitative and qualitative deficit of staff.

This paper analyses the number of people trained by federated unit in relation to number of patients and correlating them with operational and epidemiological indicators.

The modular training system adopted facilitates group training, centered on the problem-raising methodology and allowing critical reflexion, construction and reconstruction of knowledge, adoption of strategies for problem-solving and integralization of health activities.

Since 1991, the revision of trainings reinforces the assistance-teaching axis, stimulates operational research, the participation of the reference centers and the expansion of MDT as the single regimenadoped in Brazil.

TR16

IMPACT OF PERSONNEL TRAINING ON THE INDICATORS OF THE HANSEN'S DISEASE CONTROL PROGRAMME IN THE FEDERAL DISTRICT, 1990-1992

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Starting from a situation diagnosis of the Hansen's Disease Control Programme in the Federal District in 1990, the authors outline major guidelines for personnel training.

Between 1990 and 1992, the personnel training programme gave priority to professionals from fields relevant to Hansen's Disease, according to the District's Emergency Plan and adopting a methodology where the trainee can develop his capacity for reflection-action, from situations found in his own environment.

This methodology, know as "problem-raising", is being developed by Brazilian officers with the advice of the Pan American Health Organization (PAHO).

The work shows the improvement of the epidemiological and operational reached with the personnel training programme.

TR17

THE USE OF 'MATCHED QUESTIONS' IN PRE- AND POST-TESTS, TO EVALUATE TRAINEES AND FACULTY IN A LEPROSY MEDICAL OFFICERS' TRAINING PROGRAMME

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Pre-and-post-tests are an established and useful method of evaluating training programmes, and have been used at Karigiri in the Six Weeks Leprosy Medical Officers Training Course. The main objectives of these tests are two-fold. The pre-test gives a baseline impression of the level of knowledge of the group at the beginning of the course, thus enabling modification of the teaching strategy when necessary. Secondly, a comparison of pre-and-post-test scores, can be used as an indicator of the teaching effectiveness of the faculty, since each of the questions are framed such that they reflect a specific course objective or sub-objective and cover the various subject fields of the course .

The usual practice is to administer exactly the same set of questions in both the pre- and the post-test. This may not be quite satisfactory, since there is always a chance that students may just recall the pre-test question from memory, and be able to obtain a better result in the post-test, without actually having benefitted from the course. To avoid this possibility of 'practice familiarity' and 'rote reproduction', alterations were made in the presentation of the questions in the post-test.

The post-test therefore consisted of a separate set of questions compared to those in the pre-test. Care was taken to ensure that these were carefully 'matched' in such a way that the corresponding questions in both the pre- and post-test examined the understanding of the same concept or fact but were worded differently. In the case of Multiple Choice Questions this was achieved by altering either the 'stem' of the question, or the 'keys' offered. For 'True-or-False-type' questions, the statements were either modified, or rephrased, in such a way that they reflected two facets of a single concept or fact.

This paper analyses the details of the 'matched questions' format, its advantages and the results of its use over three successive courses.

TR18

LEPROSY TEACHING AT MEDICAL SCHOOL THROUGH COMMUNITY-BASED LEPROSY CONTROL IN A SLUM AREA

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THE EVALUATION OF LEPROSY PATIENT ATTENDANCE AT THE 4 PUBLIC MEDICAL SCHOOLS IN THE GREAT RIO MADE IN 1990 SHOWED A LOW LEVEL OF COMPLIANCE TO OFFICIAL NORMS OF THE NATIONAL PROGRAME.

CONSIDERING THIS WE INTRODUCED AN INTERVENTIONIST PROJECT IN ONE OF THESE MEDICAL SCHOOLS AND ITS MAIN GOAL IS TO IMPROVE THE UNIVERSITY CONCEPTS ON LEPROSY CONTROL BY MEANS OF:

MOVING THE STUDENT PRACTICE FROM THE UNIVERSITY HOSPITAL TO THE HEALTH CARE CENTRES LOCATED IN THE CAMPUS NEIGHBOURHOOD.

MAKING THE UNIVERSITY CO-RESPONSIBILE FOR CONTROL ACTIVITIES AT A DISTRICT LEVEL.

