ABSTRACTS

INTERNATIONAL
LEPROSY
CONGRESS
1993
CII2
MULTIDRUG THERAPY FOR TREATMENT OF LEPROSY PATIENTS IN NEW CALEDONIA AND FRENCH POLYNESIA. RESULTS AFTER 10 YEARS.
Maryse Crousaz, Philippe Glazig, Jean-Louis Cartel, Pierre Bobin and Jacques Gouyet
C.H.T. Gaston Bouthet, Noumea, New Caledonia, Institut Louis Nallapad, Papeete, Tahiti, French Polynesia

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 thiosalicylate 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 (28 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 > I was notified. Among the 62 patients treated with a thiosalicylate, 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.

CII3
1-YEAR SURVEILLANCE OF 451 CURED MB PATIENTS RE-TREATED WITH MDT
Zhou Dushui et al.
Shanghai Zuni Hospital, Shanghai, China

Since 1983, 451 MB patients clinically cured with DDD monotherapy together with BI of 2 or more at any site were re-treated with DDS, RFP and INH in combination. One hundred and eighty-seven of these were males and 264 were females. Their age ranged from 17 to 10 years and their disease duration ranged from 1 month to 36 years. Cured patients not re-treated were used as controls for this trail.

All patients were administered RFP and INH (120mg each once monthly with supervision and DDS 150mg daily) self-administered. This treatment was continued for 12 months and was completed within a period of 15 months. Six hundred and twenty cases (44.2%) of them completed regularly the prescribed course but 25 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 (1534 cases for more than 1 year), no relapsed case was identified. But there were 17 cases detected as relapses among the 137 control patients: giving an overall relapse rate of 12.1% and a mean annual relapse rate of 1.55%. Type I lepra reaction was seen in 3 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.

CII4
EFFECT AND SURVEILLANCE OF 1,674 LEPROSY PATIENTS TREATED WITH MDT IN SHANDONG PROVINCE OF CHINA
Yu Xia, Tang Yushu, Zhang Hongtian, Xu Wenzhang, Zhao Tian’en
Shandong Provincial Institute of Dermatology, Jin’nan, Shandong Province, China

One thousand and seventy-six active leprosy patients were detected in Shandong province from 1982 to 1991. Of these patients, 659 cases were MB and 615 were PB. 924 were new cases never treated before and 140 were re-treated 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 smear was decreased by 0.7 each year in the first 2 years. By the end of 1991, 742 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 BB, 37.2 months in BT, 33.2 months in TT and 31.3 months in indeterminate cases. As regards the five year cured rate, there was no significant difference between the newly diagnosed and relapsed cases. The 742 cases above mentioned have already been monitored after release from treatment for a total of 2,284.5 person-years. The longest period monitored was 5 years in PB and 6 years in MB. Only one BT patient relapsed. No lepromy reaction was found after stopping therapy, except neuritis with severe neuropathy occurred in one BD case.

CHEMOTHERAPY
CH5

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

Raman Dhakal and Shrikant Pande

Awadhi Municipal Hospital for Leprosy, Wadala, Bombay 400 031, India

The analysis of five year bacteriological reports available in the hospital records of 678 XL and 180 XL patients who received WHO MDT regimen for varied duration, showed that there was a progressive reduction in the respective average Bacteriological Index (BI) by 0.7% and 0.9 index per year, irrespective of the period of therapy.

At an 10 month average duration of therapy the average BI of LL patients was 1.9 (with 59% negative patients) and that of XL patients was 1.1 (with 66% negative patients). The difference observed in BI response of LL and XL patients with comparable initial BI (i.e., 3.9 and 4.4 respectively) was statistically significant that a radiographic 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 range of duration of therapy.

In 245 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 0.4 (with 95% negative patients) at the end of third year of follow up.

CH6

FIXED DURATION MULTIDRUG THERAPY (MDT) FOR MULTIBACILLARY (MB) LEPROSY IN INDIAN RURAL PROGRAMME

R Ganapati, S Hanumanth, VN Verma, J Jain & RL Gandewar

Bombay Leprosy Project, Vidyanand Bhavan, 11 TN Purav R Canapott, V Ekorbarnn, SN Jain & RL Gandewar

Bombay 400 022, India

On the basis of the available evidence of bacteriological decline after MDT (WHO regimen), for 24 months in MB patients, the National Leprosy Eradication Programme of India has adopted this procedure as a rational policy. Field level experience on operational aspects of successful practice of MDT in still lacking. In 1989 MLP gave permission to us to study MDT in Rural (Gujarat) and Chittapur (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 sites for skin smears, ensuring reliability of smear examination and reporting systems etc.

Observations on bacteriological decline over 24 to 3 years given below are in conformity with results reported earlier (Ganapati et al. 1992).

<table>
<thead>
<tr>
<th>BI at No of years</th>
<th>BI at First Year</th>
<th>BI at 2 years</th>
<th>BI at 3 years</th>
<th>BI at 5 years</th>
<th>BI at 7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 5</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>BI at 1st year</td>
<td></td>
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<tr>
<td></td>
<td>4 to 5</td>
<td>4-1</td>
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<td>2 to 3</td>
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<tr>
<td>1 to 0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total 98</td>
<td>(3%)</td>
<td>(2%)</td>
<td>(1%)</td>
<td>(2%)</td>
<td>(4%)</td>
</tr>
</tbody>
</table>

FMT: Fixed Duration MDT

Total bi: 98

TR: Treatment rendered

CH7

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

Ravi Kumar, Jayaprakash Muliyil, Abraham Joseph

CHC Unit, Parvatipuram 532 501, A.P. and CMC Vellore 632 002, South India.

This study was carried out in the Leprosy Control Unit, CHC 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 of patches (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 end of 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 < 0.005). Interestingly those who had prior dapsone monotherapy showed a significantly quicker rate of healing (P < 0.001).

Persistence 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

Y P Jayaprakash, P D Samson

The Leprosy Mission Hospital, Vizianagaram, A.P. India.

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

248 children who had completed Paucibacillary Treatment in 1985 and were followed up to 1992 were included in the study. Of the 248 children 157 were male and 91 were females. 62 (2.6%) were less than 5 years of age, 69 (25.7%) 5-9 years of age and 153 (61.7%) were 10-14 years. 20% 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 2.01/1000 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 (MDT) 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.
CH10

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

This study is supported by UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.

MTC leprosy treatment started as a routine in the State of São Paulo, Brazil, on July 1991. All the newly diagnosed cases should be evaluated. Cases of various adverse reactions from death to 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 from that date to December 1992. Cases which have been reported and investigated were classified, following clinical, laboratory and epidemiological criteria as confirmed, probable or discarded.

The patients received 203 consultations, of which 150.3% were considered confirmed, 55% probable and 21% discarded. From the confirmed cases, 43.7% were males, 43.7% in the 30 to 50 years old age group and 35.3% from 50 to 70 years old. Some 46.9% of the patients had been admitted to hospitals. The most frequent diagnoses were skin and nerve infection and diabetes-like syndrome.

In our study, we have not reported presence of 'persisters' in MDT scheme. One reason for this is the period of 8-10 years of follow-up, the median of 8 years at the time of inclusion, the possibility of continuing the evaluation and also to evaluate the special surveillance system itself.

CH11

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

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

CH12

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

We reviewed the "Disability Grading" (MIR 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 M-ISOepromadine regime was used in most patients (Rifampicin - Dapsone - ISOepromadine). 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 THERAPY IN MULTIBACILLARY LEPROSY

Dr. C. Rajendra, Dr. Claire Veillet and Dr. Cathy Pushpadass.

Profile of five relapse cases following two different regimes of Combined Therapy: Regimen A and Regimen B in 1174 HL 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 Leprosy at Hemerijckx Leprosy Centre, Polambakkam, South India.

Of the five relapses, one was MB type and the four being HL 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

MLEPRAE VIABILITY IN SKIN AND NERVE AFTER MDT AND THEIR SENSITIVITY TO ANTI-LEPROSY DRUGS

Vanaja Shetty, Suchitra Naik, Mukund Uplekar & Nashir Antia

The Foundation for Medical Research, 84-A, R.G. Thadani Marg, Worli, Bombay-400081, India.

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

End of Document.
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 RIFAMPICIN IN HIGHLY BACILLIFEROUS BL/LL SOUTH INDIAN PATIENTS**

A 10 YEAR REPORT

Aleynna Thomas, M. Nagarajan, Lalitha Hari, K. Prabhakar

Tuberculosis Research Centre, Madras, India.

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 up to 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**

Mustafa Sütülü, Türkân Saylan, İlhan Özet.

İstanbul Leprösy Hospital, İstanbul Leprösy Research Center, Istanbul, Turkey.

Between early 1982 and early 1984, 74 patients were taken into the short term course RMP-ETH-COGS 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 RAP 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 7 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**

Paul Gatt

University Department of Dermatology
Sir Paul Boffa Hospital
Floriana, Malta

Since the Malta Leprosy Eradication Programme was inaugurated in June 1972, 257 patients have been treated with Isoperodian 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 organizational 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**

Li Huan-Ying, Beijing Tropical Medicine Research Institute, Beijing 100050

Yu Xiao-Lu, Shandong Provincial Institute of Dermatology, Jinan 250022

Huang Wen-Biao, Yunnan Provincial Institute of Dermatology, Kunming 650223

During 1983, 80 untreated MB patients from Shandong and Yunnan 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 Shandong and 95.3% (41/43) of patients from Yunnan have converted to smear negative elsewhere in China.

Results at the eighth year of follow up plus their level of PGL antibody will be presented.

**CH19**

**ENFRIJAMIENTOS MULTIRACICLARES TRATADOS CON MONOTERAPIA SULFONICA**

Dr. J. Terencio de las Aguas.

Sanatorio de Fontilles, Alicante, España.
Se estudian entre 352 enfermos multibacilares (LL) tratados con monoterapia sulfonica el numero de recaidas despues de conseguirse la negativizacion.

Se observan un total de 33 recaidas entre 7 a 39 anos despues de inactividad bacteriologica.

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

CH20
RELAPSES IN 20,091 CURED LEPROSY CASES IN SHANDONG PROVINCE OF CHINA
Pan Youie, Zhan Tian'en, Wang Lei, Xu Mengtao
Shandong Provincial Institute of Dermatology
A retrospective analysis on 2001 cured leprosy cases in Shandong Province of China from 1955 to 1990 is presented. Analysed with life-table method, the relapse rates for NB and PB cases were 6.4% and 3.9% per year respectively. The levels of the relapse rates were closely related to the therapeutic drugs used in the past. In NB patients treated with DDS and DDS/RIF, the relapse rates were 7.14% (4.5-6.12%) and 1.47% (0.21-2.93%) respectively. The relapse rate is significantly higher than the latter one. In PB patients treated with thiacetazone, DDS and WHO-PB regimen the relapse rates were 12.4% (9.6-15.6%) and 0.11% (0.01-0.24%) respectively. The relapse rate in the WHO-PB regimen treated group was significantly lower than those in other two groups (0.21-2.4%). No recaida was found neither in NBI2567 nor in PB 051 cases treated with Dapsone monotherapy.

CH21
SINGLE DOSE RIFAMPIN CANNOT PREVENT RELAPSE IN SKIN-DRUG NEGATIVE MULTIBACILLARY LEPROSY PATIENTS AFTER DAPSONE MONOTHERAPY
P. Jamet, L. Blanc, O. Pave, Y. Traore, P. Robin
Between 1982 and 1985, a single dose of RMP 1500mg was administrated by 136 multibacillary leprosy patients who had become clinical and skin-smear negative after various duration of dapsone monotherapy, and then antileprosy chemotherapy was totally stopped. By the end of June 1992, 15 relapses were detected among the patients. The relapse rate per 100 patients-year was 2.125%, 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
Mahendra Dhulekar, Varsha Shetty & Noshir Antia
The Foundation for Medical Research, 84-A, R.G. Thadani Marg, Hanoi, Bombay-400018, India.

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, ethambamide and pyrazinamide. To date however, leprosy resistance to MDT has not been observed. While 58% of currently registered cases are estimated to have had 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
Roland V. Collona, Eduardo C. Dola Cruz, Tranquillo T. Fajardo, Jr., Laarni G. Villahermosa and Gerald P. Walsh
Leonard Wood Memorial, Center for Leprosy Research, Cebu, Philippines

The use of Dapsone as monotherapy in leprosy in developing countries has resulted in the occurrence of secondary DSS resistance in patients. Exposure of susceptible 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 C3H/CH 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% (Collona et al, 1989) and 3.6% (Quiro et al, 1981) 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.
N.K. Chopra
District Leprosy Officer & District Project Officer, Bharuch - 392 001 (Gujarat).

The prospective study of relapse includes paucibacillary cases of leprosy belonging to non-lepromatous group consisting of tuberculosis, neuritic and indeterminate.

6818 patients paucibacillary were screened (1115 d.q. 92) who had completed the prescribed period of treatment and now under surveillance for varying periods are evaluated for evidence of clinical relapse of their diseases. Paucibacillary leprosy 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 1 reactions, were extension of existing skin lesions, appearance of new skin lesions, paraesthesia, pain or paresthesia 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 dapson monotherapy for a minimum period of 2 years in Bharuch district using following parameters:

1. Age, 2. Sex, 3. Site, 4. Type, 5. Duration of treatment

The results indicate that short course chemotherapy.

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.

| CH25 | TREATMENT OF HIGHLY DACILITATED BULL CASES WITH A PYRAZINAMIDE CONTAINING REGIMEN
| K. R. Kothari, V. M. Matodi, M. N. Tare, C. T. Livannavar, C. Thirthawar, M. A. Patal, and A. S. Bhatia
| Central JALMA Institute for Leprosy (ICAR), Tappan, Arvind 222 001, India

Pyrazinamide has been shown to have a marked sterilizing effect on tubercle bacilli. A pilot trial earlier showed that it has some beneficial effect in leprosy also. We have carried out a trial in which highly DACILITATED untreated BULL cases were given Rifampicin 600mg once a month, Clofazimine 50mg daily and Dapone 100mg daily, tit the attainment of smear negativity combined with Pyrazinamide 150mg daily in divided doses for 1 year. The progress was monitored periodically by clinical, bacteriological, IE, mouse foot pad, bacillary ATP measurements and histopathological parameters. Smears from the same sites and biopsies were repeated yearly. 25 patients in the 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. 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 regimen at these time periods. By 3 years, 38% of patients of Pyrazinamide group became smear negative and mean BI fell from initial 4.6 to 0.7 whereas in non-Pyrazinamide group 65% 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 sterilizing effect in multibacillary leprosy.

| CH26 | CLINICAL TRIALS OF MINOCYCLINE IN LEPROMATOUS LEPROSY
| Robert H. Gelber, Lynda P. Murray, Patricia S. Miel, Mabel Tsang, and Thomas R. Lee
| Medical Research Institute of San Francisco, CA, and University of Southern California, Los Angeles, CA, USA.

In our first clinical trial of minocycline 100 mg once daily for 3 months, 8 lepromatous leprosy patients responded excellently rapidly both clinically and bacteriologically. After 1 week of therapy 6 of the patients had noticeable improvement observed in either skin lesions 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. Electrophysiological study showed as a reduction of 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 ± 0.68 μg/ml (range 0.87-5.66 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 period 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 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 BIFAMPICIN CONTAINING REGIMENS FOR MB LEPROSY YIELD HIGH RISK OF RELAPSE
| Lathe, P. Junet, O. Faye, S. Zow, A. Bobin

Between 1977 and 1991, 196 MB leprosy patients entered 12 different MDT rifampicin containing regimens in Institut MARCHOUX. Among this cohort, 100 relapses occurred during follow up time from end of treatment to January 1991. Relapses were diagnosed on clinical, bacteriological and histological criteria, to date 66 were confirmed by the presence of viable M. leprae in skin biopsy specimens and 21 results pending. All the isolated strains remained susceptible to the M. leprae. Relapse rate ranged from 2.2% (0.4-5.7) to 7.3% (4.5-8.8) per 100 patients per year, risk of relapse at year 5 ranged from 36% for regimen of one year duration to 148% (11-177) for regimen of 2 weeks duration. Average risk of relapse at year 5 was high for the 1 regimen that duration were three months or less (6.13%), compared to the one of two years duration and strain as well as in the other regimen of 2 weeks duration (13.8-17.5 respectively). For these last regimen, risk of relapse at year 10 ranged from 72% (0.13-17.5 to 93%) (17-53) but there was no evidence that the duration of therapy (one year versus two years) changed the risk of relapse. Time distribution of relapse for regimen having at least 10 years follow up showed peaks at year 7 and 9. The risk of relapse was not totally explained by the therapy. Other possible risk factors for relapse would be interesting to be analysed (bacteriological 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 | BRODHIPIMIDINS AND BRODHIPIMIDINS/RIFAMPICIN - IN VITRO AND IN VIVO RESULTS FOR A NEWLY DEVELOPED EFFECTIVE MDT AGAINST LEPROSY
| Joachim H. K. Skowy, Magdalena Rosenfeld, Ellen Wempe, Helga Bartels, Ulrich Siedler, Monika Hass, Buda Lindner, Hans-Bernd Flad, Johannes Gerdes (Borstel Research Institute, D-29016 Borstel, Germany)
| Arvind SLD-Nille (Florida Inst of Technology, Melbourne, Fla. 32901, USA)


Martin Dietz (Alert, P.O.Box 160, Addis Ababa, Ethiopia)

A new combination consisting of Dapsone (DDS) and the diphosphonate derivative Dapsone (DDS), a compound which has been developed for the treatment of leprosy. The combination of these two drugs shows strong synergistic inhibitory activity. This is demonstrated on Mycobacterium leprae in 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 parameters (area under concentration-time curves vs half-life of - 2.1 hr). On the basis of these results, trials on previously untreated patients <100 have been performed in Addis Ababa and Amsterdam/Denmark with the following regimen: A) 100 mg BID daily, B) 200 mg BID + 25 mg PO daily. In a 12-month intervention, C) 100 mg BID + 100 mg IDIS + 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. There were no unscheduled relapse control. Tolerance of all 3 regimens was generally good.

**CH29**

PROGRESS IN CHEMOTHERAPY RESEARCH OF LEPROSY (II.B). G. Pera1, P. Jomp, I. Tropar; and J. H. Gossel2 
Faculté de Médecine Pitié-Salpêtrière, Paris, France1 and Institut Marse, Bamako, Mali2

Since the last Congress in 1990, we have demonstrated that clarithromycin (CLAR) and minocycline (MINO) Alone showing promising bacillary activity against M. leprae in mice; pefloxacin (PEFOC) alone; ofloxacin (OFLG), CLAR and MINO alone displayed very powerful bacillaryidal activity in lepromatous patients, with rare and mild side effects. In mice, adverse effects were shown with the combinations of CLAR + MINO and CLAR + MINO + DOXO and with single dose of CLAR + MINO. CLAR + MINO + OXFL displayed definite bacillidal activity against M. leprae, only slightly inferior or comparable to that of single drug therapy. The results of these clinical trials indicate that these new classes of bacillidal agents are added to the list of anti-leprosy 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 regimen. In addition, these new drugs, probably in combination with doxycycline, may play an important role for the treatment of RMP-resistant leprosy.

At present, we are testing the bacillidal activities of various combinations of new antibiotics drugs in M. leprae-infected nude mice evaluating the bacillidal activities of the single dose of various combinations CLAR + MINO and CLAR + MINO + OFLO in lepromatous patients and the effect of prolonging the multidrug therapy over 6 months regimen. In addition, the three new drugs, probably in combination with doxycycline, may play an important role for the treatment of RMP-resistant leprosy.

**CH30**

MINOCYCLINE AND RIFAMPICIN IN LEPROSY 
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Tropical Disease Foundation, Makati Medical Center, Makati, Metro Manila, Philippines

Twenty (20) biopsy proven, previously untreated leprosy patients were entered into the study using a 28 day course of daily minocycline (100mg.) and rifampicin (450mg.) for 6 months. 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 LEPROREA 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 from physical but also deep psychological and social scars. Various drugs are being used in the management of the Type II lepra reaction like CLF, Steroids, 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 steroids in Type II lepra reaction. Group A consists of 30 patients treated with colchicine and Group B consists of 30 patients treated with steroids.

Colchicine was effective in controlling median to moderate degrees of neuritis & arthritis as compared to steroids. Colchicine is a safe drug except GIT symptoms. Colchicine allowed continued administration of antibioprexy 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 steroids or steroids + CLF as an anti-reactional treatment in the past. In our opinion Colchicine should be tried before starting steroids 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 submitted our preliminary observations on 38 untreated multibacillary leprosy patients with BI more than 2.0147 had BI > 3.51 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 50 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 investigations, we report here a special feature observed on 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 reaction 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 doxycycline. Rest of the reactions were mild and easily controllable with steroids. 12 out of 16 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 design should include precise neurological assessments in view of the possible effect of reactions on the nerves (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 33 lepromatous leprosy patients and 3 Borderline lepromatous leprosy patients with a Bacteriologic Index of 4+ or more were admitted into the hospital of Central Leprosy Teaching and Research Institute, Chengalpattu.
CH34 MINOCYCLINE IN LEPROMATOUS LEPROSY

T. Fajardo, Jr., L. Villahermosa, E.C. dela Cruz, R. Molina, J. Fransilano, G.P. Walsh

Leonard Wood Memorial Center for Leprosy Research, Cebu, Philippines and Gillis W. Long Hansen's Disease Center, Carville, Louisiana, U.S.A.

Minocycline, a tetracycline derivative, has recently been found to have bactericidal effects on M. leprae in the mouse footpads. In the chemotheraphy 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 bacteriological 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 radiorepiphysometry 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 clinical pathological evaluation of 510 new leprosy patients registered between 1982 and 1987 revealed:

1. 25.5% (120) infectious cases (Dharmendra's operational classification, 1986).
2. Majority of males (3:1), in their prime age group (21-45 years) were housewives or involved in manual labor.
3. 29.21% compliance rate of treatment (Modified WHO regimen) and additional 146 cases (minimum) 100mg dapsone daily for PB cases and initial intensive 2 weeks therapy with 600mg Rifampicin and 100 mg Dapsone daily through 150 mg Clofazimine EOD for MB cases.

4. M, (9%); N, (74%); PB, (79%) and 31% histological examinations of biopsies, radiographs and skin lesions for comparison.

5. Complete clinical cure in 23.6% (26; 16 PB and 19 MB) with clinical activity in 76.4% (42; 29 PB and 9 MB). Two PB cases active after 19 and 14 months therapy.

6. Untoward side effects in 13 MM/MDT cases in the form of ENL in 26.9%, ichthyosiform lesions and reddish brown pigmentation of face, conjunctive or of lesions in 11(33.33%)

7. No relapse and

8. Histological cure complementing clinical cure only in 15% (2; PB and 1 MB) cases.

Strategies of leprosy eradication by 2050 AD need revision in the light of above observations, in our view.

CH36 AN OBSERVATION ON THE EFFECT OF MDT IN THE TREATMENT OF 0.195 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 1993. Eighty and seven nine cases of them (80.24%), including 85% MB cases and 15% PB patients, were clinically cured. Out of these cured cases, 103(4.1)% (MB 96; PB 7) were markedly improved. 50 (9.19%) (MB 36; PB 14) were improved, and 136 (5.01 %) remained unchanged. The total clinical effective rate was 94.14%, showing an obvious effect within a relative short time. In 103 MB cases treated with MDT for 24 months, the annual average decrease of BL of out patients and hospitalized patients were 0.01 and 0.01, giving a declining rate of 14.14% and 8.11% respectively. In 223 hospitalized MB cases treated with MDT, after the completion of the prescribed doses, their HI (histological index) decreased from 1.28 to 5.11, with an annual average decline of 0.62 and the decrease rate of 14.14%. BI decreased in parallel with the decline of HL. The proportion of the occurrence of type II leprosy reaction in 223 previously untreated MB cases on MDT was 21.74%, similar to that of 22.12% of 56 cases with DDS monotherapy. In the above said 56 cases 26 (23.94) of type II leprosy reaction were seen when they were retreated with DDS, suggesting the limited effect of the routine dosage of DDS 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 DDS were acceptable and did not interfere the carrying out of the MDT programme. Six hundred and forty and fifty four MB and 138 PB cases were cured clinically and were followed up for 1-3 years, no relapse was detected.

CH37 THE OBSERVATION OF 120 MB CASES TREATED WITH MDT AND FOLLOW UP STUDY

Miao Zhibi et al.

Hunan Provincial Institute of Dermatology and Venereology, Changsha, Hunan Province, China

Three hundred and twenty eight MB patients were observed during the treatment with MDT (WHO regimen, 1981) for 12 months and monitored for 24 months after the end of their drug treatment. One hundred and fifty of them were previously untreated group (group 1, 164), they 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 and during and after MDT regularly. The observation indicated that there were satisfactory clinical improvements in all cases, moles disappeared in 3-6 months, and moles flattened in 1-3 months. There was a steady fall in BI value before and even after the discontinuation of the treatment. Skin tumors became negative in 102 cases 16 months after stopping the drugs. Five-year histopathological observation in 32 cases showed that all 30(D30) bacterial index of the granulomas, 16 of them decreased, and bacterial index decreased steadily. The side effects of DDS were acceptable. The authors stressed the effectiveness of MDT in shortening the duration of treatment and frequency and severity of lepra reaction and deformities.
CH38
THE EFFECT OF MDT FOR 27 MONTHS AND POST-TREATMENT SURVEILLANCE FOR 12 MONTHS IN MB CASES
Huang Weimin, Zhang Shihao, Zhu Kang
Yunnan Provincial Institute of Dermatology and Venerology, Kunming, Yunnan province, China

Forty-seven cases of active MB (topgy patients were regularly treated with MDT, Bacillus Calmette-Guérin (BCG) for 2 months with satisfactory clinical, bacteriological and histopathological improvements. The side effects were mild. MDT was also effective in controlling Type 1 leprosy reaction. After stopping MDT, there were both steady clinical improvement and steady decrease of the B1 also decreased. The number of patients whose skin lesions became negative increased to 93 cases (75.0%) and at the end of the second year of surveillance the number of patients whose skin lesions became negative increased to 93 cases (75.0%) consistently. The results observed above show the need to introduce MDT MB regimen to MB patients until the skin lesions become negative. That is to say that the 24 months of MDT for MB patients recommended by WHO (1982) is enough for the MB patients. But the real and final efficiency of MDT for MB patients recommended by WHO will be confirmed by failure in the future.

CH39
OBSERVATION OF 467 PATIENTS OF MULTIBACILLARY LEPROSY UNDER SURVEILLANCE OF THREE YEARS AFTER COMPLETION OF MULTIDRUG THERAPY
Hu Rupang, Lu Jiaji, Liu Xiaoliang, Jiao Qiang, Nie Zuyun, Li Delu
Sichuan Provincial Institute of Dermatology and Venerology, Chengdu, Sichuan Province, China

From 1984 through 1991, 467 patients of multibacillary leprosy with positive smears in 20 counties of Sichuan and Panchhua prefectures of Sichuan province had completed MDT courses, recommended by WHO in 1982, and were under surveillance for three years. Watched steady clinical and bacteriological improvements were observed. Forty-five of them were previously untreated cases with active skin lesions and B1 value of 1.10 to 4.10 at the start of MDT. Their skin lesions subsided after 12 months of MDT and the annual average decline of B1 in the period of five years was 2.58. That of the first five years was 6.81. B1 of 10 patients became negative and that of the other 9 remained positive in the third year of surveillance. A half of another 562 cases, BCG treated previously and with B1 value of 0.10 to 4.60 at the end of MDT, also had active skin lesions at the start. Their skin lesions subsided after 12 months of MDT, and the annual average decline of B1 in the period of five years was 0.31, and was 0.45 in the first three years. In the third year of surveillance, B1 of 51 cases of them decreased to zero but the smears remained positive in 43 cases. In the period of surveillance, lepra reactions, mostly only skin reactions, were seen in 9 patients (3 males, 6 females, 1.0 reaction). 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
Cheng Zhi Quan, Yang Li, He, Fan De Han and Huang Gui Yu
China Leprosy Control and Research Center

Eighty-four multibacillary (MB) patients whose skin smears were positive were treated 24 months with the regimen of multidrug treatment (MDT) for MB patient recommended by WHO (1982) since 1982. At the end of the first 12 months of MDT there 15 (17.5%) 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 surveillance the number of patients whose skin smears became negative increased to 63 cases (75.0%) and at the end of the second year of surveillance the number of patients whose skin smears became negative increased to 93 cases (75.0%) continuously. The results observed above show the need to introduce MDT MB regimen to MB patients until the skin smears become negative. That is to say that the 24 months of MDT for MB patients recommended by WHO (1982) is enough for the MB patients. But the real and final efficiency of MDT for MB patients recommended by WHO will be confirmed by failure in the future.

CH41
THE ANALYSIS OF TREATMENT TIME FOR LEPROSY CASES FUSED WITH DDS AND MDT IN YANGSHOU PREFECTURE, CHINA
YANG ZHONG-MING*, LI Wen-Zhong*, YU Gu-Fan*, LIU Xue-Ming*, LIU Jun**
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**Yangzhou Institute of Dermatology, P.R.China

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 Modified 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 shown as normal distribution, therefore we use the median (year) of cured time to compare them. By the end of the year 1990, total 4721 cases are cured by DDS with median of 11.46 years, 83 Old PB cases by WHO MDT with median of 2.09 years, 116 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, 36 New MB cases by WHO MDT with median of 4.43 years, 156 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 cured PB cases by WHO MDT need 1.5-2.5 years, MB cases with WHO MDT need 3.5-4.5 years. The difference between males and females in DDS and WHO MDT have high significance (p<0.01). The interest of time to show that the MB cases with WHO 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 JIRISH, TALA, RIZAL, PHILIPPINES
Poland, C. Samson, Jr, Jimby Damascus, MD

Multidrug treatment, following the WHO regimen was introduced at Dr. Jose M. Rodriguez Memorial Hospital, Tala, Rizal, Philippines in 1983. 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 state of the MDT group. 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 among patients recommended before the use of multidrug regimen. Few cases of...
leprosy reaction's during the treatment have been observed. There were few complaints about ofloxetine - induced photodermatitis, that gradually disappeared during the surveillance period.

We are of the opinion therefore that multi-drug 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/CHS IN RIO DE JANEIRO.


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

Four hundred and eighty six defaulters were interviewed, in order to detect the most common causes of non-attendance to the supervised monthly doses in several cases leading to default before healing. Among others, professional factors and "forsitting" the right day were frequently found. The results will be presented, analyzed and discussed by the authors in this intervention.

CH44

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

J.C.Avelleira,F.Rolz Vianna,A.B.Marcque,Y.L.G. Andrade.


Detection of JGg and IGG antibodies to phenolicglycolipid-1 by ELISA method has been used, to evaluate its usefulness in the serum diagnosis and monitoring of treatment. A group of thirty-six multibacillary patients was followed after RFT with PGL-1 titrations by the ELISA method, on a 3 months basis. The objective of the study was to evaluate the viability of this test in the early diagnosis of relapse. Patients were divided 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.

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

Between 1983 and 1992 - 15,250 patients received MDT, of which 11,552 are PAUCIBACILLARY (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, 474 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 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 6 patients who were found to be dapsone resistant. They were divided into 3 groups. One group (A) 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.

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 11% of patients with type II reactions aspects. The BI was negative in 20% and the 511 in 25 to Rifampicin. 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.

The launch of the World Health Organization'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 consistent 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.

CH50
INCORPORATION OF THE MULTITHERAPIA EN LOS ENFECHE-
MOs DE CATALUÑA: RESULTADOS E INCONVENIENTES:
Montserrat Pérez M.D, Mercedes Arneles M.D, Joan Batalla M.D., Jari Sauch A.S.
Programa de Prevencion y Control de la Enfermedad de Hansen. Salut Publica. Consellera de Sanita-

La poblacion enferma de Cataluña (España), inició la implementación multitécrica 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 DRUM IN LEPROSY - AN IMPROVEMENT TO PUT Y
Richard de Goldenhoff
Netuddha Leprosy Relief Association - Eastern Leprosy Control Project, Biratnagar, Nepal.

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 financial support from UNDP/World Bank/WHO-TRD.
CH53
SURVEY FOR SECONDARY BAPCOUS AND ISOPACTIC RESISTANCE IN CUBA.
Angel L. Gonzalez and Jorge L. Mastre.
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A total of 1521 Cuban leprosy patients treated for at least 5 years were clinically and bacteriologically examined. They were being treated according to a two-phase monotherapy regime with RSP first and BAPCO after wards. On skin smear examination, 50 patients were found positive, of then, 9 showed 0.01 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 B1 group who showed a good clinical condition except for a heavy infiltration of both earlobes were receiving a second Bapco course when examined and biopsied for this research. These 5 patients were biopsied and susceptibility tests to RSP and BAPCO were performed. The results showed that in 1 case the earlobes were resistant to both drugs, the organisms from 2 other patients were susceptible to DDS but low-grade resistant to DDS. In 3 other cases the bacilli did not multiply in any of the eight 1:2 of the strain was from the patient taking a second BAPCO course, therefore this strain might also be susceptible to DDS and resistant to BAPCO. 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 AFIs inoculated into fresh mice to repeat the tests but failed to multiply.

CH54
RELAPSE AFTER DATSON MONOTHERAPY: AN ANALYSIS OF 96 CASES IN JIANGSU PROVINCE, CHINA
Wu Zhixiang, YuHaibing and Gu Changlin.
Jiangsu Institute of Dermatology, China.
From June 1974 to June 1989 the 3034 patients treated on Jiangsu Province totaled 9,646, of whom 360 cases relapsed with a relapse rate of 0.4%. This article reviewed 360 relapse cases, who also receive DATSON monotherapy for 1 to 3 years with a regular treatment rate of 46%. The dopamine monotherapy was also given during the observation period. The interval between cure and relapse averaged 3.6 months for the MS cause and 0.7 months for those of PB. 94.1% of the relapse patients were over 20 years of age. When they developed signs of relapse and the disease course was not clear for longer than 6 months of all the 191 relapse cases, 91% had more than three skin lesions on their face, 80% on their body and 10% on the limbs. The clinical features of the MS relapse cases were mainly the necrosis of old skin lesions and the reemergence of old nerve involvement and the relapse rate was 0.46%. When a large portion of the PBs developed new skin lesions and nerve ulcers, and the relapse rate was 0.11%. It has been shown that the main precipitating factor causing relapse is nerve involvement. Both the frequency and severity differed in the various stages. The results showed that dopamine monotherapy cannot prevent relapse in the number 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.
Xu Zhishen and Jiangping.
Jiangsu Provincial Institute of Dermatology, Nanjing, China.
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 M1 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 regimens. All patients were followed once or twice a year after the completion of the re-treatment MO 12,250 cases of them (93.12%) have been released from re-treatment for 5 years or more than 5 years. By the end of 1991, no relapse was detected. But during the same period (1984 -1991), 427 relapses were released in 22,468 DDS-cured but not re-treated patients, giving a relapse rate of 0.13% (M1 12.99%, PB 0.0%).

CH56
COMBINED CHEMOTHERAPY AND IMMUNOTHERAPY FOR TREATMENT OF HIGHLY BACILLATED ULL CASES
Central JALMA Institute for Leprosy (CJILM), Tegrap, Ag Clay, 202 001, India.
Viable as well as dead bacilli are known to persist in BULL cases even after 2 years of currently recommended MDT. Our earlier studies showed that DDS had a potential immunotherapeutic effect when used in BULL patients. In this study, we have investigated the therapeutic response of combined immunotherapy along with MDT in BULL patients. Untreated BULL patients with the initial BI of 4 to 6 were serially allotted to three treatment groups. Group I patients received a slightly modified WHO regimen (rifampicin once a month, Clofazimine & Dapsone daily) and DDS 0.1 mg/day. Group II patients were administered the same MDT and Mycobacterium INH-MDR killed bacilli (MDR-MV) and group III received the same MDT with DDS 0.1 mg of distilled water. Vaccination was repeated every 6 months. Biopsies were taken from the local site of vaccination and from the distant site 105 i.e. back. The progress was monitored periodically by using clinical, histopathological and bacteriological findings, mouse foot pad, ATP and other viability parameters. The vaccine was well tolerated. There were no serious side effects. In cases of combined chemotherapy and immunotherapy, no viable bacilli were demonstrated 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 up to 2 years. With 20 months of treatment, the mean BI decreased from 4.6 to 2.54 in the group on MDT alone (control) 4.9 to 0.08 in the MDT-DDG group and 4.7 to 0.05 in the MDT-MDR group. Immunotherapy appears to have a significant effect on killing and clearance of bacilli in these cases.

CH57
EVALUATION OF SINGLE DOSE VS MULTIDOSE FOR THE TREATMENT OF LEPROSY PATIENTS IN THE RAT BURDEN MODEL
Yoko Nanri and Yoomi Kimura.
Medical Department, Yonsei University Hospital, Korea.
We undertook a 9H10-V strain triad in a single dose of 100 µg of sheep diphtheria toxoid in the evaluation of the effectiveness against leprosy. Overall preventive rate at 10 weeks strain period showed only about 10%.
In addition, evaluation of leprosy was studied and incidence was not shown with the sheep diphtheria toxoid. To contain drugs used rifampicin, lomprine and arsphenam were considered for further trial.
During the trial operation, (1946-1951), patients in experiment area (about 23%) were unable to be compared with the standard triad regimen.
So, if not to test, an alternative regimen using a single intradermal dose of 1500 µg of rifampicin and self-administered daily dose of diphtheria toxoid was introduced for 10 days.
The results were not satisfactory: morphologically all of them were after the use and bacteriologically most of them were negative after 5 years.
and thus a feasible option (using a single dose of rifampicin per year for 5 years in outreach areas) was considered helpful to change the leprosy epidemiological pattern in an area where standard regimen was impossible.

CHIS8
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 "atypical" mycobacterial diseases, enteritic diseases, staphylococcal bacterial diseases, etc., does not need additional medication for treating concurrent infections often encountered in leprosy patients, e.g., tuberculosis, "atypical" mycobacterial diseases, enteritic disease, staphylococcal disease 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. Summary: So far we have not heard of any other therapy allowing to overcome such a complex of difficulties.

CHIS9
ON THE NECESSITY OF ALTERNATIVE TREATMENTS 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 variety of conditions in an area of 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 "Isomycin" (INH + PHT + DDS), "Isomycin-RMP" (INH + PHT + DDS + RMP), "Cotrifazid" (SXT + INH + RMP), "Emetine" (SXT + PHT + RMP), Ofloxacin + INH + DDS + RMP, and a combination of PHT and DDS in more than 1970 cases of leprosy.

CH60
BACTERIAL ACTIVITY OF OFLOXACIN AGAINST Mycobacterium leprae
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Hospitál, Nacional, J.B. Sommer, Gral.Rodriguez, Buenos Aires, Argentina

Sixteen patients with infiltrated lesions of lepromatous leprosy were enrolled in this trial. The microscopic examination of their leproma, yielded bacterial indexes in from 4+ to 5+ (according to Ridley's logarithmic scale)

and morphological indexes higher than 70%. The histologic study of the lesions revealed typical LL leprosy granuloma. Patients presented disseminated erythematous plaques, papules, nodules and macules. The mouse footpad inoculation and esterase tests were positive in all patients. Suppervised multi-drug treatment (standardized 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 (nodosum erythema), other side-effects were absent. After 2 months treatment, only granular bacilli were found by smear examination; the esterase 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 reaction occurred.

CH61
K-130, A NEW INHIBITOR OF M. LEPRAE DHFROPHOLATE 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 synthesized with the aim 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 mycobacterial cell wall and 3) to possibly combine two principles of folate synthesis inhibition (dihydropterin reductase synthesis and dihydrofolate reductase inhibition respectively) by combining diaminopyrimidine derivatives with a diaminopyrimidine derivative in one "mesosynergic" 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 laef (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 controllers for permission to initiate phase I clinical trials.

CH62
GANGLIOSIDES DESCRIBED AS LL LEPROSY NEUROPATHY.
A Randomized, Placebo controlled trial.
A. Sallana, G. Chaunan, A. Mattan, D. Lobo

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

Method: Randomized double-blind placebo controlled trial of Cransoll conducted in 6 centres in India. Of the 120 patients who entered the trial only 114 completed it as per protocol. Only 86 BL 11 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: I) Age between 18 & 50, (2) At least 2 nerves have moderate to severe damage as assessed with Patracha's instruments, WHO thermal tester, skin thermometre, VDT, (3) The damage must be of not less than 2 years duration, so as to rule out spontaneous recovery.
The therapy: 40mg/Crohnssniul i.n. 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 symptoms at baseline and after 90, 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 & subjective functions. Circa 45% of Crohnssnai patients recovered in toto all sensory modalities: touch, 2-point discrimination, pin-prick, temperature, as against the placebo group, of which only 15% had improvement of only one or two sensory modalities. The VMS score & the sympathetic functions were significantly better in the drug group. A follow-up of 2 years in 36% of cases showed that the placebo had a poorer score (compared to their last one) while the Crohnssnai group had consistent or even better results.

CH63

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

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Anti-leprosy effect of deoxytryptophan serotonin for which evidence is available prompted trials of a tryptophan-enriched diet - "Nourriture Anti-Lepric" (NAL), administered to multilocular leprosy patients to study the clinical and bacteriological effects attributable to the therapeutic effect of free tryptophan as serotonin precursor in blood. A trial group of 12 MB patients with H1 = 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 PDT 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 noticed 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 inoculations prior to the trial and subsequent 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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National chemotherapy of an infectious disease involves identifying an essential metabolic activity of the causative agent and suppressing that activity with an appropriate inhibitory compound to achieve the arrest and suppression of the disease. The drug of choice for the suppression of the enzyme, L-lactamase, in B. lactis or Mycobacteria is a carbapenem treated with penicillin benzathine. M. tuberculosis has been shown to contain a constitutive L-lactamase. We have been able to develop resistance against the generally used anti-leprosy agents. To overcome this problem, multidrug therapy is being promoted widely, and has had remarkable successes. When M. tuberculosis becomes 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 must safely deny the possibility of the emergence of MDR leprosy. Mycobacteria, in general, synthesise L-lactamase and are insensitive to penicillins and cephalosporins. We screened the effect of L-lactam/L-lactamase-inhibitor combinations on growth of M. leprae in mouse foot pads, and on M. tuberculosis H37Ra, H37Rv, R. atroseptica, and BCG (drug-susceptible as well as drug-resistant strains). We tested four different drug combinations: ampicillin/sublactam (PL14), ampicillin/TEM 9200 (Taisho), amoxicillin/clavulinate (SmithKline Beecham), piperacillin/tazobactam (Cyancam). All of them suppressed growth of the bacteria, including that of drug-resistant Mycobacteria. Our results also showed better activity than the others in which the proportion of inhibition to antibiotic is higher than that of amoxicillin/clavulanate or piperacillin/tazobactam.

Apparently, L-lactam/L-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 anti-therapeutic phenamine 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 synthesized to produce a more widely effective agent with less toxic effects. Two of these agents (B4099 and B4106) have been shown to be particularly promising. Before further maximization 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 some 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 CLOFAZIME

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Clofazimine (B606) is an anti-leprosy agent which has also been successfully used to treat other mycobacterial diseases, including M. avium infection in AIDS. An attempt to optimize and increase the therapeutic potential of B606, a number of compounds have been synthesized 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 phenotype compounds. The chromatographic system consists of a C18 column with a mobile phase of THF: Water (9: 40 - 549: 5) with 2.5 mM hexane sulfonic acid and UV detection at 265 nm.

Phenazine compounds (B606, B379P, B395, B4099, B4106) were extracted from biological samples into dichloromethane containing another phenazine with a suitable different retention time as internal standard. Using peak height ratios, the extraction ranges were linear in the range 0.50-50 mg/L.

This method uses an easier extraction protocol for phenotype 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 NONOTHERAPY

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A follow-up physical and bacteriological examination of 1,445 leprosy patients cured with DDS nonotherapy was carried out in 22 counties in Hubei province was carried out in 1993. Among them 35
CH68
CLOFAZIMINE DISTRIBUTION IN HUMAN MILK
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Clofazimine, (3-(p-chloroanilino)-10-(p-chlorophenyl)-
2,10-dihydro-2-isopropylimidino) phenazine, is used in che-
motherapy of leprosy. In addition it exhibits anti-inflamma-
tory 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
coming 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 CHAUWOGA 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
treated leprosy with Chauwoga oil even in Southern Song
Dynasty (from 12th to 13th century). The following evidences are considered as major arguments, 1) Bai Yuchan(1193-1228), a famous
Taoist priest, poet and doctor, treated leprosy with chauwoga
oil and his prescription was collected in the monograph—"Jie Wei Yon Mei" written by Shen Zhou in the Ming Dynasty; 2) Some medical
works, such as "Benzhai Zhili Fang", in which the mentioned
prescription was collected, were lost in the Ming Dynasty, but fortunately, it had been collected in "Yi Fang [et al]" and "Zhang Yao Zhichang Fang", edited by Korean doctors in the 15th century
and published by the Japanese afterwards; 3) Invasiveness of importing chauwoga oil could be found in some historical literatures,
such as "SiWang Annals"; 4) Some historical relics from harbour
rungs of Quanzhou Bay also provide evidences. The authors 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 chauwoga oil and many other valuable medical
materials.
CH70
TREATMENT COMPLIANCE IN THE SOUTH SULAWESI LEPROSY CONTROL PROGRAMME, INDONESIA
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Leprosy Control Programme; 2) Medical Student, University of Amsterdam, the Netherlands; 3) Hasanuddin University, Ujung Pandang; 4) Prov.
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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 for unsupervised MDT for up to 3
months. Although not encouraged, leprosy workers are allowed to deliver DOT 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 dapsonex 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, route 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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Centre.
G.W.Long Hansen Disease Center at LSU, Baton Rouge, LA
Mycobacterium bovis, strain 44 (BCG P, vaccine strain) was
incubated with "C-palmitic acid in an axenic culture. Release of "C02
was detected by liquid scintillation using Whiteman No.42 filter paper
soaked in liqscinturar concentrate; PPO, Triton X 100; 4 N NaOH.
Rifampicin at concentrations of 2.0, 0.2, 0.02, 0.002, 0.0002, 0.00002 g/ml was added to the cultures on the first day. The
evolution of "C02 was monitored daily for 5 days. Rifampicin
significantly inhibited the ability of BCG to oxidize "C-palmitic acid
and release "CO2. 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 mg/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 utilised in Ethiopia to screen extracts of plants,
used in traditional medicine, for their mycobactericidal activity; and to
calculate the concentration of rifampicin in various body fluids and
tissues.
CH72
EFFECTS INDESEABLES PROVOCADOS POR LA RIFAMPICINA.

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

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

CH73
ELECTRON MICROSCOPY, POLYMERASE CHAIN REACTION AND SERODIAGNOSIS AS TOOLS FOR ASSESSING LEPROSY TREATMENT.

This study was done on diagnosed leprosy patients receiving the WHO regimen of treatment (MDR) 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 (NI)-n. ASO and four iLA, tests were done using two and indirect ELISA tests.

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

CH74
THE EFFECT OF ANTI-LEPROSY DRUGS ON BIOLOGICAL RHYTHMS.

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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 rhythms, development of desynchronoses, resulting in the formation of different pathological states and toxic complications have been described. The effect on biological rhythms 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 rhythms of fluctuations. Erythrocyte count, glucose and hemoglobin concentrations were changed according to circannual rhythms. Rythmical fluctuations of other blood indices differed from circannual rhythms. Prolonged administration of DDS caused desynchronization of the previously synchronised 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 bioythes. The preliminary results suggest new possibilities of development of antimicrobial drug 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 promising 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. 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 radioreceptor based 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 radiorepirometry and the mouse footpad assay clarithromycin had been found to be the most active macrolide against M. leprae. Its in vitro activity being closely 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). Radiorepirometric 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.
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 leprosy patients. Patients received a single 400 mg loading dose followed by 200 mg daily for 6 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, radioscintigraphy 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. Radioscintigraphic activity correlated well with the mouse footpad data; all biopsies became 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 sparfl oxacin appear to be comparable with that found previously in trials of 400 mg ofloxacin.

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

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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 leprosy 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 chemotherapy to longstanding LL and BL patients, of whom many had received thianthrosine 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.

IMMUNOTHERAPY OF MB LEPROSY PATIENTS WITH THE ANTI-LEPROSY VACCINE MUCOBACTERIUM N

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Immunotherapy with Mucobacterium 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.

1) 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 positive 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.

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 potential for 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 an immunocytochemical technique. Intracellular localization of drugs specifically in macrophages and Schwann cells was carried out with polyvalent (rabbit) anti-RS2 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.

Intracellular localization of dapsone and Rifampicin was carried out in skin and nerve (21182 particularly in nerves of MB patients. A graded difference was seen in staining intensity in cases of leprosy. All the nerves under extracellular staining in the skin and nerve (61, 4 time (>6 mths) after stopping treatment nerve lesion. It was also noted that the drug (metabolite) persists over a long period of time (>6 mths) after stopping treatment specifically in macrophages and Schwann cells 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.

LYMPHANGIOGRAPHY AS AN ADVERSE EFFECT OF CLOFAZIMINE THERAPY IN LEPROSY

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Podal 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. 20 of these patients were noted to have significant podal edema on one or both feet after the clofazimine therapy was started.

Systemic causes of podal 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 paucibacillary leprosy showed normal lymphatic drainage.

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

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

With the multidrug treatment (MDT), the overall results have been satisfactory. However, the presence of residual activity, worsening of residual disability, late reactions/relapse after the stoppage of treatment especially in case of fixed duration of 6 months regimen have been reported by several investigations. 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 months duration, modified 12 months 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 dopaque multidrug therapy days and in some of the studies later. The significance of these findings need to be debated and investigated by further studies.

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 examiner's finger, asking the patient to compare sensation between areas innervated by the ulnar and median nerves. In this study the quick tests have been compared to a more standard VMT and 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 seem to indicate that the quick test 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 320 fresh Multibacillary cases without deformity or neuritis registered during 1986-1990 at The Leprosy Centre 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 17.05%. 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 MULTIBACILLARY DURING SURVEILLANCE

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During the course of surveillance we encountered interesting events among MB leprosy patients after completion of M.D.T. recommended multidrug 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 lepro reactions. These manifestations responded to steroid therapy (without specific chemothera- py for leprosy).

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-Hidley 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 LACEROPHALMOS

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In outpatient in eastern Nepal we tested the hypothesis based on clinical impression that in every clinically significant lacrohthalmos also other facial muscles are involved. 44 of the 57 (81%) examined patients with lacrohthalmos (mean duration 23.8 months) had involvement of at least one other facial muscle group. In patients with a pain at mild closure of 3 cm or more (5/50 60%) had involvement of an other muscle group. In LL patients there is a symmetrical, "mask" involvement of the facial muscles. In BL the ipsilateral muscles are more often involved than the contralateral muscles which is the norm of involvement of a nerve trunk. We found that in lacrohthalmos 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 anesthetic cornea and noted that the type of Bell's phenomenon and the way of

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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 PROGRAM FOR RESEARCH AND TRAINING IN TROPICAL DISEASES.
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**CL8**

**CLINICALLY ATYPICAL RELAPSES IN MULTIBACILLARY PATIENTS**

**P. JANMT and F. BONIN**

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 several clinically atypical because lesions are very mild or because they do not seem active leprosy.

Photographs 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.**

**M. Duncan, T. Miko, S. Menzel, R. Nelson, D. Frommel.**

Department of Medical Microbiology, University of Edinburgh, UK; Armauer Hansen Research Institute, Addis Ababa, Ethiopia.

149 children of mothers with leprosy (MB and PB) and healthy mothers (NL) living in the same environment were followed: 89 children (49MB, 25PB, 15NL) at puberty aged 12-15 years (Phase 4); 86 children (mothers: 48MB, 23PB, 15NL) were reassessed at age 3-4 years (Phase 3); 9 had macules without sensory loss and 7 had palpable/slightly enlarged nerves (diagnosed as early leprosy); and 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 (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 3); 1 had flattened nerves and slightly enlarged nerves (diagnosed as early leprosy); and 1 had bluish hyperpigmentation with slightly enlarged nerves. The meningeal involvement of the mothers of these children during pregnancy and/or lactation was: 1 child with 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 (49MB and 25PB) and healthy mothers (NL) living in the same environment were followed: 89 children (49MB, 23PB, 15NL) were reassessed at age 3-4 years (Phase 2); 86 children (mothers: 48MB, 23PB, 15NL) at age 7-8 years (Phase 3); and 99 children (mothers: 49MB, 25PB, 15NL) were studied from birth up to 2 years of age (Phase 1). Reassessments were as follows: 89 children (49MB, 23PB, 15NL) were reassessed at age 3-4 years (Phase 2); 86 children (mothers: 48MB, 23PB, 15NL) at age 7-8 years (Phase 3); and 99 children (mothers: 49MB, 25PB, 15NL) 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. 25/45 (175) died before Phase 1 (Llk 24%, NLK 14%, MBK 12%, PBK 14%, mean height/weights at Phases 2 and 3 were 90cm/12.7kg and 117.7cm/20.1kg with no significant differences between sexes or groups of children aged 3y 7m and 3y 10a 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 (136cm). Triceps skinfold, arm and head circumference were 7.0mm, 19.6cm, 53.8cm and 5.2mm, 19.2cm, 53.6cm for girls and boys respectively. Medical records showed hospital treatment for infections: intestinal worms (5%), respiratory 50%, ear/raditis media - MBK 20%, PBK 20%, NLK 20%, eyes all infections (trauma - MBK 70%, PBK 85%, NLK 25%); skin all infections/scabies - MBK 67%, PBK 85%, NLK 25%.

**CL11**

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

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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 were classified into "cured" (new nerve damage following RFT, or no problem appearing), "clinically atypical because lesions are very mild or because they do not seem active leprosy, (1), or had incomplete records). Of 67 mothers with leprosy 60% had new nerve damage (cured BT, RFT, 36% had neuritis with new sensory or motor loss; 41% had stocking and glove anesthesia (not confined to MB patients), and 65 had tender nerves. 44 patients had their new post-MDT RFT nerve damage in association with pregnancy, 45% postpartum. 62% episodes appeared to be "silent" neuritis. In addition 9% relapsed with new leprosy, 65% post partum, 1st healthy controls developed new leprosy. These findings contrast with those at an interim assessment in 1978 where 76 mothers with leprosy had just stopped DDS or had just started MDT/MB/RFT; 47% "improved," 45% "no change," only 8% worse. While NL 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 neurophysiologic 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 childbearing. 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 sensitivity tests that were not commonly used at our hospital, an extended nerve function assessment (NEFA) was done on 50 in- and out patients with an established leprosy diagnosis (100 hands and feet). The NEFA consisted of Semmes-Weinstein Monofilament Testing (SWMT), Moving 2-Point Discrimination (MPD), 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 patients' in order to get a better idea of the prevalence of sensory impairment as measured with the
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. Tests sites were the pulp over the distal phalane of the index finger, little finger and big toe. Correlation between the SWMT and each of the other tests proved statistically significant: the closest correlations were between the SWMT and M2PD and PP for both ulnar and median nerves (r=0.7, P<0.0001). In comparing SWMT with VMT results, the best correlation was found between SWMT and abductor pollicis brevis for the median nerve (r=0.7, P<0.0001) and SWMT and abductor digiti minimi for the ulnar nerve (r=0.67, P<0.0001). It is argued that the first tests to show nerve function impairment (NFI) are the M2PD and PP, and serial biopsies, immunological tests like MT-MDT. There was no evidence of Type-1 reaction on stopping MDT, but new lesions appeared in many patients without clinical evidence, type-1 reaction under MT-MDT in skin lesions was put forward in a few patients. The finding that the onset of leprosy during adolescence is most frequent has 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 (r=0.7\(\frac{\text{ll}}{\text{ll}}\))) (X'=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 onset of leprosy was over 60 years developed ENL. The age of the patient at first admission was not correlated with the development of ENL (X=47.5, P<0.025). 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 highly inducible around the time of puberty. The basic for these observations is not known but they suggest that maturation and emergence of human immunity, and the relationship between the immune and endocrine systems, may be areas for further study in leprosy.
Abstracts of Congress Papers

61.4

Sensitivity of skin smears in one hundred cases of multibacillary leprosy

Miriam Gutierrez, Jair Ferreira, Miriam Perez

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

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% sensitivity (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.

Investigation of patients with longstanding high levels of antibody to phenolic glycolipid I (PGLI) 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 study 9 multibacillary (PB) 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 0.993 (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 ear lobes, elbow and nape and stained with Fite-Faraco-Wade staining: in all samples no acid-fast material was found. At the time of presentation 26 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-reactivity. 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.

Liquefying nodular panniculitis 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 undergo 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 atypical features and clinical characteristics of LNP with 30 years of evolution.

Thalidomide: A Clinical Study of 33 Cases of Type II Lepra Reaction

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Thalidomide is N-phthalyl-glutamim-acid-imide, a mild sedative, causing two serious side effects - neuritic syndromes and characteristic foetal anomalies, for which it was withdrawn from the market in 1961. It is indicated in Type II Leprous 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 Tuberculosis, 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.

Natural History and Clinical Features of Reversal Reaction in Hyderabad, India

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The paper will be discussed in detail at the time of presentation.
A retrospective survey of the notes of all patients attending Dhoppet Leprosy Research Centre during 1985 was done to establish the frequency, timing and clinical features of Reversal (Type I) reactions. 404 case notes were examined and clinical evidence of a reversal reaction was found in 44 cases (10.9%). Reactions were commont in borderline patients with 11.4% and 11.8% of HT and LB patients developing reactions. Prevention of reaction was common with 41.3% of patients having signs of reaction at the time of diagnosis. 45.1% of patients had only skin lesions, 22.7% had both skin lesions and neuritis, whilst 31.9% 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. Second 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.

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FACTORS AFFECTING RISK OF TYPE I REACTION AMONG MULTIBACILLARY PATIENTS
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Community Health Department,
Christian Medical College, Vellore

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. In this view, a historical cohort study was carried out on fresh multicellular 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 end 2 years was 54/1000 and 19/1000 respectively. The cumulative risk of reaction of the presence of thinned nerves at registration (RR = 4), B1 positivity (RR = 2) and palmoplantar anaesthesia (RR = 2.4) were associated with risk of reaction. The probability of reaction increased with number of patches. The incidence less than 40 had greater risk of reaction when compared with those aged more than 40. 18.6% of the patients who had reaction had developed visible deformities.

CI23
REACIONS IMMUNOLOGIQUES OBSERVEES A L'INSTITUT CARDINAL LEPER PENDANT UNE PERIODE DE 6 ANS.
Claude A.Louvill, Nicole Beliard, Gyoste Blanc.
Real Charlebois, Marlene Danuville.
Florence Foucaud, Florence Davoust, Claude Peam.
Institut Cardinal Leger contre le leprose (MATI).

Sur une population de 720 patients enregistres, 55 ont presente un etat reactiouneal:
33 eczemad nousieux leporex
23 reactions reverses
1) la representation des etats reactioonals selon l'age, le sexe et le type clinique
2) les variables telles que la periode moyenne d'apparition des symptomes, le rythme des eczemes, l'induration et la duree de l'hospitalisation et le traitement.

CI24
CLINICAL STUDY OF LEPROSY IN 123 CASES TREATED BY MDT.
Roughdy W. Mohareb.
Skin and Leprosy Clinic, Ramses Bld., Ramses Sq. Cairo, Egypt.

An attempt was made to investigate the incidence & behaviour of lep. reactions in a group of 123 cases treated during the last few years with MDT. Classification of the cases is as follows: II.T.T. 4 (6.5 %), B.T. 47 (38.2 %), B.L. 21 (17 %), L.L. 47 (38.2 %).

47 Lep. reaction cases were recorded, of which 20 belong to type 1, 27 to type 2. 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. developed severe bullous pustular lesions with toxemia & tendency to relapse while under M.T.D., mild chronic recurrent type of E.M. lesions occured in 4 cases. Crops of few small subcutaneous nodules appear 2-4 days after the monthly dose of rifampicin, a clear up in 10 to 14 days. (Herd Niemen Like Reaction)

The above observations suggest that M.D.T had little effect in preventing or ameliorating leprox reactions. One of the study cases developed type 2 R. after a complete 2 year 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.

CI25
REVOLUTION RATION IN MULTIBACILLARY LEPROSY PATIENTS FOLLOWING M.D.T./HIV/REFUGEE THERAPY WITH A CANDIDATE ANTI-LEPROSY VACCINE, MYCOBACTERIUM W.
A.K. SHARMA, H.K. KAR, S.A. CARRIER
Department of SKT and Leprosy, Dr. RML Hospital, New Delhi - 110 001.

Immunotherapy with a candidate antiglycoprotein vaccine, FycoBacterium W was given in addition to standard multidrug therapy (MDT) to 53 multibacillary lepromin negative patients belonging to 38, BL and LL types of leprosy (Vaccine group). An equal control group of similar age and sex received M.D.T. and injections of microbial 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. Reacational episodes were analysed with reference to incidence, onset, frequency and severity before and after release from treatment (RF).-1.

Incidence of reversal reaction(AR) was marginally higher in vaccine group (22.6%) vaccine group vs. 15% control group). All cases with history of downgrading type 1 reaction developed AR during therapy. Most episodes occurred within first year of commencement of therapy-half developed within 3 months. Late reversal reactions after (RF) were observed in 3.8% of cases in both groups. Half the reactors in control group and 1/3rd in vaccine group had repeated reaction episodes. Incidence of neuritis associated with AR as well as isolated neuritis were equally frequent in both groups.

CI26
SIGNIFICANCE & MANAGEMENT OF REACTIVE PATCHES IN LEPROSY TYPE 1 REACTION
UDAYA KERAN, V.SOLUNAM, J.N.A.STANLEY, SULAI.S.
Dhoppet Leprosy Research Centre,Hyd., A.P., INDIA.
In this study 350 cases of Type 1 reaction have been included. These are from the leprosy patients registered at Sivananda Leprosy Research Centre, Hyderabad during 1986-92.

All cases were classified according to Ridley Jeppings Classification. Classifying done carefully, this made true VDT done routinely and biopsy taken in most cases.

These cases were analyzed as regards to classifications, presentation of reaction with regard to leprosy treatment, local effect of these reactive patches on the skin involved, hist and underlying structures will be mentioned. Significance of the location and size of reactive patches to the cases damaged about/median/lateralsocial will be dealt.

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

CL27

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

M.K. Chopra, B.Ganapati & M.S. Tripathi
District Leprosy Officer and District Project Officer, Harjuch - 322001 (Gujarath, India)

The occurrence of the reversal reaction in leprosy 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, leucoderma and borderline - tuberculoid) detected by different methods in multidrug therapy project in Harjuch district. These cases completed Multi Drug Treatment during the year 1986-90 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 (PBR). 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 diagnosis 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.

Department of Dermato-Venerology, Di Jkzigt Hospital, Erasmus University, Rotterdam, The Netherlands. Department of Dermato-Venerology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands.

Reversal reaction in leprosy is usually described as a classic example of Type IV hypersensitivity reaction. Therefore, treatment with corticosteroids is considered the mainstay 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 hands. However, an 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.

F.F.V. Hamerlink1, W.R. Faber1, P.R. Klatser1, J.D. Bos1
1Department of Dermatology, University of Amsterdam.
2Academic Medical Centre and Royal Tropical Institute, Amsterdam, The Netherlands.

Reversal reaction (RR) is supposed to be a delayed type hypersensitivity 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 Philippines. It appeared that neopterin levels were increased in RR and ENL compared to untreated TT/RL and BL/LL patients. (Hamerlink 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 paralleled the increase of serum neopterin levels 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 support 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.

Samanth Reddy, V.V.Gurunath Babu and Sr.Annie Sivananda Rehabilitation Home, Kukatpally, Hyderabad-500 872 (A.P.)

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 3.0 per 1000 person-years of risk. The criteria applied for diagnosis of reversal reactions were clinical and bacteriological after excluding relapses with therapeutic 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 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
OPHTHALMIC FINDINGS OF LEPROSY CASES THAT WERE DIAGNOSED AT ISTANBUL LEPROSY HOSPITAL
Tulay Çakınan, Murat A. Karapooğlu, Turan Saylan
Istanbul Leprosy Hospital, Istanbul Leprosy Research Center, Istanbul, Turkey.

Ophthalmic 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 years, and average disease duration was 5.71±0.63 years.

56.66% of cases had bilateral corneal nerve thickening, 57.14% had palpebral fistula in the right eye and 61.90% in the left eye, 9,52% had bilateral pannus, 33,53% had subepithelial scar in the right eye and 28.57% in the left eye.

52.36% of cases were still on anti-leprosy treatment.

CL32
THE EXTENT OF LEPROSY RELATED DISABILITIES IN TURKEY
Tulay Çakınan, Arşı ş Ebişi, Gülcen Dökan, Arşıvê Yûksel, Ayta Külah, Türkân Saylan
Istanbul Leprosy Hospital, Istanbul Leprosy Research Center, Istanbul, Turkey.

Turkey has a national population of approximately 75 million and there are 3,562 registered leprosy cases at the end of 1999.

In this study, realized between January 1996 and January 1998, 7,111 leprosy patients were evaluated according to their age, sex, province they live, classification of their disease and disability using WHO grouping.

The average age of patients was 50.07±13.50 years and average disease duration was 25.73±13.29 years.

50% had lagophthalmos, edema or keratitis in both eyes and 9.4% had severe loss of vision or blindness.

27.4% had ulcer, mental claw fingers or slight absorption.

18.1% had wound drop, stiff joints or severe abscess.

45.25% had plantar ulcers, clawed toes, foot drop or slight absorption in both feet, 10.4% had contractures, severe absorption or amputations.

CL33
OCULAR STUDY OF HANSEN’S DISEASE AT A DERMATOLOGICAL HOSPITAL, THE PREVENTION IN OUR HANDS.
Fredyco Orfeice, Leilana Werner
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 broken down 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, broken down as follows: Virchow’s (275), Tuberculosis (75), Indeterminate (29) and Disorganised (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 LEPROSUS OUT PATIENTS
Lilian Monteiro, Wesley Campos, Fernando Orefice, Maria Aparecida Grossi
Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

In this study, 397 leprosy 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 (10.7%) of the Indeterminate type.

314 patients (31.5%) showed ocular adnexa lesions and 389 (39%) showed eyelash 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
BACKDROCGSIOGRAPHICAL STUDY OF PATIENTS BEARING HANSEN’S DISEASE.
Leilana Werner, Fernando Orfeice, Liliana Werner.
Leprosy Unit, Department of Ophthalmology - Universidade Federal de Minas Gerais Belo Horizonte - Minas Gerais - Brazil.

A dacriocistographical study of 290 patients were performed in order to detect an early damage of the 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 diagnosing help in detecting an early damage of the VII nerve.

CL36
USE OF CLOFAZIMINE IN PATIENTS WITH OECULO-CUTANEOUS ALBINOISM IN BEARS OF VIRCHOW’S FORM OF HANSEN’S DISEASE.
Wesley Campos, Fernando Orfeice, 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-cutaneous albinism, sex male , 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 mucous.

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 melanosomes of Clofazimine be correlated to albinism?

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

CL37
CONJUNCTIVAL AND SCLERAL PIGMENTATION DUE TO CLOFAZIMINE.
Wesley Campos, Maria Aparecida Grossi, Liliana Werner.
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 dose of 324 g.

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

The exam at slit lamp showed a very “vivid green” aspect of the scleral pigmentation.

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

CL38
PSEUDO ACUTE ABDOMEN DUE USE OF CLOFAZIMINE.
Frederico Dos Santos, Maria Aparecida Grossi, Wesley Campos, Fernando Orfeice.
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 impression of parietal peritonem and omentum with dark spots at the 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 surgical picture and that this picture should be included in a differential diagnosis of acute abdomen, mostly in countries where Hansen’s disease is endemic and Clofazimine is used as therapy.
BILATERAL HIODOCYCLITIS CAUSED BY MYCOBACTERIUM LEPRAE DIAGNOSED THROUGH PARACENTESIS.

Wesley Carpes, Fernando Orceio, Maria Aparecida Grossi, Carlos Rodrigues.

Leprosy Unit, Departament 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 iridocyclitis.

The paracentesis was performed in out patient.

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

This study shows that Mycobacterium leprae is one 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.

ANALYSIS OF LAGOPHTHALMOS AMONG 2,114 CASES OF LEPROSY

Yan Lianping, Zhang Guocheng, Li Weichong

Institute of Dermatology, CAMS. Nanjing, China

Two thousand one hundred and fourteen cases with lagophthalmos among 2,114 cases of leprosy in Jiangsu were analyzed. The results were as follows: 1,121 cases had uni-lateral lagophthalmos and 993 had bilateral lagophthalmos.

The prevalence of lagophthalmos was 44.03% comprising 31.31% of all eye complications in leprosy.

In the lagophthalmos group, 41.6% of the cases had loss of sensation of the cornea.(t=2.461), which was higher than that in the non-lagophthalmos group, the eye complications in leprosy varied with type of leprosy and duration. For PB cases, 58.2% of the cases had lagophthalmos within four years after the onset of the disease. For MB cases, 44.9% of the cases had lagophthalmos over 10 years after the onset of the disease. Most of them were bilateral lagophthalmos. The approach to eye complications prevention has been proposed according to the findings. Emphasis was laid on the early detection and treatment of eye complications.

EVALUATION OF PRE-CORNEAL FILM IN LEPROSY

ALAPUR SATYAR A CDU

SIVAGANDHA REHABILITATION HOME

KURAPPALLY, KERALA

The number of registered cases of leprosy was 3.7 million in 1990, 25% of them have got ocular involvement and may be 50% do have blindness. The present study aimed at investigating the pre-corneal tearfilm abnormalities in patients of various types of leprosy. This study was conducted on 500 eyes of patients attending Sivagandha Rehabilitation Home. The patients were subjected for Schirmer's Test, 1% Rose Bengal Test, Tearfilm break up time with Fluorescin and Conjunctival impression cytology. It is observed that tearfilm abnormalities are important factors contributing for corneal morbidity. This work has been carried out at Sivagandha Rehabilitation Home, Pookkatty, Kerala.

DERMATOLITHIC ASPRITS IN LEPROSY PATIENTS AND THEIR RELATION IN ALABAMA

M.A. Nakuci & M.Nakuci

(CLINIC OF DERMATOLOGY, TIRANA, ALBANIA)

Genetic predispositions in leprosy are demonstrated in some works with pedigrees similar to the·specific gene in HLA-DR4, DQ7 marten. We have study aspects of dermatolithic area in 21 leprosy patients, 11 relatives persons and 110 health persons (group of control).

In 1097 fingers of health persons there are: 62.8% Loops, 30.8% Whorls, 4.6% Arches. In 269 fingers of leprosy patients there are: 47.1% Loops, 23.7% Whorls, 5.6% Arches. In 440 fingers of relatives 62.7% Whorls, 31.8% Whorls, 5.4% Arches. If in the leprosy patients the Whorls are higher (t=2.524, p<0.01) the Whorls and Arches are lower (t=2.414, p<0.050 in comparing with the group of control.

Important is that the third finger in the leprosy patient the loops there are (very higher) 77.2% in comparison with health persons, which have 64.5% (t=2.99, p<0.05)

Furnarher index (F=100W/L) is for the health persons 91.85%, in the leprosy patients 35.85% (very low), in the relatives 55.18%

In the study of tridimensional (n=300) 24%, in health persons, n=50% in leprony patients, n=65% 67.5% in relatives. There are significant differences (a=0.1, a=0.5)

The conclusion is that:

1. This data confirm genetic predisposition of the leprosy patient for this disease.

2. This method can play in the control of the people in the endemic zones to know the predisposition of this populations for leprosy.

A CLINICAL ANALYSIS OF 187 CHILDREN LEPROSY

We Yongquan

Xining Leprosy Hospital, Haikuo, Hainan Province, China

Xining Leprosy Hospital was established in 1913. The accumulative number of hospitalized patients is 2,873 including 187 children patients (0-14 years of age), accounting for 15.6%. Of these children patients, 41 (21.9%) and 46 (24.5%) were detected before and after the fifties respectively, males 112 (59.9%), females 55 (40.1%), male:female = 2.04:1. The duration of disease was 1.2 years for paticnary and 2.8 years for multibacillary leprosy. The appearance of skin lesions in most cases (71.2%) was a nodule or a plaque. Most of the cases belonged to bacteriologic borderline bacilli or borderline, with polar groups being distinctly uncommon. Then minimized 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 59.2% of the cases was clinicalhistopathologic correlation obtained again.

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1. This date confirm genetic predisposition of the leprosy patient for this disease.

2. This method can play in the control of the people in the endemic zones to know the predisposition of this populations for leprosy.
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 three drugs.

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

Dapsone induced pulmonary eosinophilia 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.

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.

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

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We discuss and present the alternative treatment plans evolved in the management of this patient.
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 season 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 griseovine plus local application of one of the imidazole anti fungal group of drugs.

CL51
ZOSTER-FORM BORDERLINE-LEPROMATOUS LEPROSY.
Jane T. Yamashita, Mitie T., R.F. Brasil, Renée Jabur, Regina M.C. Fortunato, Nilceo S.Michalany, and Osumar Rotta
Dermatology Unit, Escola Paulista de Medicina, R. Botucatu, 740 4023900, São Paulo, SP, Brazil.

RG in a 32-year-old dark-skinned man with 8 month history of cutaneous lesions. He presented multiple and infiltrated lesions with symmetrical 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, poly morphic, well-defined in some areas and poorly demarcated in others.

The histopathology of the lesion showed thinned epidermis, with inflammatory-cell infiltrate separated from epidermis by a narrow zone of collagen. The infiltrate was represented by foam-cells, some forming large nodules throughout the dermis with little epithelioid-cells. Bacterial index of skin smear was 5+ and lepromin reaction was 9.5 mm. The culture for mycobacteria was negative and lepromin reaction was 9.5 mm. The culture for mycobacteria was negative, showing that there was not association with other mycobacteria.

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

CL52
KERATOSIC PRESENTATION ON TUBERCULOID LEPROSY
Dermatology Unit, Escola Paulista de Medicina, R. Botucatu, 740 4023900, São Paulo, SP, Brazil.

RG in a 45-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 exam was also negative and lepromin reaction was 9.5 mm. The culture for mycobacteria was negative, showing that there was no association with other mycobacteria.

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

CL53
ASPECT CLINIQUE DIFFERENTIEL DE LA LEPRE EN HAITI.
Cyrielle Noel, Claude Fleur, Raymond Bernardin.
Institut Cardinal Leger contre la lepre ( HAITI )

Presentation iconographique des principaux pathologies cutanees pouvant ressembler a des pigres en pratique courante de dermatologie.

CL54
ASPECTS CLINIQUES PARTICULIERES DE LA MALADIE DE BUKON EN HAITI.
Institut Cardinal Leger contre la lepre ( HAITI )

Cas n° 1 - Femme, de 51 ans, presente un placard erythematous squameux de couleur violine a resolution centrale localisee au dos du pied droit, accompagne d'une lesion satellite angiomateuse.

Cas n° 2 - Homme, de 70 ans, avec de multiples nodules dissemines d'aspect syphilitique en niveau des doigt. ( Diapo )

Cas n° 3 - Femme, de 47 ans, lepromatose avec de multiples nodules en groupe de raie sur le nez et disseminés sur le corps.

Cas n° 4 - Femme, de 20 ans, avec des lesiones a type d'epithelo-polymorph de la paume des mains.

Cas n° 5 - Aspect similaire de lesiones nodulaires observe chez un patient lepromateux de 44 ans.

CL55
LOCALIZATION OF SINGLE LESIONS IN LEPROSY.
J.C.Avelo, L.R. Reis Vianna, J. Coutinho, A.B. Marques

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

Focality of lesions in covered sites, even when considered the percentage body areas occupied by those regions favours this impression; also the significant occurrence of dorsal lesions more common in men than women reinforce this point of view.
Prevalence of facial lesions in the age group under suggests that another factors, besides exposition, interact in the distribution of lesions in this group. Important differences were found when compared with data from other places and times. In vacuolar 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, which do not depend of transmission's form.

flat hypopigmented macule with defined edge (2 - 1 was shiny; slightly raised hypopigmented macule (11); reddish/coppery macule (6 - 4 were shiny); flat-topped nodules (10 - 1 patient only). The largest lesions were seen on the buttocks and thighs. Light touch sensation in lesion: lost (25), reduced (38), intact (10), variable (4). Site of lesions: trunk (14); buttocks (11); back (9); chest (5); scapular (6); hip (1); upper arms - elbow (10); thigh - knee (7); forearms (2), face (2). Condition of nerves: just palpable (2), easily palpable (3); slightly enlarged (4); number of nerves easily palpable/enlarged per child: 1 (8), 2 (6), 3 or 4 nerves (1). Biopsies were done in lesions: 111; Mitsuda reaction was - (9), (+) (1), (++) (4), (+++) (1), (++++) (1).

CL56
CLINICAL ASSESSMENT OF MONOLESION LEPROSY CASES
V. Paj, CR Pavankar, ML Gandowar, KL Bandekar & E Eupeotis Bombay Leprosy Project, Vidyanagar, 11th Purur Paharg, Slon-Chumabati, Bombay 400 022

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

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

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

Results:
Out of 829 cases which were treated with WHO-PH-MOT regimen for 6 months, 562 (67.8%) were found to be inactive at Release From Treatment (RFT). From the remaining 267 cases, wall at 264 (99%) attains inactivity at Release From Surveillance (RFS). Out of 5 cases, 2 patients dropped out during surveillance period and were lost for follow-up. 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 mono-lesions, as well as those involving single nerves in relation to PB as well as MB regimen.

CL58
CLINICAL-HISTOPATHOLOGICAL CORRELATION IN PATIENTS SUSPECTED OF HAVING LEPROSY
A.P. Schettini, A.A.F. Alencar, I.S. Melo, L.C. Dias, C.B.R. Ribao,
Instituto de Dermatologia Tropical "Alfredo da Matta" Rua Codai•ti, 25, Cachoeirinha, Manaus CEP 69.063-130 Amazonas BRAZIL

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 incidence in percentage terms of clinical and histopathological diagnosis with 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 INFECTION AND LEPROSY
Pedro Cangaïtes, Eniko Garcia, Juan Garcia, Carmen Logroñ, Robert Jurado, Jose Kincheloe and Manuel Ola, Hospital "Maria Soffia", School of Medicine University of Cordoba, Spain.

Among 50 patients with leprosy, 12 (24%) had radiographic evidence of bone infection in feet and/or hand. Fifteen lesions were recorded with a marked predominance to the upper extremity (90% cent were located in the hand). Considered asymptomatic, these lesions were painful only in two cases (both located in hand's phalange). Xylogene discoule encartacinales, and bone sclerosis.

We think that these lesions are due to a mucosal pathogenetique like leptome narine, and they are a kind of specific bone change due to invasion of bone 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
Ana Maria de Almeida, M.D. Ana Maria F. Riosling, M.D., Ph.D.,
Samuel F. Aragão, M.D., Ph.D. 
FACULTY OF MEDICINE OF SÃO PAULO UNIVERSITY OF SÃO PAULO BRAZIL

Among 50 patients with leprosy, 12 (24%) had radiographic evidence of bone infection in feet and/or hand. Fifteen lesions were recorded with a marked predominance to the upper extremity (90% cent were located in the hand). Considered asymptomatic, these lesions were painful only in two cases (both located in hand's phalange). Xylogene discoule encartacinales, and bone sclerosis.

We think that these lesions are due to a mucosal pathogenetique like leptome narine, and they are a kind of specific bone change due to invasion of bone 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.
The authors present a clinical case of association of histoid leprosy and pulmonary tuberculosis involving a 17-year-old female student from Goias, Brazil. In October 1985, she was diagnosed to have pulmonary tuberculosis. After 1 week of treatment with a triple drug schedule (isoniazid, pyrazinamide and rifampicin), the patient presented skin lesions of a progressive nature. After 6 months, 3 nODULES, erythematous-desquamating hypotrophic lesions with infiltrated borders were observed on the face and upper limbs at the Dermatology Service of FMUSP.

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

- LST: negative
- Mituto reactions: positive 120 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 leprae alters the immunological equilibrium of the patient and triggered the skin manifestations of leprosy.

CL63
STUDIES ON SSW - ANTITRYPsin INHIBITORY CAPACITY OF LEPROSY PATIENTS
Chen Han Gao Xingying
Faculty of Dermatology, Bengbu Medical College, Bengbu, Anhui Province, China

Modified Eriksson's method was used to evaluate serum-antitrypsin inhibitory capacity (ATI of 68 healthy subjects control group) and 55 patients with leprosy, including TT, LL, Borderline group (BB, BT, BO) 30, LL 10. The results showed that the values of serum-AT were 1.21±0.31 mg/ml for the control group, 1.42±0.26 mg/ml for Borderline group compared with control group, significant difference. P<0.05, 1.52±0.28 mg/ml for Borderline group compared with control group, significant difference. P<0.05. 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
HOMOGENEITY ASSESSING FUNCTION IN LEPROSY PATIENTS AND THEIR HOUSEHOLDS - A PRELIMINARY STUDY
Lu Dexian Deng Yufu Lu Zhihong Li Shupeng Wang Shaoming
Skin Disease Control Station of Chenzhou County, Hunan Province, China

Eighty-one leprosy patients and their household members were monitored with RCCB3bkR, RBCCICR, RFER and RFIR from 1985 to 1995. The results showed that there was a significant difference of the values of RCCB3bkR, RBCCICR, RRER and RFIR between the patient group and the group of household members, but significant difference of the values of RCCB3bkR was found between the two groups just mentioned. The results also showed that the values of RCCB3bkR, RBCCICR, 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 Hercin adhering 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-PHENYL GLYOXALID (PGL-1) ANTIBODY IN MULTIBACTERIAL LEPROSY PATIENTS
Ma Jiaju Deng Yunting Meng Weibai
Hanzhong Leprosy Hospital, Hanzhong, Shanxi Province, China

With NT-P-BSA as antigen, ELISA was used to detect anti-PGL-1 antibodies (IgM) in WD patients with different clinical status of disease and different durations. The following were the results: the average OD value (ODv) of 154 healthy individuals was 0.11±0.06 (x±SD) with 0.27 as the cut off point of positivity and a positivity rate (PR) of 5.9%. The initial OD of 20 previously untreated patients was 0.11±0.06 with a PR of 14.3% and the initial OD of 20 previously treated patients was 0.11±0.06 with a PR of 20%. The OD of active cases after 12 doses of MDT, 24 cases after 24 doses of MDT and 52 clinically cured cases were 0.23±0.25 and 0.33±0.27 with 0.21 and 0.45%, and 0.26±0.17 and 0.42%, respectively; OD and PR of 16 relapses were 0.33±0.22 and 44.2%, the OD of active case was remarkably higher than that of cured, and there was also a significant difference between OD of cured and healthy persons. The annual mean falls of OD and PR of patients on MDT were 0.25 and 8.65, respectively. This reduces the role of MDT and predicting the possibility of relapse.
CL66
THE METHOD FOR QUALITY CONTROL AND ITS APPLICATION IN LEPROSY SKIN SMEAR EXAMINATION
Zheng Mayunzh2, Zhang Zhenzh3, Liu Yuening3
1 Guangdong Provincial Institute of Dermatology, China
2 Chronic Disease Control Program, Guangzhou Provincial Health Service, China

Five workshops on Skin Smear Examination were conducted in Guangdong province since 1981. Every participant was required to take tissue fluid from active leprosy skin lesions (4-6 sites for each patient). Totally 81 slides including 65 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" (MTCAI, modified by adding BI value of smear spots) were used to evaluate the quality of skin smear made by 51 participants. According to TCAM, the results were, grade A: 71.6%, grade B: 28.4%, grade C and D: 1.4% each, but according to TCAM grade A was 71.6%, grade B was 28.4%, grade C 0%, grade D: 0%. All slides of grade B assessed by TCAM were regarded as 10 fresh smears with TCAM, the results were changed as follows: grade A: 30.6%, grade B: 49.3%, grade C: 18.6%, and grade D: 0.8%. The authors suggested that TCAM, if used for skin smear quality control, could not fully reflect the quality of bacteriological examination. MTCAI might be pre-ferrable.

CL67
THE RELATIONSHIP BETWEEN ANTIBIOTIC RESISTANCE (AMR) LEVELS AND RELAPSES IN THE CURED LEPROSY PATIENTS
Sun Chuanzh1, Tang Guilin1, Jin Qiaobo1, Liang Zhe1, Zhu Youyang1, Wang Weihong1, Xue Yi2, Wu Xingzhong1
Guangdong Autonomous Institute of Dermatology and Venerology, Nanning, China

Three hundred and thirteen cured leprosy patients (MO 117; PB 112) were clinically, bacteriologically and serologically monitored for 2 years in Guangdong Autonomous Region, ELISA and MLPA with NT-P-BSA as antigen, were used to detect PGL-I (198). Sera from 235 local healthy people (MO:250; PB:24) served as the cut-off point of ELISA or the positivity threshold of MLPA (x±2.3). The results showed that, the anti-PGL-I antibody (1/3) were detectable over a considerable period of time in leprosy patients after cure. The mean OD values of PGL-I antibody for ELISA was 5.133, with a positive rate of 19.7% (27/133). Much higher than those of the PB, the latter being 0.096 and 3.52±1.42, respectively, 12.8% (23/171) of cured PB was regarded as MLPA positive, but all cured PB were MLPA negative. 2) (1/4) relapses from cured PB were detected in NT-P-BSA-ELISA positive PB patients. Furthermore, the levels of specific antibody in the sera of both cases steadily increased eight weeks before relapses appeared, but no relapsed case was found in 21 NT-P-BSA-ELISA negative patients. The results suggested that relapses were more likely to appear in cured patients with positive serological results, and 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 RELAPSES IN SMERS FROM NASAL MUCOSA
Robert Macnaghy1, Steven Naoum3, Kevanu (Manduca) Leprosy Control Project, F.G. Box 140, Lilongwe, Malawi

Smears from the nasal mucosa of 171 newly detected multibacillary leprosy patients were taken over a five year period in the LCPH 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 OT of the slit skin smears. The correlation shows a mildly positive

CL69
HEMATOLOGIC DATA OF OLD PATIENTS WITH LEPROSY
Shigeru Matsumi1, Sunao Tanaka1, and Tsugio Nakawara2
National Leprosarium Koryu Rakusen-en* and Gumi University*, Gumi, Japan

Hematologic values, in a retrospective three-year (1989-1991) longitudinal study, were analyzed for 315 old leprosy patients who were 163 males (ranged in 47-99 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. WBC counts were not statistically different. BB values for leprosous form were lower than those of tuberculoid form and decreased significantly with advancing age.

Sex Age n 19\(\text{Ht}^{0.05}\) 1B n (10) 1P n (10) BB n (10)
Male 50-59 13 14.6±1.1 4.39±0.32 4.42±0.46 5.6±1.5
60-69 63 13.8±1.4 4.36±0.46 4.31±0.57 6.2±2.1
70-79 60 13.5±1.5 4.27±0.49 4.07±1.4 6.0±1.2
80-89 23 13.7±1.0 4.31±0.49 4.04±1.7 6.0±1.3
Female 50-59 13 13.4±1.0 4.36±0.35 4.51±1.2 6.3±0.8
60-69 45 13.4±1.0 4.31±0.34 4.04±1.5 5.9±1.2
70-79 60 13.2±1.0 4.20±0.35 3.94±1.1 6.7±1.2
80-89 26 12.8±1.2 4.10±0.44 3.86±0.34 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.

CL70
ETUDES DE L'INDICE BACTERIOLOGIQUE CHEZ LES PATIENTS MULTIBACILLAIRES
Institul Cardinal Leger centre le Lepre ( HAITE)

Sens considérés:
1) les variations de l'I'B chez les patients multibacillaire réguliers au traitement,
2) les variations de l'I'B dans les cas de non-compliance au traitement,
3) les variations de l'I'B dans les cas d'abandon du traitement.

CL71
THE ROLE OF SKIN-SMUR EXAMINATION IN MULTIBACILLARY LEPROSY
Devansh V. Salin A. Khan, Lilly Ravisimmar, Nobleraj A, Lebo D.

International Journal of Leprosy
1993

32A

correlation (r=-0.47). A majority (approx. 75%) of the patients for whom the highest OT 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. If the 171 patients had a positive nasal mucosa smear, if of those, 50 could be followed until the nasal smear become negative, the majority (75%) became negative during the first six months of treatment with the standard multidrug regimen.
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.

Despite 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 1983, a total of 450 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 underwent 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 facilities worldwide.

CL72
POLYMERASE CHAIN REACTION IN THE LEPROSY,


2) Sanatorio Fontilles Alicante (Spain), Departamento Microbiología Facultad de Medicina Valencia (Spain), Durviz S.L. (Spain).

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

Se presentan los resultados preliminares obtenidos y se hacen consideración de la importancia de esta técnica para detectar formas paucibacterianas, causas 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 áreas endémicas.

CL73
BACTERIOLOGICAL AND IMMUNOLOGICAL STUDIES ON ACTIVE AND TREATED PATIENTS.

Sawsan H.M., El Tayeb, Abd-El Hamid A. Mohamed, Jiri Kaye, Er El Regal Khannis, Nahid El Shabrawy, Fazl M. Naar.

Al Azhar University, Medical College Egypt.

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 nerve system. Bacteriological investigations were done including the bacteriological and morphological index. 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, Fazl M. Naar, Abdel Hamid A. Mohamed, Er El Regal Khannis, Nahid El Shabrawy.

Al Azhar University, Medical College, Egypt.

Hematological investigations as blood hemoglobin, total and differential leukocyte count, and biochemical investigations 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. Those patients had a higher hemoglobin level than the under treated patients. All the biochemical result showed some significant increase or decrease values compared with the control group.

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

CL75
SECRETE LACTOFEHRIN IN LEPROMATOUS LEPROSY PATIENTS.


Central JALGA Institute for Leprosy (ICM), Taj Ganj, Agra-212001 (India).

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-I reaction. The mean lactoferrin levels in both types of patients (18.8±26.81 mg/l; 32.9±10.3 mg/l respectively) were observed to be significantly higher than those in healthy volunteers. The serum lactoferrin levels were found to be associated with bacterial load and CO2%. Majority of lepromatous patients without reactions (湍=3) had normal levels whereas 6/11 of lepromatous leprosy patients suffering from reactions showed a significant increase in the levels of lactoferrin. These findings suggest that the use in lepromatous leprosy is associated mainly with occurrence of reactions in lepromatous patients. The results and their possible use in diagnosis and understanding the pathogenesis of type-I reactions would be discussed.

CL76
EFFECT OF MULTIDRUG THERAPY ON PLASMA LEVEL OF HIGH DENSITY LIPOPROTEIN CHOLESTEROL (HDL-C) IN PATIENTS OF LEPROMATOUS LEPROSY.

Nigal Kumar and B.L. Sharma.

Civil Hospital and Danida assisted leprosy project, J-10, Gandhi Nagar, Gwalior-474002 INDIA.

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 62 ± 4.04 Kg) who received multi drug Therapy & declared free of disease (as per WHO tech. report

Abstracts of Congress Papers 33A
ADAPTATION HORMONES AND AUTOSENSIBILIZATION TO CONNECTIVE TISSUE IN LEPROSY

E. Balybin, L. Vinnick, V. Naumov, L. Gerovitch

Leprosy Research Institute, Astrakhan, Russia

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 hypophysal somatotropic hormone (HSU), hydrocortisone, triiodothyronine (T3), thyroxin (T4), and for T- cell suppressor activity (TSL) with using ELIA. 22 otherwise healthy persons were used as controls. In active patients Abe and ABe levels were significantly elevated remaining such in cases after 10 years and more of their controls. In active patients ARc and ABe levels were in the normal range. There was a strong relationship of the titers of the hormones studied and TSL-activity and decreased TSL-activity and nutritional status and weight improvement was noticed in last two groups. Relapse rate remained 5% in list group and nil in other two groups.

It is opened that HDL-C plays an important role not only in disease process but also has role in relapse of lepromatous leprosy. We suggest to give trial of lipolytic drugs along with NDT in cases of lepromatous leprosy.

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

Solomon Yinnakhma,1 Jo Coombes2 and Dana Lockwood3.

1. Dholpet Leprosy Research Unit, Karwan, Hyderabad, India
2. Type of Clinical Sciences, London School of Hygiene and Tropical Medicine, London WC1E 7HT.

Erythema nodosum lepromum (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 multibacillary 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 11. and 52 % 911. Overall 22.1% (range 10.7-57.5%) of 11. and 3.7% (range 0.6-5.9%) of 911. patients presented with ENL. Of the 1989 cohort 32% of 11. and 9.5% of 911. patients have developed 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.

AGRAVULOCYTOSIS SUPPOSED CAUSED BY CLOFACAZINE IN A LEPROMATOUS PATIENT

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Dermatologia Sanitaria, Secretaria Estadual de Saúde do Estado de Santa Catarina, Brasil

This abstract is about a case of agranulocytosis in a lepromatous patient who was under treatment for leprosy and, during administration of 2 doses administrates clofazimine, rifampin, dapsone, developed agranulocytosis and needed hospitalization in C.T.1.

After discharge from the hospital, he used only dapsone without a problem but when clofazimine was developed agranulocytosis in the patient was again.

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

This is not a very uncommon phenomena after the implementation of Multi Drug Therapy.

APPLICATION OF ELECTROACTIVATED SOLUTIONS FOR TREATMENT OF OSTEOMYELITIS IN LEPROSY PATIENTS

E. Shats

Leprosy Research Institute, Astrakhan, Russia

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. Juschenko, 1992). The results of treatment of 46 leprosy patients with osteomyelitic 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 necrotic 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 amolyte, i.e. the fraction (pH7) with marked bactericidal properties. As inflammation subsided amolyte was substituted for local catalyte (pH7), i.e. the fraction with regenerating properties. Clinical observations showed that applications of electroactivated solutions resulted in a noted and disappearance of foci of infection with healing of ulcers. In addition, these solutions are free of allergic complications.
THE EXPERIENCE OF USING REFLEXOTHERAPY IN LEPROSY PATIENTS WITH CHRONIC NEURITIS

E. Shata, V. Naumov, E. Baliybin
Leprosy Research Institute, Astrakhan, Russia

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 AR28, 31, 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-endorphins 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.

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

Dean R. Goodless, Ana L. Viana, Ribe J. Padua and Phillip Ruiz
University of Miami School of Medicine, Department of Dermatology & Cutaneous Surgery, and Department of Pathology division of Immunopathology, Miami, Florida USA

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 eumamous, anesthetic, annular plaques. Histology was consistent with borderline tuberculoid leprosy and M. leprae was detected by PCR. The lesions responded rapidly to MT6. The percentage and absolute number of CD4+ peripheral blood lymphocytes (PBL) was decreased (969/μl) 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 granuloma consisted principally of CD4+ cells surrounded by a mantle of CD8+ cells, with less than 5% (CD2+)

Neoplastic transformation of chronic ulcers in leprosy

Niyi Awafeso, Aq. Director,
National Tb. and Leprosy Training Centre P.M.B. 1089, Zaria, Nigeria

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 planter ulcers is said to be rare, the fact that, for instance 2 patients were detected within a month from among 25 patients admitted for care at the NLEIC, Zaria is a reminder that this unpleasant complication does occur. Since the proprin in leprosy is slower with delay in diagnosis, it is important that health workers, and especially those looking after leprosy patients should recognize the possibility of malignant change in patients with reffrocted planter ulcers. In addition, this condition should be emphasized in textbooks and handbooks on leprosy. Most importantly early diagnosis and effective treatment of leprosy patients will prevent malignant transformation of trophic ulcers.
for H1Ag (ELISA, Abbott), whereas in 53 samples from the same original population HCV seropositivity was assessed (ELISA, Abbott and Covalent). H1Ag seropositivity (2.6%) did not differ between leprosy cases and healthy control. HCV seropositivity was found 18.9%. A near significant difference was observed between patients and healthy controls (A: 9.9%). Total seropositivity rates revealed a statistically significant difference (p = 0.04) between the prevalence of HCV and HIV. It is concluded that the prevalence of hepatitis C is increased among Greek leprosy patients. In both form of hepatitis, seropositivity rates do not differ between pauciarticular and multibacillary forms of leprosy.

**CL87**

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

Sapan K. Samanta and I. S. Roy

Community Ophthalmology Service, Upgraded Dept. of Ophthalmology, B. S. Medical College, Bankura, West Bengal, India.

Social stigma had kept the leprosy sufferers away from the general hospital and private clinics for ophthalmic care. Till up to late eighties 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 (especially in cases of patients with deformity). Their eye care were mainly adapted by the weekly eye clinics of the leprosy hospitals and the field clinics which were conducted by P. M. S. Medical Officer and in a very few instances by the ophthalmologist.

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 O.P.D. 6 operation theatre respectively. At the same time most of the 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. It is certain that eye specialists 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 GMFL'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 involved 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**

Ogendo P A, Obwu A, Girolo C M, Gatura M, Olika F, Aroko H R, were M

KENYA MEDICAL RESEARCH INSTITUTE

Alupe Leprosy and Skin Diseases Research Centre, P.O. Box 5, Bura, Kenya.

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, development of type I or type II reactions and occurrence of relapse among leprosy patients who had been treated with MDT.

Cases were HIV positive patients who were put on MT 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, 95% CI = 1.0-23.4 p = 0.07). 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 (X² = 4.4 p = 0.04). Relapse/retreatment was found to be higher among cases (26%) as opposed to controls (5) (OR = 6.5 X 3 p = 0.07).

These findings would not have implications on the national control programmes which are implementing MT in areas where both diseases endemic.

**CL90**

**HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND LEPROSY**


Department of Dermato-Venereology, Dijkzigt Hospital, Erasmus University, Rotterdam, The Netherlands.

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 hyper- sensitivity reaction. During a HIV infection, this may well not be possible. The bacillus 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 antigen discussed.