SINCE 1991 WE HAVE BEEN DEVELOPING THE MAIN ACTIVITIES LISTED BELOW WITH A SUCCESSFUL ACCEPTANCE AMONG STUDENTS:

IMPLEMENTING LEPROSY CONTROL IN R.DE JANEIRO CITY AT DISTRICT LEVEL ORGANIZATION - TWO MORE HEALTH UNITS ARE ATTENDING PATIENTS IN A SLUM AREA.
IMPROVING THE UNIVERSITY CONCEPTS ABOUT LEPROSY AND CONTROL PROGRAMME- THE STUDENTS OF BIOMEDICAL AREAS HAVE CONTACT WITH LEPROSY PATIENTS IN SEVERAL OPPORTUNITIES SUCH AS: PRIMARY HEALTH CARE PROGRAM IN HEALTH CENTRES, IN THEORETICAL ACTIVITIES IN PREVENTIVE MEDICINE, TROUGH PRACTICE ATTENDANCE AT THE UNIVERSITY HOSPITAL IN THE SERVICES OF DERMATOLOGY, GENERALMEDICINE, TROPICAL DISEASE, NEUROLOGY AND REHABILITATION MEDICINE. IN ADDITION THEY CAN PARTICIPATE IN THE OPERATIONAL RESEARCH ON FIELD THROUGH THE PROGRAM OF SCIENTIFIC INITIATION; E.G. THE SELECTION OF CLUSTES AREAS FOR LEPROSY PROSPECTIVE STUDIES HAS ALREADY BEEN DONE.

THE CURRENT RESULTS MAKE US RECOMEND THAT BRAZILIAN UNIVERSITIES SHOULD WIDEN OPPORTUNITIES TO TEACH LEPROSY WITH LOW INVESTMENT.

TR19

TASK ORIENTED TRAINING OF PRIMARY HEALTH CARE PERSONNEL IN LEPROSY CASE DETECTION - AN ASSESSMENT

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For the successful involvement of primary health care staff in leprosy control, initial effective training is crucial. The current training modules at

initial stage seem to be too elaborate and sometimes confusing to a beginner. Hence it was decided to try out a simple task-oriented training just for leprosy case detection as a first step. A half a day training was offered to Primary Health Care staff in Raipur, Madhya Pradesh Multidrug treatment district emphasizing only three suspecious symptoms - 1) hypopigmented, anaesthetic patches, 2) shiny oily skin and 3) deformities of limbs. Colour photographs and patients were used for demonstration.

232 multipurpose workers of 8 Primary Health Centres undertook "Photo survey" of 840 villages covering a population of 5,27,160 in 15 days during their annual family welfare ennumeration programme. They detected 200 new cases (MB : 32, PB : 168) and reidentified 543 (MB : 206, PB : 337) old known cases.

This experience showed that a simple task-oriented training of PH Care staff just to suspect leprosy as a first step may go a long way in augmenting leprosy case detection even in vertical leprosy programme. Similar training in stepwise fashion for treatment, case-holding and deformity care could perhaps lead to a gradual process of integration of leprosy work with general health services. However, further operational research in this direction is needed.

TR20

EARLY DETECTION OF OCULAR LEPROSY

ALAMPUR SAIBABA GOUD

SIVANANDA REHABILITATION HOME
KUKATPALLY , HYDERABAD

The number of registered cases of Leprosy was 3.7 millions in 1990. 25% of them have got ocular involvement and may be 5% do have blind ness. This high incidence of blindness is due to ignorance on the part of the non-medical assistants and Medical Officers on one hand and patients on the other. The patient will approach the doctor in late stages,as he does not have acute signs and symptoms.

This paper deals with various methods of training to detect early ocular involvement to non-medical assistants and medical officers including health education to the patients. This work has been carried out at Sivananda Rehabilitation Home,Kukatpally,Hyderabad.

TR21

"SIMULATION GAME" AS A MODEL OF HEALTH EDUCATION IN LEPROSY. AN EXPERIENCE FROM THE RURAL LEPROSY CONTROL PROJECT IN NGANJUK REGENCY, EAST JAVA .