We expect an initial decrease in leprosy which can be seen in many countries in which HIV infection is widespread and which is commonly attributed to BCG vaccination or Multiple Drug Therapy (MDT) programme. Thereafter we expect an increase of leprosy infections among those not infected with HIV.
CL91

MALIGNANT TRANSFORMATION OF CHRONIC PLANTAR ULCERS IN LEPROSY PATIENTS

Michel-Yves Grauwin, Bernard Gentile, Alcina Chevalland and Jean-Louis Carcel
Institut de Léprologie Appliquée, Dakar, Sénégal.

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 differentiation 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: 15 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 (depending on healing possibility and functional capacities of the foot). In case of carcinoma, the regional lymphnode dissection should not be systematically considered.

From available data in literature, 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.

CONTROL AND ERADICATION

CO1

ON THE ROLE OF THE GOVERNMENT IN LEPROSY CONTROL,

Zhang Hongyun, Pan Hongyi, Li Zengyi and Fang Qiyun

Wen Zuijun, Zhang Lixing, Lu Peichao and He Guowei

Guangxi Autonomous Regional Institute of Dermatology and Venereology, Nanning, China

Health Bureau, Guangxi Autonomous Region, China

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 programmes and have provided with necessary resources including manpower, funds 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 1992 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 government, especially in the third world countries where leprosy is seriously endemic.

CL92

SQUAMOUS CELL CARCINOMA IN CHRONIC ULCERS OF LEPROSY PATIENTS

Jan Hendrik Richardus and Trevor C Smith

McKean Rehabilitation Centre, P O Box 53, Chiangmai 50000, Thailand

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. Metastatic spread was observed in 2 cases (5%), both instances leading to death. The common 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 race 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.

CO2

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

Helen Verheggh

S. L. B. Bukkuru, Nigeria

The strategy of accelerated implementation of NTD presupposes the political commitment for the allocation of resources, a well-motivated leprosy control organisation and a relatively stable political and social environment.

The result of this strategy in S. 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 MCH or combination with TB control do not address sufficiently the problems of care of disabled patients, the motivation of health personnel and theinstability of the political and social environment. In addition or as an alternative to these solutions the systematic participation of leprosy patients and patient associations is discussed. The experience with testpaticipants in voluntary leprosy workers has shown that they could become powerful
partners in leprosy control and could contribute orately to the sustainability of leprosy control in the next decade.

C03

COMPREHENSIVE LEPROSY CARE PROJECT, "OORSAD MODEL" - A NEW APPROACH TO LEPROSY ELIMINATION
Atul Shek and R Ganapatig

The Comprehensive Leprosy Care Project envisions the combination of governmental efforts and specialists brought together by Rapid surveys to supplement the international assistance to develop a new approach where a leprosy patient at any stage of the disease process needing medical, surgical or medical care was given an opportunity to overcome the disease. In rural field situation at Burdwan in West Bengal (population 3,70,0000) 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 splints (c) identification of early neuritis, reactions and relapses for medical or surgical intervention (d) care of insensitive extremities (f) recognition of handicap and required economic assistance and (g) rehabilitation of advanced deformed patients by Modular grip aid.

During the past four years of its existence the project has detected 885 new patients, started MDT in predominantly monotherapy area, provided deformity care services to 498 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 minimizing the chances of elimination in true sense. The detailed observations will be presented.

C04

A COMPARATIVE STUDY ON THE EFFECTIVENESS OF DIFFERENT METHODS OF CASE DETECTION IN NORTH INDIA
M N Cassabianco, W Kerkerlo and P K Roy

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

This study was conducted in two endemic areas, Muzaffarpur and Maini 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 are analysed in relation to the main hours spent on the survey and the profile of the cases detected such as age, sex, type, deformity and bacteriological index, etc.

A population of 9,692 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 25 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 15.9 man hours per case detected. More male cases were detected by rapid survey (11:1) than in the mass survey (1:2:1). More adult cases were detected in rapid survey (7:1:0) than in the mass survey (4:1:0). More single lesions were detected in 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.

C05

GUIDELINES AND STRATEGIES OF THE PROGRAMME FOR THE CONTROL AND ELIMINATION OF HANSEN'S DISEASE IN BOLIVIA IN THE PERIOD 1990-1994
Germain O. Perna, Rolofsia H. R. Poncea, Paulo F. R. Rebelo e Carmona F. M. Peixe

Coordenacion Nacional de Dermatologia Sanitaria, Ministerio de la Salde, Brasilia, Brazil.

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 classify small infectious areas, with the objective of having an impact on the endemic through activities of disease prevention, early diagnosis and ready treatment with MDT and POT and thereby reducing the incidence of leprosy.

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

C06

EPIDEMIC LA TRANSMISION DE LA LEpra PARA 1994: POLITICA PARA LA ACCION EN MEXICO
José Rodriguez-Dominguez MD, MPH, Lucía B. Yepez Velasco MD, MSc; Francisco Castellanos García MD, MPH

En 1989 el Gobierno Mexican° emiti6 la politica de eliminar la lepra como problema de salud publica certeando su transmisi6n mediante incorporaci6n de los 16,700 enfermos provenientes y los nuevos casos a los esquemas de poliquimioterapia (POT o MDT) recomendado por la OMS. Se implement6 un plan entre el Gobierno de Mexico y dos organizaciones internacionales de ILEP (MWF y ALM) para intensificar acciones de salud y de atenci6n primaria.

La distribuci6n 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 el pais; por lo que se consider6 prioritaria a esta area geografica, para iniciar la primera fase de locali-

zaci6n e incorporaci6n al tratamiento de los enfermos. Las principales dificultades para lograrlo han sido la recurrencia y no localizaci6n de casos; por ello se disi6ron estrategias de capacitaci6n en leprologia, de promoci6n y fomento de la salud usando como tema la curabilidad de la lepra; implementaci6n de un programa de rehabilitaci6n de incapacidades; supervisi6n continua y evaluaci6n peri6dica.

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

La tasa de prevalencia del pais al iniciar la POT era de 21 X 10,000, actualmente ha bajado a 1.8. Para 1994 se pretende bajarla a menos de 1 X 10,000 h/s.

C07

EVOLUTION OF THE ILEP INFORMATION SYSTEM FOR LEPROSY CONTROL PROJECTS 1966 - 1993
Dominique Martineau-Needham and Sarah Lacey

International Federation of Anti-Leprosy Associations 234 Blythe Road, London W14 0HL, United Kingdom

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.

It's 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.

CO0
RAPID PHOTO SURVEY AS A TOOL FOR CASE DETECTION IN URBAN AREAS
Lobo D, Mathews R, Alexander M, Kamudripa 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: 704/690
- New Case detection rate: 0.68/1000

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

CO9
COMPARATIVE CASE-OUTPUT THROUGH DIFFERENT CASE-DETECTION METHODS IN URBAN AREAS
Mathews R, Alexander M, Thirunavakarasu S, Lobo D, Kothandapani C, Maria Dominic A.

In urban areas and metropolitan conglomerates, it is impossible to employ a 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 CREMALTES 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:

<table>
<thead>
<tr>
<th>Method</th>
<th>Pop. Covered</th>
<th>PB</th>
<th>MD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive</td>
<td>859,046</td>
<td>747</td>
<td>669</td>
<td>1,200</td>
</tr>
<tr>
<td>Rapid Photo</td>
<td>1,669,019</td>
<td>1,280</td>
<td>52</td>
<td>1,332</td>
</tr>
<tr>
<td>Health Camps</td>
<td>12,631</td>
<td>44</td>
<td>02</td>
<td>46</td>
</tr>
</tbody>
</table>

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
Joint Director of Health Services (Leprosy), Pune, India.

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 worker (K). District, Satara, (Maharashtra) was selected with total population, 25000 distributed in 10 villages.

A microlevel experiment with special stress on personal contacts, was given with the help of visual aids. After two years successive efforts following spectacular 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 RAP change, individual approach is extremely effective.

CO11
RAPID VILLAGES (RVS), ANALternative METHOD TO THE ESTIMATION OF LEPROSY PREVALENCE
Panna Singh, S.S. Sharma, P.A. Schenker, Chawatkal A.

The MULEP Project P.O. Box 8, Khon Kaen University 40002, Thailand.

This study aim 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. VHS case-detection was used. Found cases would be confirmed by leplogist. 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 announced 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 group technique would be tried. Registered cases (known cases) and their contacts would also be tried. 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 absence 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 20385 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 TVS was reportedly it was a small village. The statistical analysis showed no significant difference between the two methods (TVS and PSS) in terms of prevalence. The TVS 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**

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

Leprosy is prevalent in the Kingdom but not equally distributed. Some in Terai Districts and Hill Districts in Western Nepal & Eastern Regions. Leprosy control started since early 1960 with a prevalence of 10/1000, after a survey in 1956 (Nepal Government). In 1964 Leprosy Control Program was established in a Pilot Project till 1980. About 10 districts have the prevalence more than 17/10000 in 1990 (country prevalence 12/1000). M.DT 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 MINI (Nepal Ministry Government) and WHO (Fudziloketuberculosis program in the last 6 years; 1967/9 to 97/2) prevalence rate dropped from 15.7 to 2.6 in the detection rate from 3.6 to 3.2/1000, 0th coverage 23% to 1997. Action plan to improve control activities for achieving better achievements are:

1. Training programs for DPI-10 (District Public Health Officer), Leprosy supervisors and Basic health workers are put as a priority. Improvement of the services in clinics/health posts, supervision from National and Districts level will be done more systematically and frequently to the district Leprosy supervisors and clinics/health posts workers in the field. Distribution of leprosy drugs will be maintained regularly.

2. Action plan for more better achievement are:
   - Training programs for DPI (District Public Health Officer), Leprosy supervisors and Basic health workers will be put as a priority. Improvement of the services in clinics/health posts, supervision from National and Districts level will be done more systematically 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 REDUCTION OF LEPROSY PREVALENCE IN RURAL SOUTH INDIA AT ANGULUS KEDRA LAST THREE AND A HALF DECADES AMONG 1.5 LANDS OF FATEHPUR DISTRICT BY INDEPENDENT INITIATING AND EFFORT IN THE STUDY PERIOD ATTENDED BY MINI SUPPORTED ALREADY.


2. SECOND PHASE OF MODIFIED MDT, 1984-87 GIVEN ONLY FOR PROGRESSIVE (IL AND LS)-106 CASES (BECAUSE OF LIMITED FUNDS). 2% OF 186 CASES WERE CONVERTED NEGATIVE IN THE FIRST YEAR ITSELF WE RECEIVED GOOD PUBLIC REACTION FROM ALL, MODIFIED MDT WAS GIVEN FOR THE REMAINING KHOI NEGATIVE CASES (IN IT) OF THE WHOLE PROJECT AREA.

3. THIRD PHASE OF REGULAR MDT (FULLY REGION) AFTER ANOTHER ENQUIRY SURVEY IN THE AREA COMPLETELY WITH GOVERNMENT FREE DISC SUPPLY AND INCENTIVE SUPPLY, NOT GOVERNMENT 100% AND CLINIC ATTENDANCE 99%. CASE DOWNS TO 24/1000 AND INCIDENT RATE 4/1000, 187 CASES TO CHILDREN 3/1000, UNIDENTIFIED CASES 2/1000, INTEGRATED APPROACH ADOPTED THROUGH 22 PRIMARY HEALTH CENTER, COMMUNITY HEALTH WORKER CASE-HOLDING, LEPROSY PARAOCLIC, WASHING CASE-SURVEY, DETECTION AND SURVEILLANCE - NICE Hoping to eradicate almost all cases of LEPROSY AND MAKE INCREASE DROP TO ALMOST NULL BY TURN OF THE CENTURY (2000 AD).

4. FOURTH PHASE OF PLANNING REDUCTION OF THE PROJECT ALREADY TAKEN UP THE CURE, CAPPING AND SECOND SURVEY OF ALL TREATED.

**CO14 UTILIZATION OF BARANGAY HEALTH VOLUNTEERS IN THE IMPLEMENTATION OF THE LEPROSY CONTROL PROGRAM**

Soledad S. Grino, B.S.E., M.P.H.

The Philippine Department of Health integrated leprosy services with NDT as the main approach in 1983. After 1 1/2 years of implementation, problems in case finding, case holding, surveillance, and information dissemination arose due to difficulties in 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 NIDT 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.

Cagayan, Ilocos Sur, with a Prevalence Rate of 4.5 per 1000 and a Case Detection Rate of 1.8 per 1000 was chosen as the study site. At this time, 7 Rural Health Units are implementing the health program with 17 Barangay Health Workers helping them. A 2-week training (with 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 health aides had 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.

* Village
CO16
INTEGRATION OF EYE CARE IN LEPROSY CONTROL IN SOUTHERN NIGERIA
Rien Verhage, Margaret Hopewell
Netherlands Leprosy Relief Association, Amsterdam, The Netherlands

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 25% 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, organizational 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 levels, 2) an appropriate and efficient referral system and 3) the maintenance of a distribution system for standardized equipment and medicines.

CO17
Hamsa Chum, Kwatanga Gumareh, Putra Graf
National Tuberculosis and Leprosy Programme, Tanzania. TB/Leprosy Central Unit, Dar es Salaam, 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
Shao Kuanwei Jiang Zhilin Hong Baoying
Fujian Provincial Institute of Dermatology and Venereology, Fuzhou, Fujian Province, China

Since 1986 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 services 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% of the total number of new cases were detected, and 95% 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, 2166 patients received MDT with a coverage of 95% and regularity rate of 95%.

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 1934 - 3423 per year. This included chronic diseases (e.g., TB, HBD, STIs, epilepsy) immunization and antenatal care. The extra cost incurred was an average of 68,12,500 ($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 illustrated 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.

CO19
COST AND EFFECTIVENESS OF INTEGRATING LEPROSY WITH PRIMARY CARE
K.R. John, Jayaprakash Mulyili
Christian Medical College, Yellore

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. This 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.

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CO20
THE SIGNIFICANCE OF TAKING CARE OF LEPROSY IN-PATIENTS WITH COMPLICATIONS IN GENERAL HOSPITAL
Nguyen Van Son, Nguyen Van Hu, Nguyen To Nga
Dermatology Department, Viet-Tac Hospital, Haiphong, Vietnam

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 treatments. 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-Tac general hospital has been determined to do its best to receive and treat them.

The care and treatment for leprosy in-patients have created more favourable conditions for the dermatology department. Nowadays, there is also a Dermatology Department in the Haiphong Medical College to contribute valuable experiences in early detection of leprosy patients to treat them with the best success and to prevent the development of leprosy reactions, as well as the treatment of leprosy reactions in order to avoid nerves damage, thus preserving disability for leprosy patients.
CO21
INTEGRATION OF A LEPROSY-TUBERCULOSIS-ONCHOCERCIASIS-CONTROL-PROGRAMME INTO A PHC-PROGRAMME IN THE FOREST REGION OF GUINEA

Hannes Wither, Abdourrahmane Sherif
Mission Philalfricaine en Guinée, Macenta, Guinea

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 riverine onchocerciasis component was added. Starting from 1989/90 the national leprosy control programme was formulated. 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

Tori O. Majoh
Specialist Hospital, Osun, formerly Bendel State of Nigeria.

MDT was introduced in the state in October 1995 as a pilot project in one clinic. By December 1996, the whole treatment centre 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 33 at Dec. 1998. Factors that accounted for the fall in this prevalence are discussed. Relapses have been few, the reasons and the place of R.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.

CO23
SAMPLE SURVEY OF LEPROSY AFTER THREE YEARS OF MDT IN BHUTAN TALUK OF PERIYAR DISTRICT, TAMIL NADU, INDIA

Dr. M. S. Shanmugam, P. Mahaswamy, S. Louis and D. G. Puran

V. Ilaha, Leprosy Project, Sakthinagar, Periyar District, Trivandrum, 699015, South India.

A sample survey of Bhutan 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 4555 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 38 days. 177 active cases were detected. 265 cases were new. 5.55 were bacteriologically positive for AFB. The child rate was 13.57/1000 new cases. Whereas according to the programme the prevalence has come down to 3.4% from 13.0%, according to the sample survey the prevalence rate is 9.30 with a prevalence of new cases of 6.93. This is much higher than the expected ten fold reduction of prevalence under MDT. Indirect assessment of MDT 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

Paul Jakeman, Witi Jakeman, Jigmi Singay
National Leprosy Control Programme, Bhutan

Bhutan introduced MDT in 1992, following the WHO regimen. A marked decline in prevalence has been seen during the past decade, from 4 per thousand to 0.3 per thousand. However, incidence 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 encouragement that 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
TRENDS OF LEPROSY IN MULTIDRUG TREATMENT AREA OF NANDA

Firuz Thapar and Nilu-Mital-Grewal

Leprosy Control Programme in Jammu was started in 1992 with intensive case detection and Multidrug therapy. Of the country's 14 states/districts, six divisions constitute 91.6% of the total registered cases in 1992 and were designated as hyperendemic areas. In these divisions WHO Multidrug Therapy was introduced in 1996. The MDT delivery was by the Vertical staff but was integrated into the activities of the Basic Health Staff (BHS) during second half of 1997.

Epidemiological indicators were calculated from the annual reports (1990 to 1991) of the leprosy control programme.

Among the registered cases, number and prevalence rate declined progressively but was not marked after introduction of MDT. The Multibacillary rate declined but was noted marked two years after introduction of MDT. The Multibacillary proportion increased after introduction of MDT. There was decrease in under 14 years proportion.
**CO26**

**COSTING OF LEPROSY CONTROL PROGRAMMES BEFORE AND AFTER INTRODUCTION OF MDT**

Jayakumar 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 255-2974 with an average of 1625 patients. The budget of the leprosy control programmes varied between Rs6,60,000 to Rs 3,69,700 and the average budget Rs2,20,278. The cost per patient treated varied from Rs.6,037 to Rs 10,678 with an average cost of Rs6,423.

Due to decrease in size head before MDT was started, the number of patients in these centres varied from 109-1566 with an average of 526. The budget of the leprosy control programme varied from Rs.1,11,860 to Rs 6,96,556 with an average cost of 232,227.

The cost per patient increased from Rs.126 prior to MDT to Rs.1054 per patient/year.

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

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**CO29**

**ECONOMIC ANALYSIS OF VARIOUS THERAPY SCHEDULES IN THE MANAGEMENT OF LEPROSY IN BRAZIL**

Domingos L. Rodrigues, Gerson R. Penna, Gerson F. M. Pereira & Maria C. C. Magalhaes.

Coordenação Nacional de Dermatologia e Saúde Pública, Ministério da Saúde, Brazil.

Six years after the official implementation of MDT in Brazil (1988-1992), an analysis allowed us to see the difficulties found in the area support of supplies needed for the treatment of the 250,000 registered patients.

Brazil is a continental country, with a prevalence of 17 cases per 10,000 population, with a policy for the national production, distribution and control of drugs, and the central level monitoring of three drugs (rifampicin, isoniazid and dapsone) provided by different laboratories, had to obtain support from the Brazilian Ministry of Health Inventory.

This paper shows and discusses the programmed use and the coverage reached in 1991, the missed patients, under the monitoring of the central, state and municipal levels.

The table presented 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.
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 ILLEP 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 ILLEP were receiving MDT. At the end of 1991, 65% 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

L.M. BECCHELLI, Faculdade de Medicina de Ribeirao Preto, Universidade de São Paulo, Brasil.

Formerly Chief LFU Unit, WHO, Geneva, Switzerland

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 DDS was adopted (1982) the duration of treatments 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 anticipated 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

Jool Almeida

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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) diagnosed and awaiting treatment, or ii) disabled by leprosy, will probably double the initial number, and almost certainly no less than 125% of the initial number.

**CO33**

DECLINING OF LEPROSY IN MALUKU INDONESIA AFTER INTRODUCING MDT IN 1982

Nisitanno Sugiono, D.Jugono Tanusala and Andy L. Lohanesrjo

Leprosy was known in Maluku Province, Indonesia since last century, until now still prevalent but not equally distributed. New patients found in Ambo town, North Maluku, in Kei Islands in 1973, in Central Maluku in 1984, epidemiological situation since last 1980's was:

- Prevalence rate from 41.8 to 12.0/10000, case detection rate from 2.8 to 0.6/10000, cure coverage from 2.3% to 93%, cure rate from 5% to 95% and cumulative cure coverage from 12.5% to 76.5% (1982/83 to 1991/92).

- Leprosy patients were treated since early 1910's in several leprosy hospitals/hepaprastal in Maluku, central Maluku, Ambo town and in 2.5 Maluku, leprosy control program (MDT) started since 1965, in Ambo town and Central Maluku, 1970 in North Maluku, and in 1971 in Kei Islands, 2.5 Maluku, Kalam and Labuan until 1987 started with combined regimen introduced by WHO in October 1981.

- In the first few years after the introduction of MDT the coverage was still limited to very active cases and in preponderant districts due to lack of drugs.

The WHO program in Maluku Province was carried out by Government Health Staff and workers assisted by the WHO Ciba Geigy, Danish Save the Children Organization, WHO and Sanatata Memorial Health Foundation.

Effort is made to continue strengthening the activities to achieve the goal 1 per 10000 by the year 2000.

**CO34**

TEN YEARS OF MULTIDRUG THERAPY IN ZIMBABWE

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National Leprosy Control Programme, Department of Epidemiology and Disease Control, Ministry of Health and Child Welfare, Zimbabwe.

A national Leprosy Control Programme based on WHO recommended Multidrug Therapy was implemented in 1994.

From 1996, a gradual integration of control into Primary Health Care was initiated after training of health workers from the districts.

The results show 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 show 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 (7/100 of new cases have more than WHO grade 1 disability).

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

DELENA LEPRA
ORGANIZATION OF THE STUDIO FOR ERADICATION OF LEPRA IN ALBANIA
H. Puka and M. M. Jakość
(Clinic of Dermatology, Tirana, Albania)

Since 1944-1992 (50 years) we have treated 88 cases of leprosy (67 LL, 17 LT, 4 LL), long period of infection of leprosy (30-40 years) present for us the duty to control 512 household, 2585 people in 15% time 1 year for long time clinically and serologically. Also we must control all the people in endemic areas one time in two years. In this we can find early the patient, oligosymptomatic or subclinical 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.

FORM OF THE PROGRAM

I. Diagnostic
1. Clinical control of the patients 1/2 time/year, for new patients and treat them rigorously and free of charge.
2. Control of real and projected zones, for short period 1-2 months, every two years, if needed.
3. Serological control for the people in endemic zones, for the presence of leprosy patients and contact persons and contact persons with ELISA positive, with Rifadin or Lesinol 25 mg/kg, a single dose. Repeat them after 2-3 years (2).
4. Education.

CO36

FORMATION OF A NEW LEPROSY CONTROL PROGRAMME IN REPUBLIC OF TENEM AS COOPERATION BETWEEN CLRA AND MOPH.
Tasha Al Qubati, and M.G. Al Nahhasi
Dermatology and Veneral Disease Hospital, City of Light, Post Box No.55722, Taiz, Republic of Yemen.

Tenem Republic is the land of the Queen of Shiba. Historically known as the "Arabia Felix". It has an area of about 3,50,000 sq.km. and a population of about 12.5 million. It is the most densely populated country in the Arabian Peninsula.

Leprosy in Tenem is well documented since 600 AC with very interesting stories. In the two large leprosaria built since 1940 the country lacked a programme for leprosy control up to 1990.

In 1989 an agreement between CLRA and MOPH brought to the country its first LCP.

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 CLRA to the NLCP, an immediate 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 Tenem.

CO37

COMMUNITY-BASED LEPROSY CONTROL PROGRAMME
A CASE STUDY IN NAKHONRATCHASIMA PROVINCE, THAILAND
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Leprosy Center Zone 5, Nakhonratchasima Province, 30000 Thailand

Village leaders and village health volunteers from Ban Sai, 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 trips 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 now in the leprosy colony. As a result, when they come back to their community, they provide health education to their community, referral cases of leprosy to the Leprosy Center. 2) Patients with deformities organized themselves for occupational training in their village.

CO38

CHINA LEPRA SURVEILLANCE SYSTEM
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The China Leprosy Surveillance System is a specialized system under Department of Epidemic Prevention of MOHP. 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 program. 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, together with guidelines and manuals of procedures. 3) Computer equipments and software.

The system uses 4 individual forms specially designed for (a) 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 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 and correctly 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 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
Des Soares, C. Ruth Bultin, James Nakami, Win Theuvenet, Kumar Jedsadan
Anandaban Leprosy Hospital, The Leprosy Mission, P.O. Box 151, Kathmandu, NEPAL.

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...
C040

DRUG RESISTANCE IN NEPAL LEPROSY PATIENTS
C. Ruth Bullington, Kapil Neupane, Aliyam Morgan, Warren Britton
Amidabad Leprosy Hospital, P.O. Box 153, Kathmandu, Nepal

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 4 year period, 105 outpatients with B1,2,74 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 25 cases there was no growth in control mice.

Of 59 biopsies from previously untreated patients, 5X showed dapsone resistant strains. Of 27 biopsies from previously treated patients, 4X demonstrated dapsone resistant strains.

Of 66 biopsies tested for primary rifampicin resistance initially showed growth, but the RF assays were sensitive to 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 4X of treated cases tested exhibited secondary dapsone resistant strains. Rifampicin resistance was not confirmed.

CO41

LA LUCHA ANTILEPROSA EN LA REGION Suroeste de la Republica Dominicana PROGRAMA NUEVO CON PARTICIPACION DE LA COMUNIDAD
Rafael Isa Isa, Socrates Canario y Rafael Isa Isa

La lucha antileprosa en la region Suroeste de Republica Dominicana se desarrolla en 4 provincias con una poblacion de 350,000 habitantes, presentando niveles criticos en cuanto a pobreza se refiere. La unidad dermatologica Suroeste ejecuta un programa modelo con participacion de la comunidad y coordinacion con las diferentes estructuras de salud del area.

Todas las metas programadas en lo que se refiere a descubrimiento de casos nuevos, revisiones a enfermos de lepra, tratamiento a enfermos, consulta dermatologica por auxiliares y por medicos, contactos intradomiciliarios y extradomiciliarios, exámenes escolares etc., se vienen cumpliendo rigurosamente. La unidad tiene 595 enfermos de lepra inscritos: 227 han sido dados de alta; 210 estan activos en control; 36 enfermos multibacilares en tratamiento y 83 sin tratamiento; 54 enfermos pauticulares en tratamiento y 37 sin tratamiento. No hay enfermos remanentes y solo dos estan perdidos.

CO42

RECIDIVAS EN ENFERMOS DE LEPRA MULTIBACILLARES Y PACHYBACILLARES TRATADOS CON TRES DROGAS
REPUBLICA DOMINICANA OCTUBRE 1982 - DICIEMBRE 1992
Rafael Isa, Roberto Bogart, Freddy Sinnes, Socrates Canario.

Se hace una revision de los 1,472 casos tratados con tres drogas en el periodo octubre 1982 a diciembre 1992 para determinar el porcentaje de recidivados que se han presentado al finalizar la multiterapia. Se dividen los pacientes por forma clinica y de estos, los que estan en revision postterapeutica y los que han sido dados de alta por curacion. Se precisa ademas el lapso en meses transcurridos antes de la presentacion de la recidiva, el numero de lesiones que presentaba el paciente al examen inicial y el sexo al cual pertenecia. Se observa que la frecuencia global de las recidivadas es del 0.22% con 0.25% en pacientes multibacilares y 0.23% en pauticulares.

De los once enfermos que han presentado recidiva, 7 son varones y 4 mujeres.

CO43

COMPUTERIZED MONITORING OF LEPROSY PROGRAMME
OF RAYMOND R. RAVANSEK, S. KEENLEY, M. AKPER, M. KAPIL NEUPANE AND R. BOGART
Bombay Leprosy Project, Vidyvan Bhavan, 11, VN Purvaz Mary, Sion-Chaabibathi, Bombay 400 022 and Dehradun, 42, NOSE1, New Delhi 110049, India.

For improved monitoring both at the macro and micro levels some of the important computer software were designed. This simple software helps programme managers to obtain data on a large scale for better planning especially for metropolitan leprosy programmes.

1. Computerised Central Registry.
2. Prevention and care of Disability.
3. General management of Leprosy.

CO44

STRENGTHENING OF ACTIVE CASE-FINDING STRATEGIES AND CLINICAL STUDY OF HOUSEHOLD LEPROSY CONTACTS IN MEXICO
Department of Dermatology and Medical Mycology, National Medical Centre, DF55, Ministry of Health, SSA, and **Health Centre, SSA, Culiacan, Sinal., Mexico.

Leprosy in Mexico has a prevalence of 0.20/1000 inhabitants. Most cases (95%) are distributed in 18 hyperepidemic areas.
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 Simonis State, a hyper-endemic leprosy area on the Pacific coast. Patients from several endemic areas of the country were also studied in a specialized hospital in Mexico City. A total of 129 leprosy patients were diagnosed by trained dermatologists and were classified according to the Ridley and Joplin criteria.

Household contacts of patients were thoroughly studied and epidemiological 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 emphasize 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 made 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
C. Malau and R.H. Gueran
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In the 1960's and 1970's, leprosy control in Papua New Guinea was progressively phased out as a separate program 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 tuberculocidal and leprosy consolidated into one program within the integrated health services.

Review of epidemiological data at the end of 1988 showed that the declining trend 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; consultation; 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
Hecleda M. Metello, Zenaide L. Lessa, Wagner Nogueira, Marcia R. Buzan, Otelia S.J. Goncalves

Since the State Secretary of Health of Sao Paulo started the Special Program for Hansen's Disease in 1984, initiatives were set up for the 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, extended with the integration of actions with the Instituto Dr. Luiz de Souza Lemos.

More than 5,000 technicians from the 65 administrative sub-regions of the State were upgraded during this period and evaluation of the distribution of such personnel by level of training and qualification responsible for the training can be made by maps.
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 system, may well serve as a model for the near future.

CO50
SURVEILLANCE SYSTEM FOR LEPROSY: A FIELD APPROACH
L. Blanc, A. Tiendrébego, Y. Rinani, B. Dauwerie
Institut Malanchose BP 291 BAMAKO MALI

Leprosy control programme in West Africa was using in 1989 a surveillance system conceived 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 peripheral 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 containing only these informations developed. Treatment notebook allowed calculation of prevalence rate, detection rate, proportion of disabled and proportion of HD patients among new cases, proportion of compliant patients, MDT coverage in order to avoid form compilation. An annual statistical 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 center nurses.

CO51
ROLE DE L'AGENT DE SANTE DANS UN PROJET DE CONTROLE DE LA LEPRE: EXPERIENCE D'UNE ANNNE
Guyette Blanc, Florence Desvarieux, Claude A. Levalle, Claude Fran.

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 inrat et extra-domestiques, le nombre de visites, passage repetes, le nombre de fistules bacteriologiques seront evolues. Des facteurs socio-economiques et culturels seront aussi discute.

Institut Cardinal Leger contre la lepre (HAITI).

CO52
INVOLVEMENT OF SCOUTING MOVEMENT IN LEPROSY CONTROL
Kalpana Mutatka, Ranga Rao
WHP Leprosy Relief Organisation, 9A, Amini Park, Amin, Pund, India.

The work of Scout's 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 showing leprosy control including case detection in schools.

The role of appropriate health education material in must nearly 4.5 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
T. Jayam Dinshaw, C.S. Cheriyann, Director, GLRA/ALES
Regional Secretariat, 4, C. Rajgopathi Street, Chennai, Madras 600 032

Relying on the fundamental principles of Social Work, a community based action programme was initiated for controlling leprosy in Nigrija 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 familiarizing with them through a known voluntary organisation in the community.
- Interacted with the community and made them aware the role and function.
- Motivated the community and made them interested in leprosy control and eradication work.
- A core group was formed comprising of volunteers who are interested in leprosy eradication work.
- A Radar Sangam (Mother's Group) and a youth group was formed as core group.
- Providing 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 centre.

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 PLANIFICACION ESTRATEGICA DE MERCADOTECNIA UTILIZADA PARA ERRADICAR LA TRANSMISION DE LA LEpra EN MEXICO.

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

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 precio 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 proyecto temático para 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.

**COS5**

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

Eduardo Falconi, Pedro Legua, Ciro Naguiaza y Gilma Ruiz. Instituto de Medicina Tropical "Alexander von Humboldt" de la Universidad Peruana Cayetano Heredia y Centro de Investigación en Salud "Dr. Hugo Lumbreras Pena" 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 cases, the working area was divided in two parts: trees and the rest of the province (rural area), with a total population estimated in 99,700 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 Turunumpa, trese health auxiliaries and one nurse (female) were trained. Additionally, short training courses (one week) were done for health auxiliaries and promoters of the whole province. The area was combed house by house, visiting every villager 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 Turunumpa, 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 the period, total registered patients were 101, which makes a prevalence of leprosy for the area of 1.4 per thousand population. Number of active disease was shown. Patients were treated with WHO recommended regimen (MDT). Results were as follows:

- **Number:**
  - Old Cases: 59
  - New Cases: 43
- **Age:**
  - Mean in years (range): Males 43 (29-89) Females 43 (27-87)
- **Sex:**
  - Males: 52 (21-94)
  - Females: 15 (20-64)
- **Means of detection:**
  - Search + contact tracing: 8 (14%) 26 (61)
  - Self reporting: 25 (43) 10 (23)
- **Diagnosis:**
  - Multibacillary: 23 (43) 20 (47)
  - Paucibacillary: 25 (43) 22 (53)
- **Illness duration:**
  - Mean (range): 19 (2-118)
- **Nerve trunk involvement:**
  - Enlargement only: 53 (94) 38 (86)
  - Enlargement + infiltration: 14 (24) 13 (30)
  - Paraesthesia: 23 (43) 9 (22)
- **Normal hands:**
  - 22 (38) 25 (57)
  - Normal feet: 22 (38) 25 (57)
- **Normal eyes:**
  - 25 (43) 26 (60)
- **Complications during treatment:**
  - Type 1 or 2 reactions: 13 (24) 2 (5)

Prevalence of leprosy in the province was 1.4 per thousand population. The active search for leprosy cases allows the detection of patients in early stages of their illness and with less typical leprosy.

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**COS7**

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

N.K. Chopra, Mrs. M.P. Triyedi y R.K. Gupta. The epidemiological impact of multi-drug therapy project in Leprosy eradication program was present in tribes. Leprosy eradication program and the study showed that WHO can be implemented in tribal rural urban population with high rate of implementation.

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**COS8**

**STUDY OF FIELD TRIALS OF COMBINED CHEMOTHERAPY AND FIXED DURATION COMBINED CHEMOTHERAPY IN MULTIBACILLARY LEPROSY IN WDT 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 resisters and preisters 2) to achieve the more rapid arrest of transmission of the disease 3) to prevent relapse. VO drugs were treated as per regimen recommended by World Health Organisation. Treatment was continued for maximum of two years or till bacteriological negativit
which ever is later. Total 356 M.B. patients were
included in the study till Dec.92. 138 M.B.
cases were positive prior to M.D.T. 237 (29.8%) 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 evaluated. 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 M.D.T. Only 137 (39.0%) MB patient who have completed 2
years treatment show gradual bacteriological
clearance even after cessation of Chemotherapy.

Data from 702 person-year follow-up on relapse
and encountered.

C059
SKIN DISEASE DIAGNOSTIC, TREATMENT & EDUCATION (S.D.T.E.) CAMPS: A TOOL FOR COMMUNITY EDUCATION IN TRIBAL DISTRICT BHARUCH (GUJARAT) INDIA.
N.K. CHOPRA Mrs, M.P. TRIVEDI and R.K. GUPTA

71 Skin disease diagnostic, treatment and education
 camps were organized in prepratory and intensive phase of M.D.T. Programmed in forms of
Local Festivals in different rural and tribal
villages in Bharuch district during 1989-92.

The idea was basically used for bringing awareness
towards skin disease. The second objective was new
case detection. The gathering in the camps
usually comprised of patients, their relatives,
teachers, social worker, and the NLEP-PMC functioning
authorities. Case selection and demonstration for
 differential diagnosis was used as a method of
Health Education. The method used to increase
familiarity of the community's knowledge gained from known to unknown
167 leprosy cases (82 New and 65 old) including
13 deformed cases were detected in these camps. 3555 other skin ailments cases were also benefited.
The services offered was free of charge. The
role of community was vital in such camps as
they were the organizers and NLEP functionaries
were helpers and guides. Primary health were
system was mainly responsible for diagnostic facilitation.

C060
AN EXPERIMENTAL STUDY OF INVOLVEMENT OF GENERAL HEALTH WORKERS IN LEPROSY WORK.
S.K. DANDYPOHAT

Although the NLP 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 Belampur 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 management of the programme in which
they could participate. Annual meetings of these
workers were held for 4 years in which the
program 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 95 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.
"DEFORMITY CARE CLINICS" - A NEW APPROACH TO INTEGRATE 'CARE AFTER CURE' CONCEPT IN ROUTINE MDT PROGRAMME

P.V. Dave, A Shah and R Ganapatil

Comprehensive Leprosy Care Project, Leprosy Management Training Centre, Ciba Compound, Diana Lane, Tardeo, Bombay 400 034, India

The aim of the 4 years preliminary study was to analyze 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 2.1 million.

During this study the existing problems with the vertical leprosy control programme, segregated leprosy patients' concept, 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 PSC 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 encouraging.

CO66

INTERVENTION FOLLOW-UP STUDY OF GENERAL HEALTH STAFF TRAINED IN LEPROSY IN WARAKHDISTRICT - INDIA.

Fishor Landge, Mukund Kanade, V. Prabhakar Rao.

Gandhi Memorial Leprosy Foundation, P.0,Hindi Nagar, WARDHA - 442 103, Maharashtra - 411101.

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 direction.

A prerequisite 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 mutual consultations.

After one year, a detailed questionnaire was framed and administered to evaluate the knowledge of health staff in leprosy, their participation and the difficulties by them in this work. 120 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

Ben Nwakpa and Ugbogu

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ABSTRACT This paper presents the preliminary analysis and synthesis of the application of cybernetics in the management of MDT. Some operational problems of MDT implementation were also discussed in the context of the cybernetics and its application.

The theoretical basis of this article is the advance concept, feedback control and feedback control of the cybernetics, which are the most important one in the field content. The application of cybernetics in the MDT implementation is that the feedback control can be used in the regulation of treatment, especially the monitoring, dosage and the daily and weekly doses of drugs. The more the level of dose content, the higher the treatment rate will be.
the scientific management can help in the improvement of both the personnel and the basic health system.

The enhancement of efficiency and responsibility of all the people concerned, including the patients, themselves, in the scientific management is also the task of the control. The more the measure of control, the better the quality the MDT will have.

The International Conference 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 paper proved that the scientific management of MDT contributes to the increase of quality and effect of the leprosy control last but also adds 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
Paul Jakeman

National leprosy Control Programme, Bhutan

Bhutan is a small mountainous country in the eastern Himalaya, 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 it 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 EPIDEMIOLOGICAL IMPACT OF MDT ON LEPROSY IN GUANGDONG PROVINCE
Chen Junliang, Liang Zhangxue
Guangdong Provincial Institute of Dermatology and Venereology

A province-wide comparative analysis of leprosy data of D0S monotherapy period (D0S) of 1982-1984 and that of MDT period (MDT's of 1987-1991) was reported.

The cure rates of the D0S and the MDT groups were 52.64% and 64.35% respectively, with an increment of 21.7% (11.72%) in the MDT group. In the period of drug-free monotherapy of 1982-1984, the highest rate of such increment was 19% only.

The prevalence rates in the D0S and the MDT groups were reduced from 66.55% and 83.26% respectively, and they were reduced either by 13.11% and 26.91% annually in the average in the D0S and MDT groups respectively.

The age specific incidence rate of 0-14 year group was decreased by 32.64% in MDT as compared with that in D0S.

After the implementation of MDT for 5 years, the number of endemic counties (prevalence rate >0.1%) decreased from 12 (9.65%) to 5 (%) and the number of non endemic counties increased from 84 in 1987 to 95, including 41 counties with a prevalence of 0.01%.

The results showed that the implementation of MDT has given a positive impact on leprosy control in Guangdong province.
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 1983 and 1992, a period coinciding with the National Programme's restructuring and the implementation of MDT/WHO.

COT75

TEN-YEAR COHORT ANALYSIS OF MULTIBACILLARY LEPROSY PATIENTS WHO RECEIVED MULTI-DRUG THERAPY

Renuka Ramakrishnan, Narayan R, Devantu V, Lobo O, Ramamurji R.

Our institution GREMATES based in Madras is a pioneer in URBAN Leprosy Control. We initiated Multi Drug Treatment (MDT) in 1982. Between 1983 and 1992 - 11,250 patients received MDT, of which 1650 are Multibacillary (MB).

A COHORT analysis of all the 88 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 Programmes is discussed.

COT76

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 13% in 1982 to 6.4% in 1992.

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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 65% 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 2.5% were found to be active, detection rate of 1.3/1000, in 1982 - 1986.

The implementation of MBD in 1982, was successfully initiated Multi Drug Treatment (MDT) in 1983.

The proportion of new cases presenting with deformities fell from 13% in 1982 to 6.4% in 1992.
CO77

**ÉPIDÉMIOLOGIE ET POLYCHIMIOGRAPHIE APPLIQUÉES AU PROGRAMME DE LA LEPRE EN TUNISIE**

La Tunisie, pays méditerranéen situé au nord-est de l'Afrique, a une prévalence de 0,03% malgré cette faible endemicité le besoin d'entreprendre une action de lutte contre ce fléau a été rendu nécessaire par la pandémie de la TL lempyrame et l'existence de foyers dispersés.

On a pu mettre en place un programme de lutte antilépreux 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 médicale mobile qui a pour tache : la prise en charge des malades, le dépistage, l'ouverture des contacts, la distribution et la surveillance de la P.T.
- Au centre hospitalier de traiter les complications de la maladie et de réunir tous les dons sur l'escale dans un fichier central.

Jusqu'en 1992, 200 cas sont fictus et répertoriés. Les régions les plus concernées sont Bizerte 60 cas, Medenine 51 cas, Elar 45 cas.

La contamination reste essentiellement familiale.

Les résultats apres 7 ans sont pratiquement identiques avec un contrôle clinique et surtout bacteriologique régulier.

CO78

**MARTINEAU : Évaluation de 1980 à 1991 de la polyarthrité lempyramique (PAL) ou polyarthrométrie (POT) traitement de la lepre**

H. CONSTANT-JEANPIERE ROSE, B.JI
J. GROSSET, H. SANFREDIC
R. BEILLANGE, C. BALLOI, P. PIVIIILO-LOGE
R. KEBBIKAL, JC. SAINT-SEYB, P. SCAT
J. Madeleine, JC CAROLINA, A. LEFEBRE

L'abord de la maladie en toute de cette nouvelle approche thérapeutique a nécessité une démarche communicative utile à la participation du personnel soignant et de beaucoup d'action sociales germane à la santé et à la promotion culturelle. Avec l'aide du laboratoire de bactériologie du CNS Pital Salpétrière de PARIS la surveillance des malades sous POT a été évocée dans le choix des antibiotiques, en fonction de la fréquence des récidives et de leur association et la durée du traitement.

En ce cas la 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

**PATIENT COMPLIANCE AND DRUG THREAT: AN ANALYSIS OF EFFECTIVENESS OF MULTIDRUG AND MULTIDRUG THERAPY(MDT) TREATMENT**

Saravanabavan **G**, Shunhsu, Shaela, **G**. - Department of Geography, National Taiwan University, National, Taiwan.

The Department of Geography of the National Taiwan University in different districts of Tamilnadu has been analysed to understand the health situation of Tamilnadu and its status in the recent years before and after the implemention of MDT. The present study was made an attempt to bring out the effectiveness of MDT in controlling the prevalence rate of leprosy in most part of the distri-

C080

**LONG-TERM EVALUATION OF A PROVINCE-WIDE CLUE SURVEY FOR LEPROSY IN LIAONING**

Yu Anxin Yang Weixion Li Shier

Dalian Municipal Institute of Dermatology, Dalian, China

Based on the effective health education activities, a province-wide clue survey was carried out from 1977 to 1978 in Liaoning Province. Through this survey, 7,862 suspected cases were reported, among them 5,404 new leprosy patients, including 1,092 multibacillary (21.4%) and 353 paucibacillary (6.8%), were diagnosed.

The survey was completed in the end of 1978. From that time on to the end of 1988, various order of leprosy were 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 continuously in order to detect leprosy patients as early as possible. The results of the past 13 years showed that the number of newly detected leprosy cases has reduced significantly.

During the period of 1977 through 1983, the total number of newly detected patients in the whole province was 8,678 only 13 of them were late cases. We probably can say that the reported province-wide clue survey had detected 81% of the patient population which existed at the time the survey was implemented, and only 2%-3% were missed. Among them may be because of the absence when the health education was given, or their symptoms might have been very slight.

In the period of 20 years before and 13 years after the implementation of the province-wide survey, the incidence rate of leprosy in Liaoning province decreased by 94% and 93% respectively. It is evident that the province-wide clue survey accelerated (facilitated) the declining incidence rate of leprosy in Liaoning province.

CO81

**AN EVALUATION OF THE ACHIEVEMENTS OF COMMUNITY-BASED LEPROSY CONTROL FOR 35 YEARS IN CHENGDU COUNTY, SHANXI PROVINCE, CHINA**

Wang Bojun Wang Zhenhua Xue Xuezhi Wang Wentang Huang Lingzhao Ying Zheng

Health and Epidemic Prevention Station of Chengg County, Shanxi Province, China

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 carried out in Chengdu County, Shanxi Province. The accumulative number of registered leprosy patients was 1,360. Excluding cured (1,095, 80.7%) and migrated cases, there were only 365(26.9%) active cases at the end of 1990. The prevalence reduced from 2.1% in 1953 to 0.022% in 1990.

*The principle of Prevention First and Active Treatment on Community Basis means a thorough and continuous public health education on leprosy and active leprosy control in community for the purpose of early detection and early treatment.
The average incidence rate of 5 years decreased from 20.07/100,000 (1411.598, PB 130) of the period 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 728 relapsed patients worsened, among active cases increased from 0.10 (1957-1961 period) to 0.88. (0.88). The average relapse rate increased and the duration from cure to the occurrence of relapse of NB (7 years) was much higher than that of cured cases (8.31). The average duration from cure to the occurrence of relapse of NB (1 year and 4 months) was much longer than that of TB (5 years and 2 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 0.14% (1957-1961 period) to 1.16%. The existing disabilities of 247 (31.4%) of 788 relapsed patients worsened. Disability worsening of relapse was more common in MB (41.4%). Since 1986, 2,152 patients (MB 1,161, PB 295) have been cured with MDT. No relapse was found up to now. The authors emphasize that preventing cured leprosy patients was 28,458 in Fujian province, among them 21,878

By the end of 1991, the cumulative number of registered leprosy patients was 29,458 in Fujian province, among them 21,478 cases (MB 1,161, PB 130) of time relapsed the relapse rate 7.75% (Naik et al., Ind. J. Lepr., 1990, 62, 305). The incidence of children (0-14 years of age) also declined from 728 relapsed patients worsened, among active cases increased from 0.10• (1957-1961 period) to 0.88. (0.88). The average relapse rate increased and the duration from cure to the occurrence of relapse of NB (7 years) was much higher than that of cured cases (8.31). The average duration from cure to the occurrence of relapse of NB (1 year and 4 months) was much longer than that of TB (5 years and 2 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 0.14% (1957-1961 period) to 1.16%. The existing disabilities of 247 (31.4%) of 788 relapsed patients worsened. Disability worsening of relapse was more common in MB (41.4%). Since 1986, 2,152 patients (MB 1,161, PB 295) have been cured with MDT. No relapse was found up to now. The authors emphasize that preventing cured leprosy patients was 28,458 in Fujian province, among them 21,878

The authors present a cohort study of leprosy patients detected and registered in the state of Amazonas in 1988. Clinical, labotorial 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.

The NORTHERN REGION, WITH 9.3% OF BRAZILIAN POPULATION AND 22.3% OF REGISTERED CASES OF LEPROSY (1991) IS THE LARGEST REGION OF THE COUNTRY.

The confirmatory smear positive cases rate was 46.4% in centres having different regional and population set up was made. During last 5 years (1988-1992), total 1,597 new cases (324 MB and 1,263 PB) registered by conventional methods of SST. The analysis showed that there is 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 areas of educated and stable population.
NEVERTHELESS, THIS REPORT REMAINS CONCERN THE PERSPECTIVE RELATED TO OPERATIONAL IMPROVEMENT OF THE PROGRAMME ACTIVITIES WHICH HAVE BEEN COMING TRUE IN MOST STATES THE PROPORTION OF DEFORMED NEW PATIENTS IS LOWER THAN 3% AND THE NOT COVERAGE IS THE HIGHEST IN THE COUNTRY.

FOLLOWING THE AMAZON AND ACORE STATES EXPERIENCE THE MACHINEREGIONAL 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 THE PREVALENCE RATES BUT ALSO CONSOLIDATING THE STRATEGIES INITIATED IN ORDER TO CHANGE THE ENEMY'S TRENDS IN A LONG TERM.

C087

SITUATION OF LEPROSY ELIMINATION IN THE AMERICAS
Clavio Lombardi
Pan 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, observations 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.

C088

THE INTER-L. CONFERENCE AND OTHER PROMINENT EVENTS IN THE STUDY, EPIDEMIOLOGY AND ELIMINATION OF L. (WITH BIBLIOGRAPHY AND PHOTOS OF NEARLY ALL)

BARIJA LOIS M. and VALDEZ PAUL P. Hospitals Argentia and de Clinicas,av.Alvarado 1890 (1129 ) Buenos Aires, Argentina

1973 A. Hansen starts the scientific era.

1992 II Int.L.Congress on L.(Berline)Viroch Pres."L. is produced by a microbe, not hereditary and is possible to prevent it" 1992 II Int.L.Congress on L.(Bergen)Pathologists and dermatologists under the honor,Presid.Nansen 1932 II Int.L.Congress on L.(Paris) a meeting that provides the birth of ILA,Presid.B.Jansel,Viroch Pres."L. is produced by a microbe, not hereditary and it is possible to prevent it" 1932 II Int.L.Congress on L.(Berlin)Presid.B.Jansel,Viroch Pres."L. is produced by a microbe, not hereditary and it is possible to prevent it" 1932 II Int.L.Congress on L.(Berlin)Presid.B.Jansel,Viroch Pres."L. is produced by a microbe, not hereditary and it is possible to prevent it" 1932 II Int.L.Congress on L.(Berlin)Presid.B.Jansel,Viroch Pres."L. is produced by a microbe, not hereditary and it is possible to prevent it" 1932 II Int.L.Congress on L.(Berlin)Presid.B.Jansel,Viroch Pres."L. is produced by a microbe, not hereditary and it is possible to prevent it"

C089

LEPROSY CONTROL IN KARAKALPAKSTAN
T.Kuchanov, 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 3rd 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 specialized 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 sanitation. Effectiveness of such an approach is proved by more than 10-fold decrease in leprosy incidence in average by 24 annually.

C090

LEPROSY CONTROL IN KARAKALPAKSTAN

BARIJA LOIS M. and VALDEZ PAUL P.

Instituto "Pedro Roqf", La Habana, Cuba.

C091

FOURTEEN YEARS OF HD CONTROL IN ACORE STATE.

William John Woods, Leila Borges Marques, Alvaro Romero,

Secretaria de Saude, Acre State, Brazil.

The most remote of all Brazilian states Acre had an average prevalence of HD of 10.5/1000 for over 20 years. With no roads and only river travel most patients were attended only 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 implantation of MDT, even in remote areas and a 5 year follow up of patients not included in MDT is presented. The rehabilitation, 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 Lima Brasileirinha, Silvano Renzo,* Luiz Perreiras*
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 administration and patients were attended by para-medical workers at 3 monthly intervals. To initiate MDT and to re-release from treatment each patient was evaluated and orientated by the medical supervisor. To initiate MDT in these circumstances took 3 years and involved travelling on 30 different rivers.

The clinical results compared with a sample of 50 histopathological oxames have been satisfactory.

CO93
A Health Education Intervention in Cuba to diminish the delay in diagnosis of leprosy.
Viviane de Ruijo, Olivia Hernández, Reinaldo Gil.
Institute 'Pedro Kouri', 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 (GL) 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, 5.0 GL). In GL the patients sought medical attention 3 months after the initial clinical manifestations while in HC they did so during the first month. These findings allowed us to design 5 different interventions: in HC to increase physician index of clinical suspicion; and in GL 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 GL 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 immediate medical attention. In HC the in GL, 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
Dr. V.Kandaswami, Damien Foundation, AL 189, Annanagar [west], Madras 600 040, India.

One of the district in Kerala State, with a population of 16,78,629 (1991 census) has been taken up for this study. The literacy rate in this region is high.45 PHC/2 LCDs and 2 ULCs exist in the area, most of the patients 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.
E.D. Bhardak, G.S. Mane
Maharashtra Lokahita Seva Mandal, Bexlay, 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 in 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 Scheme 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.
**Lutte contre la Lepre au Zaire 1987 - 1991**

Mputu Luengu Boyau, Bureau National de la Lepre, Zaire

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**EPIDEMIOLOGICAL CHANGES IN AN URBAN LEPROSY CONTROL PROGRAM: 15 YEARS OBSERVATIONS IN HOWRA**

C R Porepuk, PH Pai, D Girija, SS Deshpande, K treatment, VV Pai, Nirmala Hame & AA Ganapati

Bombay Leprosy Project, Vidyanay Bhavan, 11 VN Purav Marg, Sion-Charnabouhiti, Bombay 400 022, India.

Leprosy control in metropolitan and other developing cities in endemic countries, is becoming a major public health problem. Due to heterogeneity in socio-economic conditions with artificial living habits, health practice behavior etc., the epidemiological trends in leprosy could vary from rural areas. No studies are yet available on impact of the 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 blue 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.

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**EXPERIENCES WITH EVALUATION OF LEPROSY CONTROL**

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Evaluation Unit, The Leprosy Mission, MB-06 Golden Mile Tower, CO1 Beach Road, Singapore 0719

Experience has been gained in the evaluation of more than 30 leprosy centers in over 10 countries in Africa, Asia, the Far East and the Western Pacific regions. The different methods used in evaluation include questionnaires, field visits and sample surveys. The evaluation covered epidemiological aspects both descriptive and analytical, operational and organizational/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 analyzed and presented in the paper.

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**CHANCE IN LEPROSY PROFILE IN A HYPER ENDEMIC BOMBAY SLUM OVER 15 YEARS**

R Ganapati, RS Jerewar, and D Girija

Bombay Leprosy Project, Vidyanay Bhavan, 11, VN Purav Marg Sion-Charnabouhiti, Bombay 400 022, India.

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 sure 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 Dates Enus Exu Cases Total F**

<table>
<thead>
<tr>
<th>Year</th>
<th>Slum</th>
<th>Ini</th>
<th>Exu</th>
<th>MB</th>
<th>Cases</th>
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<tbody>
<tr>
<td>1977</td>
<td>272</td>
<td>3812</td>
<td>3710</td>
<td>83</td>
<td>13</td>
</tr>
<tr>
<td>1980</td>
<td>603</td>
<td>6335</td>
<td>569</td>
<td>8</td>
<td>41</td>
</tr>
</tbody>
</table>

**All 4 patients had monolesions and had migrated from other slums.** Prevalence expressed as Rate per total slum population enumerated.
This transformation was brought about by present-ing attendance of all the patients in the slums at a nearby "integrated" clinic where success in treatment to infectious reservoirs in the community through effective training of workers. Rapid increase in the population density in large urban slums poses logistic problems in the crucial factor in overcoming leprosy transmission.

**CO101**

**PRELIMINARY EVALUATION TO MEASURE THE MORTALITY EFFECTS OF HOMOZYGOSITY ON THE CONTROL OF HUMAN LEPROSY IN THE MEGALOPOLIS REGIONAL AREA OF BELO HORIZONTE, MINAS GERAIAS-BRAZIL, FROM 1960 TO 1990.**

Maria Ana LeBomb, 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 studies performed in 1990. The use of this preliminary evaluation is a baseline for measuring the future impact of training health care workers and decentralization of MDT control in the municipality of Belo Horizonte.

**CO102**

**CONTROL AND ELIMINATION OF LEPROSY:** A RURAL/URBAN STRATEGY ANALYSIS.

L. Jayral Devasag, Thomas Abraham, Director of Health, Regional Secretariat, 4 Gajapathi Street, Hyderabad, India.

Control and elimination are not synonymous. The two terms indicate two phases of activities towards eradication of the disease. Multi Drug Therapy is no doubt essential for the control and elimination of leprosy 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 4.4/1000 in urban and 2.6/1000 in rural areas.

- It was observed that the urban/rural case load per worker though differs numerically (76 and 146 cases), it was 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.**


Urban Leprosy Centre, Safdarjang Hospital, New Delhi.

Rapid industrialization 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, 1991-400). A trend showing an upward trend (1983=48.2, 1989=54.0, 1990=57.5, 1991=58%) while MDT has gone down. Childhood leprosy has nearly doubled and deformity rate has remained static. The most depression 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-1 IMMUNOLOGY FOR LEPROSY CONTROL: PRELIMINARY RESULTS.**

Ana Gonzalez-Abru 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 4000 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. The strategy is being used as a pilot area to test a control strategy based on PGL-1 serology which consists in performing serological tests by ELISA to the whole population above the age of 9 years as well as clinical examination of leprosy and bacteriological tests performed on the whole study population. The implications of these findings are discussed and a coordinated plan of action is suggested for finding actual and potential PGL-1 "transmitters" which would lead to an earlier administration of chemoprophylaxis and of chemoprophylaxis, and in this way, to an effective cut off of the chain of transmission. To date, 10,048 individuals have been tested for PGL-1 antibody. Of them, 660 (6.6%) showed O.D. readings higher than 0.500 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 on the clinical examination, bacteriological and lepromin tests on seropositive individuals will be presented.

**CO105**

**LEPROSY CONTROL PROGRAMME IN SANTA FE PROVINCE, ARGENTINA: RESULTS AFTER 30 YEARS.**

Pedro Caprini, Adolfo Balle Fontana, Silvia Fares, Ana Luisa Baccaro.

Sanitary Dermatology Control Program, Santa Fe, Argentina.

The Leprosy Control Program in Santa Fe Province was launched in 1963. 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; (2) Two facts have been observed in association with the falling incidence rates: an increase in mean age at onset (43/52) and an increase in the proportion of multibacillary forms among new cases (43/63); (3) There is a high proportion of cases (43/63) without any antecedent of infectious contact; (4) Intrafamilial transmission is higher among consanguineous contacts. It suggests the importance of genetic factors; (5) 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 1992. The current coverage is about 45%; (3) A high percentage of cases is under private assistance (45%). This sector is not yet adequately integrated; (4) Case finding, defaulters retrieval, training of personnel and research have so far been the main activities of the Program; (5) Active case finding activities have been somewhat neglected and are still to be reorganised.

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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Zheng Da-Yo, Weifang Prefectural Institute of Dermatology, Shandong 260131
Ran Shan-Peng, Wenshan Prefectural Institute of Dermatology, Yunnan 663000

Weifang of Shandong and Wenshan of Yunnan were highly prevalent for leprosy in the 1950s. 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% (1.4 - 0.009/1000) 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 cumulative incidence of leprosy in Wenshan appears to be still in the level of 1960's in 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 LEPROSY SERVICES AMONG THE TRIBAL AND NON TRIBAL POPULATION IN THREE SELECTED DISTRICTS OF MADHYA PRADESH, IN INDIA

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Directorate General of Health Services, Ministry of Health, New Delhi, 110011, India

The tribal population constitutes 7.7% of India's population. In the selected leprosy endemic districts the tribal population in 18,15 in Raipur,12,62 in Durg and 25,12 in Rajnandgaon. A beneficiary study of leprosy services conducted in the above three districts indicated 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 DAIIDA assistance. Both tribal & non-tribal community members have inadequate knowledge and awareness about cause of leprosy. Although majority of tribal and non-tribal people say Ayurveda is the best treatment available for leprosy, (84 - 90%), a small percentage of people still feel Ayurveda and Homoeopathy as better remedy for leprosy. Women in tribal areas & girls students in both tribal & non-tribal areas are less aware about leprosy compared to the male groups of the same villages./schools.
FIVE-YEAR EVALUATION OF A PROGRAM OF CHEMOPROPHYLAXIS FOR LEPROSY USING A SINGLE DOSE OF 25 MG/KG RIFAMPIN

Jean-Louis Cartel, Suzanne Chancieu, Philippe Glaziou, Jean-Félix Roux and Jacques Grouzet
Institut Louis Malardé, Papetee, Tahiti, French Polynesia

In January-February 1988, a program of chemotherapy for leprosy was implemented in French Polynesia. 2,786 (98.7%) residents of the Southern Marquesas, a remote archipelago, and 3,144 South Marquesan "emigrants" in other islands and their families were given a single superimposed 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 chemotherapy was given); the first, a 4 months and the second, 21 months after chemotherapy, 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 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.
Yang Li He, Yin Bo, Jinn Bei and Chenn Zhi Clang
EPIDEMIC AND CONTROL OF LEPROSY IN TIBET

... Among newly detected patients were 3(1.6%) (1985), 22.6% (1986), 21.9% (1987), 20.8% (1988), 18.5% (1989), 13.3% (1990), and 12.6% (1991). The median in females (2.0 years) is significantly longer than in males (1.8 years, 0.95% 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 (>2.2 years). 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 service 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.

CO116
EPIDEMIC AND CONTROL OF LEPROSY IN TIBET
Yang Li Be, Yuan Bo, Jing Bei and Chenn Zhi Clang
China Leprosy Control and Research Center, Guangzhou, China

Leprosy is an old disease in Tibet. It has a long history of more than 1,000 years. From 1952 to 1991 there 3,401 leprosy patients were detected and 2,100 cases were cured. By the end of 1991, the number of active cases was 808 and the prevalence rate was 0.00239 of 0.02, 110,000 respectively in this big city at the end of 1991.

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 years, 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 T7 and LL cases have longer delay (>2.2 year) and RH shorter delay (<1 year). The delay in females (2.0 years) is significantly longer than in males (1.8 years, 0.95% 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 (45% and 65% age group) have the longest delay (>2.2 years). 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 service 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.
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 mobility or strength, and to monitor both the extent of change and the effect on nerve function and the rate of incidence.
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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With the generalization of new combined treatments (PCT) the leprosy endemicity has been declining considerably since the 1980’s, particularly since 1990. Recently (1992) the prevalence has been estimated at 0.22 per 1000 versus 3.18 in 1986. With the generalization of new combined treatments (PCT), the prevalence rate appears to be high i.e. around 1% 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 results under discussion are:
(a) case finding methods for approaching each child and school child out of school child.
(b) labelling of child cases in view of possibility of self-healing leprosy in the context of social stigma.
(c) ratio of P8:MB cases among children and its implications from control.
(d) primary health care approach and integration of case finding methods with other child services.
(e) need for epidemiological studies.
(f) role of NGOs
(g) problems of street children

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.

CO121
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.

(These papers were financially supported by Red Barnet-Leprosy Control Project.)
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.

### 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 eliminating disease": it is certainly significant for researching and evaluating the prevalent features of infectious diseases and the effect of the disease control programmes. In this paper the author uses an improved two-stage catalytic model (log(TCM)) 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 eliminating 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 positively 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 1.48% in 1972. Since 1983, all the active cases were treated with MDT recommended by WHO. At the end of 1993, 1176(MB 021 and PB 555) patients have been treated with MDT. Through the comparative analysis of the theoretical endemic indicators of 1982-1993 calculated by the mathematical models of DOD, mono-therapy (1973-1982) and the actual situations, the results showed that the detection and prevalence rates after MDT were usually higher than the theoretical ones (difference between theoretical and observed values, \( \triangle Y_{b} \) and \( \triangle Y_{y} \) values decreased significantly after 1985, moreover, \( \triangle Y_{b} \) was less than 0 in some countries. 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 model \( e^{\text{ax}} \) with \( b \) and \( K'd_{0} = 0.058 \) except one county with \( K' \) of 8.4027.

#### 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 Gujratthan 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  
Philippe Glaziou, Jean-Louis Cartel, Jean-Paul Mouila-Pelat, Lam N'Guyen Ngox, Suzanne Chanteau, Régis Pichard and Jacques Grosset  Institut Louis Malardé, Papeete, Tahiti, French Polynesia

From 1902 onwards, notification and lifelong follow-up of leprosy patients has been systematic in French Polynesia. Since 1993, the number of new cases has decreased substantially. However, the epidemiological situation of leprosy and tuberculosis in Polynesia is far from being stable. The importance of leprosy and tuberculosis has been due to their high economic burden. Two explanatory factors can be underlined: the high rate of tunneling (70%) and the absence of specific funding for leprosy and tuberculosis. The points outlined above will be discussed along with some other relevant issues (definition of cure, current trends in the number of cases, monitoring the impact 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.
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 368 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 (3.5%) developed tuberculosis.

From 1902 to 1999, mortality from tuberculosis occurred significantly more frequently in multibacillary patients (13%) than in paucibacillary (4%), Relative Risk (RR) = 3.2, p = (1.003). From 1980 to 1991, incidence of tuberculosis scored 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 USING TO CHINA LEPROSY SURVEILLANCE SYSTEM
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Computers have been widely 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 input 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 automatically 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 1/100000 marks. The method of inputting data with OMR provides a powerful tool to input large amount of data not only in leprosy epidemiology, but also in other fields.

EP6
A TWENTY YEAR FOLLOWUP STUDY OF INCIDENCE RATES OF LEPROSY IN DOS PROPHYLAXIS AND CONTROL GROUPS
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DOS 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 DOS has inhibitory effect on CT1.

The author has analysed the post-prophylactic data of incidence rates during the last 20 years in the project of Gandhi Memorial Leprosy Foundation where DOS as prophylaxis was given for 6 years to 1 group of 9250 adults and 6 months to 925 (Lw) and 18674 (Lw) were kept under placebo. The analysis was done to assess whether DOS exerted any prophylactic value or was inhibitory to CT1.

In the 20-year period, 153 cases occurred in Lw (mid-term population 5120), 171 in Lw (5361) and 354 in U (11103) groups. The respective cumulative incidence rates were 24.6, 31.8 and 31.8. No significant differences were noticed in incidence rates, DOS did not seem to have either prophylactic value or inhibitory effect on CT1.

Further detailed analysis of age-type occurrence, deformity & relapse rates and responses to treatment were made and discussed.

EP7
LEPROSY AND HIV IN TANZANIA
National Tuberculosis and Leprosy Programme, Tanzania TB/Leprosy Central Unit, Dar es Salam, Tanzania.

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 / antenatal 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 blood samples. 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

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.
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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$2500 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 prevalence.

These between country and within country analyses demonstrate the relevance of socio-economic development to the decline prevalence and incidence of leprosy.

The study of trends Hansen's Disease in Brazil has been used to assess the endemic's evolution and estimate targets for the annual programming of control activities.

We used the historical series of detection rates for the country, the notifications and each state of the federation, from 1973 to 1992, applying the exponential adjustment method. For each region, we build three curves of the endemic'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 endemic's evolution in the country.

Intensive case finding and combined treatment regimens for all patients were introduced in Anjouan in 1981. The mean yearly detection was 38 per 100000 inhabitants (in population) during successive 4 year periods was for 1981-84: 9 per 10000, for 1985-88: 4.8 and for 1989-92: 5 per 10000. The MDT rate during the same periods was 20, 34 and 30 respectively. The % of children (< 15 yrs) at diagnosis among PPD skin tested from 57 to 52 and 48; among MDT 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 after 10 years of intensive anti-leprosy activities the incidence of the disease finally declines.

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 nine new cases per year. Multibacillary forms prevail (56%). Formerly 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. ~ 5% 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.

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LEPROSY PREVALENCE IN RUSSIA

Leprosy was never a major problem of public health in the former USSR. The highest number of leprosy cases were 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 multidacillary 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 beginning 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 - 164, Armenia - 40, Georgia - 21, Moldova - 6, Latvia - 22, Lithuania - 1, Estonia - 25. There are 12 antileprosy centres where 1185 cases were registered, Russian Federation - 1152, the Ukraine - 75, Byelorussia - 2, Kazakhstan - 1185, Uzbekistan - 1003, Tadjikistan - 166, Turkmenistan - 141, Kirgizia - 33, Azerbaijan - 164, Armenia - 40, Georgia - 21, Moldova - 6, Latvia - 22, Lithuania - 1, Estonia - 25. There are 2 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. Therefore economic hardships adversely affect the care of the patients and surveillance of leprosy contacts and every efforts are required to escape worsening epidemiological situation.
EPI4

1012 YEARS FOLLOW-UP OF HEALTHY CONTACTS OF LEPROSY CASES USING FLA-AGS AND LEPRORIN 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 CIDR, Asr more than 100 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 Mycobacterium-specific antibodies by fluorescent antibody absorption test (FLA-AGS) was recorded. During the follow-up of more than a decade, a large number of contacts have developed disease ranging from tuberculoid to lepromatous type. Various risk factors including the predictability to get disease either using FLA-AGS, lepromin skin or in various combinations has been statistically evaluated. Analysis of the results indicates that FLA-AGS test is a very sensitive test for monitoring tuberculosis infection in the community specially the childhood contacts. It was also observed that by the combination of FLA-AGS and lepromin tests, the relative risk can be better predicted than using these tests alone. The contacts with initial FLA-AGS positivity and lepromin negativity were found to be at significantly higher risk in compared to other groups. FLA-AGS positivity was observed to appear before lepromin response 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-AGS 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.

EPI5

A SEROEPIDEMIOLOGICAL STUDY OF LEPROSY IN HOUSEHOLD CONTACTS AND HOSPITAL PATIENTS IN HENAN, CHINA USING NON-O-BSA AN PGL-1 AS ANTIGENS

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Using the ELISA assay of detecting antibodies to ND-0-BSA and PGL-1 as antigens.

EPI14

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.
Florida but it is widely distributed among all others. There are no directional trends in its prevalence distribution that might suggest a role. Leprosy appears to be indigenous to armadillos. Both the desirability and transmissibility 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 1844 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 infected 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**

**A NEW SIMULATION MODEL FOR PREDICTING INCIDENCE AND PREVALENCE TRENDS IN SEVAGRAM DISTRICT, MAHARASHTRA, INDIA**

Mukund Ranade

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Epidemiometric models are useful tools for studying dynamics of disease in populations. Simulation models 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 1932 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 equation based on experience of rate from 1952 to 1990 could 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 ninety seven 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 age at inception 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 1962 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 LEPROSY EPIDEMIC WITH STEPWISE REGRESSION MODEL**

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The basic data were taken from the records in Bose Prefecture of Guangxi from 1955 to 1993, with leprosy morbidity (yj), and case rate (yi) as dependent variables, the per capita gross value of industrial and agricultural production (xj), per capita national income (x2), proportion of agricultural population (x3), proportion of public health personnel (x4), average annual temperature (x5), and average annual rainfall (x6) as independent variables. Multiple regression model of y; on xj, x2, x3, x4, x5, x6 was built with stepwise regression method, respectively. The simple and multiple correlation coefficients between such variables and independent in the model were analyzed. It is illustrated that population, economy and air temperature have effects on leprosy epidemic in varied degrees, among which x5, x6, x2 have greater effects on y1, x1, x2, x3 have more obvious effects on y2.

Key words: Multiple regression; stepwise regression; partial regression coefficients; morbidity; case rate.
3 levels: <2, 2-10 and >10 years. The cured time is a dependent variable which is divided into 2 levels: delay (cured time) and >= 4 years. The results in single factor show that above 36+ age group has high Odds 1.660 in comparison with young age group (Odds = 0.692), differences between males and females (males Odds =1.880), and delays (1 - 2 year Odds =1.0815) show no significance (p=0.05). Mod MDT has the highest Odds 6.253 compared with New MB (Odds = 0.20) and this indicates the longest time to cure. The cases in group of < 2 year delay of treatment has an Odds 2.290, but MD MDT less than 2 years indicates the lowest treatment efficiency(Odds=0.255). In multiple factors, the male MB with Mod MDT in median 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 few MB cases in young age group with WHO MDT (Odds=0.1273).

EP25
TREND OF LEPROSY DURING THE MDT ERA
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S L R T C Korigiri, Tamilnadu, India 632 106

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 20 years or more. In the absence of any primary prevention measures, it becomes obvious that the only possible area of intervention is to block the known source of infection i.e. a case. S L R T C Korigiri, in Gudiyattam town, (population 570,000) has been implementing a leprosy control programme, with intensive case finding activities, since 1982, 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 marginal reduction. The available data suggest that the quantum of disease transmission in the community has not changed appreciably.

EP23
THE ANALYSIS OF StepWISE REgression AND INDICATORS FOR REFLECTING LEPROSY DETERMINING FACTORS IN YANGZHOU, CHINA

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Total 19478 cases have been detected (1949-1990) in Yangzhou Prefecture located in East of China with 9 260 000(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’ complaints), 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 (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, III/II 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 completeness MDT, date of cure, date of relapsed, type of leprosy, disabilities grade and population in the area.

EP26
STUDY OF LEPROSY IN CHILDREN IN MULTI-DRUG THERAPY IN BARIARBH DISTRICT BHARATPUR INDIA

N.K. CHOPRA, R.CANAVATI, MRS. M.P. DUBEY
Multi-drug therapy project commenced since 1st March 1982 with the financial collaboration of Government of India and WHO. Total no of patients brought under MDT till Dec 1992 are 11447 (4533 old active area + 6914 new detected cases). So of child below 15 years detected between commencement of MDT and till Dec 1992 are 1378,(12.01%), of which 187 (13.5%) are MB and remaining 1191 are P.B. (86.49%) 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 previous, intensive and maintenance phase of MDT. The study showed that child incidence rate was at commencement of MDT was 21.19% and after 3 years of intensive phase in the year 1992 which increased to 28.9% Child hood rate in the year 1988-89 in preparatory phase was 16.25% and it was increased to 23.84% in the year 91-92.

The other vital epidemiological parameters such as 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

Wu Xinhong and Ning Yong
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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 1990 to 1991; 131 of them were HC of MB and 94 were non-HC the ratio for risk for MB HC, PB HC, and non-HC being 13:1:3.1. The case detection rate gradually reduced annually in the three kinds of contacts. The annual average declining speeds were 29.94, 41.12 and 40.21, 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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EP29
THE LEPROSY IN ALGERIA.

Ahmed Adoun, Ahmedrcia El-Hadj Haddad, Department of Preventive Medicine, University Hospital of Tlemcen (West-Algeria).

Leprosy is not a problem for public health in Algeria. For one century (from 1900 to 1980) a maximum of 200 cases were reported, 70% of them were females, and 51 caught the disease in Algeria.

In July 1989, a couple from Tlemcen (West Algeria) living in Mali came to our service for consultation. They had the same type of lesions, non pruriginous achromatic spots of 0.5 cm diameter. These lesions reside on the forearms, the legs and the feet. A biopsy of an injury was performed. Histo logical examination shows a subcutaneous granuloma composed of a large amount of histiocytic cells with clear cytoplasm. The aspect is compatible with a lepromatous lesion. 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 continuous surveillance, because of multiple exchanges with the neighbouring countries where there is a high lepromatous endemicity.

EP30
THE ACTUAL STATE OF LEPROSY IN THE BALTIC STATES.

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Heinrich Heine University, History of Medicine, Dusseldorf, Germany.

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 and economical 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 economic 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 = 0.9429 > r= 0.798. 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 economical development and government plan. Our research maybe also suggest that it was along with economical 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

*Dr. Jayasree De and **Harshit Sinha.

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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 continuity of the disease in these 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.

Chen Xiaosheng Li Minzhong Ye Guiyu Huang Weihua.

Dr. Jin Shikang Zhan Xingzhe Teng Taishong.

Institute of Dermatology, CAMS, Nanjing, China.

A total of 1,522 samples from 435 families in two leprosy-endemic counties within Yunnan Province of China were tested for anti- M.laeprae antibody based on ELISA using ND-O-BSA as antigens.
Abstracts of Congress Papers

For the purpose of the epidemiological analysis, the 95% percentile value of DB (8,14) 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 analyzed using the theoretical models of Poisson, negative binomial and logarithmic distributions, respectively. The results showed that the different age groups, the introducing rates had significant difference (P<0.001) and the highest rate was 82.2% 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. The actual distribution of infection in families was consistent with the negative binomial and logarithmic distributions, but not with the Poisson one. This showed that the leprosy infection was significantly clustered in families.

In this paper, the applications 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 Yichon Prefecture of Jiangxi Province, China
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Anti-Schistantosomiasis Office of Yichon Prefecture, Jiangxi Province, China

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 Yichon Prefecture, Jiangxi Province in 1990. The results of this survey showed that the prevalence rate was 0.0835%. 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 regression equation instead of random distribution. Aggregation exponent K was 0.7256. There was a significant difference between prevalence rate and population density (P<0.05) and the linear regression equation was y=3.13-0.0386x-0.0414.

EP35
Profil Epidemiologique de la Leprose en Haiti
Claude Preu, Silvano Nathelier, Jean Olivier, Reol Charlot-Toin, Gary Bien-Aime, Michel Norius, Fritz Janiez, Edinor Toussaint
Institut Cardinal Leger, Port-au-Prince, Haiti

Les auteurs utilisent les différents paramètres epidemiologiques de l'endemie leprose au niveau de deux centres de reference en Haiti.

EP36
Hansen's Disease in Children in the State of Amazonas, Brazil, 1980 to 1990
Silvana Pessini, Paula F.B. Rebellio e Maria F. Maroja
Coordenacao Nacional de Dermatologia Saude, Ministra, do Saude, Brasilia, Brasil.

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 prevalence 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 paper analyzes the contribution of several characteristics of dwellings and households to the definition of leprosy. Dwellings with diagnosed cases of illness are compared with randomly selected dwellings located in the same urban area, in the outskirts of the Metropolitan Area of Rio de Janeiro.

The paired analysis of patients reveals a high association with age and educational level as a measure of socioeconomic status. In the group of dwellings and households distant from the focus area, age and type of house are the probable differential 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
Tutana Sabita (1), A. M. Kh. Ahan Ali (2)
(1): Medical Officer, Dhanjuri Leprosy Project-Khulna Branch (ONS Sisters), Dampara Road,boro Round, Khulna-9, Cell (2): Director, TB & Leprosy Project, Khulna, Daka, People's Republic of Bangladesh.

Since there was not any leprosy control program in the south of Bangladesh by 1996, the prevalence rate of leprosy in this area still unknown. This report is about the results of a case detecting activity which was done from February to Jule 1992 both for villagers and for slum dwellers in Khulna municipal area and to give some idea of the prevalence rate of leprosy in the south of Bangladesh.

Khulna is the biggest city in the south of Bangladesh with 0.7 million population, which has expanded along the west side of the big river, Dugha. It can be divided into two characteristic areas 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 months.

The number of total population who were checked from February to June 1992 was 19,037 and 107 cases were found to be leprosy. The overall prevalence rate was 0.67 per thousand population. The numbers of villages and slum dwellers checked were 15,791 and 3,241 and the member of cases found were 87 and 40 respectively. The prevalence rate in villages was 5.7% and that of slum dwellers was 12.54%, which was extremely high but of the same order of that of the slum in Bombay.

EP39
M. Gemma C. Canayao, M.D., M.P.H.
Skin Clinic Physician
EP42

A LONGITUDINAL STUDY OF THE PREDICTIVE VALUE OF THE LEPROSIN 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=161) or PGL-1 AB positive status (definite positive n=64, borderline n=94) or lepromin negative and PGL-1 AB positive (definite positive n=4; borderline n=23), total n=300 were clinically and serologically examined more frequently. There was no statistical difference in PGL-1 AB positivity rate in male and female children. Twelve new cases developed during the study period of which 11 were of non-cutaneous (OT) and only one OT (female). (7 females and 5 males). Statistical evaluation showed that lepromin negativity alone or PGL-1 AB 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.

Sandip Joshi, Vrushali Kathe, and Shared Hall.

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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 (10%) indicating continued infection in Bombay. The sponsorship programme which provided...
such simple "social services programmes" has potential for prevention of dehabilitation. Such simple "social services programmes" has potential for prevention of dehabilitation. Such simple "social services programmes" has potential for prevention of dehabilitation.

OPPORTUNITY FOR PERSONALITY DEVELOPMENT ENABLED 126

Although the number of patients coming from different provinces has diminished significantly, there was an increasing incidence among the indigenous population as shown by the 7,591,000 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 population. The extent of transmission and infective going on before MDT was a big question, however treatment of active cases, which are potential reservoirs of infection have been addressed by the MDT program. New patients were re-examined and finger prick samples collected from the 159 index cases and 403 contacts of leprosy patients in the low endemic area. The role of anti-Mycobacterium leprae-specific PGL-1 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-1 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 1958 and multidrug therapy (MDT) was introduced in 1993. Between 1986 and 1990 a mass intensive survey detected 234 new cases (new detection rate 2.7/10,000). In 1991-1992 new patients were re-examined and finger prick samples collected from the 159 index cases and 403 contacts of leprosy. The study monitored the efficacy of MDT, determined relapse rates and measured PGL-1 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.

Population data included 67 cases of leprosy (28%, 28% of males and 5% of females). The socioeconomic status of the cases was assessed by means of a questionnaire. The results were analyzed using the chi-squared test (P < 0.05). The results indicated that there was no significant difference between the groups with regard to age, sex, and disease type. The mean age of the patients was 41 years, and the proportion of women was 56.6%. The patients were divided into two groups: Group A (cases with disease duration less than 5 years) and Group B (cases with disease duration of 5 years or more). The mean duration of disease was 8.5 years in Group A and 15.2 years in Group B. The difference in the mean duration of disease between the two groups was statistically significant (P < 0.01). The percentage of patients with advanced disease (anesthetic, sensory, and visual loss) was higher in Group B than in Group A (P < 0.01).

The results of detecting M. leprae-specific antigen-phenolic glycolipid (PGL-1) with our modified method—Western ELISA are reported. The sera were from 63 cases of household contacts of leprosy patients (HCA), 61 cases of non-household contacts of leprosy patients (NHC), 16 cases of household contacts of non-leprosy patients (HCAC), and 16 cases of non-household contacts of non-leprosy patients (HCNC). The sera was also examined from 40 sera of healthy contacts (HC), 40 sera of antibiotic treated contacts (ACT), 12 sera of seropositive contacts of leprosy patients (SPC), and 16 sera of seropositive contacts of non-leprosy patients (SNC). The results showed that the antibody levels of PGL-1 in the sera of HCAC and HCNC were significantly higher than those in HC. There was a significant difference (P < 0.01) between the antibody levels of PGL-1 in the sera of HCAC, HCNC, HCA, and NHC. The antibody levels of PGL-1 in the sera of HCAC, HCNC, and NHC were significantly higher than those in HC.

In conclusion, the results of this study suggest that the serology of PGL-1 antibodies in the contacts of leprosy patients has potential for use in the detection and monitoring of leprosy.
screening tool in a leprosy control program. Seroreactivity to PGL-1 antigens correlated with the prevalence rate of a defined population. The use of M. leprae specific antigens, such as PGL-1, in immunosorbent 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 endemic areas and in leprosy patients. IgG antibodies were found in significant quantities in individuals staying in low prevalence communities and in leprosy patients treated over a long period of time. A relative particle agglutination test (MPAS) which detects IgM anti-M. leprae was used as a field test in the seroepidemiological studies in Malaysia and was shown to have very good concordance with the reference ELSA test.

EP49
A NATURAL RESERVOIR FOR LEPROSY RELATED CHEMILOPHOTOTROPHIC NITROGEN-FIXING BACTERIA: TRANSMISSION OF LEPROSY RACETES TO HUMANS FROM FOSSIL FUELS RICH SOILS

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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 tillage 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 cases and figures in various paintings, 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 missionaries as frequent occurrences of facial leprosy among the Maya 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 report 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 80,000 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=0.07). 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

According to WHO estimation there are about 15 million leprosy 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 pathologists of infections declare that leprosy specialists in not present in Isfahan area. We began an investigation either to approve or to pull out this idea. We searched the records about all of the registered patients in leprosy registered center were 21. Of whom were Afghan, one was Irani and the reminder were Iranian who were infected in other provinces and then migrated to Isfahan. The analysis the results proved that there are not any cases of leprosy 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-ACQUIRED IMMUNITY TO LEPROSY

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We report incidence rates of leprosy among 58,000 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.
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 MSLA 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.

In this paper we describe the importance of active surveillance by hospital-based survey is emphasized and may be designed to focus on persons below 15 years, with intensive follow-up for first 5 years. This model is feasible and can be integrated into general health service of any hospital.

### EPS4

**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 *pss*-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 UTP/UNG. False-nega-
tive 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 8.1% 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 popula-
tion. 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*.**

Bobby J. Gormus, Keyu Xu, Wayne M. Meyers, Gerald P. Walsh, Rudolph P. Bohm, Jr., Gary B. Baskin, Susumu Ohkawa, Marion S. Ratteree, Pamela A. Mack and James L. Blanchard

Tulane Primate Research Center, Covington, LA; AFIP, Washington, DC and Leonard Wood Memorial, Rockville, MD, USA.

Groups of 10 tussus monkeys (RM) and 7 sooty mangabeys (SM) were immunized and boosted with either live BCG alone or BCG + low dose heat killed *M. leprae* (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 (LP) and Foot soluble protein antigen (FSpA) 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, CD40/44B, CD42/49H and CD16.

Ab profiles to ML-specific glycopoligand-I (PGL-I) Ag by EUSA showed elevated IgG and little IgM in groups receiving BCG + HKML compared to others. We previously reported that this pattern is present in leprosy-resistant 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 CYNOLODUS MONKEYS (MACACA FASCICULARIS).**

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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 nanaopy-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 due to 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 [tGm] correlated well with the appearance of AFB in nasal secretions. No lesions are apparent at the cutaneous inoculation sites. The colonisation of the nasal mucosa with *M. leprae* in the absence of other clinical manifestations implies 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, an increase in *M. leprae*-specific 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 < 0.05) 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 < 0.05) and normal BALB/c mice (P < 0.05).

Flow cytometric analysis of spleen confirmed effective reconstitution with both CD4+ and CD8+ 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-4 141.72 ng and 600.800 pg per 10^9 cells, respectively.

These experiments demonstrate that *M. leprae*-immune 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 (severely 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 do not support replication 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-y 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 SPORE/MAID 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 (CWF), afforded protection when the amount of material solubilized was as little as 10^4 CFU derived from 10^6 *M. leprae*, while 10^3 or more killed *M. leprae* or further refined cell wall fractions derived from 10^6 or more *M. leprae* were required to provide protection.

In subsequent studies, we found that vaccination with a SDS-soluble fraction of CWF, "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* (CWF and PFC) generally 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 (fractions 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 AgNO3 suggests that the likely critical protective *M. leprae* proteins therein are probably the 12KD protein and 1-3KDa proteins, and, to a lesser extent, the 65 KD protein.

**EX6**

**BACILLARY PERSISTENTS 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. leprae* and in order to obtain a shorter survival time (SVT) of animals and to ensure 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 26 days, and by 74 days, pSA by 124 days, and by 214 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
EX7
UV-B IRRADIATION OF MICE INHIBITS THE PHAGOCYTIC ABILITY OF MACHROPHAGES,
DECREASES IMMUNITY TO MYCOBACTERIUM LEPRAE, AND INHIBITS DISEASE PROGRESSION.

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Ultra violet (UV) radiation decreases immune response 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 UV (200 - 320 nm) radiation can decrease immune function. These findings have raised concerns that increased environmental UV 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 bovis (MC) is inoculated into the hind footpad and disease progression is monitored by assessing the number of bacteria in the infected hind footpad and inguinal organs. We demonstrated that exposure of BALB/c mice to a single dose of UV radiation, varying from 0.35 to 3.0 kJ/m², from the UV lamp suppressed the induction of a delayed type hypersensitivity (DTH) response to MC in a dose-dependent manner. This was associated with an increase in the number of bacteria in the infected hind footpad and the inguinal organs. Furthermore, UV radiation reduced the survival time of mice infected either in the footpad or intravenously with MC. In order to determine whether the impaired clearance of bacteria seen after UV radiation was associated with altered macrophage function, we studied the uptake of MC by macrophages collected from the peritoneal cavity of UV-irradiated mice. Macrophages obtained from mice exposed to doses of UV radiation at or above 1.4 kJ/m² showed a significant reduction in their phagocytic ability when infected with MC. These studies demonstrate that UV radiation can alter the immune response to UV 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 FUNCTION AND THEIR MODULATION BY MACROPHAGES.

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Macrophages (Mφ) constitute the bulk of inflammatory cells in nerves of leprosy patients. Earlier studies indicate dysfunction in both Mφ infected human leprosy bacilli as well as murine Swiss white (SW) mice. 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 response to M. leprae infection. The parameters examined were: a) Ability to support intracellular M. leprae growth b) Expression of IGF & NgCAM c) Production of secretory proteins viz. fibronectin and collagen.

Constitutionally, DSC of the 2 strains responded differently to M. leprae infection with respect to release of secretory proteins and NgCAM expression. However differences in m.o.i of the 2 strains played no role in modulation of growth of M. leprae in their culture medium or in expression of NgCAM & IGF. Their role in modulating secretory proteins was at best temporary. Preliminary results of intraneural injections with supernatents of normal and patient Mφ displayed diversity in the composition of intraneurul granulomas that ensued.

EX9
THERAPEUTIC EFFICACY OF KRM-1648 IN COMBINATION WITH OTHER ANTIMICROBIALS AGAINST M. LEPRAE INFECTION INDUCED IN NUDE MICE.

Shimane Medical University, Izumo, Japan and KASHKA Corporation, Takasaki, Japan.

A new benzoxazinorifamycin derivative, KRM-1648 (KASHKA Corporation), is known to have excellent effect 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 DOX or chloramphenicol (CP), was evaluated against M. leprae infection induced in athymic nude mice. BALB/c nude mice infected sc with 1 x 10³ of M. leprae Thai-53 strain were given test drugs by gavage, once daily six times per week, for up to 60 days from day 31 to day 80. The growth of M. leprae was observed in the hind footpad during the 17 months following infection, by counting the number of acid-fast bacilli in the tissue homogenate, by using Sheperd’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 DOX (0.2 mg/mouse) and CPZ (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
COMBINATION OF RIFAMPICIN OR RIFABUTIN PLUS FLUOROQUINOLONES AGAINST MYCOBACTERIUM LEPRAE.

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The treatment of leprosy worldwide is limited mainly to dapsone, chloramphenicol, 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 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, ofloxacin, clinafloxacin, ofloxacin, sparfloxacin, temafloxacin and sparfloxacin were found to be most active against M. leprae, with MIC ranging from 0.35 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, clinafloxacin, temafloxacin or temafloxacin was combined with rifabutin, but not with rifampicin. When Rifampicin or Rifabutin were incorporated into MDT regimes it was found to be more active than ciprofloxacin, with MIC ranging from 0.35 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 ciprofloxacin, clinafloxacin, sparfloxacin or temafloxacin was combined with rifabutin, but not with rifampicin. Therefore, it seems there are more effective candidates now available for incorporating into MDT regimes in leprosy.
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 $\geq 10^5$, 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 $10^6$ to $10^7$) in NTLR. M. leprae from treated NTLR were judged viable if 1 year after subpassage either: (1) an increase of 5-10-fold M. leprae was found in any single NTLR subpassage 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 (1/1), 2 schedules of rifampin + daptomycin (0/2), daptomycin + 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<0.002) than with the previously described regimen when treatment consisted of: (1) rifampin + minocycline (0/15), (2) rifampin + ofloxacin (1/16), 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
ASSAYS OF MONOCLONAL ANTIBODIES AGAINST MYCOBACTERIUM LEPRAE FOR USE IN IMMUNOCHROMATOGRAPHIC AND IMMUNOSTRUCTURAL LOCALIZATION STUDIES.


We have developed a trial based on the recently described model of the "persister" state in experimental leprosy.

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 (PGI I) of M. leprae, we have revealed that the haemolytic specificity of PGI I was on the sugar part of PGI I. To
study the roles of such sugar-constructs, various kinds of sugar analogs were synthesized. They included the outer monosaccharide (NM-I), outer disaccharide (NM-II), trisaccharide (NM-III) inner monosaccharide (IM-I), inner disaccharide (IM-II) 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 micro-ELISA. MAB recognizing outer monosaccharide (who 1-24), MAB (1-25), outer disaccharide (PG08581, mi B2, mi B23), trisaccharide (SF-1), inner monosaccharide (OI), AB 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 quanitation of PGL I, immunohistochemistry and so on.

EX16

DENDENATED MUSCLE AUTOGRAPTS 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 intramuscular injection of cobalt-irradiated Mycobacterium leprae. \(^\text{1}\) 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 measurement 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 6, 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

SUPPLAMEMEAL LINEAR DENSITIES IN MONONUCLEAR CELLS INDUCED BY AN ANTIGEN IN HUMAN SENSORY PERIPHERAL NERVE.

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Subplasmamemal 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 10 mg was used as an 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 mononuclear cells occurring in sarcoidosis, which have SPLDs. These are now considered to be precursors of epitheloid cells.

EX18

OBSERVATION ON PHAGOCYTOSIS OF M. LEPRAE BY CULTURED HUMAN SCHWANN CELLS

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Schwann cells from 25 control rats (13 adult, 12 of human peripheral nerves have been successfully cultured by means of tissue plastination method. Among these the Schwann cells of 3 fetuses could be sub-cultured 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 lysosomes and Glial's complex in the cytoplasm. Even when fragments of peripheral nerve tissue or the cell suspension were stored in liquid nitrogen for several months, the nerve tissue or the cells could still alive to survive and proliferate after rapid thawing.

The Schwann cells and M. Leprae were co-cultured by cover-slip method, and the cover-slip were stained (acid-fast stain). The phagocytosis of M. Leprae by Schwann cells was observed under light microscopy in regular intervals. About 10% of Schwann cells phagocytsed M. Leprae 10 hours after infection. Later, on the number of the cells phagocytsed M. Leprae steadily increased and reached the peak (15%) of phagocytic index 72 hours after co-culture. M. Leprae could not 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 phagocytsed 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 + HD HKML > BCG + HD.
EX20

DETECTION OF Ig A, Anti-Pd-1 IN MAMMARY TISSUE ASSOCIATED WITH MYCOBACTERIAL INFECTION

N. leprae affects different parts of the body but especially the peripheral nerves, skin and mucosa, where bacilli are found in large amount. Pd-1 patients, long after the infection, escaped the attention. The little knowledge about the development of the immune response in leprosy patients is caused by the difficulty to make longitudinal study in human leprosy, because of the slow course of transmission and long incubation period.

The mabangay monkey has been reported to be a good model to study the immune response in leprosy, since the course of the infection with N. leprae in this host is similar to human.

Using sera from 6 mabangay monkeys we could demonstrate that IgA antibodies against N. leprae specific Pd-1 patients were present in sera of some monkeys. These monkey sera were obtained in the course of 36 months before and after Ig level experimental infection with N. leprae suspensions, where by two monkeys each were inoculated with different numbers of bacilli.

In A, an antibody levels to Pd-1 in mokey sera were compared with Ig G and Ig M antibody levels and clinical course of infections.

EX21

A NEW PATHOGENICITY MODEL OF LEPROSY: MIGRATION OF T.GES IN MICE EXPERIMENTALLY INFECTED WITH M. LEPRAE/GEN CANBACERIA

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The leprosy bacillus has been shown to multiply outside the human body, chiefly in the mouse footpads, armadillos and some non-human primates, yet no animal model is 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 / 10^6/10^7 CFU of CAN2, leprae bacteria in 0.05 ml volume containing 40 % of sterile colloid (type VII, Hyphasol, Sigma Labs., USA). Each batch consisted of 20 mice. Controls consisted of un inoculated mice of the same litters as well as those inoculated with colloid alone. The animals were observed for 6 months.

Migration developed in several animals belonging to different test batches after 3 months or later with or without being accompanied or followed by dermatitis or contractures. None of the control animals living in the same environment develop dermatitis/deformities. Microbiological and histopathological study of the lesions showed significant bacillary proliferation with disintegration/resolution of the connective tissue and their replacement by fibrous tissues in the affected areas.

EX22

EVALUATION OF SEQUENCE STABILITY OF OCTOPAUS AND CHELESTORINE ON MODEL, EXPERIMENTALLY INFECTED WITH MYCOBACTERIUM LEPRAE FROM HUMAN LEPROSY.

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The in vitro effects of any one of the currently used drugs on 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 cultured in vitro a large number of leprosy strains of chemostatotrophic nocardoidum (CAN) bacteria which appear to have a very close parallelism with the leprosy bacillus; these have been examined for in vitro susceptibility to Na-salbutamolone (a pentavertical agent), urea, salbutamol, norepin, ritanserin, IES, as well as, in vivo effects of these agents on the multiplication of the freshly harvested leprosy bacillus from human leprosy and inoculated into the mouse footpads; pathological changes in the footpads as well as the internal organs were also studied.

We found that Na-salbutamolone most significantly reduced the bacterial multiplication and degradation of lesions in the internal organs compared with urea and all other drugs, and also significantly with respect to the untreated but infected control mice.

EX23

UTILITY OF BEIGE MOUSE IN CHEMOTHERAPIC 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 (C5713116/bg)/bg mice to leprosy patient's bacilli, and their own immunity, a very close parallelism with the leprosy bacillus. These investigations are an extension of 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, not in BALB/c mice, following iv or ip inoculation. Bacilli harvested from Beige mice exhibited all the characteristics of M. leprae.

M. leprae inoculated into footpads 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 0.005% dapson, 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 infected macrophage compartment of their immunity were proposed and developed by Professor F.E. Vishnevetsky, now 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 (Gerva, 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 DAPSOE, RIFAMPICIN AND CLARITROMYCIN INTO MACROPHAGES AND MYCOBACTERIA

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Recently, attempts have been made to correlate the presence of a drug inside the mycobacteria with the phagocytic cells. In this paper we have examined the penetration of three antibiotics directly into murine peritoneal macrophages and into M. leprae, and compared the results with those obtained when mycobacteria were treated outside the macrophages. The penetration of Polyether conjugated dapsone was compared with that of dapsone only. After longer incubation periods, an increase in drug penetration was observed.