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Dept.of Dermatology, Airlangga Medical Faculty ,
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A "simulation game" has been introduced as a part of the Leprosy Training Course for village caders in the Regency of Nganjuk, East Java. The aim of this activity is to improve their knowledge and ability in solving the leprosy problems in the community, by simulating these in a "play" situation .
The game is played by a group of 10-20 caders, sitting around an illustrated playing chart (80x120cm) which contains some written questions from No.1 - 20. Conducted by a leader as a moderator, the cader throw a dice to get the number of question to be naswered. The other participants are requested to give a comment, addition or objection to the statement from the answer. The questions are chosen from everyday's experience in leprosy problems found in the community.
This programme has been conducted to 20 groups of leprosy caders from several districts of Nganjuk. Evaluation on the individual ability and performance of leprosy caders showed a better attitude and more self confidence, which is very helpful in reducing the stigma of leprosy in the community.
As a conclusion, the method of Simulation Game in Leprosy seems a good model for the Community Health Education which eventually could be applied for other program of disease control .

TR22

TRAINING FOR NATIONAL TB/LEPROSY PROGRAM IN TANZANIA SINCE JULY 1977

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National Tuberculosis and Leprosy Programme Tanzania. TB/Leprosy Central Unit, Dar es Salaam Tanzania.

Training for National TB/Leprosy Programme has been one of the important activities when the programme started in July 1977. With the commitment of the Government officials Health staff at all levels, (Central, Regional District and Dispensary) Politicians and the community have been trained. Each group had a training schedule ranging from 2-30 days depending on the type of training R.T.L.C. meeting, D.T.L.C. course, zonal seminar, District seminar, laboratory seminars. Regular training has been conducted for both diseases on a yearly Plan of Training. Since we have on systematic Plan of training every year, the programme has been running successfully for both components of the programme.

In the wake of the H.I.V. endemic new training topics have to be chosen, after all for the close relationship of H.I.V. Infection and T.B.

TR23

HANSENIASIS EN LAS ESCUELAS

Dora Martins Cypreste, Nuciclea Barbosa dos Santos, Sara Aguiar Campos and Regina Lucia Fraga Borgo

Exposicion en poster de la Cartilha Educativa.

TR24

FIELD TESTING OF THE COMMUNITY HEALTH EDUCATION LEAFLET DEVELOPED AT THE NATIONAL LEPROSY TRAINING CENTRE,UJUNG PANDANG,INDONESIA

Djohan Kurnia, Norma Aspar

National Leprosy Training Centre,Ujung Pandang,Ministry of Health, Indonesia

The leaflet developed at the National Leprosy Training Centre,Ujung Pandang,Indonesia was field tested on two occasions for its effectiveness and its acceptability, and for the community opinions. All target community groups (students year 4,5,6, their teachers and the village community leaders) showed an increase in their average test scores (reflecting the extent of the essential knowledge in leprosy given in the leaflet that the community members had or gained) after they had read the leaflet for ten minutes. The scores increased further after the leaflet had been explained and discussed. Thirty two out of 44 answers received rated the leaflet was very attractive or attractive. Tweenty six out of 50 rated the leaflet was very horrible or horrible.Sixteen out of 24 said that the leaflet was too small. Sixteen out of 18 said there were too few pictures, and 14 out of 23 said there were too few words in the leaflet.

TR25

ASSESSING EFFECTIVENESS OF LEPROSY EDUCATION IN RURAL INDIA: A RANDOMISED-CONTROLLED COMMUNITY-BASED INTERVENTION TRIAL

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A randomised-controlled community-based trial was carried out in a rural area of a leprosy endemic district of Central India to evaluate a leprosy education intervention during one year in terms of its impact on knowledge and attitude and its influence on case detection and case holding.

'Education rate' and 'education rate difference'statistics were derived for assessment of effect of the treatment. 'Education rate' was defined as per cent increase in knowledge level among those who were found without 'correct' knowledge initially. 'Education rate difference' like an 'attributable risk' is defined as the difference of 'education rates' in treatment and control areas. It should take into account any extraneous effects in control areas and thus estimate the effectiveness of treatment per se.

The education program was most effective in teaching villagers the early presenting symptom of leprosy as 'patch with anaesthesia' ('education rate difference'=43 per cent). The second strongest effect was seen for knowledge about deformity that not all patients have deformity('education rate difference=32 per cent). For cause as 'germ', it was 27 per cent, for curability 20 per cent. Attitudes also improved with treatment. Increase in knowledge levels were also observed in control area and are discussed and phenomenas like 'secular effect', 'diffusion effect','interview effect' has been suggested for the increase in control area.