EX26
THE ACTIVITY OF COMBINATIONS OF EFFECTIVE 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.

Groups of female BALB/c mice were infected by both ears with 5,000 M. leprae and treated from day 60-150 afterwards with low but active schedules of the following 4 drugs singly and in all possible combinations: rifampin (R), dapsone (D), clarithromycin (C) and minocycline (M). At the end of therapy the number of AFB was less than in untreated controls. Bacteriostatic (BS) if multiplication was still observed, partial bactericidal (PBC) if multiplication increased, and fully bactericidal (FB) if multiplication was completely stopped. The results of the first 2 harvest intervals all single drugs were 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 of the 4 drug regimens (S + R, S + M, S + D, R + B). The 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.

EX27
THE ACTIVITY OF CERTAIN NEWER QUINOLONE ANTIBIOTICS AGAINST M. LEPRAE-INFECTED MICE

Robert Gelber, Ali Iramnesh, Patricia Siu, Mabel Tsang, and Lydia Murray. Medical Research Institute, San Francisco, CA, USA.

Previously, ofloxacin and pefloxacin 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 several recently developed fluoroquinolones (loxacin, ofloxacin, PD 124816, WIN 57273, ternafluoracin, 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, 15, 30 mg/kg; 5 times weekly. The number of M. leprae in footpad of 2 mice (4 feet) from untreated controls and all treated groups was enumerated. All fluoroquinolones studied were active against M. leprae, ternafluoracin 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%-0.15% 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 3 drug regimens clarithromycin and clarithromycin being found
more active than roxithromycin. Later, we found by proportional bactericidal test that the minimal inhibitory concentration for M. leprae was 0.01% in diet. Furthermore, we found that clarithromycin's minimal inhibitory concentration and minimal bactericidal concentration for M. leprae was 0.001% and 0.01% in diet, respectively.

It was also found that clarithromycin's minimal inhibitory concentration for M. leprae was 0.001% in diet, and 0.01% in diet for M. leprae, while 0.01% in diet of both clarithromycin and clarithromycin showed similar effect on the immune response in the BALB/c mice.

EX29
STUDIES ON THE ACTIVITY OF MINOCYCLINE AGAINST M. LEPRAE-INFECTED MICE.
Robert H. Gelber, Patricia Siu, Mabel Tsung, 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 of 0.17 and 0.51 µg/ml, respectively, which were achieved in mice treated with 0.1% minocycline in the diet. We also found that 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 (0.001 µg/ml) partially inhibited 5 of these strains, while 0.001% minocycline was consistently active.

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 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%, and 0.1% in the diet were completely and partially inhibitory of these strains, respectively.

EX30
LONG-TERM EFFECTS OF DAPSONE ON IMMUNE RESPONSES IN BALB/c MICE.
M. E. Reddy and P. L. Rao
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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 0.02% 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 BCG, proliferation and IL-2 production to T-cell mitogen Con A by spleen cells were suppressed to both the concentrations of dapsone throughout the exposure period with a sharp initial increase at 4 week exposure. Lymphocyte proliferation to T-cell mitogen Con A and PFC numbers to T-dependent (SRBC) and T-independent (NP-CFA) 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 4 week exposure. Suppression of early stimulation and later suppression was higher at 0.01% dapsone concentration when compared to 0.005% concentration. This indicated a concentration-dependent response of identical nature.

The implication of these results will be discussed.

EX31
STUDY ON MOUSE INOCULATED WITH MYCOBACTERIA LEPRAE BY THE MULTIPLE ROUTES.
Wang Hengyi, Zhang Weiyan, Tsa Liechong, Shi Meiqin, Liu Jihie
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The immune-deficient nude mice were inoculated with nude mouse-derived mycobacteria leprae by multiple routes (subcutaneously and intradermally), and the results showed that these inoculated animals were capable of producing a great amount of Mycobacteria leprae in the liver and spleen of nude mice. It was particularly found that the sites with lower body temperature were more active and the lesions were more prominent.

The authors suggest that the experimental leprosy is a new useful tool in leprosy research, especially in the countries without leprosy. The administration of multiple routes inoculation reported previously, the multiple-route inoculation is of more practical value.

EX32
EXPERIMENTAL LEPROSY IN Dasypus hybridus IN ARGENTINA.

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, we decided to focus the research on the armadillo. Appropriate facilities for the procurement of lepromin and other antigens used in serological assays were prepared. A general examination was performed on the armadillo and lepromin was detected in the infected tissues. The inoculum was injected with a tuberculin syringe in the external femoral vein under anaesthesia. It was prepared with a human lepra obtained from an untreated patient. One milliliter of this inoculum adjusted to 105/µl was inoculated to each animal. Two animals showed disseminated leprosy 26 months after inoculation. Abundant solid bacilli appeared in the skin ulcer (lepra), liver, spleen and lymph nodes. It was possible to purify bacilli from the infected tissues. In the inoculated armadillo the inoculation of bacilli into mouse foot pad and Piridin extraction were positive. The culture in different medium were negative.

EX33
NERVE CONDUCTION STUDY TECHNIQUE IN THE ARMY.
Jose Garzon, Jorge Almeida, Marcos Vilempo.
EX34

THE ARMADILLO AS A MODEL FOR LEPROSY

Eleanor E. Storrs, Florida Institute of Technology, Melbourne FL, U.S.A.

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 leproma-A, a reagent used to predict the course of disease; and PGL-1, a reagent used to stimulate sites distally below the ankles, and proximally just close to the knee in the foot pad of the lower limbs. The stimulating sites were distally, between the ankle, and proximally just close to the knee in the foot pad of the lower limbs. The distance between these two points was measured with a tape measure and the temperature was measured by means of an infrared skin thermometer which was placed half way of the above mentioned points, in both sites. We concluded that the motor nerve conduction study in the armadillo is a feasible and easy technique to be performed in a standard laboratory and could be of utmost importance to be used in experimental leprosy, neural involvement. Our data with statistics studies will be presented.

IM1

THE 65 KDA PROTEIN OF MYCOBACTERIUM 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 H37rv and M. leprae infections in mice. It stimulates cell-mediated immune responses and shares several immunomodulating properties with these mycobacteria.

The 65 KDa protein of this mycobacterium has been isolated in pure form by isoelectric focusing. The isolated protein was run on SDS-PAGE gel, alongside molecular weight markers, electro-transferred, immunostained, and probed with two monoclonal antibodies (mAb) 1H8 and 1H9, 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 x 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 no stoppage of migration and had shown strong lymphoproliferative response under antigenic influence. Strong CM responses have been generated by this protein in animal against hom and heterologous antigens.

EX35

LEPROSY IN WILD ARMADILLOS

Eleanor E. Storrs, Florida Institute of Technology, Melbourne FL, U.S.A.

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, a few 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 the transmission of leprosy in wild animal populations.
IM3
CLONING AND CHARACTERISATION OF A 42-KDA SERINE-RICH ANTIGEN FROM MYCOBACTERIUM LEPRAE.


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4 Department of Medical Microbiology, University of Antwerp, Belgium.
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In order to identify and characterise protein antigens from Mycobacterium leprae which are relevant in the immune response to this organism, a screening strategy of a lgt11 library was carried out using pooled sera from lepromatous leprosy patients. Four positive plaques were identified which contained an identical 1.7kbp insert coding for an immuno-reactive 145-kDa galactosidase fusion protein. The 1.7kbp insert was subcloned into the lacZ gene in pUC19 and sequenced. Analysis of the end adjacent to lacZ revealed an 42-kDa protein with a significant homology to sequences already reported, but in order to isolate the gene for this protein, the 1.7kbp insert was used to screen an M. leprae cosmid library by hybridisation techniques. Screening of 1.5 million clones identified, and M. leprae 1.8-kbp HindIII fragment was subcloned from one of these clones, which was sequenced. A 1.27-kbp OEF 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 leprosy patients (44 & 60% 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 cross-reacts with the cross-reactive determinants of sera from patients with active pulmonary tuberculosis who had antibodies recognising this 42,466-Da protein.

IM4
HEAT SHOCK PROTEINS IN LEPROSY REVERSAL REACTIONS.

Diana Lockwood, Douglas Young, Jo Colston, John Stanley, and Satroy Young.

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Heat shock proteins are synthesized 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 reactive patients to determine whether heat shock proteins play a role in these cutaneous 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 HSP 70 in reactive human 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 T cells of healthy leprosy contacts who are presumed to have protective immunity (Dockrell et al., Infect. Immun. 57:2979 (1989)), which might make it a candidate leprosy vaccine. However BCG-vaccinated mice, not previously exposed to leprosy, can also be induced to this protein. We have used a panel of M. leprae 18kDa reactive human T cell clones, and a series of direct overlapping peptides which span the M. leprae 18kDa sequence, to map the peptides recognised by the M. leprae-specific T cells. 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 18kDa antigen previously described as 18kDa (Verbon et al., J. Exp. Med. 174:3132 (1991)).
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; SoPCW, soluble proteins extracted from the cell wall of M. leprae; and MCP-I, recombinant major cyclodextrin protein of M. leprae. The SP antigen is similar to the skin test antigens of Rees (STA, Leprosin, MLSA) and of Convit (STA, SPA, SA) except that cross-reactive "suppressive" carbohydrates and lipids were removed. SoPCW 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 SP antigen which is known to be persistent and cause a false positive reaction to a subsequent test, will be eliminated. The recombinant MCP-I protein is identical to the skin test antigens of Rees in sensitized guinea pigs resulted in a strong DTH response. Based on these data, an investigational new drug (IND) application has been submitted to the Federal Drug Administration. Upon approval, phase I testing in humans will be conducted by Dr. G.P. Walsh in Cebu, Philippines.

Work supported by NIAID Contract NO1 AI-05074.


cell wall of M. leprae. The recombinant MCP-I protein is identical to the skin test antigens of Rees (STA, Leprosin, MLSA) and of Convit (STA, SPA, SA) except that cross-reactive "suppressive" carbohydrates and lipids were removed. SoPCW 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 SP antigen which is known to be persistent and cause a false positive reaction to a subsequent test, will be eliminated. The recombinant MCP-I protein is identical to the skin test antigens of Rees in sensitized guinea pigs resulted in a strong DTH response. Based on these data, an investigational new drug (IND) application has been submitted to the Federal Drug Administration. Upon approval, phase I testing in humans will be conducted by Dr. G.P. Walsh in Cebu, Philippines.

Work supported by NIAID Contract NO1 AI-05074.

IM8

B-CELL EPITOPES OF M. leprae IN THE AUTOIMMUNE DISEASES

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Nat. Ins. For Lepr. Research 47-1, Aoba-cho Higashimurayama-shi

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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 M. leprae 14KD for exogenous 65kD protein. The convalescent sera but not acute phase sera of KD reacted with both of these peptides for endogenous and exogenous proteins. On the other hand, sera from mice immunized with M. leprae lysate or purified 65kD reacted with 17T85 epitope, but did not react with the PI epitope.

In leprosy, 20% of lepromatous leprosy patients and 28% of tuberculous leprosy patients showed 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 in leprosy. 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-KILOCALORR ANTIGENS OF MYCOBACTERIUM ICRC BY ANTI-MYCOBACTERIUM LEPRAE ANTIBODIES

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ICRC, a cultivable mycobacterium isolated from human leprosy in undergoing clinical trials as an anti-leprosy vaccine in India. Antigens of ICRC share cross-reactive epitopes with antigens of Mycobacterium leprae. Radioimmunoprecipitation of 125I-labelled ICRC antigens with sera from lepromatous leprosy patients, borderline lepromatous leprosy patients, tuberculosis leprosy patients, healthy controls, tuberculous patients and healthy individuals, demonstrated that 21- kD antigen of ICRC was exclusively precipitated by sera from all lepromatous leprosy patients and those underlying erythema nodosum leprosis reaction. The 14-kD antigen of ICRC was identified by sera from a few lepromatous leprosy donors (5 of 25) and in all the controls. 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 WM9 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 polyvalent 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. Pattaraya, Institute of Immunology, Bogota, Columbia and M. Gildon, MIR, Bill 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 (Lakshmi et al. PNAS, 89, 104-05, 1991). They were screened in a cell proliferation assay using peripheral blood lymphocytes 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/LI patients who showed unresponsiveness to the total leprosy 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% of the cases of leprosy. This was not true for the 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 tuberculous leprosy patients fell below the cut-off point. The present study was therefore, conducted to find out the level of Ag/Ab in such situations in the lesions. Using a cross reactive anti-IgG antibody about 92% per cent of the tuberculous leprosy patients were described in the lesions and skin smear samples. It was interesting to note that many of these samples were negative 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 kbp fragment. Nucleotide sequence analysis of the 1.2 kbp fragment revealed the presence of three open reading frames (ORF II), 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. tuberculoides. One of the yllM. leprae clones (LL) 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
ANTIGEN RESPONSE OF PATIENTS WITH BORDERLINE LEPROMA-TOS AND BORDEROIL IDELE TUBEROSIS LEPROSY TO MYCOBACTERIAL 29/33 KDA DOUBLET AND 65 KDA SINGLET ANTIGENS.

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Using immunoblot assays (InBA) and enzyme-linked immunoblot assays (ELISA) we have demonstrated the presence of a 29/33 kDa doublet and 65 kDa mycobacterial antigen (InA) in CRAC respectively (J Clin Microbiol 1990; 28: 379-380).

Furthermore, we proposed that measurement of antibodies to these antigens by 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 ELISA and InBA have been extensively used for diagnosing and distinguishing different stages of leprosy, particularly those of borderline groups (borderline lepromatous (BL) and borderline tuberculoid (BT)). The patient groups consisted of 31 LL, 20 BT, 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 HUMAN IL-6 AND Ag85 OF M. BOVIS BCG EACH EXPRESSING THE 185 KB ANTIGEN OF MYCOBACTERIUM leprae.

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The 185 kDa 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, recognize a number of epitopes within this antigen following infection with M. leprae or immunization with M. leprae vaccines. Whether immune responses to this particular antigen can play a role in 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, IV using vaccine virus and M. bovis BCG were prepared. The gene for the 185 kDa protein was inserted into the thymidine kinase region for the VV vectors under control of the early and late promoter. The gene for the 185 kDa protein was inserted into BCG vectors under the control of either the early or the 65 kDa shoot promoter. Different strains were infected with viable VV (10 PFU) or BCG vectors (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 185 kDa antigen were assayed by ELISA from all strains once, although the vaccine strains induced the highest specific antibody titers. T cell proliferative responses to the 185 kDa antigen, were minimal in 8-12 kDa mice after subcutaneous immunization with either construct at 2 weeks. Reombinant BCG stimulated delayed type hypersensitivity responses to soluble 185 kDa antigen in guinea pigs. Prior vaccination with VV expressing the 185 kDa antigen conferred partial protection to BCG-185, 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.


Peripheral blood leucocytes from 9 paucibacillary and 12 multibacillary leprosy patients, 18 healthy controls and 4 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, 10/10 lepromin positive controls and in 25/25 lepromin positive contacts. The 70 kDa hsp was less active T cell stimulant. 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 cell responses in 8/10 lepromin positive controls of 20/25 lepromin positive contacts. The 18 kDa hsp elicited only 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 sub-tuberculoid leprosy patients and lepromin negative controls, the 70 kDa hsp was the only antigen capable of inducing significant IL-6 production. In lepromin positive healthy contacts, Ag85 and the 18 kDa hsp induced substantial IL-6 titer. 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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In 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 TNFα seems to correlate with the intensity of their clinical symptoms. Although high TNFα levels are associated to the fatal outcome in other syndromes, elevated TNFα 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 in peripheral blood mononuclear cell cultures from 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 range of 690 ± 826 pg/ml, 20% of 587 ± 286 pg/ml, ranging from 0 to 4,880 pg/ml. Although
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IL-6 is also overproduced during the reactinal state. IL-6 values were inversely related to those of TNFα. The amount of TNFα (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 RNL, can justify at least in part the benign course of reactions in leprosy.

Supported by grants from TDR/WHO.

IM17

ASSOCIATION OF NK(DD1+) CELLS AND CYTOKINES WITH M. LEPRAE-SPECIFIC RESPONSES IN TYPE I REACTIONS


During Type I reaction(T1R), a leprosy manifestation more frequent on borderline lepromatous patients, and associated with peripheral neuritis, there is emergence of antigen-specific immune response to M. leprae, in previously unresponsive individuals. Enhancement of natural killer function also was observed during the course of T1R(Crude & G Hjerm, 1986). So far, we evaluated the participation of antigen-specific immunity and innate response in T1R, we analyzed 18 patients(10 BL, 4 BB, and 4 LL: 12 male and 6 female).

The 18 patients were previously negative for leprosy skin test and turned positive during T1R. The relative proportion of CD85 on peripheral blood mononuclear cells(PBMCs) had a 3x increase during T1R(13,0±0.9%, n=7) when compared with values post T1R(4,6±0.8%, n=10). T-lymphocyte in vitro proliferation to M. leprae, and production of TNF-α were also present during T1R but returned to absence of response after the end of the reaction (50,0±12.0 U/ml during T1R, n=5; and 3.5±3.2 U/ml after T1R, n=3). In the course of T1R, serum levels of IL-6 were similar to BT and NV(6.0±0.4 pg/ml vs. 34.3±9.8 pg/ml). These observations are consistent with an enhancement of NK function during T1R as a consequence of increment in NK cell marker in the PBMCs. It remains to be determined if the appearance of M. leprae-specific immune response during T1R is a consequence of the transient increase in the level of NK activity, or if the antigen-specific immune response drives the innate function during the reactional episode. Supported by grain from TDR/WHO and CNPq.

IM18

PROBLEMS IN DETECTION OF SECRETORY ANTIGENS OF INTRACELLULAR MYCOBACTERIA IN MACROPHAGE AND SCHINN CELL TISSUE CULTURE

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Identification of mycobacterial (ML and H37 Rv) antigens in supernatants of infected growth promoting host cells vir. Schwann cells (Sc) and mgs 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 culture ELISA & 2-D electrophoresis for testing of supernatants derived from ML/H37 Rv infected murine Sc/mgs respectively. A significant problem 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 a specifically 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 y-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 as Type 1 cells. The mycobacteria reactive CD8+ clones produced little y-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, y-IFN and IL-10. In contrast the CD4+ cytotoxic clones secreted y-IFN, IL-4 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+ clones, IL-4 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 LEPROREA REACTION

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Cytokines are involved in the immunopathological complications of several infectious diseases, 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 (378±182) and 3,000 pg/ml of IL-6 (223±194) 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 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 MOITIES IN MYCOBACTERIUM HABUAN

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M. habuau, a nonpathogenic, cultivatable mycobacterium offers protection against experimental infection with M. leprae and M. tuberculosis. Present study aimed at subcellular localization of protective moieties in this candidate vaccine.

The cell wall, cell membrane and cytoplasmic fractions were prepared by sonication and differential centrifugation of the bacilli grown in liquid shake cultures. Groups of mice were immunized with these fractions (doses adjusted in relation to the size of intact vaccine) in addition to the integral vaccine (killed M. habuau) and placebo and subsequently challenged with M. tuberculosis H37Rv. The animals were examined for survivals and associated parameters.

Preliminary results indicate that the protective moieties most probably are located in the cell membrane. Data on morphological, biochemical and immunological characterization of M. habuau 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 treatment of leprosy depends on identification of antigens relevant for eliciting T cell responses. Several approaches to identify immunoreactive 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 blotting indicated that most M. leprae reactive T cell lines developed from lepromin positive individuals recognized an antigen of 10KD mole. wt. The gene encoding this antigen was isolated from Lambia gill library and sequenced. The deduced amino acid sequence of M. leprae 10KD protein was found to have 51% identity with 10K GroEL 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 pUC119 expression vector, to produce the recombinant 10KD protein in large quantities for further evaluation. The immunological studies using recombinant protein show significant lymphoproliferation in vitro of PBMC from leprosy contacts and T cells from leprosy patients infected with whole M. leprae plus unique phenolic glycolipid I (PGL-I) of M. leprae and M. leprae sonicate supernatant fluid (MSS) as immunogen. Primary identification of the M. leprae 10KD protein can secrete MoAb against the epitope of PGL-I. The expression of the MoAb cell line can secrete MoAb against PGL-I and MSS as cell line only against whole M. leprae. The uses of these MoAbs in characterization of leprosy, identification of M. leprae, analysis of M. lepra antigens, and key problems in technology for producing MoAbs against M. leprae were also discussed.

IM23
STUDIES ON POTENTIAL USES OF MLPA IN LEPROSY

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Radioimmunoassay of Leporosin Assaying 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 these, we conducted systematic comparison of MA with NE, samples—leprosy patients 15(56), BL 55, BT 20, TT 20). Household contacts (HC) 55; random population (RP) 46; normal controls (NC) 40.

Results: MA at 1:32 serial dilution (MA 1:32) positivity rate (PR) was 79.4%, NC 1:16—97.6% PR of NE (OD0 1:10) was 98.0% of NE (OD0 1:10) was 98.0%. The individual agreement (RA) were more than 90% between MA 1:16 and NE, while the MA were more than 70% between MA 1:16 and NE, in multibacillary patients(NB), the IA were 84~100% between MA 1:16 and NE and 82~96% 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 NB.

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 differences were no significances between ELISA and dried blood (P0.05), 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%).

Comparison of U-bottom plate with V-bottom plate, the differences of results were of no significance between U-bottom and V-bottom plate (T -test, P0.05). 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(MoAbs) were produced by means of fusion between mouse myeloma cells SP2/0-Ag14 and spleen cells from M. leprae immunized with whole M. leprae plus unique phenolic glycolipid I (PGL-I) of M. leprae and M. leprae sonicate supernatant fluid (MSS) as immunogen. Primary identification indicated that the MoAbs can secrete MoAbs against the epitope of PGL-I. The expression cell line can secrete MoAbs against PGL-I and MSS as MoAb cell line only against whole M. leprae. The uses of these MoAbs in characterization of leprosy, identification of M. leprae, analysis of M. leprae antigens, and key problems in technology for producing MoAbs against M. leprae were also discussed.

IM25
REACTIVITY OF LEPROSY PATIENTS TO THE DERMATOLGICAL CENTRE, SSA, #Health Centre, SSA, Culiacan, Mexico; **Microbiology, Aga Khan University, Pakistan, and Departments of Dermatology, National Medical Centre, IMSS, Dermatological Centre, SSA, #Health Centre, SSA, Culiacan, Mexico; **Microbiology, Aga Khan University, Pakistan, and National Medical Centre, IMSS, Mexico; **Microbiology, Aga Khan University, Pakistan, and National Medical Centre, IMSS, Mexico; **Microbiology, Aga Khan University, Pakistan, and National Medical Centre, IMSS, Mexico.

Western blotting 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 murine-derived M. leprae sonicate EBSACG and a M. leprae PGL-I 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-kba were the most frequently identified. In particular, 831 of patients with a history of Mycobacterium leprae leprosy (MLN) had antibodies directed to the 33-kDa protein; a similar band was recognised by 161 of tuberculosis patients but not by sera from endemic controls.

A 60-kDa protein that was partially purified and initially expressed as a 16S-14S-puriied fusion protein was recognised by 75% of 76 individual leprosy sera. Analysis of recognition patterns by different patient groups revealed that 78% multibacillary and 60% paucibacillary cases had antibodies directed to this molecule. The recombinant antigen was recognised by 94% of patients with a history of MLN, 84% of tuberculosis patients, and none of the control sera. Statistical analysis of recognition patterns among patient groups and controls suggested that the 60-kDa protein has a potential as a marker of leprosy reactions.

**IM26**

**M. LEPRAE ANTIGENS CAN BE RECOGNISED BY BOTH TH1- AND TH2-LIKE HUMAN T CELLS**

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Recent studies have suggested that tuberculosis leprosy may represent a Th1 form of the disease, while T cells with the properties of Th2 are predominant in leprosy. A panel of human T cell clones have been obtained from IG booster doses who responded to M. leprae vacuolate and to the L. leprae recombinant 18kDa antigen. Cloning was performed in the presence of antigen, IL-2 and autologous irradiated peripheral blood mononuclear cell antigen-presenting cells. Clones were chosen by the ability to incorporate tritiated thymidine in a dose dependent fashion to the antigen used for cloning. Supernatant from antigen-stimulated cultures of cells were screened for the secretion of interferon 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 cells. A small 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 18kDa antigen, produced IL-4, defined by ELISA. All the clones were CD4+ CDS+, CD25+ and IFN-g+. Thus, even in donors with predominant Th1 T cell responses, a minority of Th2-like T cells responsive to mycobacterial antigens are present, at the absence of any clear ongoing Th2 response to allergens or worms. We are now investigating the role of other cytokines in the development of Th1 and Th2 CDS+ 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 antigen on monocytes could explain the antigen specific T cell energy 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 CD14 as a marker for monocytes. MHC class-II antigen expression was induced with lipopolysaccharide, interferon-gamma (IFN-gamma) and lepromatous (BL/LL) leprosy patients. This was independent of antigenic stimuli. The expression of HLA-DR, -DQ and -DP was 6-10 fold more than that of HLA-GQ 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 Mycobacterium H37Rv.

**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, 7/12 of paucibacillary patients, 20/25 Mitisuda positive contacts and 6/9 of Mitsuda negative controls recognized the 70 kDa protein.

IgG activity towards the hsp 65 was higher in patients with positive Mitsuda reaction than in 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 controls 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 10 kDa molecule.

**IM29**

**RECOGNITION OF ANTIGENS OF MYCOBACTERIUM LEPRAE IN PATIENTS HANDELING**

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Las células mononucleares (linfocitos) de pacientes con lepra tuberculoides, ojos 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 line productions, de una respuesta positiva de células mononucleares de sangre periférica provenientes de dichos pacientes y familiares. Contactos sinus, M. leprae positivos frente a antígenos proteicos separados por SDS-PAGE. Se encontró actividad en las fracciones con intervalos de peso molecular de 45-29, 29-18 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 lepromatosisi. Se detecto actividad frente a alguno de esos mismos antígenos (15, 16 y 14 kDa) después de la absorción de dichos sueros con M. lepra, evidenciando una alta especificidad con respecto a M. leprae.

**IM30**

**SEROLOGICAL RESPONSE AGAINST CROSS REACTIVE CELL-WALL ANTIGENS (65 18 65 PROTEIN A) IN LEPROSY**

Elangovanmer S. Sethibhimur S, Menaka K. Jayashree M. and Ram, P.S.,

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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.hovis BCG, M.fortuitum.
was noticed in adult contacts only. The occupational contacts with M.bovis BCG, and significantly very high response against LAM-B of the subjects included in this study.

A cell elicted significantly higher response against all the antigen, body response against M. leprae, M. bovis BCG and LAM-B by ELISA with the objective of discriminating antibody response against M. leprae and 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 contacts along with the questioning of the subjects included in this study.

**IM31**

**DETECTION OF 65 KILODAHOT SHOCK PROTEIN FROM Sera OF LEPROSY PATIENTS - IMMUNOLOGICAL ROLE AGAINST THIS ANTIGEN.**

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Sera from 167 leprosy cases of 65 kilodalton heat shock protein antigen by Reverse Passive Haemagglutination(RPHA). The antigenicity of this protein was well detected from 1:100 dilution along the clinical spectrum of leprosy. The same sera were also examined for the presence of IgG antibody to recombinant 65 kDa protein by ELISA. 60% 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 removed from treatment. The 65 kDa antigen detection by RPHA found to be more sensitive than the antigen 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.

**IM32**

**MAJOR ANTIGENS OF Mycobacterium habana RECOGNIZED BY Sera OF PATIENTS WITH LEPROSY PATIENTS**

Magdalena Vichay, José Esparraga, Fausto Queveda-Pascual, Sergio Estrada-Parras, Alanis Islas, and Iris Estrada*


Although Mycobacterium leprae infection of mice is self-limiting, it is possible to vaccinate mice such that they are protected against bovid infection. Intra-dendritic immunisation with killed M.leprae is the most effective means for vaccination. Of the cultivable mycobacteria which have been tested in this system, only M.bovis BCG has been found to give consistent 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 were 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 tuberculous 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 so far they are only recognized by IgG Abs we suggest they may play a role in protection.

We also identified a similar doublet in M.leprosus BCG and M.tuberculosis with our LL sera. It is possible that the M.habana doublet is the signature of a doublet (30/28 kDa) 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.

*Corinna de GOFFA*

This work was supported by the British Leprosy Relief Association

**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 cross-reacted 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 in 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 reactivation 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 M. HABANA VACCINE**

_Mycobacterium habana_ shares T and B cell determinants with M. leprae and M. tuberculosis.

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Peripheral T cell repertoire of M. w vaccinated leprosy patients was analysed using fractionated antigens of Mycobacterium _w_ Response of unimmunised lepromatous patients, tuberculous leprosy patients and healthy contacts (HC) were also analysed. All the subjects, except the unimunised 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 and HC. This antigen(s) mimicked _M. leprae_ in the sense that the unimmune 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 suggest that it has homologues present in _M. leprae_ as well as _M. tuberculosis_ DTH studies carried out in guinea pigs with a different strain of _M. leprae_ also showed a positive DTH response.
IM35

IMMUNOCHEMICAL CHARACTERIZATION OF 22 KD CYTOSOLIC PROTEIN OF MYCOBACTERIUM HABANA: A CANDIDATE VACCINE

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The known adverse effects of certain constituents of integrin mycobacterial vaccines have reemphasized the need for subunit vaccines based on immunoprotective 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 g for 1 h) of the culture 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 precipitated at 60 to 85% ammonium sulfate concentration. Purity of the isolated protein was checked by silver staining, HPLC and isoelectric focusing. Initial immunological characterization was done by immunoblotting using homologous and heterologous polyclonal antibodies, LTT and IHA.

IM36

PGL-1 LIKE ANTIGEN IN RENAL CARCINOMA

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Many methods for sero-diagnosis of leprosy have been established using M. leprae specific phenolic glycolipid I (PGL-I) as an antigen. Gelatin agglutination test by Imai et al. and micro hemagglutination test by Miyawaki et al. are two of the most popular methods and used widely. By using Imai's gelatin particle agglutination 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 antibody titers very high. In extensive studies, we examined sera from patients suffering from some kinds of cancer. We will discuss about the relationship between PGL-1 like antigen and renal carcinoma.

RESULTS AND DISCUSSIONS
1) Anti-PGL-I antibody titer in serum: 2(140,000 g x 1 h) of the culture of logarithmic growth of M. leprae. Pattern of cytosolic protein was analysed by SDS-PAGE. The major protein (Mr ~22 kd) was identified which almost exclusively got precipitated at 60 to 85% ammonium sulfate concentration. Purity of the isolated protein was checked by silver staining, HPLC and isoelectric focusing. Initial immunological characterization was done by immunoblotting using homologous and heterologous polyclonal antibodies, LTT and IHA.

IM37

IGG HUMORAL RESPONSE AGAINST THE ANTIGEN 85 COMPLEX HOMOLOGS IN LEPROSY

Antigen 85 complex is the major protein component present in M. leprae 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. kansasi, 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 (PB/BB) 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 pattern of these different antigen 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 CYTOTOXICITY AGAINST M.LEPRAE BY CYTOKINES IN LEPROSY PATIENTS.

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We studied the lack of cytotoxicity induced by M.lepraue in multibacillary patients (MB), to determine whether it was due to a deficiency of activating factors, peripheral blood mononuclear cells (PBMC) (2xl0^6cells/ml) were cultured for 7 days in tissue culture medium (RPMI-PCS) in the presence or absence of whole M.leprae (1X10^7 bac/ml), and then used as effector cells (E) [19 MB(6 BL, 12 LL), 6 paucibacillary (PB) (2 BT, 4 TT) and 7 BCG vaccinated healthy individuals (CH)]. Adherent cells were cultured in RPMI-PCS for 6 days, pulsed overnight with M.lepraue and used as target cells (T). IL-2 (50U/ml), IL-4(10U/ml) and IL-4 (200U/ml) were added at the beginning of the PBMC incubation period, and IFN-g(100U/ml) 18hr before performing the cytotoxicity assay. 51Cr release was measured after 4 hr incubation of E + radio-labelled T (E/T=40/1). Results were expressed as % cytotoxicity (MeanSEM). Basal: MB:16±2, PB:33±4, N:25±2; +IL-2: MB:16±2, PB:11±4, N:24±1; +IFN-γ: MB:20±2, PB:43±4, N:36±2; +IL-6: MB:20±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:24±3, PB:49±4, N:47±2; +IL-4: MB:21±1, PB:39±2, N:36±1; +IL-4+IFN-γ: MB:25±2, PB:54±4, N:46± 2. Statistical differences were found for IFN-γ and IL-6 alone (p<.05) 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.lepraue.
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 opioid receptors identified, f receptor has immunostimulatory and r receptor has immuno suppressive effects. Using Met enkephalins which binds to both receptors and f selective (DPDPE), and f selective (TAPA) peptides, we have demonstrated modulation of lymphocytes derived from leprosy patients and healthy controls.

Antigen specific lymphoproliferation and numbers of rosette forming T cells were significantly (p < 0.05) enhanced in vitro treated with Met enkephalins in both tuberculoid and lepromatous patients. This was further increased (p < 0.001) in the presence of the f selective DPDPE. In contrast, treatment with f selective TAPA 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) TAPA may be useful as an immunosuppressant agent in reactive leprosy.

IM40
SUBMISSION OF LEPROSY MONOCLONAL CYTOKINE RESEARCH BY HOMER GLAVINDAUR (MS-1) OF MYCOBACTERIUM LEPRAE
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Selective 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 MS-1 plays a role as protectors of resident M. leprae within phagocytes. Therefore we have examined macrophage activation by cytokine release in response to 1% in the presence or absence of MS-1.

Peripheral blood mononuclear cells (PBMC) from healthy individuals were incubated in the presence of medium only or in the presence of absence of MS-1 and LPS. After incubation for 4 h, culture medium was aspirated and THS, IL-1 and IL-6 concentrations determined by using ELISA kits.

Over a concentration range of 0.1-10 uM, MS-1 did not significantly stimulate production of IL-1, IL-6 or INF-1 observed in cultured monocytes when compared to that observed for monocytes stimulated with LPS. The results were similar to those found for PBMC in the presence of medium alone. In contrast, a significantly increased (p < 0.05) levels of suppression of cytokine release was observed by the addition of MS-1 (1 uM) within the LPS-stimulated PBMC cultures. Thus, the percent suppression ranged from 35-74% for IL-1, 42-68% for INF-1 and 58-71% 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 secretion of cytokines from specifically sensitized T cells and activated macrophages interest by means of cytokines to give rise to a state of protective immunity to this class of human pathogen.

IM41
EFFECTS OF GLUCOCORTICOID, 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 dermatitis like dermatis herpetiformis and erythema elevatum diutinum. Thalidomide was developed as a hypnic and sedative since the 1950s, 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-1 mRNA production in U937 cells measured by Northern blot method and IL-1 production in the supernatant of human adherent monocyte-stimulated peripheral blood mononuclear cells which was measured by ELISA concomitant 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-1 mRNA production of U937 cells and IL-1 production of human adherent mononuclear leukocytes were not suppressed by either the treatment with DDS (1 uM/ml, 10 uM/ml, 100 uM/ml) or thalidomide (1 uM, 10 uM).
2. IL-1 mRNA production of U937 cells was well suppressed by 15’3’ 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-1 mRNA production in 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 as the problem is expected to be exaggerated due to relentless deterioration of HIV incidence and its 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 PGL, sonicates of M. leprae and M. habana, arabinomannans 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 sera than urine. Several negative doubtful paucibacillary cases were also detectable and confirmed semiquantitatively for initiation of treatment. Significance of these findings has been discussed.

IM43
1-MICROGLOBULIN ANTIBODIES TO PGL-1 BY ELISA IN HEALTHY SUBJECTS AND LEPROSY PATIENTS
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Serum from 90 healthy subjects and 416 leprosy patients were tested for anti-PGL-1 antibodies (AGP-1) by ELISA with 1:2000.
The results and discussion showed that, (1) The mean OD550 and positivity rate of healthy females (0.049) and (2) Women significantly higher than those of healthy males (0.044 and 0.207), and there was a similar trend 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 cutoff of OD of males and females must be calculated separately. (2) The levels of APGL-I were of slow distribution in all groups except the active MB patient group, suggesting it was not suitable to calculate cut-off point of OD according to OD550 based on normal distribution. Therefore, the comparison of 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) OD and positivity rate were still significantly higher in inactive MB and FB patients than those in healthy subjects. It remains to be proved what are their clinical and epidemiological significance and if they can serve as an applicable parameter in detecting relapses. In order to have a good quality control of the detection at different levels and in different laboratories, the procedure and requests and especially the control panel sera for correcting results, must be standardized.

**IM44**

**LIPPA RABDINOMANNAN (LAM) BASED ENZYME-LINKED IMMUNOSORPTION 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 Lipparabinomannan (LAM) antigen were assayed. 40 leprosy patients, their household contacts which comprised of 31 individuals and 46 controls which included 46 apparently healthy individuals and 46 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 immunosorbent assay. The 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 AFL, the difference was significant by McNemar test for changes. A positive linear correlation was observed between titerary index and anti-LAM antibody level. The relevance of these findings to the serodiagnosis of leprosy and its importance in household contacts of leprosy patients is discussed.

**IM45**

**THE IMMUNE RESPONSES TO VARIOUS ANTIGENS IN M. LEPRAE IN HUMANS WITH OR IN RELATION TO LEPROSY**

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The immunological activation to various M. leprae specific antigens include (100, 650, 350, 700, 723, 1021, 223, 1101, 1203, 3315, 2201, 3501) are in the sera of 11 patients classified Clinically Pathologically as BB. In patients classified Clinically Pathologically as MB and NB, the sera from 72 patients and 10 normal healthy volunteers. The sera from 75 patients were collected periodically at monthly intervals for 6-9 months during treatment and rest were collected only once.

A similar pattern of reduction of Antibody responses in both BB and MB groups suggests that steroids do not influence the antibody responses in the majority of patients. The results of these studies indicate that anti-LAM IgG antibodies are highest in sera from leprosy patients than from healthy subjects. The female false positivity rate would be increased if calculated by overall positive criteria. Thus the authors suggested that the positive cutoff of OD of males and females must be calculated separately. (2) The levels of APGL-I were of slow distribution in all groups except the active MB patient group, suggesting it was not suitable to calculate cut-off point of OD according to OD550 based on normal distribution. Therefore, the comparison of 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) OD and positivity rate were still significantly higher in inactive MB and FB patients than those in healthy subjects. It remains to be proved what are their clinical and epidemiological significance and if they can serve as an applicable parameter in detecting relapses. In order to have a good quality control of the detection at different levels and in different laboratories, the procedure and requests and especially the control panel sera for correcting results, must be standardized.

**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 from tuberculoid patients (levels were in 24/24 and 5/16, respectively, outside 95% confidence levels of levels in control sera). Anti-sulphatide IgG was also present in sera from lepromatous patients.

Lack of variation (p < 0.05 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 assess their role in leprosy, the humoral immune response to these lipid antigens as well as to ceramide, sulphotides and human Myelin Basic Protein (MBP ) was quantitated by microtitre enzyme linked immunosorbent assay. Sera from 219 leprosy patients, 18 neuropathic patients and 43 normal healthy controls were screened. High titers of IgM antibodies directed to total nerve lipids (TNL), Galc and ceramide were present in patients across the spectrum while the antibodies to sulphotides 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 correlation was observed between anti-TNL and anti-Galc antibodies in TT and neuropitic patients. However anti-MBP antibodies were significantly high in LL-RL patients with evident nerve damage. These observations suggest that the neural pathology in these two forms of disease may be different.
IM48
CONCILCATION 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 analogues 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 Mindanao, 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%) was much higher than that in PB patients (61.8%). The concordant rate, ranged from 92% in normal populations and 57.85% in household contacts, Chi-square tests 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 specificity of both GPAT and ELISA in MB patients (93.04%) was much higher than those in PB patients (88.2%).

The seropositivity of both GPAT and ELISA in multibacillary patients (86.7%) was higher as compared with the titers of anti-M. leprae antibodies in patients with chronic specific polyneuritis.

IM50
THE INFLUENCE OF BCG VACCINATION AND CLOSE CONTACT WITH LEPROSY PATIENTS ON THE RESULTS OF SKIN TESTS WITH A NEW TUBERCULIN BCG

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Our study in Sao Paulo Province of Brazil investigated the results of skin tests with Tuberculin, Leprosin A, and Tuberculostatin A on 672 young adults residing in a leprosy endemic area. Of them, 350 were index cases, usually relatives, of 68 patients. 67 were similar contacts of MB 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 concordant rates of BCG scar were 83.04% and 88.2%, respectively. Chi-square test of homogeneity and the relative risk were considered individually for each antigen, and by responder categories (Category 1, no reactions to all antigens; Category 2, 1 reactant to all antigens; Category 3, 2 reactants to all antigens). Age made no difference to categorization, but the presence of a BCG scar significantly increased reactions in categories 1 and 3 at the expense of 2 (p = 0.03). A similar finding was recorded in leprosy cases when compared to MB and PB contacts (p = 0.03). 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.

IM49
A PROGNOSTIC VALUE OF SEROLOGICAL ASSAYS IN RECESSIVE LEPROSY

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610 patients 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-destructed M. leprae (USS-M) and a semi-synthetic analogue of PGL-1 (ND-O-RSA) (provided by WHO, Bank) were used. Among the patients with inactive leprosy (Bi < 0.5) 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 polyneuritis, visceral and eye pathologies (hepatitis, orchitis, ulcers, etc.). Only in 15% of the patients from this group antibody titers to ND-O-RSA were significantly higher as compared with the titers of antibodies to USS-M. In other cases the ratios were inverse indicating the necessity of serological testing of repressed leprosy patients with either antigens. 26 patients relapsed, 80% out of them being seropositive 1-3 years before the occurrence of relapse. 23 (80,4%) cases out of them had high levels of antibodies to both antigens that is characteristic to active leprosy. Leprosy 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 repressed leprosy for assessment of the effectiveness of chemotherapy and early prognosis of relapses.
IM52
INDUCTION OF LEPRORIN POSITIVITY BY A CANDIDATE ANTI-LEPROSY VACCINE MYCOBACTERIUM W AND ITS IMMUNOMODULATORY EFFECTS ON LEPROSY NEGATIVE HEALTHY CONTACTS OF MULTICALLARY 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 (14.94%) were found to be having leprosy. The remaining 308 apparently healthy contacts were lepromin tested and 169 (54.1%) were observed to be negative to Mitsuda lepromin. M.w vaccine was administered intradermally to 90% of these 169 lepromin negative contacts. Sixty eight of them could be retested for lepromin A reactivity. Fifty six (82.53%) 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 reversal of lepromin positivity back to negativity status. Among original lepromin positive contacts, so far for cases of Paucibacillary leprosy have been detected, but none from vacine induced lepromin converted contacts.

IM53
M. LEPROSIRESISTIVE TLYMPHOCYTE AND THEIR MOBILIZATION IN A RARE FORMATION OF LEPROSY, THE LUPICIOUS FORM.

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The Lupis phenomenon (LP), a leprosy reaction, characterized by necrosis of peripheral nerve, was investigated in 17 polar lepromatous (LL) patients (LP1, LP2, LP3, male, 65 to 76 years old). 10 in LP 1 stage, 6 in LP 2 stage of treatment. Lesions with thalidomide (LP1, LP3) or thalidomide plus glycolic acid (LP2), before treatment, patients had increased levels of TNF-α (p<0.01 LP3 vs LP1, LP2, LP3) and their peripheral blood mononuclear leukocytes (PBML) generated spontaneous TNF activity in vitro, as well as very high levels of oxidative metabolism intermediates (chemiluminescence, ILP2, LP3). TNF analysis of PBML demonstrated absence or reduction of the CD8+ and CD4+ cells. On day 7, the lesions were healing. The parameters above with the exception of IL-6 levels were returned to normal or diminishing; and surprisingly the PBML (LP2, LP3) proliferated in vitro in response to M. leprae, but without IFNγ 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. (Presented in part at the 10th World Congress of Leprosy, September 1996).

IM54
LYMPHOCYTE SUBPOPULATIONS AND THEIR FUNCTIONAL PROPERTIES IN LEPROPSMY LEPROSY

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Lymphocytes from LL patients were studied for their proliferative responses to PPD, ConA, PWM, and specific M. Leprae antigen (lepromin).

Besides, the functional activity of ConA-induced T suppressors and T cell subsets with CD4+, CD8+, CD95 phenotypes were studied. It was shown that in active leprosy patients lymphoproliferation to mitogens, function of nonspecific T suppressors and the relative percentage of CD4+ 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 lepromin 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 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 in circulation to replenish their functional deficiency. Thus, in LL patients there is a definite interrelationship between immune alterations and their disease status. Prolonged specific therapy results only in partial recovery of disturbed functional activity and changed contents of lymphocyte subpopulations.

IM55
IMMUNOGEGIC 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 population were assessed. In our investigation presented was aimed at studying a role of HLA class I and II antigens in leprosy susceptibility. Patients with leprosy and healthy controls were selected. HLA typing was performed. Overall comparison of a whole series of antigens tested statistically significant differences remained only for HLA B7 (P=0.001) and DR3 antigens (P=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 (S=0.67). Thus, based on these results it was concluded that HLA-B7 (possibly, haplotype B7-DR2) and HLA-DR3 might be the markers of susceptibility to leprosy in Russians that should be borne in mind when identifying risk groups among leprosy contacts.

IM56
RULES OF LYMPHOCYTE SUBPOPULATIONS IN ERYTHMA NODOSUM LEPRORUM AND ACUTE ANTERIOR UVEITIS

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One of the many clinical complications of leprosy is a reactional state known as erythema nodosum leprosum (ENL). During ENL, some patients develop acute anterior uveitis (AAU). AAU is still unknown, some patients develop AAU during ENL and others do not.
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 N. 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 footpad. We have been conducting autoradiography studies to evaluate the 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 ABF bacilli and more than ten silver 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 (PGE) which inhibit gamma interferon in the microenvironment of LL granuloma. To find any difference following IFN-γ, ECG, IL-2 treatment in vitro, we have examined levels of PGE production by radiolmmunoassay and toxoplasmascindial effect of MACs from LL granuloma.

IM58

KILLING OF MYCOBACTERIA-INFECTED MACROPHAGES BY LAK CELLS FROM LEPROSY PATIENTS

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Immunology Division, Cancer Research Institute, Bombay; * Richardson Leprosy Hospital, Miraj, India

Most 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 lysose 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 MACROPHAGES/MACROPHAGES OF LEPROSY PATIENTS BY TUFTEIN FOR BIOCHEMICAL AND IMMUNOGENIC FUNCTIONS.

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Mycobacterium leprae is an obligate intercellular pathogen that is acquired and proliferate within the cells of Monocytes/Macrophages (M). Intercellular pathogen may escape killing mechanism either by inhibiting production of reactive oxygen intermediates (ROI) or by neutralizing these intermediates. We have investigated the effect of tuftein (plant "tofesia") on immunogenic functions of monocytes/M derived from leprosy patients as a function of in vitro culture age. Since we have earlier observed an aberrant phagocytic and microbicidal activity of monocytes/M from LL patients towards tufitin pulsing, we have undertaken to correlate the microbicidal functions (by measuring Qa, NADPH) and maturation profile (by measuring reduced granulocyte macrophage (G-M) activity of monocytes/M). Further the signal transduction by measuring Qa, NADPH by measuring Qa, NADPH, and determining the no membrane by tufitin and tufitin receptor expression (by radio receptor assay) on these M were studied in detail. ROI production and (Qa^-) release towards tufitin pulsing showed a progressive increase with increasing in vitro culture age till day 3, then tapered off in older cultures of normal and LL/MM. BL/M were unable to undergo tufitin mediated ROI production and (Qa^-) release after day 3. ADA activity was found to be maximum in the early culture of BL/MM. These results indicate that BL/MM has a differential maturation profile and these may be specific enzyme(s) defect associated with ROI production. From the study it can be concluded that there is defective signalling during Qa activation and finally these defects may lie at the tufitin receptor expression.

IM60

IN 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 nerves appear 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 more than hundred leprosy patients belonging to the entire spectrum of the disease, along with sera from normal human volunteers 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 antibody 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 IgG type and none tested positive for the IgM 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=31), patients with neuropathies other than leprosy (n=27) and normal healthy volunteers (n=31) using microtiter 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 resistivity was minimal with normal healthy volunteers as only 2 (6.4%) patients showed detectable levels of 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/T 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 any 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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Department of Microbiology, Yonsei University College of Medicine, Seoul, Korea, and Leonard Wood Memorial Center for Leprosy Research, Seoul, Philippines.

Nerve damage is a major clinical manifestation in leprosy. As an effort to elucidate the pathogenetic 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 galactocerebroside (GC) were prepared, and the prevalence of antibodies to the antigens and asialo-GM1 (AGM) was determined among leprosy patients and controls. The major immune globulin class to the nerve lipid antigens was IgG; therefore, only IgG class to the antigens was analyzed. Of 291 Korean controls who had no history of having transferred to leprosy, 34 (11.6%) had elevated antibodies to ceramide, 54 (18.6%) to AGM, and 24 (8.2%) to GC, respectively, and 81 (27.6%) of at least one of the three antigens. In contrast, among 170 Philippine controls, 52 (31%) were seroreactive to ceramide, 30 (22.4%) to AGM, and 16 (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 (54.2%) were seropositive to ceramide, 40 (38.1%) to AGM, and 42 (40.0%) to GC, respectively, and 109 (54.3%) 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 extentiveness of anesthesia and nerve enlargement. The results suggest that anti-neural antibodies are closely associated with neurologic damage following Mycobacterium leprae infection.
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 DH2 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 2001 individuals from 408 families were taken for the study. The normal healthy sibs were taken as controls. None of the HLA-A-B-C and DR antigens showed any significant correlation with the disease types except for BB group only. In this group HLA-A10 specificity showed a significant association (P<0.001) even after correction of the P value. Certain haplotypes also showed some significant associations which will be presented and discussed.

In in vitro systems, 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 and after treatment had poor positive response in the two parameters. The normally leprosy resistant individuals in an endemic city like Bombay, showed two to three fold higher negative reactions in their macrophages. This has been consistently found to be true in subjects analysed 30 patients BB, BL, TT, normal control (3). Cells were obtained from fluid aspirated from suction-induced blister directly over nonreactive skin lesions. Significant differences were observed between T-helper and normal control by HLADR, Leu-la, Leu-2a. The BL, BT group had higher positive rate than the TT,BT group and normal controls. The T-helper/suppressor ratio (Leu-3a-Leu-2a) was 0.39 in LL,BL and 2.39 in TT,BT. This indicated that even macrophages containing phagocyted 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 lymphoblast absence, IL-2R is also decreased in LL,BL. On the other hand, Leu-2a positive cells (suppressor cells) were increased in LL,TT group and normal controls. No significant difference was observed between LL and TT,BT in Leu-3a/Leu-2a cells. This indicates that perhaps NE cells are not important in cell-mediated immunity in leprosy. Macrophages had higher levels in LL than TT,BT from nonreactive skin blister. This is inadequately understood as yet.

This study attempts to evaluate changes in T-cell subsets, macrophages and natural-killer by cells using Leu-3a, Leu-2a, Leu-1a. Interleukin-2 receptors (IL-2R) and HLA-DR antigens in 24 leprosy patients and healthy normal controls. BL, BS, BT, TT, normal control (1). Significant differences were observed between LL and normal control by HLADR, Leu-la, Leu-2a. The LL,BL group had lower positive rate than the TT,BT group and normal controls. The T-helper/suppressor ratio (Leu-3a-Leu-2a) was 0.39 in LL,BL and 2.39 in TT,BT. This indicated that even macrophages containing phagocyted 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 lymphoblast absence, IL-2R is also decreased in LL,BL. On the other hand, Leu-2a positive cells (suppressor cells) were increased in LL,TT group and normal controls. No significant difference was observed between LL and TT,BT in Leu-3a/Leu-2a cells. This indicates that perhaps NE cells are not important in cell-mediated immunity in leprosy. Macrophages had higher levels in LL than TT,BT from nonreactive skin blister. This is inadequately understood as yet.

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IM 68

OBSERVATION ON SUBCUTANEOUS IMMUNE CELLS IN SITU IN LEPROSY NONMEDITATIVE SKIN LESIONS

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This study attempts to evaluate changes in T-cell subsets, macrophages and natural-killer by cells using Leu-3a, Leu-2a, Leu-1a. Interleukin-2 receptors (IL-2R) and HLA-DR antigens in situ in leprosy nonmigrative skin lesion of 24 leprosy patients and healthy normal controls. BL, BS, BT, TT, normal control (1). Significant differences were observed between LL and normal control by HLADR, Leu-la, Leu-2a. The LL,BL group had lower positive rate than the TT,BT group and normal controls. The T-helper/suppressor ratio (Leu-3a-Leu-2a) was 0.39 in LL,BL and 2.39 in TT,BT. This indicated that even macrophages containing phagocyted 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 lymphoblast absence, IL-2R is also decreased in LL,BL. On the other hand, Leu-2a positive cells (suppressor cells) were increased in LL,TT group and normal controls. No significant difference was observed between LL and TT,BT in Leu-3a/Leu-2a cells. This indicates that perhaps NE cells are not important in cell-mediated immunity in leprosy. Macrophages had higher levels in LL than TT,BT from nonreactive skin blister. This is inadequately understood as yet.

IM 69

BORDERLINE TUBERCULOID HANSENIAIS: PARAMETERS OF IMMUNOLOGICAL 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 circumscribing the disease in the skin (number of cutaneous lesions) and in the peripheral nerves (number of affected nerves). These clinical features were compared to each other, and to an immunological test (ELISA test for PGL-I, phenolic glycolipid spe-
cific from Mycobacterium leprae) and to cellular immunity tests "in vivo" (cutaneous Mitsuda test) and "in vitro" (lymphocyte proliferation stimulated by M. leprae and gamma-interferon detection in lymphocyte culture stimulated by M. leprae supernatant). The cellular immunity test that best related to the capacity of the patients in limiting their disease, with reference to the skin, was the gamma-interferon detection test. BF form of Hanseniasis seems to be of systemic nature, though with tendency to circumscribe the lesions to the skin, whereas in the intermediate form the lesions may be in the skin and/or in peripheral nerves, one feature not necessarily being accompanied by the other.

IM70
A POTENTIAL MARKER FOR THE PREDICTION OF ENL REACTIONS
Department of Biotechnology, AI Asia India University of Medical Sciences: Department of Dermatology, Safdarjung Hospital*, New Delhi; VHS Leprosy Project, Shahnik Nagar, TM India; National Institute for Medical Research, Mill Hill, London, UK.

A double blind study was conducted to identify a serological marker for the prediction of ENL reactions from patients with lepromatous leprosy (LE). ENL reactions occur in lepromatous patients. 538 sera samples (ENL, stable LL, LL with history of reactions (H/0 REACTION), BT-77, FF, Familial contacts (FC), Non contacts (NC), Pulmonary Tuberculosis (TB)) obtained from endemic and non endemic areas of India were screened in an ELISA. Results showed a significant (P < 0.001) for peptides 2, 3, 13, & LSR. Peptide 13 was found to be cross reactive with H. influenzae and L. pneumophila (P < 0.001). In the stable LL patients, the antibody response to PGL-1 was significantly higher in females at every age level. Clinical leprosy of all forms was more frequent in females. The highest frequency in females occurred in the 15-24 year age group. The response to the LSR antigen in comparison to only 68% of the ENL patients recognised peptides 2 (GVTYEIDLTNKNAA), showed seroreactivity to the LSR antigen in comparison to only 68% of the ENL patients in females; 92% of the ENL patients recognised peptides 2 (GVTYEIDLTNKNAA), the stable LL patients. In contrast none of the NC individuals were 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 SITI USING SUCTION-INDUCED BISTERS: CELL CHANGES WITH IGM ANTIBODY TO PGL-1 AND INTERLEUKIN-2 RECEPTOR IN CLINICAL SUBGROUPS OF ERYTHEMA NODOSUM LEPROSY.

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Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand.

To examine the immunopathogenesis of type 2 erythema nodosum leprosy (ENL) reactions in leprosy, we studied cellular and soluble immunologic components of skin lesions in 37 patients with reactions (29 acute ENL and 8 chronic ENL), 60 active patients without reactions, and 33 control patients whose leprosy had been treated and cured. Cells, IgM antibody to PGL-1 and T cell peptide levels were obtained from fluid aspirated from biopsies induced by suction 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) T cell 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 intracellular CD8+ cell population and IgM antibody to PGL-1 but not increase CD8+ cell population and IgM antibody to PGL-1. The lesions of ENL patients showed a relative decrease of CD8+ cells and increased CD4+/CD8+ ratio compared to those in acute ENL and non-reactional leprosy. The degree of seroreactivity to the Optical Density (OD) values showed highly significant differences between stable and reactional patients (P value < 0.01) 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.

IM72
LEPROSY IN WOMEN: CLINICAL AND IMMUNOLOGICAL ASPECTS

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Recently interest has been shown in the impact of tropical diseases in women. One of the basic areas of interest in the analysis of leprosy is gender differences and gender differences are 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 compared to those in acute ENL and non-reactional leprosy; b) Tac peptide and IgM antibody to PGL-1 levels were increased helper/suppressor ratio as compared to those in acute ENL and non-reactional leprosy. These dataare consistent with previous findings and with those obtained in other studies. The degree of seroreactivity to M. leprae soluble extract (MSE) in females the antibody response to PGL-1 was significantly higher in females at every age level. Clinical leprosy of all forms was more frequent in females. The highest frequency in females occurred in the 15-24 year age group. The degree of seroreactivity to the LSR antigen in comparison to only 68% of the ENL patients recognised peptides 2 (GVTYEIDLTNKNAA), showed seroreactivity to the LSR antigen in comparison to only 68% of the ENL patients in females; 92% of the ENL patients recognised peptides 2 (GVTYEIDLTNKNAA), the stable LL patients. In contrast none of the NC individuals were 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.

IM73
THE INFLUENCE OF THALIDOMIDE ON THE IMMUNOLOGICAL MANIFESTATIONS OF ERYTHEMA NODOSUM LEPROSY (ENL) IN PATIENTS OF VENEAZUELA.

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Leprosy patient with reactions in the 15 to 30 year age group, in Venezeula, usually are identified as part of the ENL group when the LSR test is positive. The ENL group is divided in subgroups. ENL reactional leprosy has been divided in subgroups: ENL reactional leprosy; b) Tac peptide and IgM antibody to PGL-1 levels were 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 intracellular CD8+ cell population and IgM antibody to PGL-1 but not increase CD8+ cell population and IgM antibody to PGL-1. The lesions of ENL patients showed a relative decrease of CD8+ cells and increased CD4+/CD8+ ratio compared to those in acute ENL and non-reactional leprosy. The degree of seroreactivity to the Optical Density (OD) values showed highly significant differences between stable and reactional patients (P value < 0.01) 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.
IM74
LIPOPOLYSACCHARIDE (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 1137Ea. 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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**Dept. of Dermato-Venerology; Erasmus University, Rotterdam, The Netherlands.

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 differences 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
LEPSES 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 explore the significance of specific factors manifested in AAU we determined the levels of circulating immune complexes (CIC), IgA, IgM, C3 and C4 as well as Paucibacillary and Multibacillary 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 these experiments will be presented.

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 tuberculosis (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. DBR1, DBR3, DBR5, DQA1, DQB1 and DRB1 alleles were studied in 93 patients and 47 normal controls. DBR1*1501 and DBR1*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 S Leprae lipopolysaccharide LPS antigens.

 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.
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IM79
GLUCOCORTICOIDS 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. Immunoreactivity to glucocorticoids and interleukin-1 (IL-1) was assessed. It was found out that in active leprosy hydrocortisone levels were increased while glucocorticoid receptors were 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 glucocorticoids 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 hypothalamic-hypophysial and adrenal levels. Proliferative and regulatory potential of lymphocytes is dependent on the state of glucocorticoids production. These findings as well as the peculiarities of lymphocyte response to IL-1 in leprosy reaction represent the interrelationships among immune and neuro-endocrine systems and might be used for prognosis of the course of leprosy and optimization of pathogenetic therapy with glucocorticoids and immune modulators.

IM80
EFEKTO DEL IONOFORO A23187 Y PMA SOBRE LA PROLIFERACION DE LINFOCITOS T DE PACIENTES CON LEPROSIA MULTIBACILLAR
Fernandina Alfaro, Gabriela Echave, Anado Gonzalez, Martin Arce, Alfonso Islas, Roberto Norales, Mary Fafutis, Centro de Investigaicón en Immunología y Dermatologia, Universidad de Guadalajara/Instituto Dermatológico de Guadalajara (SSBS), Unidad de Patología Clínica, Guadalajara, Jalisco MÉXICO.

The ion transport via systemic circulation is assured by IIF a serum globulin which binds iron and conveys it to high-affinity TfR on cell surfaces. It has been shown that the complex IIF/Tf-R plays an important role in the progression of the antigen and/or mitogen, that lead to the expression of interleukin-2 (IL-2) and its receptor. We have reported (Int. J. Leprosy 55:561, 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 i125(iodination) and the expression of TfR by flow cytometric analysis in PMA stimulated T lymphocytes from 25 LL patients. In this work we found that T lymphocytes from LL patients under PMA stimulation, present a diminished percent of TfR positive cells and the serum Tf levels are not significantly different from those of normal subjects.

IM82
RECOMBINANT IL-2 IN UNTREATED AND TREATED LEPROMATOUS LEPROSY PATIENTS
L.G. Villar, R.I. Ballos, T.E. Fajardo, Jr., E.L. de la Cruz, and G.P. Walsh
Leonard Wood Memorial Center for Leprosy Research, Cebu, Philippines.

Interleukin 2 (IL-2), a 15-kilodalton single chain protein produced by thymus-derived lymphocytes and is believed to stimulate T-cell proliferation after antigenic stimulation.

Ten lepromatous patients: 5 untreated, 3 currently receiving W60-BHT 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 11 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

The iron transport via systemic circulation is assured by Tf a serum globulin which binds iron and conveys it to high-affinity TfR on cell surfaces. It has been shown that the complex IIF/Tf-R plays an important role in the progression of the antigen and/or mitogen, that lead to the expression of interleukin-2 (IL-2) and its receptor. We have reported (Int. J. Leprosy 55:561, 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 i125(iodination) and the expression of TfR by flow cytometric analysis in PMA stimulated T lymphocytes from 25 LL patients. In this work we found that T lymphocytes from LL patients under PMA stimulation, present a diminished percent of TfR positive cells and the serum Tf levels are not significantly different from those of normal subjects.
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 designated 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 treat type II reactions. To evaluate the potential role of TNF in type II reactions and the effects 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 who had clinically recovered from the reaction (no clinical symptoms, one month on thalidomide). TNF levels in second samples were measured by a bioassay with L1210 cells. Levels of TNF in the first sample (reaction and no thalidomide) were high (x=253.7 U/ml). In the second sample (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 patient was compared to a control 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<0.05), 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 triggered 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 suggests that type II reaction is accompanied by the production of TNF inhibitors.

"Secoros de Costa"
61A Abstracts of Congress Papers

IM88
POST-VACCINATION SENSITIZATION WITH ICRC VACCINE
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CIIl Field Unit (Indian Council of Medical Research),
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I CRC is one of the anti-leprosy vaccines tested in the multi-armed Leprosy Vaccine Trial being conducted at four localities in India, South India. A study was conducted in 368 Individuals, from one village and a nearby school in Chilongadipet, to obtain information on local reaction after ICRC vaccination and post-vaccination sensitization.

Each individual received either ICRC vaccine, in a dose of 5 MLU, 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' MLA, Lepromin-A (early) or 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
Medical Research Institute of San Francisco, CA, Colorado State University, Fort Collins, CO, and Albert Einstein Medical School, Bronx, NY, USA.

Groups of 10 mice were vaccinated intradermally in the right hind footpad with in Freund's incomplete adjuvant (FIA, negative control), 10⁸ killed M. leprae (positive control), and 10 μg of a 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 lung 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 the protective effect was reduced when mice were vaccinated with each of the proteins found to be protective there was induction of significant T cell responses in vivo to somatic M. leprae (stimulation indices ≥ 2). These studies suggest which M. leprae protein epitopes are important to protective immunity and those responses can be manipulated with cytokine treatment, even though they cannot, as yet, be activated to inhibit the bacilli in vitro.

IM90
BCG VACCINATION PROTECTS AGAINST LEPROSY IN VENEZUELA
Jacintn Convit, Peter G. Smith, Marian Ulrich, Celsa Sampson, Manuel Zuiga and Vctor Garcia
Instituto de Biomedicina, Caracas, Venezuela.

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 we carried out a pilot study to determine if the 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 67,670 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, 1.51 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 (5 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.
Michael F. S. Guta, Elaine Finley, and John L. Stanford.
Hospital for Tropical Diseases, London, and School of Pathology, UCHMMS, London.

Six 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 (15 patients) or BCG plus 6 x 10⁸ killed M. leprae (18 patients) or BCG plus 1 x 10⁷ dead M. leprae (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 nocardobacterial antigens.
including standard lepromin and non-stimulated 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 Mistry, 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 RECOMBINANT.

A double blind field trial was started with an anti-leprosy recombinant vaccine that was administered in skin-test antigen-positive patients. A positive skin test was an immunotherapeutic and immunoprophylactic agent in a highly endemic region of Rampur District in the Northern Indian State of Uttar Pradesh. A total of 21732 eligible contacts have been screened for mycobacterial infection triggers by a 1M93 booster dose for immunoprophylaxis has been given to contacts of vaccine/placebo showing a complainco rate of 83.41.

IM94 T CELL RECEPTOR USAGE IN BLOOD AND SKIN LESIONS IN LEPROSY.

Caroline Cross1, Maggie Hacken1, Sebastian Luca1, Rabia Haszain1, and Hazel Dookeran1

1 Department of Clinical Sciences, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. 2 Department of Histopathology, University College & Middlesex School of Medicine and 3 Microbiology Department, Age Khan University Medical Centre, PO Box 1500, Stadium Road, Karachi 74000, Pakistan.

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 V and Vh genes in leprosy. In peripheral blood, positive cells were quantitated by FACSscan, while immunohistochemistry was used to stain lesional T cells. T cells expressing V22, V23, V30, V12, V12.5, V5, V66, V82, and V82 were analysed. There was no evidence for deletion of any family of T cell receptor genes in the lesional pathy. Comparing blood and lesional T cells, lesional skin lesions contained more V22 and V23.5 positive T cells than the blood, although there was no connection with the clinical status of the patient. These results show that V22 and V23.5 positive T cells are attractd to or preferentially expanded in leprosy skin lesions - perhaps stimulated by a leprosy superantigen.

IM95 T CELL RECEPTOR USAGE IN BLOOD AND SKIN LESIONS IN LEPROSY.

Caroline Cross1, Maggie Hacken1, Sebastian Luca1, Rabia Haszain1, and Hazel Dookeran1

1 Department of Clinical Sciences, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. 2 Department of Histopathology, University College & Middlesex School of Medicine and 3 Microbiology Department, Age Khan University Medical Centre, PO Box 1500, Stadium Road, Karachi 74000, Pakistan.

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IM93 HUMAN T CELL CLONES RECOGNIZE MYCOBACTERIAL SPECIFIC AND SHARED EPITOPES ON MYCOBACTERIUM LEPRAE 70kD PROTEIN.

Adams E, Britton W J, & Baston A.

Hospita! Center, 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 T cell epitopes we scored 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 (T1-0, restricted by HLA A2 or A4) spans a region containing a deletion restricted to the mycobacterial sequences. The second mycobacterial specific epitope (241-250) was DR1 restricted. A further two epitopes towards the C-terminal end show partial homology with human hsp70. The minimal epitope length of these is 6-4-47 and 471-496. 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 H2Kb and TNF-a, but one also released IL-4 in comparable amounts. Functionally each clone was cytotoxic against autologous EBV targets pulsed with M. leprae sonicate, hsp70 or the specific peptide. Analysis of other C4A 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 specificy were non-cytolytic. Therefore there is a spectrum in cytoxic activity in M. leprae C4A T cell clones.

In summary, the defined T cell epitopes are present in regions distant from major human antibody determinants of M. leprae hsp70.

IM96 MYCOBACTERIUM LEPRAE INFECTION TRIGGERS SYNTHESIS OF STRESS INDUCIBLE hsp 70 IN SCHWANN CELLS AND ANTI hsp 70 ANTIBODIES IN BLOOD.

Vasini Misra, 1 Douglas Young, 2, and Bama Mukherjee 3

1 Department of International Medicine and Microbiology Department, Aga Khan University, Box 3500, Stadium Road, Karachi 7-18101, Pakistan. 2 Medical Centre, Aga Khan University, Box 3500, Stadium Road, Karachi 7-18101, Pakistan. 3 National Institute of Immunology, New Delhi-110094.
National Institute of Immunology, Shalib Jec

Marine 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 marine and primate Schwann cells by metabolic labelling and by immunoblotting with specific monoclonal antibody. 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 IMMUNODEPRESSANT SKIN REACTION MOLECULES ON CELLS WITH IMMUNE POTENTIAL.

R.J. Shannon, Rcclean K., Howo, R.C.,
Hastings, R.C.
1Laboratory Research Branch, GML HD Center at L.OU, P.O. Box 27072, Baton Rouge, La. and 2New York University Medical Center.

Immunocompetent cells of human leprosy patients and in healthy subjects were studied for melanocyte-depleting ability of their surface molecules, ICAM-1 and cytokines such as IL-1 and IL-6. Interestingly, using in situ hybridization and by immunohistochemical methods, we could demonstrate that MC can express NOC class II/tumor necrosis factor (TNF)- and cytokines e.g. IL-1, IL-2, and IL-6. It was shown by using competitive microarray microcytometry and FACScan analysis we could show that normal human MC are capable of phagocytosis. These results are suggestive of an antigen presenting and processing ability for melanocytes. Indeed we could demonstrate that cultured human MC can process intact HSP-65 as well as whole BCG and can present processed antigenic peptides to CD8* cytotoxic and proliferative Th1-like T-cell clones in a MHC-restricted manner. These T-cell clones are specific for HSP-65 and able to destroy melanoma cells. Therefore, these results strongly support the role of T-cell clones in the immunologic destruction of tumor cells of patients suffering from leprosy.

IM89
IMUNOLOGY OF MELANOYCTES IN RELATION TO HYPOMIGENETATION IN LEPOROSY.

Caroline Le Pooie, Tuna Muntas, Rm. M.J.G.J. van den Wijngaard, Wieke Van Denderen,

Departments of Dermatology and Pathology, Academic Medical Center, Unio Amsterdam, and Department of Immunohematology, Leiden, Leiden.

Hypomigration is a feature of all forms of leprosy and predilects for neuronal division of the disease. However, it is strikingly more common in paucibacillary tuberculoid type of the disease. Although there is no strong correlation between cellular infiltrate and hypomigration in leprosy, it is assumed that destruction of melanocytes (MC) which originate from neural crest, is a consequence of local T-cell mediated immune response. The potential importance of MC in the localized 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; Expl.Cell Res. in press, 1993; Expl.Dermatol., 1, p. 95, 1992). Using immunohistochemical methods, we could demonstrate that MC can express NOC class II/tumor necrosis factor (TNF)- and cytokines e.g. IL-1, IL-2, and IL-6. Interestingly, using in situ hybridization and by immunohistochemical methods, we could demonstrate that normal human MC are capable of phagocytosis. These results are suggestive of an antigen presenting and processing ability for melanocytes. Indeed we could demonstrate that cultured human MC can process intact HSP-65 as well as whole BCG and can present processed antigenic peptides to CD8* cytotoxic and proliferative Th1-like T-cell clones in a MHC-restricted manner. These T-cell clones are specific for HSP-65 and able to destroy melanoma cells. Therefore, these results strongly support the role of T-cell clones in the immunologic destruction of tumor cells of patients suffering from leprosy.

IM98
SOLUBLE M. LEPRAE ANTIGEN SKIN TESTING AND LEPROMIN REACTIONS IN CHILDREN WITH LEPOROSY AND THEIR FAMILY MEMBERS.

M.E. Duncan, T.Mike, R. Howe, Demisie, S. Mekoeal, R.Mokets, D.Freese.
Department of Medical Microbiology, University of Edinburgh, UK. Arzuvar Hansen Research Institute, Addis Ababa, Ethiopia.

149 children (K) of patients with leprosy (MB and PB) and healthy controls (NC) were examined. In the study, a positive skin test was defined as a 4-mm induration at 24 hours. The test was considered positive if there was an induration of at least 4 mm at 48 hours. The test was considered positive if there was an induration of at least 4 mm at 72 hours.

IM100
NATURAL KILLERS IN LEPOROSUS LEPOROSY.

L.Saroyants, A.Juscenko, L.Alexseyev.
Leprosy Research Institute, Astrakhan, Russia.

The present work is aimed at studying functional activity of natural killers (NK) in vivo distribution of HLA class I antigens in LL patients belonging to the Russian nationalities. Cytotoxic activity of NK in leprosy patients and in healthy subjects was determined by their response to labelled cells of myelolocytic line K-562. HLA-typing by class I antigens was performed by standard microlymphocytotoxicity test.

IM101
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leprosy functional activity of NK was decreased as compared to healthy donors and inactive patients (p<0.05), being higher in the late 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 $\gamma$<$\delta$ T CELLS

J. Sanchez-Garcia, P. Jenner and M. Colston

National Institute for Medical Research, London, UK.

Most T lymphocytes in human peripheral blood (hpb) express the $\gamma$<$\delta$ T cell receptor (TCR). $\gamma$<$\delta$ T cells expressing the $\gamma$ 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 $\gamma$<$\delta$ T cells. The nature of the $\gamma$<$\delta$ stimulatory molecule(s) is controversial. In this study we have used a variety of fractionation methods to identify these molecules, and to characterise the $\gamma$<$\delta$ T cell response.

We find that virtually all individuals tested show a stimulation of $\gamma$<$\delta$ 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 $\gamma$<$\delta$ T cell response to these molecules has been further characterised 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 RHOMBOID PROTEIN

Cristina Passos, Aimee Stanley, and Patrick J. Brennan

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Fort Collins, Colorado 80523 USA.

The high abundance of some specific polypeptides in uranyl-acetate images of Mycobacterium leprae has permitted their purification in enough quantities to perform their complete amino acid sequence (see Passos et al., Abstract this Congress). In anticipation of the biochemical definition of such proteins, the following approach has recently been undertaken in order 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 66% homology in a 17 amino acid stretch with the N-terminal region of the Streptococcus pyogenes L12 rhomboid 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 rhomboid 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 rhomboids, the characterization of the M. leprae L12 rhomboid gene may favor the cloning of genes commonly arranged in the same operon, such as the genes that code for the $\beta$ subunit of RNA polymerase, the well-known target of the drug rifampin.

(Work supported by NIH, MARD Contract NIH AI-45074)

**MI3**

DETECTION OF MYCOBACTERIUM LEPRAE DNA BY PCR IN SKIN SCRAPIINGS AND NASAL SECRETIONS FROM MULTIBACILLARY AND PAUCIBACILLARY LEPROSY PATIENTS.

T.P. Gillis, E.V. Tan, D.L. Williams, L.G. Villahermosa, M.V.F. Balagon and G.P. Walsh

G.W. Long Hansen's Disease Center, Baton Rouge, LA, Leonard Wood Memorial, Cebu City, Philippines.

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 95% 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 biopsies 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 ml each of transport medium containing Tweens 20 (0.05%). The particulate fraction was recovered by centrifugation and resuspended in 100 μl 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 biopsies 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 optimized. 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 buls 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 observed 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 bul material for diagnosis of both multicenal and paucibacillary patients in early stages of the disease and, additionally, use of nasal secretion for monitoring the therapeutic regimens.

This project was supported by UNDP/W110 Special Program for Research and Training on Tropical Diseases (TDR).

**M15**

NUCLEIC ACID SEQUENCE-BASED AMPLIFICATION (NASBA) FOR IDENTIFICATION AND VIABILITY ASSESSMENT OF M.LEPREAE 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 primer set 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.

**M16**

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 large incubation period of lepr, 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 20 % 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.

**M17**

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 Mycobacterium Database. The following M. leprae DNA sequences were analysed: 65 kba, 36 kba, 28 kba and 10 kba. 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.


**M18**

DETERMINATION OF THE ADENYLATE ENERGY CHARGE (AEC)

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The adenylate energy charge (AEC) defines the proportion of energy-rich adenine nucleotides referred to the total amount of adenine nucleotides. The ratio is given by the equation AEC = [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.marmmatius 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.
The genes coding for antigens 85-A, 85-B and 85-C have been isolated from a 4-Dasch: 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 patterns 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 UPD/WHO Special Program for Research and Training in Tropical Diseases (TDR) and from the Consejo Nacional de Desenvolvimento Científico e Tecnológico, CNPq, Brazil.
shown that PFC is much more powerful in specific determination of M. leprae organisms in skin tissue as compared with conventional acid-fast staining method. Hybridization of the amplified fragments with digoxigenin-labeled 1 kb 36 kb gene probe increased the sensitivity of detection by 10%. A quantitative test to determine the proportion of viable bacilli in biopsy specimens by the PFC 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 SECRETIONS
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Little is known about the scope and importance of subclinical infection or carriage of M. leprae. Given that multicellular organisms 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, we decided to examine rates of nasal carriage in treated and untreated multibacillary 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 added to minimize false negative results, due to inhibitory components from nasal mucosa, swabs were treated with vancomycin-thiocetamide(CDCS) or DMSO. It was found that 59.15(13/22) untreated MB patients were positive compared to 10.52(2/16) 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 ASAY (ECL) : A HIGHLY SENSITIVE METHOD FOR THE DETECTION OF M. LEPRAE INFECTION in NASAL SECRETIONS
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Research Institute for Tropical Medicine, Alabang, Philippines

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 methods, two tests are available; the PCR method and a monoclonal test. The PCR has greater sensitivity but is very expensive, the monoclonal test in 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 FBs, three were test positive and three were negative and one neural type was slightly positive. Thirty nine individuals free of leprosy were used as 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 next 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
IMMUNODETECTION OF 3-6-PHOSPHOCHOLESTEIN (3-PCH) IN NASAL SWAB SPECIMENS
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Se ensayaron 3 sistemas de PFC para la detección de 3-6-PCH en muestras de suero y linfo de pacientes en los cuales se sospechaba la posibilidad de estar infectados con M. leprae porque tenían títulos elevados de anticuerpos en el suero contra este microorganismo.

En el suero no se detectó la presencia de las secuencias de ácidos nucleicos que estos sistemas amplifican mientras que en el linfo los resultados no permitieron detectar bacilos cuando la bacilloscopía era 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 sugar portion and the phosphate moiety in two separate steps: the compounds are re-synthesized intracellularly. Obligate intracellular parasites generally transport high-energy phosphates in the intact state from the host cells. M. leprae prepared from fresh tissues of experimentally infected armadillos or nude mice readily took up [2,8-3H]ATP. Initially, there was a rapid electrostatic binding which in energy-independent. Thisionic 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 [2,8-3H]ATP by M. leprae. Adenosine or 70-had little effect. Evidently, the organism takes up unhydrolyzed ATP by an active transport process. The bacteria possessed an E, ATPase that creates a trans-membrane potential driving transport of solutes into cells, but not an F, 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.

M18
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 cDNA R7 obtained from the lambda g1 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 1186 bp with a G+C content of 43.6%. Computer analysis showed that the GDD 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, M. leprae subsp. luteus, Escherichia coli, and Salmonella typhimurium, respectively. Miccinophilin EF-Tu of Saccharomyces cerevisiae (62.7%) and chloroplast EF-Tu of Arabidopsis thaliana (65.6%) are some of the eukaryotic EF-Tu's 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 asteroids suggests that the gene is highly conserved among these species.

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 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 unpaired cells, bacteria as well as eukaryotes, 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 Middlebrook 7119 for 2-3 weeks in the presence of disulfiram and acriflavine. The susceptibility of M. leprae to various drugs was determined by monitoring the intracellular Na+/K+-ratio. The rational behind this approach is the ability of all living unpaired cells, bacteria as well as eukaryotes, 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.

In order to determine the effect of drugs on the physiological state of M. leprae, the intracellular Na+/K+-ratio was measured. The ratio was determined by using an ion sensitive probe and an ion sensitive microelectrode. The results showed that the intracellular Na+/K+-ratio of M. leprae was significantly reduced in the presence of disulfiram and acriflavine. The reduced Na+/K+-ratio was correlated with an increased intracellular Na+ concentration. The increased Na+ concentration was not accompanied by an equivalent decrease in intracellular K+ concentration. Therefore, the reduced Na+/K+-ratio was not due to a specific effect of disulfiram and acriflavine on the Na+/K+ pump. The results suggest that disulfiram and acriflavine affect the physiological state of M. leprae by inhibiting the Na+/K+ pump.

Results of mice foot-pad harvests showed that decontamination affected the viability of M. leprae, whereas centrifugation and purification did not show any effect. Bacilli survived up to varying periods from 7 to 90 days under different conditions of maintenance and preservation. Thirty minutes of ultra-violet ray exposure killed all bacilli. However, 75% of alcohol was effective in killing bacilli within 15 minutes.

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 immunodotting, 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.

We have used immunogold ultracytochemistry to label in situ the 65 kDa heat shock protein in 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 armadillos and in skin biopsy tissues of humans with Hansen's disease, both before and after starting 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 the specific antibodies were a gift of Dr. D.A. van Embden, national Institute of Public Health and Environmental Protection, Biotenhein, The Netherlands). Interestingly, the immunocytochemical staining 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 immunodotting, 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.

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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 bacillary and antimycobacterial drugs.

M123

ASSESSING THE VIABILITY OF MYCOBACTERIUM LEPRAE ON TS 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 mycobacteria leprae in skin swabs taken from 31 previously untreated M. leprae cases in the period MDT. According to the theory of the FDA-EB staining technique, green cells were regarded as viable, red as dead, and dual stained bacilli as viable. The results of this study showed that the average percentage of green cells was 72.23% (range 7.5% to 84.4%) before MDT, 20.44% (range 1.2% to 72.3%) after 1 month, 14.74% after 3 months, 5.44% after 6 months, 1.15% after 12 months, and 0.35% after 16 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 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 16 months MDT, indicating that they were in need of a certain period of continued intensive treatment. Compared with the findings of this method, BI and MI values were not considered reliable in the assessment of the viability of Mycobacterium leprae.

M124

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 antmycobacterial 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 results were compared to the DNA and RNA content of the mycobacteria. Although no decrease in the DNA content was seen, a slide number of 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.

M125

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 IL patients), M. lipo 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 on the presence of any forming units in a solid medium. M. leprae were introduced into cathode fraction and of salt solution at a dose of 10^-6 - 10^-7 microorganisms per ml and incubated at 20°C and 37°C. In 1, 2, 3 and 4 weeks, 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 during an for 1-4 weeks, evidenced by the development of infection in mice.

M126

A RAPID IN VITRO MICROALISAY FOR 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 16S rRNA mRNA detected by reverse transcription linked PCR amplification. The hypothesis is that because of the short half-life 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 DNA purification in CsCl gradients. cDNA is synthesised from total RNA with reverse transcriptase using a 3' gene specific primer for the 70kDa antigen (DnaK homology) 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 DRAKE 1 treatment. Using a recombinant truncated artificial mRNA template for the 70kDa gene mRNA, the RT-PCR assay can detect down to 1 pg of mRNA: equivalent to 10^9 bacilli. Currently we are able to detect down to 1 fg of mRNA: equivalent to 10^7 bacilli. These results are based on a 3-log fold killing confirmed by cathele fraction and of salt solution at a dose of 10^-9 amarsidil derived M. leprae with a viability of 0.005%. Three of 6 M. leprae infected nude mouse footpad mRNA preparations gave 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.

M127

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 thymidine sodium is being reported. This has been found to be successful as the organisms, after multiplying vigorously in the thymidine 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 resilient organism is due to stimulating effect of thymidine 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 cotton mice treated with DNP 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 up a new era in the preparation of purified vaccine, the study of in-vitro drug sensitivity, and as such ensure rapid eradication of leprosy.

**M128**

**EFFECTS OF PALMITATE ON THE GROWTH OF MYCOBACTERIUM LEPRAE UNDER DIFFERENT GASEOUS ENVIRONMENTS.**

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Low oxygen tension has often been considered an important factor 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 and 20 weeks of incubation under gas mixtures containing 2.5% O2 and 5 or 10% CO2 as well as under air. The use of different gas mixtures is tedious, laborious and time consuming. Therefore, attempts were made to use only one gas mixture in the cultivation media.

Three different gas mixtures or air were used: 1. 10% CO2, 8% O2, 82% N2; 2. 2% O2, 2% CO2, 96% N2; 3. 0.2% O2, 0.1% CO2, 99.7% N2. It was found that none of the gas mixtures selected could replace the atmosphere of all of the experiments. However, of the three gas mixtures tested, the best results were obtained with the mixture of 10% CO2, 8% O2, and 82% N2. Palmitate appeared to act synergistically with the atmosphere of the growth medium. The addition of palmitate to the gas mixture increased the number of bacilli in the liquid media. Palmitate was found to be beneficial for the growth of the organism in both liquid and solid media. The growth of the organism was not significantly affected by the presence or absence of CO2 in the atmosphere. Palmitate was found to be beneficial for the growth of the organism in both liquid and solid media. The growth of the organism was not significantly affected by the presence or absence of CO2 in the atmosphere.

**M129**

**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, the 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 Ongawa media with interleukin-2, interferon-y, or O-2 alone or in combination. Incubation temperature was 36°C, without CO2. 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. Myprae and interleukin-2, 5-6 months after the initiation of the cultivation. Above colonies could be observed 1-2 months earlier in the test tubes with M. Myprae, interleukin-2, and interferon-y. But no colonies could be seen in all the test tubes without M. Myprae or interleukin-2.

2. The size of the colonies grow 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-y, and probably other cytokines, which would turn out to be the essential growth factors 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.

**M130**

**A COMPARISON OF DNA/HNA, MYCOLATES, PGL-1, ANTIENRIGENCY, ENZYMES, MORPHOLOGY AND STAINING CHARACTERISTICS OF THE LEPROSY BACILLI WITH THE LEPROSY-DERIVED CHEMOAUTOTROPHIC Nocardiform Bacteria (In vitro).**


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The chemoautotrophic nocardiform (CAN) bacteria isolated in the culture media of different LL cases so far as well as from the mouse footpads (MFP) and armadillo tissues experimentally infected with *M. leprae*. Those CAN bacteria and *M. leprae* have been compared on the basis of their morphological, staining, biochemical and enzymological characteristics, and found to be extremely similar. Both the organisms also exhibited closely similar or identical patterns of lipid profiles, energy and 'Nitrova' responses to a large number of LI and T1 cases respectively, PGL-1 specificity, as well as, for DNA characteristics and resistances to γ- and UV-radiations. All were DOPA oxidase positive and lost acid-inhibits due to pyrimid extraction. The comparative study and an evaluation of all the above characters reveal an extreme closeness of the CAN bacteria to the leprosy bacilli to a point beyond which it may not be possible to distinguish them from each other any further.

**M131**

**DETECTION OF PGL-1 IN THE CHEMOAUTOTROPHIC Nocardiform (CAN) BACTERIA.**

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PGL-1 is a unique *M. leprae* antigen, detecting which may lead to identification of *M. leprae*. We have investigated the presence of PGL-1 In the in-vitro CAN-cultures derived from human, mouse-footpad and armadillo tissues infected with leprosy bacilli.

For this purpose, antisera were produced in rabbits against the 4 CAN bacterial suspensions. Microtiter gelatin particle agglutination test (Serodia 11L1-gelatin, Japan) had been used to detect and assay anti-PGL-1 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-1 antibodies to be present in
the immune sera. Biological controls, human serum (LL) and normal rabbit serum controls were used to exclude false positive reactions 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 antibody, one way or other so as to develop strategics to characterize specificity etc. the present test becomes significant rising antibody titres.

In the light of other tests reported previously, e.g. chemosautrophism, lipid profile, DNA(RK) specificity etc. the present test becomes significant with respect to the true identity of the CAH bacteria, viz-a-viz M.leprae. The close parallelism observed between lepromin and the CAH-ALs is thus explainable.

M34

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 membranes. It was enzymes, in particular the activity of macrophage myeloperoxidase. The present work is devoted to electron cytochemical study of myeloperoxidase (MPO) activity in active LL patients. Various activity and distribution localization of MPO in macrophages correlated with the degree of completeness of M-lepraemurium 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 mycobacterial cell. A close parallelism was observed. On the contrary, in macrophages with low level of MPO activity M-lepraemurium was not viable. Observation of MPO-activity in macrophages of leprosy granulomas in long-treated BL and AV 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.

M33

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, by a reduced microcapsule, thickened cell wall and condensed cytoplasmic matrix with poorly differentiated ribosomes and nucleolide, 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 cytoplasmic membrane and rare inclusions ("homogeneous bodies") in their cytoplasm. These strains differed from the 1st passage by the absence of "homogeneous bodies", pronounced nucleolide and more developed mesosomes. For ML of the 3rd 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 ultrastructure 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 biotechnological developments as well.
the single passage on armadillos, was not disco-
covered. The data obtained should be taken into
account in taxonomical studies on M. leprae passed
on laboratory animals, and when deve-
loping novel experimental leprosy models, speci-
fic diagnosticus 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 capa-
cable 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 pro-
teins 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 overex-
pressing the proteins in E.coli as fusion pro-
teins using a variety of expression systems
(i.e. pUC8-2, pG021, pGElX-3 and pVW500).In
the present paper we will discuss the characte-
rization, 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 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
ion. However, the 4.5 kb insert DNA from this clone was sub cloned
into pBluescript expression vector and expressed in E.coli HB101
as maltose binding fusion protein. The affinity purified fusion protein
showed strong reactivity with leprosy patients 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,
and weak reactivities. Sequence determination of these clones
showed that clone R9 has part of the gene coding for 15 kDa
protein.

MI38
CHARACTERIZATION OF M. LEPRAE STRAINS BY RFLP
ANALYSIS OF AMPLIFIED tRNA
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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 cultivated only from highly bacillated
leprosy types. Earlier studies on strains grown in experi-
mental animals showed very little divergence among such
strains. In this study, nucleic acids from biopsies of
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 targeting variable regions towards the
ends and flanking regions of ribosomal RNA genes, tRNA
fragments were amplified. These were restricted with
different restriction endonucleases and hybridized with
ribosomal RNA probes by the techniques reported by us
earlier. The origin of amplified tRNA was confirmed by
using a set of oligonucleotide probes targeting specific
sequences on tRNA genes of M. leprae. The comparison of
patterns obtained after restriction with different
restriction enzymes revealed interesting findings. Overall,
strong resemblance among the different strains was observed.
However, some diversities have also been observed. The
relevance of these findings is being investigated further
at sequence level and in larger number of strains. Amplified
tRNA restriction analysis appears to be promising for rapid
identificiation and characterizing of M. leprae directly from
the lesions in leprosy cases.

MI39
DEVELOPMENT OF IMPROVED TECHNIQUES FOR EXTRACTION OF NUCLEAR 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
acids from leprosy cases have been developed. For
the optimum application of these methods, the extraction of
tissue nucleic acids is an important step. Techniques reported
for extraction of nucleic acids from tissue include physical as well as
chemical approaches. In this study, different techniques for tissue
homogenization such as freeze--
thawing, freeze-boiling, Proteinase K treatments for 1 to
16 hrs and a new modified lysyza/EDD/proteinase K method
(followed by stepwise purification whenever 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 RNA by oligonucleotide probes
and for gene amplification by primers targeting 18S,
36S genes and reverse transcription-amplification of tRNA
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 method from this study
was standardised in this laboratory. By using different
methods of nucleic acid extractions, nucleic acids
were extracted from biopsies from various
geographical locations in India,

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 (PGCL-1). The other is ELISA method using
bacterial cellular protein(s) as antigen(s). Among these methods cross
reactivity with another Mycobacterium was one of the major problems.
To establish a new reliable method, antigenicity of bacterial
protein is very important.

In this study, we planned 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 BCG complex of M. tuberculosis.

2) Recombinant α1 antigen of M. leprae has been constructed and purified by amiono resins affinity chromatography. More than 20 mg of recombinant protein was obtained from 250 ml liquid culture.

3) Antibody titer against recombinant α1 antigen in the serum of leprosy Al. antigen was lower than those between unrelated in sequence and differ in size, suggesting that there has been positive selection 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 recently reported the cloning and characterisation of the recA gene of Mycobacterium. This gene is very unusual in that it contains a protein splicing element which is removed post-transcriptionally.

We have now characterised the Mycobacterium recA and found that it too contains a protein splicing element. However the Mycobacterium and Mycobacterium 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 recA seen in Mycobacterid and Mycobacterium.

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 1 (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 and eight peptides from MMPI were sequenced 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 Dr. Brigitte Gisquiel 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 lepromatous bacillus are close to complete definition.

(Worl supported by NIH, NIAID Contract No. 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 mycolarabino-glucan-1-pentoseglucan (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 arabinose ends are occupied by branched hexa-arabinofuranosyl and linear tetra-arabinofuranosyl arrangements, giving a product now designated as AraLAM. However, the same arrangements are capped extensively with mannos-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 organic fragmentation. To minimize wastage of M. leprae, pilot studies were conducted on M. intracellulare 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 2-13 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 cytoplasmic fractions. SDS-PAGE and Western blot analysis of the fractions revealed significant differences in terms of the various proteins and carbohydrates. The 63 kDa protein was significant only in the cytoplasmic fraction. The 71 kDa and 18 kDa HSPs and the 28 kDa (GOD) protein were seen in the cell wall and cytoplasmic fractions but were totally absent in the membrane. The 63 kDa HSP was mostly membrane-associated. LAM was predominant in the cytoplasmic 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 and to assess their role in the pathogenesis of leprosy.

(Work supported by NIH, NIAID Contract No. AI-05074.)
M146
RECENT RESULTS ON IN VIVO DRUG EFICACIES 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 bacillary epithelioid cells. In this study, we found that the Na+,K+-ratio of a strain present in complex glycopilinds. As an alternate source of glucose, we incubated M. leprae in the presence of uridine-5'-diphosphoglucone (UDPG). The results revealed that significant amounts of GDP, and ATP were released in the presence of labeled UDPG. Organisms which do not glycolyze glucose, may use other metabolic pathways, e.g., glutamate oxidation. When Na+-glutamate was incubated in the presence of M. leprae, Na+ 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. These observations have therapeutic implications.

M147
THE EFFECTS OF RIFAMPICIN AND CIPROFLOXACIN ON MYCOBACTERIUM LEPRAE IN VITRO AND ITS CORRELATION WITH VIABILITY
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Rifampicin is a potent anti-nycrotbacterial drug whereas Ciprofloxacin is a broad spectrum drug also possesses anti-nycrotbacterial activity. The effect of these agents on mycyclic acids was investigated and correlated with their killing mechanisms(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 analyzed by H-TLC and ATP photometry respectively. The results showed drastic reduction in the level of mycolates which were 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, mycyclic acid contents were found to remain intact. The biosynthetic as well as catalytic processes are affected by Rifampicin at very high concentrations leading to preservation of cell wall skeleton. In case of Ciprofloxacin, catalytic process seems to be less affected thus leading to continuing degradation process. These observations have therapeutic implications.

M148
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 association 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 said colonies 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, and 20 by measuring the CTLA-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 microorganisms.
2. The IL-2 activity in the media with the autoclaved was 4-6 times higher than that in the ones with the nonautoclaved on days 10 & 20.

These data strongly suggested 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.

M149
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 biopsies, 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.

The cosensual ophthalmotonic reaction (Ton) describes a 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 Ton is mediated via a nervous reflex mechanism. In this study the Ton is introduced and without ocular involvement. The Ton and the primordial usage of the Cor I in the eye clinics will be discussed.

Chemoautotrophic nocardioform (CAN) bacteria have been repeatedly isolated from infective 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 bacillus leprae. For further studies on their taxonomical relationship with leprosy bacillus, energy or other contrarily, Mitsuda-type responses towards 4 of these CAN - AGs and a control lepromin were tested on 93 LL, 1T and borderline cases of leprosy, categorized clinically and bacteriologically. Final results were obtained from 72 cases. The antigens injected per patient varied from a maximum of 5 to a minimum of 3. The suitability standard of the control lepromin was verified first in 4 T1 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 35 TT cases showed clearer, close 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.

Periodic examination of eyes were done for leprosy patients attending this centre. The condition of eye in 649 patients for a period ranging from 5 to 20 years (mean 8.29) are discussed. Throughout this period, 438 (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.D, 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 with 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.

The cosensual ophthalmotonic reaction (Ton) 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 I is mediated via a nervous reflex mechanism. In this study the Cor I was determined in normals and in the leprosy patients with and without ocular involvement. The Ton and the primordial usage of the Cor I in the eye clinics will be discussed.

OP1
A LONUDITUDINAL FOLLOW-UP STUDY OF EYES IN 649 LEPROSY PATIENTS

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OP2
CONDENSUAL OPHTHALMOTONIC REACTION IN LEPROSY PATIENTS

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The cosensual ophthalmotonic reaction (Ton) 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 I is mediated via a nervous reflex mechanism. In this study the Cor I was determined in normals and in the leprosy patients with and without ocular involvement. The Ton and the primordial usage of the Cor I in the eye clinics will be discussed.

OP3
OCCULAR 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 RFT cases in India. This study deals with the remaining ocular lesions in such RFT cases. This series of 6,000 RFT cases (with 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 highlight 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 peroneal or paralysis of orbicularis oculi with resultant lagophthalmos. Many of the patches over the face (primary or following type-I reaction) are predisposing to the development of lesions over the face and in the orbit. 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. specific around the globe, orbit, 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. specific around the globe, orbit, or keeping the eyes at risk.