Voluntary reporting and treatment regularity of patients increased during the intervention program.

TR26

EDUCATION SANITAIRE LEPRE

Enquète dévaluation des connaissances et de la perception de la lèpre à la MARTINIQUE

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J.C CAROLINA - Dr M. CONSTANT-DESPORTES
Dr A. LEOTURE - C. CHARLES-NICOLAS
Dr J.C SAINT-ZEBY - A. YEBAKIMA

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Tout d'abord, l'enquête préliminaire menée en 1986, montrait une bonne connaissance du symptôme initial de la lèpre et mettait en évidence la transmission des messages, mais également soulignait la peur du sujet atteint de cette maladie.

La seconde enquête évaluative en 1993 permettra d'une part de confirmer oud'infirmer les précédentes observations, d'autre part d'analyser l'impact de 10 ans d'information sanitaire centrée sur une modification des mentalités.

TR27

PROMOCION PARA LA SALUD EN EL PROGRAMA CONTRA LA LEPRA EN MEXICO

Dr. F. Castellanos, ESP. A. Martinez, Lic. A. Barocio, Dr. J. Rodríguez-Domínguez.

El programa contra la lepra en México planteó como objetivo eliminar la transmisión de la enfermedad para finales de 1994, reduciendo su taso de prevalencia a menos de 1 X 10,000 hbs, por medio del tratamiento con poliquimioterapia de todos los enfermos.

Para conseguir tal propósito se elaboró un subprograma educativo para la población general y enfermos entre los servicios de salud y la colaboración técnica y financiera del Fondo Ciba-Geigy contra la lepra. Se diseñó y editó material audiovisual y gráfico dirigido a la población con el lema "La Lepra es Curable". Se difundieron por medios masivos como TV, radio y carteles, y por medios individuales, promoviendo el diagnóstico, la continuidad del tratamiento, la prevención de incapacidades con recomendaciones sobre cuidados que deben proporcionarse a los enfermos y su familia. También se diseñaron materiales educativos para capacitar al personal de salud con los temas de diagnóstico, tratamiento y prevención de incapacidades. Se realizó una encuesta de opinión dirigida a 3 grupos: enfermos, familiares y población general, en dos fases, la primera antes y la segunda un año después de la difusión del material, evaluando el grado de conocimiento de la enfermedad, su transmisibilidad y la aceptación de los enfermos, en la comununidad. Los resultados de la encuesta reportaron mayor conocimiento de la enfermedad por la población.

Derivado de lo anterior se incrementó el número de enfermos incorporados a POT.

TR28

LEPROSY LITERATURE ACCESS AND RETRIEVAL BY MICROCOMPUTER USING CD ROM

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A database of 41,160 citations selected from 2,874 books and journals published between 1913 and 1991 is available on compact disk ROM (Read Only Memory). The selection criteria for this literature are the keywords: leprosy, *Mycobacterium leprae*, diet and nutrition in connection with infection and immunological factors, and immunity. Each citation contains the author(s) name(s), Unique Identifier (UI) number where available, title, abstract (in about half of the citations) and reference. Three quarters of the data is from the United States National Medical library online service and one quarter from the Tropical Diseases Bulletin, London. About 1% of the data came from a variety of sources.

The CD ROM contains the leprosy literature data in English. The data on the compact disc may be accessed by a choice of three computer programs on the compact disc. One computer program has on line help in English; one in French; and one in German. Exhaustive and rapid selection and viewing or printing of the data is made possible by the computer programs. The equipment necessary to use the compact disc is a micro computer that is IBM compatible with at least 512 K of RAM using DOS Version 3.2 or higher and equipped with a CD ROM drive. The report will include illustrations of data selection from the compact disc with a brief explanation of how to understand the various computer screen displays encountered using the computer program to access the data.

This compact disc is obtainable from the Leprosy Research Foundation at a cost of $20.00 (U.S. currency) to cover postage and handling.

TR29

THE TEACHING OF LEPROSY IN MEDICAL COLLEGES OF ORISSA, INDIA

JAYADEV SAHU
GMLF HE Unit Khurda Road, Orissa, India

Orissa: 31 million population, 140452 leprosy cases, PR 4.82, Trial 30-40%, Literacy 48%, MDT started 1983. By the end of 1993 it is anticipated that all 13 districts of the state will be covered by MDT.