OP5

A CASE ANALYSIS OF THE PATTERNS OF CATARACT AND CORTICOSTEROID USE 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 most 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 (flare and cells). The intraoperative and postoperative complications will also be assessed. This will be done at discharge and one month after discharge.

Cataract extraction will be done using a cryoprobes under retro bulbar anesthesia. Visual acuity will be taken using a Snellen's chart. Intraocular pressure will be assessed using a Goldmann applanation tonometer. Examination of the corneal structures will be done by a slit-lamp biomicroscope. Postoperative visual acuity will be taken every two weeks after surgery.

In the leprosy group classification will be made into the type of leprosy HIF or BIF. The activity of the leprosy will be assessed by studying the histopathological and microbiological indices.

OP6

RISE 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 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 (7.12%) had monocular or binocular sight impairing cataracts. Univariate analysis showed that cataract was associated with a number of other clinical eye findings (lagophthalmos, corneal surface abnormalities, corneal hypoplasia, chronic uveitis), demographic characteristics (age), and leprosy type and monotherapy. Logistic regression analysis found that cataract was associated with chronic uveitis and chronic 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 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 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 23.5% 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 the time of 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.

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

Paul Courtright, Lu-Fang Hu, Huan-Ying Li, Susan Lewallen

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 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 23.5% 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 the time of 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.
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 it is believed to be, and may not be a very useful indicator of early intraocular involvement.

The results of the study will be presented and discussed, related to age, sex, type of leprosy, duration of the disease, occurrence of type I and type II reaction and smear status of the patient.
However differs significantly from the CS of both the control group and the paucibacillary patients. The results support our hypothesis that a loss of corneal sensation in leprosy patients is mainly due to secondary atrophy of corneal nerves or to multiple ocular pathology.

PATHOLOGY

PA1

HISTOLOGICAL AND IMMUNOHISTOCHEMICAL CHANGES OF ECCrine SWEAT GLANDS IN LEPROSY

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Histopathological and immunohistochecmical changes of eccrine sweat glands were investigated in skin biopsies taken from four hundred leprosy patients covering the whole spectrum of the disease and including indeterminate group. The histological findings that may indicate the impairment of sweat function are: 1) intralobular retention of secretory material, 2) cystic dilatation of ductal and secretory segment, 3) atrophy-vacuolization, absence and the formation or 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. 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 AND LAM-B ANTIGENS IN PARAFFIN SECTIONS OF LEPROSY SKIN LESIONS

Tiesheng Wang*, Shintco Izumi, Khalid Iqbal Butt,
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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 controls, and only the LAM-B antigen appeared in the tuberculosis specimens in which the PGL-I antigen was negative. The antigens were identified as intracytoplasmic bacillary staining, in solitary, granular as well as debris patterns; and as soluble antigenic staining in vacuolar or amorphous pattern. The PGL-I antigen was demonstrated on thirty-three samples except one IT sample and the LAM-B antigen, on all samples by the 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 unchanged. The results indicate that the specificity and sensitivity of the immunochemical staining technique used in this study are suitable for both the application of diagnostic pathology and the research on the pathogenesis of leprosy. Particularly the immunochemical 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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Shin-ichi Kitajima
National Institute for Leprosy Research, Japan

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

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

Results and discussion: (1) PGL-I and BCG were clearly stained in leprosy skin biopsies. By both antibodies, solid bacillus were stained as granular pattern, and degenerated bacillus as vaculated pattern. Even in the regression stage and Fave's staining is negative, immunostaining remained to be positive, which indicate the efficacy of PGL-I immunohistochemistry for the definite diagnosis of doubtful leprosy cases using routine paraffin sections. (2) In all the autopsy cases of cured lepromatous leprosy, PGL-I 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 ambiguous, facial, hypoglossal, 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.
The role of TGF-β in the genesis of the lesion of leprosy patients was investigated by immunohistochemical studies of skin biopsies from patients with different clinical forms of disease using a polyclonal TGF-β antibody. Our results show that the presence of moderate reaction located in basal epidermal cells of normal as well as in leprosy skin, however in patients with erythema nodulon leprosy type ENL and lepromatous leprosy LL. We also observed the presence of intense staining in dermal and hypodermal inflammatory infiltrate while lighter staining occurred in those infiltrate present on the skin biopsies from patients with tuberculoid leprosy TT. No reaction was observed in these biopsies when the TGF-β antibody was preincubated with TGF coupled to Sepharose resin. These results suggest that TGF-β may be an important factor in 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 ENL (TB) phlegmonous cases were detected in patients of ENL. The results of these cases confirmed to have leprosy on the basis of the nerve damage in the epidermal granulomas. In the ENL, 20 cases were confirmed to have leprosy based on the presence of epidermal cells in the skin sections. The S-100 protein stain provides an efficient aid to 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**

Marian Ridley and Michael Waters

Hospital for Tropical Diseases, London, UK

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 epitheloid cell granulomas due to the presence of bacilli, exerted a primary influence on both spread of infection and reaction in the associated skin area.

**PA7**

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

A.B. Marques, R. Fleury, F. Reis Vianna, J.C. Avel-leira


Ten lepromatous and two borderline-lepromatous patients were injected intradermally with 0.1ml close of BCG vaccine (Moreau-Rio strain, Atulpho 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 hiperonic ring surrounding the sixth BCG injection place; the other was done at the deltoid region of the left arm, where no Leprosy lesion could be seen. Both Lepromin tests were read after twenty-one days, and also biopsied for histopathological examination.

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

**PA8**

**HISTOPATHOLOGICAL ANALYSIS OF SPECIMENS OF BCG-IZED REGIONS OF MULTICILILLARY LEPROSY PATIENTS UNDER MULTIDRUG THERAPY.**


Fifteen lepromatous and two borderline-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 previously untreated, lepromin-negative and submitted to multidrug therapy as recommended by W.H.O.

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

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

**PA9**

**MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL FINDINGS IN ERYTHEMA MULTIFORME IN LEPROSY.**

A. Miranda, C.P. Miguel, J.A.C. Nery and E.N. Sarno.


Erythema Multiforme (EM) is an uncommon manifestation of a reactional episode in leprosy patients. It is probably due to a recurrence of the same mechanisms involved in the pathogenesis of
Erythema Nodatum Leprosium (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 4 cases of ENL were studied by biochemical 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. Fibroblast 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 T cells. These vascular findings in association with a usually thickened epidermis and concomitant lesions. To further characterize the morphological

This study was financed by WHO grants.

**PA10**

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

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

The placenta 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-iodamide fluorescent Acid-fast bacilli were found in eleven placenta and nine of them also showed villitis. Twenty percent of the newborn were premature and 25% had less than 2500 g. Newborns from mothers with lepromatous leprosy showed in average a sexed fold higher serum anti PGL-I antibodies.

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

Supported by CNPq grants.

**PA11**

**HISTOPATHOLOGICAL ANALYSIS OF SKIN BIOPSIIES 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 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 BIOPSIIES IN PAUCIBACILLARY (PB) BORDERLINE TUBERCULOUS HANSEN'S DISEASE (BTHD)**

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

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

Results: Multiple patches in 64% of patients. Maximum number of patches was 14. 83% of patients had enlarged nerves. An unusual clinical feature was detection of areas of anaesthesia in addition to patches in 64%. 50% of such patients showed AFB in the skin and/or nerves. Clinicohistological concordance by skin biopsy was in 76% and by nerve biopsy in 55% of patients. Histological correlation in the skin and nerve was seen in 56%. Among histologically diagnosed BTHD patients, 50% showed AFB in the skin biopsy while 90.9% had AFB in the biopsied nerves. Lepromin was positive in 3.4% patients.

This study emphasizes that present classification of MB and PB HD by skin smears alone is inadequate, since 83% of patients who were skin smear negative showed AFB in the skin and/or nerve.

**PA14**

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

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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 granulomatosus 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 I (classic granuloma) to 4 (anergic tuberculosis) in lymph nodes from ten HIV positive Zairians with tuberculosis arthritis. Acid-fast bacilli (AFB), Grocott Methenamine Silver (GMS), and Jones stained sections were examined. Successive sections were studied for the quantitation of L68 positive cells (T lymphocytes), CD4 positive (T helper cells), UCHL-1 positive cells (T cells), and KP-1 positive cells (macrophages). Histologic grade, relative proportions of cell types, AFB cases 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 lymphomatosus response to HIV infection alone to tuberculous lymphadenopathy in HIV infection. In the tuberculous cases, relative proportions of cell types vary according to the histologic grade. In patients with severe immunosuppression, the causative granulomatosus response was replaced by a plasmocytic infiltrate and caseous necrosis. PPDnergy correlated with absence of Langhans giant cells. AFB cases in tissue were inversely related to peripheral CD4+ counts and histologic grade, and in patients with advanced AIDS (CD4+ <10%) were not affected by any subsequent antiretroviral 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

Wu Zhihua, M.D., et al
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Five male patients with histoid leprosy occurred in the lepromatous leprosy were observed histopathologically. Age range from 14-57 years. The duration of the lesions varied from 4 months to 1.5 years. Skin biopsy was taken from the nose with surrounding healthy skin of histoid leprosy. The specimens were fixed in 10% buffered formalin solution and processed for paraffin embedding. 7 thickness sections were cut and stained with hematoxylin and eosin, toluidine blue, elenin and Farrow's acid-fast method.

In histoid leprosy, in addition to the dense infiltrates of macrophages, fibroblast, etc., the proliferation of various degree and the degradation 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

MICOBACTERIUM LEPRAE IN MAST CELLS IN HISTOID LEPROMA

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In this paper, a leprosy patient in relapse with widespread lesions of histoid leprosy was presented. Histological examination confirmed the diagnosis of histoid leprosy with high BI (4+). With Giemsa stain, the slide showed that the number of mast cells in the lesion was much more than that in the surrounding healthy skin. Under TEM, the close contact or apposition of mast cells to M. leprae was found. Meanwhile, in the cytoplasm of some mast cells, the intact M. leprae were seen. These findings had not been reported previously. The possible role of mast cells in the histopathogenesis of the lesion was discussed.

PA18

CONJUNCTIVAL BIOPSY IN PATIENTS BEARING HANSEN'S DISEASE

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

The investigation was made with biopsy of the bulbar conjunctiva on the upper temporal quadrant of the right eye. The patients were from 3 groups: 1) untreated patients, 2) during treatment and 3) those who were in observation after the end of medicamentous therapy.

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

PA19

LIDOCAIN HISTOCHEMICAL/HISTOLOGICAL STUDIES

OHSU, RSET.

# A prospective study of lidocaine involvement in leprosy was conducted in 30 patients (10 per leprosy group): 1) Indeterminate (10), 2) Borderline (10), 3) Lepromatous (10). Lidocaine was administered to patients' eyes for 20 minutes during treatment and 45 minutes post-treatment.

The authors have examined 30 patients's eyes with Hansen's disease, equally divided among the forms: Tuberculoid (10), Indeterminate (10) and Lepromatous (10).

This study was made with biopsy of the bulbar conjunctiva on the upper temporal quadrant of the right eye. The patients were from 3 groups: 1) untreated patients, 2) during treatment and 3) those who were in observation after the end of medicamentous therapy.

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

PA20

QUANTITATIVE MORPHOLOGICAL METHODS FOR ASSESSMENT OF THE EFFECTIVENESS OF ANTILEPROSY THERAPY

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Leprosy Research Institute, Astrakhan, Russia

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 system, skin granulomas in biopsied skin lesions from 50 leprosy patients were studied by the following parameters: volumes percent of "leprosy" macrophages (LM), histioccytes-monocytes (H-M), bacterial index of granuloma (BiG), lymphocytes (L) and epithelioid cells (E). Active LL patients showed the following cytohistogram: LM=80%, H-M=10%, BiG=10%, L<5%, E>50%. As the disease regresses, the cyto-
The clinical, laboratory and autopsy data of 34 patients with type II reaction (THIR) of Hansen’s Disease were collected. The clinical and laboratory aspects were evaluated and correlated with the anatomic-pathological findings. The THIR of the disease in severely ill patients are more significant in males, white, old, long term and progressive course of the disease. Virchowian form of the disease, presence of cutaneous, mucosal and neurological sequelae, irregularity of the treatment, high serum levels of bilirubin, leucocytosis and high erythrocyte sedimentation rate.

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

PA23
ANALYSIS OF 98 AUTOPSY CASES IN A JAPANESE LEPROSARIUM
Shin-ichi Katsuragawa, Masamichi Goto, Chikahiro Nakatani, Satoru Hagio, Masaomi Imaizumi, Eiichi Sato*
Shin-ichi Kitajima, Masamichi Goto, Chikahiro Nakatani, Satoru Hagio, Masaomi Imaizumi, Eiichi Sato*
Department of Pathology, Faculty of Medicine, Kagoshima Univ., Kagoshima, Japan

Histological findings on 220 biopsies from 56 LL, 26 BL, 106 BT and 32 TT cases were presented. Biopsies were taken from MB cases after 24-36 doses and from PB cases 6-12 doses of MDT. Histopathological examination showed granulated bacilli in 40% and persistent macrophage granuloma in 58% of cases. The macrophages were markedly vaculated with few giant vacules. Nucleo bodies and Riesner nests were observed in 90% and persistant macrophage granuloma in 58% of cases. The highest granuloma fraction was 40 and 25% in tuberculosis and lepromatous cases respectively. Of the cases without a granuloma 30% of leprosous and 28% of tuberculous 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.
PA24
SECONDARY AMYLOIDOSIS IN LEPROSY

A. Abulos, Tranquilino T. Payardo, Jr., Lauren G. Villahermosa and Gerald P. Walsh

Postmortem examinations were performed on 35 leprosy patients at Eversley Childs Sanitarium in 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. 1 borderline lepromatous, 1 borderline, 1 tuberculosis 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%, thyroid gland, lungs, blood vessels, prostate, lymph nodes, urinary bladder, gallbladder, and by infiltrating granulomas from the alimentary disease (5:5%).

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

PA25
ACTIVITY OF THE PROTECTIVE ENZYME SUPEROXIDE DISMUTASE AND THE LEVELS OF LIPID PEROXIDE IN THE SKIN SITES OF LEPROMATOUS LEPROSY WITH TYPE II REACTIONS

Reena Chandrashekhar, Isukapalli, Margaret, John Stanley, Solomon Vinaya Kumar and Joseph Colston

In a Japanese Leprosarium Hosuzuka-Kaien, 151 patients died of disease from 1982 to 1992, and 98 cases of them were autopsied (average age 78:1, M60, F38). There were 29 males and 6 females ranging in age from 12 to 68 years. The main cause of death was malignant tumors (33.34%), respiratory disease (29.30%), cardiovascular disease (15.15%), cerebrovascular disease (10.05%), alimentary disease (5.5%) and others (6.65%). Malignant tumors were 32 carcinomas (oesophagus: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 laryn).

Amyloidosis were three cases (L2, T1). Among the cardiovascular disease, heart disease were 9 cases (9%) and its frequency is less than the average (19%) of Japan. Dementia was observed in 14 cases (cerebral dementia, 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 lepromatous, 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.

PA26
SIGNIFICANCE OF CELLULAR MORPHOLOGY OF MITSUDA LEPROMIN RESPONSE

Vedanta K. Besikan and Rameshwar K. Girdhar

Leprosy Histopathology Centre, Sevagram 442 102 and Central JAUNA Inst. for Leprosy, Agra, India.

The lepromin reaction with Mitsuda Leprosin 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 in leprosy in different stages indicates the changes seen in different stages of disease. Lepromin tests were performed on 32 patients of leprosy. One 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 BB/BL patients, lepromin histology consistent with tuberculoid granuloma was seen in 16 cases. Likewise in BB/BB patients, macrophage granuloma was seen in 6 cases. In mid-borderline patients, the histological picture of lepromin granulomas 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 N. lepra infection.

PA27
PATTERN AND SPREAD OF OCULAR LESIONS IN MULTI-BACILLARY LEPROSY: A HISTOPATHOLOGICAL STUDY

M Jacob

S L R T Kariqiri, Tomilnoudu 632 106

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

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

The spread of bacilli is predominantly through blood vessels, neurovascular complexes and by infiltrating granulomas from the conjunctiva into the corneal, ciliary body, iris, anterior choroid and anterior ciliary nerves. The second route of dissemination is the conjunctivitis to the sclero and episclera. Macrophages with bacilli were seen around the optic nerve and sheath in one eye. The third mode is the spillage of macrophages into the...
vitreous and the inner surface of the retina, when there is heavy lepromatous infiltration of the anterior uveal tract. One eye showed changes in the posterior ciliary nerves without involvement of the adjacent tissue.

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

**PA28**

**ULTRASTRUCTURAL ALTERATIONS OF Dermal Nerves in Early Forms of Leprosy**

J.L.G. Antunes & F.N. Sarno, Department of Pathology, Hospital Antonio Pedro, Universidade Federal Fluminense, Niterói, Brazil and Department of Leprosy, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil.

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

Fernando Orfúncio, Daciane Miranda, Leucia Borato

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

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

**PA30**

**HISTOPATHOLOGICAL EVOLUTION OF FB PATIENTS UNDER WHO REGIMEN.**


Several published papers argue the efficacy of paucibacillary regimen proposed by WHO in 1982. Some authors propose an addition of six months dapson monotherapy. Histopathological examination in one criteria adopted by them to ascertain disease activity.

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

**PA31**

**THE EFFECT OF TREATMENT ON LEPROSY PATHOLOGY**


Department of Pathology, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland, UK.

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 CHEM-O-IMMUNOTHERAPY IN BD LEPROSY.**


Institute of Pathology-ICMR, National Institute of Immunology and Deptts. of Dermatology, Safdarjang & Ram Manohar Lohia Hospitals, New Delhi, India.

Under the immunotherapeutic trial being conducted at New Delhi with Mycobacterium w., 257 out of the 380 originally induced 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-ML & 21-88) from the group receiving MDT and vaccine and 127 (72-LL, 34-ML & 20-88) 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 leprosy conversion is seen in the vaccine group with the lepromin site biopsies showing well-developed DTH reactions. The histopathological observations correlate well with the clinical and bacteriological data. Nerve biopsies from 8 skin B1 negative Li cases done for persisting organ-isms 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**

Jay Palra, S P Mahesh, H A Khan, S Saral

The Leprosy Mission, Barabanki, U P, India.

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

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

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

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

**PS2**

**A STUDY ON THE NON-DEHABILITATED AND DEHABILITATED LEPROSY PATIENTS**

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

The objectives of the study are: (1) To identify the various factors involved in the process of dehabilitation of persons afflicted with leprosy. (2) To find out the causes why certain patients were not dehabilitated irrespective of their disabilities (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 help. (5) To help to reduce the number of patients who would require rehabilitation through prevention of dehabilitation.

**PS3**

**COMMUNITY PERCEPTION OF LEPROSY IN KERALA (SOUTH INDIA)**

Alexander Thomas, Rebecca Alexander, Vincent Lawrence, R K Mutatkar.

The Leprosy Mission, Pathappallym P0, Manjeri - 676 123, Kerala and Dept. of Anthropology & School of Health Services, University of Poona, India.

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

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

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

The preliminary findings indicate that there is fear about the deformity and high infectivity associated with leprosy. The community prefers to retain the confidentiality of the disease. Knowledge about the signs and symptoms, about the causation, transmission and cure has also been studied. Higher literacy has shown direct correlation 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**

C.S. Cheriyan, Jayaraj Devadas, Health Education Materials Unit, DLRA, 4, Cephaslly Street, Shenoy Nagar, Madras - 30

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 dissemination of scientific facts on leprosy to the literate and younger sections of the society, within the age group of 16-20 yrs, a study was conducted in two urban and two rural areas covered by DLRA/ALES projects in two states, in South India. 1000 persons from the urban and rural areas were interviewed.
the medium used to achieve this objective was the print medium. After due consultation with leprologists, educators, sociologists, 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 received and the medium was acclaimed and accepted as effective by more than 90% of the respondents, 95% in urban and 85% in rural areas. 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 healers, and religious leaders on various aspects of the disease is essential to achieve a change in health seeking behaviour.

Through their experiences with disability, chronic illness, death, and the struggle to retain dignity and control in the face of increasing disability, 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 old woman with leprosy when she was first diagnosed many years ago.

In this era of outpatient therapy, it is easy to forget that those 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 old woman with leprosy when she was first diagnosed many years ago.

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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 their cure. The practice of social rejection of a leprosy patient is highly significant of Care after Cure, and its usefulness and limitations are discussed.

PS10
THE IMPACT OF SOCIAL MARKETING ON THE PERCEPTION OF LEPROSY IN SRI LANKA
Padmuni Gunawardena1, Dayamal Dewapura1, Sunil Settipanyak1, Penny Grewal2

1Anti-Leprosy Campaign, Ministry of Health, Colombo, Sri Lanka; 2Ciba-Geigy Leprosy Fund, Basle, Switzerland

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 1990. 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 is self reporting (10% in 1989). This indicates that the social advertising campaign created an awareness of its early signs, and motivate patients to seek treatment. The information is utilised to suggest a Model Rehabilitation Programme for Leprosy Beggers.

PS11
GENESIS AND PROFILE OF LEPROSY BEGGARS IN MADRAS CITY AND ITS LESSONS FOR REHABILITATION PROGRAMMES
Lobo D, Darisini D, Senguttavan A, Thilagarajan Kali, Delvasigarni

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
3. Reasons for Social Displacement
4. Reasons for choosing Begging 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 Beggers.

PS12
SOCIAL MARKETING APPROACH TO LEPROSY
Dayamal Dewapura1, Padmuni Gunawardena1, Sunil Settipanyak1, Penny Grewal2

1Anti-Leprosy Campaign, Ministry of Health, Colombo, Sri Lanka; 2Ciba-Geigy Leprosy Fund, Basle, Switzerland

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 desensitise leprosy, create an awareness of its early signs, and motivate patients to seek treatment. The primary health care staff, creative 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

PS13 SOCIAL PROBLEMS OF CURED LEPROSY PATIENTS

Dr. Thomas Abraham, C.S. Cheriyen, I. Joyraj Dreads, Morogoro Leprosarium, P.O. Box 35, Parakoma, Tanzania.

The trauma inflicted on victims by leprosy are irreparable, that even the hardest of humans too will undergo aboriginal physical, psychological and social changes. This study attempts to compare the lives of two groups of cured leprosy patients accommodated 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 94% of the inhabitants in contrast to 95% in Anbunagar. While the former depend on the nearby hospital for food, the latter earn their food through begging, illicit trading of amputated and yapa. The inhabitants of Morogoro are confined to their village, whereas the inhabitants of Anbunagar are wanderers, in pursuit of their occupation. As against 39% in Morogoro, 40% of the inhabitants in Anbunagar are economically better off than the remaining.

It was evident from the responses that the inhabitants in Morogoro and Anbunagar are not upset about their predilection and ways of life.

As a striking contrast to their counterparts in Anbunagar, in Morogoro, the inhabitants are polymyelous. Though socio-cultural and moral standards of these two communities were found to be divergent, the impact of leprosy on the life styles and habits of these communities are similar. Human qualities, instincts and passing were found to be similar and universal, no matter colour, creed and geographical boundaries separate them.

PS14

SOCIAL ACTION, FOR LEPROSY CONTROL

R.K. ArvAar, Department of Anthropology, University of Poona, Pune, India.

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 withdrawing 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.

Justified social action ensures internalization 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. Few 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

Harvinder Kaur* and V. Ramasubramanian

*National Institute of Immunology, New Delhi

Leprosy is said to affect 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

Manisha Saxena and Vijay Kochhar

Sivamanda Rehabilitation Home, Kukatpally, Hyderabad-500 072 (A.P.) India

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 live 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 Sivamanda 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?

Haricase UM

Leprosy Research Centre, Yuzukuk, Abu State, Nigeria & University of Nigeria, Nsukka, Nigeria.

Throughout time, due to the leading role of medical professionals in health care delivery, Health has become commonly regarded as synonymous with Medicine. As 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 offered to the World Health Organisation describes Health as "a state of complete mental, physical, social and economic well being, not merely the absence of ailments." This means that Health is primarily a condition of "complete ... social, economic well being."
PS18

ANALYSIS OF MENTAL HEALTH STATE OF LEPROSY PATIENTS

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The present study used SCL-90 to measure and analyze the psychological reaction on 11 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 (145.549±57.214), and a higher mean score of 18 factors in SCL-90 as compared with those of the normal individuals. The SCL-90 factors in patients with disability grade I or II were significantly higher than in those with disability grade I. Mean scores of compulsion depression, passive anxiety, paranoid ideation 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 severer 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 analyzed and significant difference among (18 factor scores was observed. Socio-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 for 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, preventing disability and ensuring psychosomatic health.

PS19

PSYCHOLOGICAL ASPECTS OF LEPROSY PATIENTS IN ALTO AMAZONAS PROVINCE, LIMED REGION, PERU. OCTOBER 1987-SEPTEMBER 1990

Edgar Valenciana, Eduardo Falcón, Pedro Legua, Gladia Muñoz.

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

Thirty eight patients with leprosy were studied in Alto Amazonas. The personality dimensions, introversion and extroversion, and neuroticism were studied with Eysenck's Personality Inventory. Depression and anxiety were also studied using Zung's scale. These aspects were also analyzed 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:

- Introduce 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 segregation was almost nil.

(These paper was financially supported by Red Barnet - bewark).

PS20

A STUDY OF REHABILITATION PROCESSES OF LEPROSY PATIENTS: INDIA

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The introduction of multidrug therapy is fast bringing down the leprosy prevalence rate. This has necessitated shift toward rehabilitation of patients declared as RPT(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 well 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

Hannah Anandadul

Faculty Member, College of Social Work, Red Hills, Hyderabad-500 004, A.P. India.

Leprosy interferes with the psychological and social life of the patient thus bringing about dehabilitation 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 222 randomly selected respondents. Scores were given to them by summing up the weights of each statement. High and significant low dehabilitation, statistical tests were applied for standardizing the scale. To establish reliability split-half reliability test and item discriminant 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 discriminant analysis had a level of significance of 0.001 for 42 statements while the factor analysis explained 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

Makia Male
President, Hawaii Hansen's Disease Association,
Honolulu, Hawaii

This paper addresses the psychodynamics of transition, by an adult male patient, from twenty-five years at the leprosy settlement of Kaluupapa to his re-assimilation in the city of Honolulu.

In the absence of a mentor, an established support system, and with no analogs on which to build, the presenter 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

V. Kishore
Swastik Rehabilitation Home
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Health Education is very important to prevent and eradicate any disease, such as 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 Organization & 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, 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


The Leprosy Mission Hospital, Naini, Uttar Pradesh and Purulia, West Bengal, North India.

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 159 cases, only 20 cases are not coming in open for treatment due to STIGMA. This number is only 1.22% which is very negligible. The number of defaulted cases are as follows: - Grade I = 37 (11.6%), Grade II = 127 (8.4%), Grade III = 26 (2.26%).

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.

The Leprosy Mission Hospital, Naini, Uttar Pradesh and Purulia, West Bengal, North India.

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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.
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
Punpluan Predunnyut
Faculty of Social Sciences and Humanities
Mahidol University, Salaya, Nakhon Pathom, Thailand

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 view patients with bodily disfigurement as persons who should be shunned, they tolerate these patients if they maintain some social contacts. I discuss factors responsible for the production of the stigma of leprosy (e.g., religion, everyday use of the language, health worker activism). I also show how the stigma of leprosy is understood in relation to a person’s position in the 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 disowned all their lives.

PS28
INFORMACIÓN, CONOCIMIENTO Y ESTIGMA EN LA ENFERMEDAD DE HANSEN
Montserrat Pórez M.D.,Dulalia Puster A.S.
Mercedes Pórez M.G.
Programa de Prevención y Control de la Enfermedad de Hansen, Conselleria de Sanitat, 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 después de recibir información sobre la Enfermedad de Hansen.

El conocimiento 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 LEPROSA
Dora Martines Cypreste
Este proyecto tiene su objetivo nel combate del estigma de la lepra aun muy presente en nuestro país.

A falta de intervenciones científicas en tiempos pasados posibilitó el tratamiento inadecuado y como consecuencia las inociidades físicas, el mayor temor de la sociedad.

Por lo tanto se hace necesario un trabajo social que alcance todos los siguientes, sociales nel sentido de disminuir la lepra y posibilitar la reincorporación social de los pacientes y ex-pacientes ahora allijados de la sociedad.

Areas de actuación: Servicios de salud, educacion, grupos familiares, movimientos populares organizados, organizaciones en general, utilizandose todos los medios de comunicación de masa.

Alcanzándose a populacion en general estaremos contribuyendo 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 IDIÓZOS DEL SANATORIO DR. PEDRO FONTEs
Dora Martines Cypreste
El presente proyecto tiene como objetivo prestar atencion clinico y psico-social a los pacientes idios del hospital Dr. Pedro Fuentes. 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 idios portadores de la enfermedad, siendo nel momento el unico implantado en Brasil.

Aunqy abandonados por la familia hoy estos pacientes se sienten como seres humanos recuperando sus derechos de ciudadania.

PS31
INTEGRACIÓN SOCIAL Y ECONÓMICA DE UN GRUPO DE PACIENTES DE LEpra EN LA ZONA RURAL DE DOMINICANA CON GRAN PARTICIPACIÓN DE LA COMUNIDAD
Rafael Isa Ing., Huberto Bogaert, Socrates Canario.

Se presenta la información básica sobre un Programa de Asistencia Directa para la Integración Social y Económi-
PS32


Roberto Roparterte, Rafael Isa, Freddy Simon, Socrates Casario.

Se hace una revisión del comportamiento de la endemia ex-amiendo la incidencia y prevalencia desde el inicio de la aplicación de las medidas de control hasta el 31 de diciembre de 1992. Se observa una edad continua de la incidencia desde el año 1992 ascendente de la prevalencia a partir del año 1989. Se hace una distribución de los casos por forma clínica, sexo y edad adyacente a 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 multibacileras. 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 existen-"n de condiciones socio-económicas-culturales que se mantienen en un nivel muy crítico.

PS33

SOCIAL ADVERTISING FOR LEPROSY

Sandy Salegade1, Upali Herath1, Rohan Ryanal, Dayamal Deewapura2, Penny Grewal3, Padmini Gunawardena2, Sunil Sensinapake2

1Grams Bocelli, Colombo, Sri Lanka; 2Anti-Leprosy Campaign Ministry of Health, Colombo, Sri Lanka; 3Ciba-Geigy Leprosy Fund, Basle, Switzerland;

Leprosy continues to be one of the most neglected 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 aimed at spontaneous demand for diagnosis and treatment by making people aware of the early signs of leprosy, able to spot them in themselves and others, fearful 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, slickers, direct mailings, newspaper advertisements, etc. The campaign logo, a flower held sensibly 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 Grewal1, Dayamal Deewapura1, Padmini Gunawardena2, Sunil Sensinapake2, Francisco Castellano3, Alberto Barzola4

1Ciba-Geigy Leprosy Fund, Basle, Switzerland; 2Anti-Leprosy Campaign Ministry of Health, Colombo, Sri Lanka; 3Anti-Leprosy Campaign, Ministry of Health, Mexico; 4Ciba-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 becoming 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 organizing the services to suit the convenience of patients. Social marketing also requires the careful coordination 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

Maria Margarida Pereira Rodrigues
Maria Zelete Fabio Aranha
UNESP-Bauru, Sao Paulo, Brazil

This study had an 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 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 attributes designated by the handicapped to itself in positive. Now, when characteristicizing 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's 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 & McPoreland (1954) who verified that initial answers reproduced social characteristics and only later ones had a personal connotative. 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.

Raju M.S., Wadnerkar S.D., Bawankar B.R. and Mistiachajees, R.
Gandhi Memorial Leprosy Foundation, Wardha-442 103 (India)

Though there has been an awareness among the proper scientists about the effectiveness of psycho-social interventions in leprosy control work, the application of such techniques has not yet been achieved, due to lack of standardized methods within the reach of the Para-medical 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 psycho-social point of view.

The inferences drawn based on the exercise, presented in the paper, show that psycho-social treatment in leprosy involves a systematic procedure comprising of 3 steps: a) psycho-social diagnosis, b) prescription of needs and treatment. The paper also presents a tentative standardized methodology of treatment which could easily be modified as per the local needs, in the above mentioned 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

Miguelita SOYDAN, Turkân Selhan, Sevai Koçgöz, İstanbul Leprosy Hospital/Istanbul Leprosy Research Center, İstanbul, Turkey.

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 patients under consideration at all the different aspects of disease and conditions related to disease.

Because of leprosy people with deformities cannot earn their living and go on begging or living in very bad conditions as outcomes will continue giving the image that "leprosy is a dangerous disease" which couples 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 24 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

FOODING THE IMPLEMENTATION OF INFORMED DECISION PATIENTS LEPROSY IN KERALA (S. INDIA)

Oliveira, Bc; Valim, V; Alves, M; Oliveira, M; University Hospital (HOSPITAL) Social Worker Service

In the metropolitan areas and in the middle size cities of Tamil the health system network usually has social workers in its staff not only to assist doctors in difficult situations but also to provide case solutions for those patients where difficulties are not always been identified by other staff members. Although health service does not take full advantage of all this professionals to skills in those situations regarding leprosy patients have been increasing on the MHO scheme allows a better relationship between patients and health professionals. There experiences have shown us difficulty to make patients care for group discussion specially in urban areas where the treatment is through health centers located in the patient's residential area. One of the patient's reason for not coming to the center of the social network.

Taking into account that the anxiety perception as well as an cultural factors is responsible for such attitude the social service of the HOSPITAL has been developing an "educational Project" focusing the level of participation of 2 kinds of patients:

In the slums area, treated in Primary Health Care Center through community based program and those referred from different areas of the city, treated in the University Hospital.

Considering the illness stages from a social point of view, this video documentary shown through the case studies problematic situations demanding a social diagnose. It also show that the "role of the patients from both institutions in urban area are quite different".

PS39

COPING STYLE IN LEPROSY

DOUGLAS ERNEST HENRY, DAVID HENRY, SUREISHA

The Leprosy Mission, Chandkhuri Leprosy Hospital Baitalpur (M.P.) India.

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 Hanssen 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, accepted the situation but rejected it and find something favourable like hypopigmented patch. They were regular in treatment but they do not want to know about leprosy. 93% 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 optimist a while problem focused coping is responsible for collection of information and action, positivist 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)

Rebecca Alexander, Alexander Thomas, Vincent Lawrence, R R Mutukkar

The Leprosy Mission, Pathappilthiyam PO, Manjeri - 676 123. Kerala and School of Health Services, University of Poona, India.

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 institutional 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 in design appropriate leprosy control strategies to ensure voluntary reporting and irregularity 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 diagnosis 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**

L Jinmin

Wuhan Municipal Institute of Dermatology, Wuhan, Hubei Province, China

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 "Leper" 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, thereafter believed that there might have been leprosy patients in the Palestine area at the 20th century B.C., and by the 7th century B.C., leprosy was definitely endemic.
3) From the 10th century B.C. to the 7th century B.C., there were strong fear of and prejudice against leprosy patients in the society of the Palestine area. But Jesus, whose actual existence is still being debated among scholars, the author mentions him according to the Bible story) unlike 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**


Ruth Feis do Amaral

CEP 69.063-130 Amazonas, Brazil

The study assesses the patients' regularity regarding the MDT/MDT leprosy treatment regimen.

The patients' clinical records were compared in two different periods: one in the years 1980-1990 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**

R Prekumaram, Sujai Suneetha & Soojan Dave

c/o S L R T C (Post), Karigiri, India 632 106

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.

A part of the thesis for a privately undertaken PhD by the first author.

**PS44**

**INITIATIVES ABOUT IMPERIALITY ON AGRICULTURAL TREATMENT OF LEPROSY IN AN UNIVERSITY HOSPITAL**

Douglas Santos, C.L.C., Cantalice F.P., J.P. Oliveira, J. Oliveira, M.C. Prado, A.A.

STATE UNIVERSITY OF RIO DE JANEIRO (UERJ) - DERMATOLOGY SERVICE

We studied 305 patients with leprosy on ADSP-HEP-UEM 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, accessibility and principal occupation seems not to be an influence in therapeutic non adhesion rate, while ethnic group and interaction level suggest important association with the subject.

**PS45**

**IN-FACTORY MDT**

M.L.P. Nascimento, M.O. Prado, V.L. Pedrosa, T.T. Matos

Instituto de Dermatologia Tropical "Alfredo da Matta"

Rua Codajás, 25, Cachoeirinha, Manaus

CEP 69.062-130 Amazonas, Brasil

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 industrial 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.
# 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 insensitive media.

From popular television shows such as "M*A*S*H" and "The Simpsons" to the rock music of "Was (Not Was)", the word "leper" has been used to conjure 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 sulfa 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 PRECONCETIONS OF LEPROSY: A LINGUISTIC APPROACH

Gunnar Ryome, Marcel Mollevi and Saravjet Kair
National Inst. of Public Health, Peace Research Institute, Oslo, Norway

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 classes, have taken it for granted that segregation was practiced among lepers.

We have found as a common pattern in the co-existence in many languages of different sets of terms to denominate the disease; one set is related to religious or cultural associations, where the disease concept 'uncleanliness' or 'pollution' is important. The other, secular set of terms has no such connotations or implications.

Leprosy is a social disease and the social stigma attached to leprosy is universal 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 in low standard of living. Paleontology is one of the leading states in India to witness a high prevalence rate of leprosy. The status of leprosy as a disease caused a great concern in view of the displacement of the patient due to the disease which leads to sermons psychological, economic and social difficulties. The study is based on the analysis of socio-economic and psychological 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 socio-economic and psychological dimensions with reference to monotherapy and multidrug therapies (MDT). A study was based on questionnaires survey by direct observation methods conducted among 300 respondents chosen in various endemic areas of the districts of Tamil Nadu. 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 greater than 1.000 from 13.99 to 1.013 with a total variance of 69.06%. The dimensions include: 1. Quality of Life, 2. Family, 3. Economic Status, 4. Social, 5. Psychological, 6. Physical, 7. Environmental, 8. Educational, 9. Employment, 10. Housing, 11. Health, 12. Income, 13. Education, 14. Occupation, 15. Religion, 16. Culture, 17. Values, 18. Attitudes, 19. Beliefs, 20. Social. The study is based on the analysis of socio-economic and psychological 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.
Human Relations Research Among Leprosy Personnel and Strategies for Behaviour Modification

R Premkumar, S Satish Kumar & Sojjon Dave

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 representing five aspects of behaviour towards the group concerned.

The results indicated that a significant number of the 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.

* A part of the thesis for a privately undertaken PhD by the First author
PS55
THE PARTICIPATION OF HANSEN’S DISEASE PATIENTS IN THE GOVERNMENTAL HANSEN’S DISEASE CONTROL PROGRAM – HANSEN’S DISEASE AND THE CONSTITUTIONAL ASSEMBLY – A BRAZILIAN MINISTRY OF HEALTH’S EXPERIENCE
Darcy R. V. Ventura, Gerson O. Penna e Gerson F. M. Pereira Coordenação Nacional de Dermatologia Sanitária Ministério da Saúde, Brasília, Brasil.

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 Reintegration of Hansen’s Disease Patients – MORHAN), popular health movements, the scientific community.

This paper discusses the methodology used, which allowed the major 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 endemic’s control activities in the country and background document of subsidy 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 present participation in the Brazilian Ministry of Health’s Chamber of the National Health Council is analysed under the focus of the unforgivable of this movement.

PS56
RESTRICTING THE COLONY-ASYLUM HOSPITAL: A SHARED ACTIVITY OF THE GOVERNMENT, PATIENTS AND SOCIETY AT LARGE
Acélia L. Rodrigues, Darcy R. V. Ventura, Gerson O. Penna, Gerson F. M. Pereira, Maria C. C. Magalhães Ministério da Saúde, Brasília, Brasil.

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 those that, though cured, had difficulties in their social integration and restrictions to exercise their citizenship rights.

The specially formed Technical Social Committee, made up by technical and legal MoH staff and by participants from the representative organization of HD patients (Movimento de Reintegração do Hansenismo – 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 LEPROSARIA: ITS PLACE IN MEDICAL HISTORY
Stephen B. Ell
Department of Radiology, University of Utah, Salt Lake City, Utah

This paper is an 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 an activity contributing to the control/elimination of the leprosy endemic.

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 have a position of defense of the citizenship like other 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 whole, also concerned with the social aspects of leprosy and/or health problems in general.

PS58
BEHAVIOR CHANGE INTERVENTION ON LEPROSY CONTROL, IN SOUTH SULAWESI, INDONESIA
H. Muhammad Fasli Nugrohan,
Health Behavior Change Specialist, Dept. of Health Education and Behavioral Science, School of Public Health, Hasanuddin University, Ujung Pandang, Indonesia.

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 prevalence can help the occurrence of new cases. In 1992, there was about 2,500 new cases was found and 10% has a serious disability.

PS59
LEPROSY CONTROL IN SOUTH SULAWESI, INDONESIA

The paper is an 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 an activity contributing to the control/elimination of the leprosy endemic.

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It was used the method of qualitative research reporting the history of the Association, its political importance and posing a question to the whole, also concerned with the social aspects of leprosy and/or health problems in general.
Having a traditional health concept on leprosy and practicing leprophobia to hide to the victims a real obstacles to leprosy control in this area. Back to the leprosy transmission 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 to include Take care to subclinic patients which were caught by serologic or microbiologic detection.

PS60

QUALITATIVE AND QUANTITATIVE ASSESSMENT OF CHILDREN OF LEPROSY PATIENTS

P.S. Tan

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REHABILITATION

RE1

INTEGRATION OF LEPROSY INTO GENERAL REHABILITATION PROGRAMS - AN EXPERIMENT IN BOMBAY.

Vrushali Ketke, Sandip Joshi, and Sharad Naik

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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 anti-leprosy work through their 153 leprosy clinics. In 1985, a combined workshop was organized for representatives of these organizations to acquaint them with leprosy and discuss possibilities for including leprosy patients in general rehabilitation programmes. Periodic follow-up meetings were organized 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 organized 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 organizations 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 for their survival, and they were the symbol of fear, rejection, prejudice, hatred, and segregation, until 30 years ago. Since then, 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 villagers greatly increased, c. the symbol of fear, rejection, prejudice, hatred, and segregation, until 30 years ago. Since then, 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 villagers greatly increased, c. 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 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. Sastri, Dr. Paul Jyavraj, Mr. P. K. Roy, Mr. Shriram Shoghacker

The community based rehabilitation programme was launched in 1980 at 27 different leprosy hospitals of The Leprosy Mission, India. This programme was planned in 1980 with emphasis on proper rehabilitation 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 deformity. 42% patients were staying in thatched houses.
- 76% leprosy patients do not have agricultural land.
- 27% leprosy patients do not have agricultural land.
- 64.45% leprosy patients had a deformity, 47.4% leprosy patients had a deformity.
- 20% of the patients were rehabilitated in rural areas. 78% were male and 22% were female.

This study shows that deformity is one of the important factors of rehabilitation 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 HYPERENDMIC AREAS OF MEXICO AND ITS CORRELATION WITH CLINICAL, EPIDEMIOLOGICAL AND STRUCTURAL FINDINGS.
A.T. Martinez-Fonsucar, A. Hernandez-Berumen, and L.G. Barrera-Loan
Department of Dermatology, National Medical Centre, IMSS, and *School of Medicine, Guadalajara, Jal, Mexico

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. These patients face comprehensive problems in the availability of MDT and following withdrawal of patients who live in isolated rural areas. Moreover, multicentric 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 northwestern part of the country, and patients with this type of leprosy are frequently the last to seek medical attention. In the majority of cases, morbidity due to peripheral neuropathy increases after diagnosis. These patients face comprehensive problems in the availability of MDT and following withdrawal of patients who live in isolated rural areas. Moreover, multicentric 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.

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 Cinco Lane, Tardeo, Bombay 400 034, India

In view of lesser 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 benefit patients from existing services. In our experience over the last few years, we have observed two important advances made. 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 standardized 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 principle techniques, statistical and functional analysis of 160 patients receiving these modalities 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.
Bombay Leprosy Project, Vidyanag,Btn-Puroh, Neela Shah, Nagi Reddy and P Sankarala
Bombay Leprosy Project, Vidyanag, B jaws-Chunabhatti, Bombay 400 022, India

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 "Boswell Model" (reported elsewhere) in offering comprehensive leprosy management, integrating care of all categories of disabled with an ongoing MDT programme encouraged us to extend studies into two hyper-endemic districts, Ongole and Kunool in Andhra Pradesh, contributing to a pool of over 3000 disabled patients. Care of the highly disabled at the field level using "Modulain" 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 design of pre-fabricated splints (Atul Shah 1991). 332 patients with grade III disability received 473 grip-aid's both in the districts, coverage of deformed patients reaching 100% in Ongole. 75% of the patients found the grip-aid's 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.
B Pradhan, K Pudraji, and Samuel Solomon
S L R T C, Karigiri, Tadmal, India 632 106.

The term "Work" is used in relation to the physical and psycho-social capabilities of an individual. Many testing systems have been evolved in the past to assess this. Similarly, there are atleast 75 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 such WORK ABILITY, and HAND FUNCTION. Additions that were incorporated, were from 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. Important psycho-social parameters, such as attitude towards work, trainability, stigma etc., are evaluated.
2) HAND FUNCTION ASSESSMENT includes tests of grasp, grip, pinch strengths and fine manipulation, are now standardised and graded into three ranges Normal/Poor/Fixed, along with numerical values, 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 test, scoring techniques and interpretation of such scores.

- Hand Function Assessment...
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 during mid-stance is also found to be the highest for the advanced TD leprosy patients as compared to the normals and is about 3-4 times the normal value.

**RE12**

**DEVELOPMENT OF PLASTIC FOOTWEAR FOR ANAESTHETIC FEET IN LEPROSY**

Noshir Antia and Satish Arolkar

The Foundation for Research in Community Health, 84-A, R.G. Thadani Marg, Worli, Bombay-400018, India.

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**

Jair Ferreira, Estefany Monge, Clarissa Gama, Sergio Vitor, Geicia Miranda, Luis Carlos Campus, and Mirian Estevêz.


A set of 3029 Hansen’s disease patients 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. Of these 3029 patients, 689 (22.8%) 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 patient 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 doubles each five 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 patients); bacteriological status (higher risk for patients 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 these 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 assess 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.

**RE15**

**A SYSTEMATIC PROGRAMME FOR DISABILITY PREVENTION AT KARGIRI ("SOULFEET") A PRELIMINARY REPORT**

Samuel Solomon, and Fflyssawurisun P

S L T E Kargiri, Tamilnad, India 632 106

The feasibility of vigorous Disability Prevention being included into routine leprosy control activities was considered at the SCHOFPELIN LEPROSY RESEARCH AND TRAINING CENTRE, KARGIRI. It was noted that in the last few years, all over the world, major fundings had been accorded to the Implementation of POT. It was felt that with minimum additional resources, a systematic disability prevention programme could easily be added 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 included about 3000 patients, including those who are newly-added, under-treatment, and who have been treated at least once in the past. Patients are identified by a physician is an important risk factor for developing disability before the diagnosis; risk of having disability doubles each five 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 patients); bacteriological status (higher risk for patients 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.

**RE16**

**PLAN PARA PREVENCIÓN DE INCAPACIDADES EN MEXICO**

Dr. J. Rodriguez-Dominguez, Dra. Lucía B. Yáñez, Dr. Francisco G. Vázquez-Martínez, ESP, A. C. G. Martinez, Dr. Francisco G. Vázquez-Martínez.

El compromiso en México de eliminar la lepra con el uso de POT, ha permitido curar al 47% de los casos y el 17%
RE17

INFLUENCE OF MDT ON THE INCIDENCE OF DISABILITIES IN HANSEN'S DISEASE

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35 cases who had not disabilities before MDT were investigated. 13 cases had developed disabilities during 5 years after start of MDT. The incidence of disabilities was 0.001. Among the 35 cases, 11.4% cases (4/35) of disabilities occurred during the first year after start of MDT. 39.2% cases (15/35) of disabilities were occurred associated with leprosy reaction. Leprosy reaction is still the most common factor associated with disabilities. 46.1% of disabilities occurred without one leprosy reaction. Among them, there were 1 disabled patients were found during the first year of MDT. In addition, the incidence of disabilities was also associated with sex and leprosy type. However, it was not associated with the duration of disease and the age of patients. The incidence of disabilities in male (17.1%) was much higher than female's (6.4%). and multibacillary's (16%) was much higher than paucibacillary's (9%). All of the 15 cases were BB patients. None of BB 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 disabilities 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

Germano Traple, Mari Elaine Rodella, and Ligia Mendonça
Health Institute of Paraná - Brazil

Hansen's Disease (HD) is a peripheral neurologic disease with high incapacity risk. The surveillance of precocious disabilities can prevent deformities and interrupt the misused 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 efficiency of Simple Techniques at the HD Control Program. The hypothesis is that the adoption of routine procedures avoid disabilities, or their progression, and favors the normal activities. The present situation of the patients will be known through a questionnaire 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

Heather Currie, Suhila Reewa, Ad de Riek and Petronella Jaffero

It is generally accepted that the WHO disability grading is useful only as a measure of how effectively the programme in detecting cases early, it cannot be used for individual patient follow-up. This being so, in the WHO caused 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 10mm filament was used) are being followed up by the ALERT Leprosy Control Programme on a long visit. The condition of the foot 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.
over time and the stages through which new innovations are adopted by individuals and society.

In conclusion, the accuracy of the sensory testing instrument in Brazil facilitated the utilization of the Sah sensory testing technique. 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 excellent evaluation and treatment and lessening disability.

RE21

COMPARISON OF SENSORY RESULTS OF THE THERMAL TESTER AND THE SEMMES-MINES IN LIGHT TOUCH/PRESSURE IN PATIENTS WITH HUSSEN'S DISEASE AND DEBILITY KNUCKLE DISEASE
Linda Jezman, Janet Borenhoff
Centro Local Urban de Barreiro, Belo Horizonte, Minas Gerais, Brazil
Centro de Saúde Washington Luís Lores, São Gonçalo, Rio de Janeiro, Brazil
Hospital das Clinicas, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

Two sensory modalities tested in Hansen's disease have been hot 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 NIDRR and the Semmes-Minesis (S-M) monofilaments. The electric 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-two persons with no known disease were tested with both instruments in the same pre-selected sites on both hands and feet. Both groups were analyzed separately.

The results demonstrate a significant difference between the findings of both sensory tests. The S-M monofilaments were more sensitive in detecting and quantifying early sensory loss related to peripheral nerve involvement. The Thermal Tester detected a more gradual 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 are often difficult to compare due to lack of standardized methods, varying examination times, and subjective evaluation. Reliability is important in order to determine which simple and direct clinical examination is best suited for the field objective. Therefore, the objective of this study was to determine the reliability of the manual muscle strength testing using the Medical Research Council Scale for grading.

In 28 leprosy patients with complete or partial damage of the ulnar or median nerve or ulnar and median nerve testing of nine intrinsic hand muscles was assessed manually. Muscle strength testing was assessed for one hand only and the testing was performed by two examiners. The following strength test were performed:

Abduction and adduction of the little finger;
Abduction and adduction 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 intrater reliability. The presentation will be explained why the strength testing, testing positions and point of application of resistance, deviate from the "classical" strength test 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
1. CDEU, London School of Hygiene and Tropical Medicine, London, UK
2. Africa Leprosy and Rehabilitation Training Centre, Addis Ababa, Ethiopia
3. Amhara Leprosy Hospital, Nepal

One of the major problems in leprosy is to detect early enough changes in nerve function so as to institute changes 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 interobserver variability in the assessment of clinical signs of neuritis in leprosy patients, in Ethiopia and Nepal. Duplicate measurements were performed on random order on 50 leprosy patients by two physio-technicians (PT) and recorded using pre-arranged scoring marks. In addition, duplicate measurements were performed on 50 similar patients by two paramedical workers (PMW) in Ethiopia.

Observers are compared by plotting for each test the differences in measurements against their mean and calculating the lines 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 (WBC 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 (79% to 95% complete agreement). The assessment of motor signs is extremely variable between observers (complete agreement: 49% to 84%), with a systematic bias and a large spread of values around the mean. For sphenillamats and bell-point pen, interobserver variability depends upon the use of observer (PT or PMW), the site of the test and the states of the patients. When performed by PMWs, agreement between observers appears better for BP(73% to 92% complete agreement) than for NP (53% to 53%), partly explained by the use of a different scale. When tests are performed by PTs, the pattern is less clear, with 52% to 58% complete agreement for NP and 71% to 81% 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 decision 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, ENTER, AND 1ST DOR, ENTER, WITH REGARD TO DETERMINATION FOLLOWUP, EVALUATION OF ULCER NERVE DAMAGE
Mansarif Syed, Dr. Solomon V.K.
and K.B. Kiran
Deshopet Leprosy Research Centre, Hyderabad.

In patients with ulnar nerve damage instead of testing all the muscles in the hand for convenience, simplicity and field use it is commonly agreed to test the muscles ADM, 1st D.I. In most cases these muscles are sufficient for detection and follow up. We have studied an additional muscle in 50 cases, Palmer interossei of the little finger — adductor of the little finger. This was found to be involved earlier than the other muscles and better suited for early detection but has certain disadvantages for follow up. Whereas the other two muscles were more 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 1st dorsal interossei. Hence the gradient of the muscle on HNC scale is not possible for grading.
RE25
LATE RESPONSES IN TUBERCULOID LEPROSY
Department of Medicine, S.P. Medical College, Bikaner, India.

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 ±SD = 30.72 ±12.84 m/sec., t=7.96, 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 ±SD = 31.93 ±14.01 m/sec., t=5.54, p<.001 and H-Reflex conduction was prolonged in 9 patients (36%), mean ±SD = 49.33 ±17.34 m/sec., t=4.66, p<.001 showing involvement of H-Reflex arc which is a monosynaptic reflex depending on group la 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
Judith Bell-Krotoski
Department of Rehabilitation Research, Gillis W. Long Hansen’s Disease Center, Carville, Louisiana

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. 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 normal thresholds.

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 Center, is as high as over half of the patients measured, and that some patients who were normal by monitoring acute, and 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 in the disease, in particular loss of sensory and motor function of hands.

RE27
SEMME-WEINSTEIN MONOFILAMENT DETECTION THRESHOLDS: A COMPARATIVE STUDY
Judith Bell-Krotoski and Val Coor
Department of Rehabilitation Research, Gillis W. Long Hansen’s Disease Center, Carville, LA

Semmes-Weinstein monofilaments have been found to be repeatable within a standard deviation of 0.01 for the assessment of sensory and motor function which can be directly compared with the normal for the hand and foot.

Reduced sensitivity 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 who was experiencing reactions 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.

RE28
MONITORING PERIPHERAL NERVE INVOLVEMENT DURING REACTIONS
John Figarola
Department of Hand and Occupational Therapy, Gillis W. Long Hansen’s Disease Center, Carville, LA

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 who was experiencing reactions 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
James Birke, Win Brandhau, Ton Schreuders, and Angelika Piefer
Gillis W. Long Hansen’s Disease Center, Carville, LA, USA

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
Results demonstrated that ICC = .88 - .93 for all sites tested. Statistical analysis showed normal filament thresholds were significantly related to age in 1992 and occupation (p = .001). Subjects who performed heavy and medium work had significantly higher sensitivity 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 sensitivity tests based on normative data.

Identification of Peripheral Nerve Injury in Leprosy and Its Implications for Current Prevention

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Peripheral nerve (PN) damage is the primary cause of disability and deformity in leprosy 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 Citrolândia Health Center in Betim, Minas Gerais-Brazil from February 1987 to May 1990. The study analyzed all patients with more than 2 exams by February 1992. The study analyzed the first and last upper extremity exams of peripheral nerve (PN) involvement and compared them with the World Health Organization (WHO) Disability Grade (PG). Results demonstrated that 91% had PN involvement in the beginning compared to 26% with WHO disability. 69% 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 baseline neurological exam 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 program.

Assessment for Quiet Nerve Paralysis in Field

CJII Field Unit (Indian Council of Medical Research), 271 Nehru Bazaar, Avadi, Madras 600 054, India.

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 and then 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.

A Study on Factors Influencing the Recovery of Motor Nerve Function with Steroid Therapy

Helen Roberts, D Vijayakumar, Annamma John
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This non-concurrent prospective study was conducted on leprosy patients receiving steroid therapy for motor nerve paralysis during the period 1968-91. Patients received 30 mg prednisolone daily during the period 1968-89. 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.
greater chance of recovery if the duration of paralysis was less than 3 months. The preliminary findings suggest that higher dosage of steroids do not increase the recovery from muscle paralysis among leprosy patients.

The main histological processes and decrease of inflammation, was functionally ineffective. Nerve regeneration was confined to cutaneous sensory branches. The few regeneration clusters. 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 limbs of leprosy patients were studied. All patients (2 RT, 3 ML 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 regeneration were decreased centrifugally and were inversely proportional to the endoneurial fibrosis. 4. The dorsal nerves and superficial sensory endings were destroyed beyond recognition. The present study also contributed to the understanding of the spreading of leprosy in peripheral nerves.

Rehabilitation and Training Centre, Department of Anatomy, Addis Ababa University. All three; Addis Ababa, Ethiopia.

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 'predictive damage sites' of non-sensory nerves. The regeneration, which followed to 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 limbs of leprosy patients were studied. All patients (2 RT, 3 ML 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 regeneration were decreased centrifugally and were inversely proportional to the endoneurial fibrosis. 4. The dorsal nerves and superficial sensory endings were destroyed beyond recognition. The present study also contributed to the understanding of the spreading of leprosy in peripheral nerves.

This work was supported by LEPPRA grant No. 411/9.

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2. Dept Rehabilitation Medicine, Chiang Mai University, Chiang Mai, Thailand.

This report describes the neurological and electrophysiologically examination of 15 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 0.45 mm monofilaments (PS) and thermal sensation with a thermal sensation device (TSD). 55% of ulnar nerves had abnormality of at least one of the four tests versus 75% of radial nerves and 51% of median nerves. The most frequent lesions was 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 (71%) had minimal neuropathy, 16 (45%) moderate and 6 (41%) 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, 20% median sensory and 30% of median motor responses among the leprosy subjects. Low sensory amplitudes and drops in amplitude and NCV over the cross-affected 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 crossvalidationwith the electrophysiologic data. This yielded the following overall positive predictive values: PS=90%, PS=92%, MMT=84% and NP=89%. Overall negative predictive values were: NP=75%, PS=71%, TSD=69%, MMT=66%. Advanced neuropathy in leprosy showed a decrease of sensitivity and reproducibility for monofilament testing to nearly equivalent accuracies in predicting electrophysiologic abnormalities. Both were superior to NP and MMT in subjects who already demonstrated clinical deficits in leprosy.

The advantages/disadvantages of the procedure are discussed.

A follow-up of SEVENTY ONE (71) patients who underwent the combined procedures in our Centre from 1984-1998 is presented using the following parameters:

- Range of dorsi-flexion = 0°

The advantages/disadvantages of the procedure are discussed.
61.4  Abstracts of Congress Papers  149A

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 little 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 superficialis to attach it to the Abductor Digitii Minimi at the base of the proximal phalanx. Thus the flat transverse metacarpal arch is corrected and protection 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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A.Salafia, G.Chauhan

Soft tissue contractures in the hand are usually overcome with POP casts, skin grafts, flaps, dynamic splints. 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 devised by Dr. B.B. Joshi (used in cases of fractures): (i) Fixed flexion deformity ofPIP joints: to release soft tissue, including capsule, contracture. (ii) Thumb paralysis with fibrotic adductor. (iii) After sequestrectomy of fingers or toes, to keep temporary the normal length till further surgery is done. (iv) In wrist drop: correction after bone grafting, to keep the wrist in extension. The advantages are: (i) Lengthening of all tissues, including neurovascular bundles, is achieved gradually over a period of 3-4 weeks. (ii) The volar capsule resistance is easily overcome without surgery & risks of joint damage.

The results were achieved by that time. We feel that exterical 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 overcome these deformities, intrinsic reactivation procedure with insertion of five tails of the motor intointroversi and hypothenar tendons as performed in 236 hands at this centre since 1977. 158 of these hands were followed up for periods ranging from 1 year to 15.5 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 25.4% and poor in 6.2%. Finger closure was good in 81.9%, fair in 14.1% and poor in 4%. Restoration of distal transverse metacarpal arch was good in 76.5%, 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 HENDEL'S DISEASE

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Lasso procedure (Sancelli) is a combination of dynamic and static principle. In this technique the transferred tendon is attached to proximal pulley(A) 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, 133 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 in 80. Deformity ranged 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 seaceous infection and the other three may be due to failure of the transferred 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 with anterior chamber intraocular lens. Both lepromatous and tuberculous 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 those were treated with thalidomide. Patients were followed up for a maximum period of 5 years.

Visual recovery, post-operative complications and management are discussed.

**RE43**

1. **DENATURED MUSCLE AUTOGRAFTS IN PERIPHERAL NERVE REPAIR - SURGICAL TECHNIQUE**
   
   Jill Perlitz, Jill Curtis and JL Turk
   
   Royal College of Surgeons of England, Lincoln’s Inn Fields, London WC2A 3PN, UK.
   
   DD Palande, A Subramanian and TS Narayanakumar
   
   Sacred Heart Leprosy Centre, Kumbakonam, Thanjavur District, South India 612401

   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. Localised 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 be described in the accompanying papers.

**RE44**

2. **DENATURED MUSCLE AUTOGRAFTS IN PERIPHERAL NERVE REPAIR - RESULTS ON LEPROSY PATIENTS**

   Jill Perlitz, Jill Curtis and JL Turk
   
   Royal College of Surgeons of England, Lincoln’s Inn Fields, London WC2A 3PN, UK.
   
   DD Palande, A Subramanian and TS Narayanakumar
   
   Sacred Heart Leprosy Centre, Kumbakonam, Thanjavur District, South India 612401

   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 anaesthesia 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 - up 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 OF HANDS AND FEET IN LEPROSY PATIENTS WITH FREEZE-TAUGHT MUSCLE AS GRAFT MATERIAL.

Roland Kaban, Tivader Moko, Connie le Maitre, Zewdu Kebebe.

All Africa Leprosy and Rehabilitation Training Centre, Addis Ababa, Ethiopia.

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 peri-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 Bermon

Institut Cardinal Leger contre la Lepre (BATTI)

Ecole de 162 cas de decompression et neurolyse pratique a l’Hopital Cardinal Leger de Sigoulasse,

Ensa 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.

Thirty 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 epineurotomy. 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, Ayruu Mong, Philomena Commons.

Christian Leprosy Centre Chandrughonu, 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 those cases. We believe that this operation should be considered a standard procedure for the anesthetic foot.

RE50

A TEN-YEAR OBSERVATION ON THE CURATIVE EFFECT OF SURGICAL OPERATIONS FOR CORRECTION OF LEPROSY DEFECTS — A REPORT OF 46 CASES

Nie Songling, Li Fujuan, Xu Shirui, Liu Kunwu, Zhang Xiaobing

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Several kinds of surgical operation for correction of leprosy deformities performed on 46 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 shink deformities and they believe that the corrections of foot and ankle deformities are important in the treatment of planter ulcer.
RE53

EYEBROW RECONSTRUCTION BY MEANS OF A FREE GRAFT TAKEN FROM THE HAIR BEARING SCALP OF LEPROTIC PATIENTS

Monica Jeha Mavkarou, Aldemar Vilela de Castro, Joao Aranha Moreira Neto, Fernando Orfeice
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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 the 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, SALIN, 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, Salin, 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

Department of Dermatology and Medical Mycology, National Medical Centre, IMSS, and 'Hand Surgeon, Medical Services, DGJ, Mexico.

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 electrophysiology and other clinical data was performed. The role of secondary angiogenesis 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

Atul Shah, P. Dave, S. Kingsley, Neela Shah and R Ganapati
Comprehensive Leprosy Care Project, Leprosy Management Training Centre, Ciba Compound, Diana Cinema Lane, Tardeo, Bombay 400 034, India

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 "Modulan Model" was 'Modulan' grip aids. The grip aids were provided to 34 patients on 59 articles used for daily living and economic activity and rehabilitation. 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 98% 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 psychologically, physically and economic independence but also help the patients to get fresh grip on life. The grip aids were prepared by leprosy workers trained by physiotherapist 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

Atul Shah, Neela Shah, S. Kingsley and R Ganapati
Comprehensive Leprosy Care Project, Leprosy Management Training Centre, Ciba Compound, Diana Cinema Lane, Tardeo, Bombay 400 034, India

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 was recorded 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 in, unassisted,
assisted, contractural angles cannot be taught to leprosy workers in the field area. As well as patient knowledge, our observations 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 leprosy workers in the field area. 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

Yu. Shoumei and Jean M. Watson

Hubei Provincial Health Bureau, P.R. of China

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, 55 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

Yu, Shoumei and Jean M. Watson

Leprosy Assoc. of Hubei Province, P.R. of China

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 AESTHETIC LIMBS?

Ratna Philip, Jayaprakash Mulyil and C. Vijayakumar.

CHC Unit, Paravathiparam, 532 501, A.P. and CMC, Bhagam, Vellore, S. India 632 002.

In the control program run by CRAD hospital Bhagam 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 20 patients with ulcers and 20 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 -

Eben Baskaran, Ramprasad S, Rupert Samuel,

Alban Y and Selvin Sam Joy

Dayapuram Leprosy Control Project, Manamadurai, Tamilnadu, South India - 623 606.

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.

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
SYSTEMATIC APPROACH TO PREVENTION OF SOLE WOUNDS
MANAGEMENT STEPS NEEDED TO IMPLEMENT A
present and former patients having sole sensory reduction in sole wounds in a selected group of required to endeavour to obtain a year to year systematically improving foot-care and footwear. cases result in a reduction in the prevalence of disability prevention activity, can in many demonstrate that improved management of 30 projects in 9 countries took part. The objective of this presentation is to 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 encountered 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.

RE63
THE EFFECT OF THE ILEP JOINT STUDY PROJECT ON SOLE WOUND PREVALENCE
Jean M Watson
The Leprosy Mission International
80 Windmill Road, Middlesex TW8 0QH, England

The objective of this presentation is to demonstrate that improved management of disability prevention activities 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 aim of the study was to: - 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 encountered 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
Jean M Watson and Paul Sommerfield
The Leprosy Mission International
80 Windmill Road, Middlesex TW8 0QH, England

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.

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.

RE65
MANAGEMENT OF COMMON PERONEAL NERVE DAMAGE (FOOT DROP) IN HANSEN’S DISEASES
DIDOOF LEPROSY RESEARCH CENTRE APPROACH
Dr. Solomun V.K.
Mr. Nazliki, Mr. Shahin 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 POI. They were given instructions with regard to care of the foot, on weak muscles, anaesthesia and earlness. 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/foot wear/special foot wear/for such patients it may still be possible to give acceptable good results in cases of foot drop. Since this approach is simple and acceptable, this 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).

Didayaf Leprosy Research Centre (DRLC) Hyd.

RE66
EFFECTIVENESS OF PROTECTIVE ORTHOPAEDIC SHOES IN NEUROPATHIC AND DEFORMED FEET IN LEPROSY
Ayse Tükel, Nur Uerik
Istanbul Leprosy Research Center, Istanbul, Turkey.

The orthopaedic shoe workshop was initiated in our hospital in 1983. It was 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 study 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 those cases came from rural areas. 56 % were women. 37 % of them were unemployed and 80 % of them were seen to have
The importance of (social and economic) rehabilitation of leprosy patients. Moreover, of the initial 69 ulcers showed that the shoe satisfied 77.5% of the patients. An evaluation of the shoe was done. Patients who have done no have Leon able to return to a meaningful existence. Treatment may also be a failure because patients who have lost their ability 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 medical treatment alone is impossible, because patients who have lost their ability 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 medical treatment alone is impossible, because patients who have lost their ability to expose themselves for treatment unless they can see that others who have done so have been able to return to a meaningful existence.

To realize the dream of eliminating Leprosy by the year 2000 AU will be possible if, and only if the problem of (social and economic) rehabilitation of leprosy persons is effectively addressed.

The bilateral static slings used to be taken for the correction of this deformity, but the long-term result was not good. It suggests that at last acceptable, durable and affordable leprosy footwear has been developed.

PREVENTION OF FUNCTIONAL IMPAIRMENT, DISABILITIES AND DEFORMITIES
Claudia Hitec, Michel-Yves Grauwin and Jean-Claude Naudin
Institut de Leprologie Applique, Dakar, Senegal

The early 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 active 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.

AN EPIDEMIOLOGICAL SURVEY OF DEFORMITIES AND DISABILITIES AMONG 14,257 CASES OF LEPROSY
Zhang Guocheng Li Wenzhong Yan Lingshui
Institute of Dermatology, CAMS, Nanjing, China

This study was planned and conducted in Yangzhou Prefecture covering 11 counties. Out of 14,257 leprosy patients, 8,122 (56.91%) cases with deformities and disabilities were found. The disability rate was much higher in patients with MB leprosy (41.15%) than in BB (5.80%). Males were more often disabled than females (58.2% for males, 53.68% for females). The disabilities became more common and more serious with the increase of age, The disability rate increased with increasing duration of disease. Out of 8,122 cases disabled, 4,254 belonged to Grade 3.

Among 14,257 cases of leprosy, 3,656 (25.64%) lost sensation of the hands, 6,142 (43.69%) and 5,044 (35.00%) had hand deformities as claw hand and thumb paralysis respectively. 3,027 (21.50%) lost sensation of the feet, 2,235 (15.48%) had foot drop needing surgical treatment, 1,882 (13.28%) had plantar ulcers (498 single ulcers, 1,384 complicated ulcers), 1,114 (8.14%) had cutaneous foot deformities such as claw hand and thumb paralysis respectively. 2,064 (14.48%) had hand deformities as claw hand and thumb paralysis respectively. 3,270 (23.10%) lost sensation of the feet, 2,235 (15.48%) had foot drop needing surgical treatment, 1,882 (13.28%) had plantar ulcers (498 single ulcers, 1,384 complicated ulcers), 1,114 (8.14%) had cutaneous foot deformities such as claw hand and thumb paralysis respectively. 2,064 (14.48%) had hand deformities as claw hand and thumb paralysis respectively. 3,270 (23.10%) lost sensation of the feet, 2,235 (15.48%) had foot drop needing surgical treatment, 1,882 (13.28%) had plantar ulcers (498 single ulcers, 1,384 complicated ulcers), 1,114 (8.14%) had cutaneous foot deformities such as claw hand and thumb paralysis respectively.
PREVALENCE OF DEFORMITIES IN THE LEPROSY PATIENTS IN PÜZAPUIQUE.

M. Cerrano A., MacArthur A., Barneria K.S., Sen A.

Coimbatore Leprosy Eradication Scheme (CULES), Coimbatore, Tamilnadu, India

Deformity rate (Grade I and II) among 5555 Urban and 6104 Rural patients were selected to receive Chemotherapy was 13.5% and 19.0% respectively. The rate was higher among M3 patients; a slightly higher rate was encountered in rural patients.

During the course of therapy, deformity status downgraded in 1.8% of Urban and 2% of Rural patients. 25% of Urban and 19.5% of Rural patients manifested some recovery of sensation.

Deformity rate in newly 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.

RE72
"DISCAPACIDADES EN EL ENFERMO DE LEPRA"
REPUBLICA DOMINICANA
1979-1992
Rafael Isa Ina, Freddy Simeon, Escrato Canario.

Se hace un análisis de las discapacidades producidas por la enfermedad del lepra en un grupo de 1270 enfermos diagnosticados en el periodo 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 dos tercios de los discapacitados, el grado II alcanza el 8.4% y que la forma leprosa 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 CMH RURAL PROJECT
Thomas Abraham, Vijay Shankar, Jayaraj Devadas & Venkata Ramana

Coimbatore Leprosy Eradication Scheme (CULES), Coimbatore, Tamilnadu, India

Deformity rate (Grade I and II) among 5655 Urban and 6104 Rural patients who were selected to receive Chemotherapy was 13.5% and 19.0% respectively. The rate was higher among M3 patients; a slightly higher rate was encountered in rural patients.

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RE74
PREVALENCE OF DEFORMITIES IN THE LEPROSY PATIENTS IN MOCAMBIQUE.
Compostella L., Gersono A., Saraceno G. and Macumber A.
National Tuberculosis Programme, Min. of health, PBD 5540, Maputo (MZ)

Mocambique is one of the African countries with the highest prevalence of leprosy (L), (1.7%, Africa 0.6%). It is generally believed that among the L pts there is a high prevalence of deformities (Dif) and disabilities, with considerable variations between different areas. No data were available for Mocambique.

So, during 1992, all active pts in two different areas were observed and the presence, kind, grade (40 criteria) of Dif were registered along with sex, age and Clinical classification (Mb or Ms). The results show that:

1- a rural area (Nampula town, ML) with a high prevalence of L (4.7%) and less organized health services: 550 pts, 307 males, 243 females; 166 MB and 384 Ms.
2- an urban area (Maputo town, MPT) with low prevalence (0.2%) and better organized services: 101 pts, 15 males, 86 females; 39 MB and 62 ML.

Statistical analysis: Epi-Info 5.1 computer programme.

A prevalence graph of Def was encountered and showed differences, with considerable variations between different areas.

RE75
THE APPLICATION OF CIRCULAR DISTRIBUTION METHOD TO ANALYSES OF 14258 LEPROSY CASES FOR DEFORMITIES SURVEY IN YANGZHOU, CHINA


* Institute of Dermatology, CAMS, P.R.China
** Yangzhou Institute of Dermatology, P.R.China

The purpose of this study was to analyse the regularity of time distribution for onset, detection and occurrence of deformities in 14258 leprosy cases. In this paper the author applies a circular distribution method to analyse the data collected in a survey of deformities in Yangzhou, China. The results indicate that the periods of peak (15% of the total cases) of onset, detection and deformities in these cases have occurred in March-June, May-August and March-June respectively. The periods of peak (about 6 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.

Dr.R.K.Dutta M.D., Dr.Mrs.S.Dutta and Dr.A.K.Sen.

Jashedpur Skin Research Institute, Prasathanghar, Jashedpur - 831 002, India.

An oil based Herball 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 three sets of patients included in the study. The results were documented and analyzed.

It has been observed that in most cases exercises improved wasting of muscles. The improvement was more and faster than was expected 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
Sunil Sentinayake1, Asad Shah2
1Anti-leprosy Campaign, Ministry of Health, Sri Lanka; 2Director, Leprosy Management Training Centre, Borehunya, India

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 in the early 1990s, a cost-effective approach to deformity care was adopted, based on the experience of the Comprehensive Leprosy Care project in Borsad Talaka, India.

Deformity care services are provided by the leprosy public health inspectors after training in basic physiotherapy measures 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 decreased the risk of shear stress and chance of injury from the device itself.

Another important aspect of treatment is providing protective devices that are also functional in activities of daily living. One such device is a custom-made finger cap. Customized latex caps are 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 and other materials also exhibit 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, improved durability, and enhanced gripping properties of the latex.

RE79
PHYSIOTHERAPY AND HEALTH EDUCATION - A DHOLPUPET APPROACH
M.U.S. MIZAFFARULLAH, Dr. SULTON, Dr. UDAW KIRAN
DHOLPUPET 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, Dichgalli situated at 150 Kms from Hyderabad.

Being a reputed institution, more number of probies cases, self selected patients come to DLR. 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.I., 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 H/I/Physio which were applicable on an out patient basis and whose patient acceptability was good.

The simple exercises we advised, how 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 how we transferred the responsibility to the patient to achieve good results and also on how we planned our available resources in providing them (where they could not get immediately) will be discussed.

Colour transparencies 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 FILAMENT IN TESTING SENSORY FUNCTION OF PATIENTS WITH LEPROSY IN NEPAL AND ETHIOPIA
C. LeMaire1, P. Rasquin2, R Pasqua1, C. Le Maitre1, J. Wheeler1
1Communicable Disease Epidemiology Unit, London School of Hygiene and Tropical Medicine, London, UK
2Anandaban Leprosy Hospital, Nepal
3All Africa Leprosy & Rehabilitation Training Centre (ALERT), Addis Ababa, Ethiopia

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 pairs 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 ulcer and median nerves, when applied on similar conditions by a trained observer (75% to 90% complete agreement). Kappa statistics lie between 0.50 and 0.74, showing moderate to good agreement. Compare well for the posterior tibial nerves (40% to 50% 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, where there is full sensation or complete anesthesia. Reasons for these discrepancies are examined in relation to 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?
Roland Ramos, Heather Currie and Zewdu Kebrat.
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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 over temperature.

20 cases undergoing neuritis treatment, 20 with LGG (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-neurologists without any nerve damage were tested for control.

All patients were assessed with standard methods such as VMT-5 (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
PORTUGUESE SENSATION IN NORMAL SUBJECTS IN ETHIOPIA
Heather Currie and Peter Byass
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Finding a reliable instrument to measure sensation is still a problem in most control programs. In ALERT, we use 10cm filaments for both the hands and the foot. Many health workers complain that they are registering false findings of anesthesia on footsoles. Therefore 200 normal subjects were tested using 5, 10, 20, 30 and 50cm 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 (0.10 was recorded at 6 sites on the footsole.

The results show a difference between highland and lowland, and call into question the use of 10cm 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 SENSOR-METRIS THERMOMETER
Sandra Lyon, Sonya Goncalves, Cristina Fonseca, Aparecida Grossi, Linda Lehman
Centro Social Urbano do Bairro, Belo Horizonte, Minas Gerais, Brazil

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, 20 of whom have their skin patches mapped using the Sensor-Metris thermometers. 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 Lebeuf
Coordenacao Estadual de Controle de Hansenio, Secretaria de Estado da Saúde de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

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 100 disability grades 1, 2 and 3.

The results of the preliminary findings demonstrate that deformity in newly detected cases has decreased in the state from 13.95 in 1988 to 7.65 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
Bal Kishan Gupta, D.K. Kochar, Anjli Gupta
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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 involvement in leprosy is segmental in nature.

Interpeak latency N7-N18 (Proximal Conduction Time) was prolonged in 3 patients while Interpeak latency N18-N55 (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
Judith Bell-Krotoski
Department of Rehabilitation Research, Gillis W. Long Hansen's Disease Center, Carville, Louisiana

Sensory threshold is an important aspect of the Semmes-Weinstein filament testing. These filaments are being increasingly used for testing sensibility in Hansen's Disease patients, 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 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 biomechanical 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
SENSORY-WEINSTEIN MONOFILAMENT TESTING TO DETERMINE NORMAL SENSORY THRESHOLDS IN THE FOOT AND HAND: A COMPARATIVE STUDY IN INDIA
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ALM International, 1 ALM Way, Greenville, S.C., USA

This study was undertaken in order to enable the PMU, 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 choices of tools and methods.

This paper discusses minimum threshold of each 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 biomechanical 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.

RE88
THE WINKLING TEST IN LEPROSY PATIENTS
Marcos Virmond, Lucia Camargo and Rosemarie Baccearelli

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 revealed 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
No Inoke Potter
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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 recognize 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 is 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
PAIN-SENSORY LOSS IN LEPROSY-CASE REPORTS.
Shubhada Pandya* and Waman Bhatki**

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We report the clinical and investigative features of seven patients (3 males, 4 females, age 28yr-61yr) with polymyelitic 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 limbs. Detailed investigation for other causes of this type of proprioceptive loss were negative in all lone 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 patient described is probably not the mixed nerve trunks or 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 satisfactory and it is suggested that further elucidation of spinal ganglion or root involvement be obtained by exploiting a primate experimental model for polynuromatous leprosy.


RE91

CLAV-TOES CORRECTION. PERSONAL TECHNIQUE

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A. Salisn, J. S. Shah, G. Chauhan

Clav-toes are common deformities in leprosy. Frisch has identified 3 degrees of deformity I & II are the most common in our clinical experience. We propose a 4th degree which can be corrected in 20 minutes and it is usually done along with foot-drop correction.

TECHNIQUE: With a tenotomy knife a stab incision is made midway between the FIP and MP joint of each toe on the plantar aspect. In grade I a stab incision is sufficient. In grade II, we prefer a star-shaped incision. The knife is pushed down to the bone and both flexor tendons are cut. The whole toe is forcibly kept in dorsiflexion. As the tendons are cut, usually "gives in." Often the volar capsule of FIP and/or MP joint acts as contracting forces. By moving the knife a few millimeters, both capsules can be reached and incised. Now the toe can be dorsiflexed maximally. The tendons are cut, usually "gives in." Often the volar capsule of the FIP and/or MP joint act as contracting forces. By moving the knife a few millimeters, 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. The procedure was POP with toes in manual extension. The technique of finger dynamography is simple, requires minimal tools and can be performed at the bedside.

The modification consists in joining one digital stump portion of the sublimis tendon with the flexor profundus tendon of the donor finger.

During the next two and half years, 72 cases were studied, who either underwent sublimis-tendon transfer or sublimis tendon transfer. In most of the cases, a considerable degree of passive hyperextension of the proximal interphalangeal joint was present in the donor finger and the modification indicated.

In no case, where the modified surgical procedure was used, signs of post-operative sublimis-minor deformity developed.

The results are discussed.
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 woeitic 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.

RE96
RESULTS OF SURGICAL CORRECTION OF LAGOPHTHALMOS (GILLIES TECHNIQUE) IN LEPROSY PATIENTS
ROSEMARIE BACCARELLI, MARCOS VIRMOND, FRANK DURKSEN

THE RESULTS OF THE TEMPORALIS MUSCLE TRANSFER (GILLIES TECHNIQUE), in 51 EYES (54 PATIENTS) HAVE BEEN ANALYSED. THE MAIN OBJECTIVE WAS TO EVALUATE THE DEGREE AND TIME NEEDED TO RECOVER VOLUNTARY EYELID BLINKING, IF ANY OF THE OPERATED EYES, IN 34 (66.67%) EYES.

ALTHOUGH THERE WAS NO RETURN OF INCOMPULSIVE EYELID CLOSURE IN ANY OF THE OPERATED CASES, IN 34 (66.67%) THERE WAS COMPLETE AND LASTING VOLUNTARY EYELID OCCLUSION, FEW (25%) 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 EPHIPHORA HAS BEEN SEEN IN 15 (35.65%) EYES.


RE97
NURSING CARE FOR LEPROSY PLANTAR ULCERS CURED WITH DORSO-PEDIS VESSEL PEDICLE FLAP
Ling Xinhua, Yu Bing
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Plantar ulcers of 10 leprosy patients were successfully managed by transplantation of dorsopedis vessel pedicle flap in combination with the implementation of comprehensive nursing care. Among these patients, there were 8 males and 2 females, 2 NB and 8 PB. The age and duration ranged 18-25 years and 6-12 years respectively. The duration of ulcers ranged from 6 to 10 years with a size varying from 2×3 cm to 4×4 cm. Excluding one case of failure resulted from necrosis of flap 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 3 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 that "plantar ulcers are curable" as long as they cooperate well with the nurses during the whole period of treatment. 2) Keep wounds clean and sterilized and observe their related facilities to prevent cross infection. 3) Monitor the status of flaps, including their temperature, color and elasticity closely. 4) Guide the 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 LEPROSY PLANTAR ULCERS
Wang Zaiming, Li Fatima, Dong Liwen
Shanghai Zanyi Hospital, Shanghai, China

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 6 months to 20 years with a size of 4 cm to 80 cm². The locations of ulcers were heel; 4; lateral border of the foot; 10; central area of the sole; 1; head of the first metatarsal bone; 1; and head of the 3rd-5th metatarsal bones; 26. As for the status of deformities, 7 cases with talipes equinovarus, 4 with club foot, 3 with boat-shaped foot (crest reversed) and 6 with enlarged plantar areas.

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, usually for those ulcers not suitable for skin grafting (group 3).

All patients were protected shoes and were trained in self care of foot. After an observation for more than 5 years, the overall recurrence rate of ulcers was 35% (13/55). The recurrence rates of group 1, 2 and 3 were 43% (13/30), 10% (2/20, the lowest) and 8% (4/55, 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
localised at the planter side of the feet or the lower legs. If necrotic muscle and necrotic-infused tissue were removed surgically. In case of infection, proven by bacterial cultures, systemic antibiotic therapy was given. Preoperative preparation consisted of three times daily changing of gauze pads moistened in physiological saline until the wound was clean and granulating. Five or 6 mm full-thickness punch grafts were taken from the upper leg and laid approximately 5 cm apart on the ulcer bed and were fixed by a paraffine gauze and bandaged. The first dressing change was performed after 5 days. In superficial wounds repithelialisation 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
Satish Arolkar and Noshir Antia
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Traditional surgical decompression of the posterior tibial neurovascular structure yields equivocal results. The authors postulate that the posterior tibial artery is the most compromised structure in the posterior tibial neurovascular compartment. The best surgical results in healing of plantar ulcers are 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
Frank Duerksen, Carlos Kiens, Alvin Stahl
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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 Disease 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 (20-87). Thirty patients were classified as Lepromatous, 2 Borderline and 4 Tuberculoid. The indications for amputation were: Foot ulcers (11) - malignancy (7) - leg stasis ulcers (6) and Charcot, rigid equinus-varus, P.V.D., (3) each. Average time of follow-up was 6 years (1-20). Most patients with below knee and transmetatarsal amputations had recurring 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. Preoperative and post-operative rehabilitation is an effective option for many patients suffering from the typical "claw hand" deformity resulting from Hansen's disease.

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 underlying 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
Wang Xinshuai, Wang Jixia, Yan Zikuan, Wang Guoxin, Sun Xiusian
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Eyebrows are not able to regrow in MB patients with anaesthesia. Eyebrow transplantations with single autologous hair were performed for 274 HD 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 aneuralized with antibiotic liquid. The shape of transplanted eyebrows was designed as "taker-shaped" for males and "curved-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 200 hairs on each side for females. The region implanted was tied up with pressure dressing. The patients were given some analgesics and/or antibiotics after transplantation.
TRI
THE DEVELOPMENT OF MULTIPROFESSIONAL PREVENTION AND CONTROL OF DISABILITY COURSES IN MINAS GERAIS, BRAZIL, FROM 1988 TO 1992
Linda Lohmar, Aparecida Grossi, Beatriz Orsini
Coordenacao Estadual de Controle de Hansenose, Secretaria de Estado da Saude de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

Limited resources have made it necessary to prioritize programs and services. In leprosy the 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 teach 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 techniques and results will be demonstrated.

TR2
ACTION KIT: A MEANS OF PROMOTING LEPROSY AWARENESS
Mathilde Gruner
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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
DEMEDIUMING VIDEO - TRAINING HEALTH WORKERS IN ELEMENTARY VIDEO PRODUCTION
Michael Joseph
Schieffelin Leprosy Research & Training Centre, Karigiri-632106, India

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 videoclip 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 up 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
Pushpika Pratap, Indira Johnson
SHARE, 16A, Adarsh Apts., Golibar Road, Santa Cruz (E), Bombay 400 055, India

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
Testaye Hults and Neil Aldred
ALERT. P.O.Box 165, Addis Abeba. Ethiopia

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
Ananth Reddy, Hannah Anandaraj and Manisha S. Rehabilitation Home, Kukatpally, Hyderabad-500872, (A.P.) India

Health Education in leprosy involves educating the people by communicating scientific facts towards adopting a rational attitude and practices. This action-research was an attempt to identify the communication methods employed.

The study respondents were 9th class students from 29 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 (C1)

Secondly the schools were divided into clusters of five and in each cluster, one of the five methods namely lecture, exhibition of films, 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 (C2) which indicated the present level of awareness.

Statistical analysis was done. Results pertain to the significance of difference between pre and post scores (C1>C2) and among the different methods. The reliability of the questionnaire was also tested and the methodology is discussed.

* Tests of variance.

TR7
MANAGEMENT STRATEGIES IN THE CONTROL OF HOOKER'S DISEASE IN THE STATE OF MINAS GERAIS-BRAZIL FROM 1988 TO 1992
Aparecida Grossi, Maria Ana Leboeuf, Eli Nagathées, Maria Tereza, Linda Vebre
Coordenacao Estadual de Controle de Hansenismo, Secretaria de Estado da Saude de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

The authors discuss some of the epidemiological and operational aspects of leprosy's disease control in the state of Minas Gerais, Brazil, from 1988 to 1992. In 1988 the state of Minas Gerais had 37,182 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 was to develop human resource capabilities: to implement a decentralised control program, to expand the use of multijoint 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 new cases detected and, the number of services treating the disease with MDT.

TR8
MEASURES AND EFFECTS OF LEPROSY PROPAGANDA IN SICHUAN PROVINCE
Wang Baoguo
Sichuan Provincial Institute of Dermatology and Venereology, Chengdu, Sichuan Province, China

Leprosy propaganda is associated closely with realizing 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 programmes of local government at different levels. 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 260 persons times per year, making people get rid of their fears of leprosy. A simple social survey showed that 81% of the population surveyed recognized that the infectivity of leprosy is not strong. 74% considered leprosy is curable and 94% have a view that leprosy patients should have a right of work after cure. As a result of continuous and intensified propaganda activities about the knowledge 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 0.14% (1984) to 0.04% (1991).

TR9
PARTICIPANTS' EVALUATION OF A TRAINING PROGRAMME
Arunthathi S and Ebenezer Daniel
S L R T C Karigiri, Tamilnadu, India 632 106

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 Abbott.

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 (SW5) 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 SW5.

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
Linda Spencer Ph.D., Bjorn Kurnia M.D., Stephen Cole Ph.D.
National Leprosy Training Centre, Ujung Pandang, Indonesia and Georgia Baptist College of Nursing Atlanta, Georgia

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=103) 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 .59, 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 - IMAGING HINDS AND CHALLENGES
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Health Education as an essential component of the service delivery system for the management and eradication of leprosy has been emphasized time and again in almost all forums for several decades. It is an 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 areas namely, 'the degree of meaning' and 'the degree of effort'. The factors influencing evaluation of health education methods and programmes, interpersonal 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 subject of interest, biocromism and 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 power 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 PROGRAMME IN SENEGAL
Jean-Claude Naudin, Pape Malick Sylla, Gregoire Deneau and Wally Woye
DAHW, Dakar, Senegal

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 set up with 4 main components: 1) training for health 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, booklet, 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
ADECIONES EDUCATIVAS Y HANSSEN'S DISEASE CONTROL PROGRAM IN THE STATE OF SAO PAULO - BRAZIL
Zemerli L. Lima, Ottilia S J, González, Helevreda M. Abriolo, Wander N. Nascimento, Magda Maria, 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 implementing educational actions for Hansen’s Disease Control Program, developed by the Health Teams in the 65 Regional Health Offices of the State of Sao Paulo.

Its major objective is socialization of scientistic 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 ludopoagological techniques, regarding a problem raisignpedagogical option. Until the year of 1992,
professionals were prepared to develop these actions including local planning of educative actions.

Pedagogical advisory and educative material complement conditions to ensure that educative actions will reach the impact previewed by the Hansen's Disease Control Program for the State of Sao Paulo.

TR15  
THE IMPACT OF PERSONNEL TRAINING ON THE EPIDEMIOLOGICAL AND OPERATIONAL INDICATORS - BRAZIL, 1986 TO 1997  
Aécila L. Rodrigues, Durcy R. V. Ventura, Gerson O. Penna, Gerson F. M. Pereira e Maria C. C. Magalhães

Coordenação Nacional de Dermatologia Sanitária, Ministério da Saúde, Brasília, Brazil.

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 endemic, in a service network with a quantitative and qualitative deficit of staff. This paper analyzes 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 reflection, construction and reconstruction of knowledge, adoption of strategies for problem-solving and integration of health activities. Since 1991, the revision of training programs reinforced the assistance-teaching axis, stimulating operational research, the participation of the reference centers and the expansion of RDT as the single region named in Brazil.

TR16  
Arlete A. Sampaio e Maria B. R. Moreira

Coordenação Nacional de Dermatologia Sanitária, Ministério da Saúde, Brasília, Brazil.

Starting from a situation diagnosis of the Hansen's Disease Control Programme in the Federal District in 1990, the authors outline main guidelines for personal training. Between 1990 and 1992, the personnel training program 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, known 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 program.

TR17  
THE USE OF "MATCHED QUESTIONS" IN PRE- AND POST-TESTS, TO EVALUATE TRAINEES AND FACULTY IN A LEPROSY MEDICAL OFFICERS' TRAINING PROGRAMME  
K S Satish Kumar, Sivaji Suresh, Hemmanth Daniel & Arvindnath S

S L T Kargiri, Tilamada, India 632 106

Pre-and-post-tests are an established and useful method of evaluating training programs, and have been used at Kargiri in the Six Mass Leprosy Medical Officers' training course. The main objectives of these tests are two-folds. 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 post-tests. 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 benefited 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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Federal University of Rio de Janeiro/MS/HUCCFF

The evaluation of leprosy patient attendance at the 4 public medical schools in the great RIO made in 1960 showed a low level of compliance to official norms of the national program.

Considering this we introduced an Interventionist Project in one of these medical schools and its main goal is to develop University concepts on leprosy control by means of moving the student practice from the University hospital to the Health Care centers located in the Campus neighborhood.

Making the University Co-Responsible 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 at District level organization - The more health units are attending patients in a slum area improving the University concepts about leprosy and control programmes. The students of biomedical areas have contact with leprosy patients in several opportunities such as primary health care program in health centres in theoretical and practical aspects. The students are being involved in the leprosy practice attendance at the University hospital in the Services of Dermatology, General Medicine, 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 select leprosy prospective studies has already been done.

The current results make us recommend 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  
Dr. Ravender, VK Meshul, KG Gopamary, MK Khan, CS Jaiswal 5 Gupta, S Parete and R Ganapati

Bombay Leprosy Project, Vidyanand Bhavan, VN Purav Marg, Sen-Chunabhatti, Bombay 400 022 and District Leprosy Unit, Raipur, India

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 multi drug treatment district emphasizing only three suspicious symptoms - 1) hypopigmented, anaesthetic patches; 2) shiny oily skin and 3) deformities of limbs. Colour photographs and patients were used for demonstration.

22 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 usual family welfare enumeration 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 defuxsion care could perhaps lead to a gradual process of integration of leprosy work with general health care services. However further operational research in this direction is needed.

TR20
EARLY DETECTION OF OCULAR LEPROSY
KUNAL SINGH, MANU MEHRA
SRIVANSA REHABILITATION HOME, KOLKATA, INDIAN

The number of registered cases of leprosy was 3.2 million in 1990, 25% of these have got ocular involvement and may be 50% may have blindness. 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 stances, 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 Srivansah Rehabilitation Home, Kolakata, India.

TR21
"SIMULATION GAME" AS A MODEL OF HEALTH EDUCATION IN LEPROSY: AN EXPERIENCE FROM THE HUMAN LEPROSY CONTROL PROJECT IN MAHARASHTRA, INDIA
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A "simulation game" has been introduced as a part of the Lepr0sy Training Course for village ctadets in the Regency of Sidoarjo, 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 cadets, sitting around an illustrated playing chart (80x120cm) which contains some written questions from No.1 - 20. Conducted by a leader as a moderator, the order throw a dice to get the number of question to be answered. The other participants are requested to give a comment, additional information or reaction 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 cadets from several districts of Sidoarjo. Evaluation on the individual ability and performance of leprosy cadets showed a better ability 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
Namza Chum, Petra Graf, Nustanga Gunzareth
National Tuberculosis and Leprosy Programme, Dar es Salaam, Tanzania

Training for National TB/Lepr0sy 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 Dispensarey) Politicians and the community have been trained. Each group had a training schedule ranging from 2-30 days depending on the type of training B.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 now training topics have to be chosen, after all for the close relationship of H.I.V. Infection and T.B.

TR23
HANSENIAISIS EN LAS ESCUELAS
Dora Martina Cyprente, RocileCas Barbara dos Santos, Sara Aquilar 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
Djihan 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. Twenty 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 16 out of 23 said there were too few words in the leaflet.
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 otherwise.

"Interview effect" has been suggested for the increase in control area.

Voluntary reporting and treatment regularly of patients increased during the intervention program.

TR26
EDUCATION SANITAIRE LEPROSE
Enquete dévaluation des connaissances et de la perception de la lépre à la MARTINIQUE

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J.C CAROLINA - PA H. CONSTANT-RESPORTES
PA A. LEOTLONG - C. CHARLES-NICOLAS
PA J.C SAINT-BENECHA
***************
Tout d'abord, l'enquête préliminaire menée en 1986, montrait une bonne connaissance du symptôme initial de la lépre et attestait en évidence la transmission des messages, mais également soulignait la peur du sujet atteint de cette maladie.
La seconde enquête évaluative en 1993 permet d'assurer des constatations et observations, d'autre part d'analyser l'impact de 10 ans d'intervention 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. Rodriguez-Domenech.

El programa contra la lepra en México plantó como objetivo eliminar la transmisión de la enfermedad para finales de 1994, reduciendo su tasa 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 lineamientos 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 incapacidad con recomendaciones sobre cuidados que deben proporcionarse a los enfermos y su familia. También se diseñaron materiales audiovisuales para capacitar al personal de salud con los temas de diagnóstico, tratamiento y prevención de incapacidades.

También 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 nuevos conocimientos, en la comunidad. Los resultados de la encuesta mostraron mayor conocimiento de la enfermedad por la población.

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 3.3 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, 140542 leprosy cases, PR 4.82, Trial 30-40%, Literacy 48%, NDT started 1983. By the end of 1993 it is anticipated that all 33 districts of the state will be covered by NDT.

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 & SPH.

Seminars of Students Academic Society, 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 appear in MBBS MCQ (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 EDUCATION, DECREASE AND EFFECTS OF A WOUND REDUCTION PROGRAM FOR 72 WORKERS WITH HANSEN'S DISEASE IN TAMAI, MINAS GERAIS-BRAZIL

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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-PROCEED 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 34%. 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 man 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 propagating health awareness to their families (community).

To control spread of infection-public education regarding disgusting antisocial habits like indiscriminate spitting, unattired 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.