GMLF HE Unit Khurda Road for past 12 years involving three medical colleges of Orissa at UG PG Staff level recommending leprosy teaching in main stream syllabus with no extra time but as part of routine teaching process. Thus leprosy used as a Model in teaching Anatomy, Physiology, Biochemistry, Immuno-pathology, Pharmacology, Microbiology, Medicine, Surgery, Orthopaedics, Plastic, Paediatrics, Dermatology, ENT, Dental, Neurology, Ophthalmology, Physiotherapy & SPM.

Seminars of Students Academic Socity, Interdisciplinary Workshops of Staff Academic Society, using teaching and learning materials with searching questions from UG PG staff made teaching and learning improved significantly Questions on leprosy appear in MBBS MD (Ophthalmology) Examinations.

Syllabus on Intensification of teaching leprosy circulated to all medical colleges in India with the hope that future medical graduates will successfully implement MDT and eliminate leprosy from Orissa and India.

TR30

EVALUATION OF THE HEALTH EDUCATIONAL METHODS AND EFFECTS OF A WOUND REDUCTION PROGRAM FOR 72 WORKERS WITH HANSEN'S DISEASE IN BAMBUI, MINAS GERAIS-BRAZIL

Linda Lehman

Hospital São Francisco de Assis, Fundação Hospitalar do Estado de Minas Gerais, Bambui, Minas Gerais, Brazil

This study evaluated the effects of a wound Reduction Program in 1986 on 72 workers who had Hansen's disease and lived and worked at the Hospital São Francisco de Assis.

The health education intervention was evaluated by using both qualitative and quantitative data. The PRECEDE Model and Social Learning Theory were effective theoretical frameworks for planning, implementing, and evaluating the health education intervention program which aimed to change and sustain behavior change over time. This behavior change was necessary for improving quality of life by preventing disability and deformity progression caused by wounds and their complications.

The wound prevalence before the intervention was 58%. There was a significant decrease in wounds of 71% from March to December 1986. The wound prevalence in 1988 demonstrated a sustained wound reduction prevalence of 24%.

This study demonstrates the importance of health care worker training in health education methodology and its application in both control and prevention of disease and disability intervention programs. It further demonstrates that public health and rehabilitation need to be intermixed to assure quality of life for persons with Hansen's disease.

TITLE ONLY

T1

PUBLIC EDUCATION

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From the times of recorded history, Education has been associated with liberation of men from restraints of ignorance, poverty and illness.

We have the drugs, physiotherapy and various surgical procedures. However, what will finally take us to a conclusive victory in the war against leprosy - its fallacies - and many other communicable diseases, will be EXTENSIVE PUBLIC EDUCATION.

Education begins at a very tender age under the protection of Mother and then right through school to University and even thereafter. Education moulds and develops children into healthy youth who become rich dividends of the country in propogating health awareness to their families (community).

To control spread of infection-public education regarding disgusting antisocial habits like indiscriminate spitting, unstiffled sneeze, spurious cough, hygienic living conditions, good sanitation and overcrowding, unknown in the West, but a major problem in our country and other developing countries.

Improving literacy and status of women and female children has to be given the highest priority. Rightful place of women in the household will play a vital role - eliminate poverty and lead the country towards advancement. (Association of poverty with overpopulation and vice versa).

PUBLIC EDUCATION removes IGNORANCE, POVERTY ILLNESS ___ PROMOTES HEALTH Human Development HAPPY LIVING ___ COUNTRY'S DEVELOPMENT.

T2

THE EFFECT OF OFLOXACIN TO MDT RESISTANCE, A CASE REPORT

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Several cases are supposed to be MDT resistance even in our project located in the south of Bangladesh, where MDT has been given since 1987. Ofloxacin combined with Rifampicin has been given to such cases. This report is a case report of one patient who was supposed to be MDT resistance and administrated with Ofloxacin combined with Rifampicin for one month. Skin biopsy was taken before and after the administration of the new regimen.

The case is 30 year-old female, lepromatous, initial B.I. was 5.66 in 1987, who had taken MDT irregularly for 5 years. B.I.in 1992 was 2.33. Histologically intact AFBs were seen in the cystic Giant cells, foam cells & etc, which suggests active borderline leprosy before the new regimen. But AFBs were seen degenerated after it.