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CONGRESS ABSTRACTS

The abstracts of the papers and posters presented at the XIII International Leprosy Congress were published prior to the Congress as an issue of *Health Cooperation Papers,* Professor E. Nunzi, Editor. As a cost-saving measure, these have been photoreproduced here without editorial changes.—RCH

ABSTRACTS

FREE PAPERS
FP 001 - FP 265

FP 001

MONOCLONAL ANTIBODY BASED DOUBLE ANTIBODY SANDWICH ASSAY FOR DETECTION OF ANTIGEN IN SERUM OF LEPROSY PATIENTS.

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The present day serodiagnostic tests for leprosy are based on antibody detection against M.leprae sonicate (protein antigens), M.leprae specific lipid (phenolic glycolipid) and surface antigens of M.leprae.

While the presnece of antigen either in body fluids or in tissues may indicate an active state of infection, presence of antibody on the other hand generally appears later during infection and lasts much longer even after the disease is subsided.

Using monoclonal antibodies a double antibody sandwich immunoradiometric assay was standardised, and the tudy was conducted on different types of patients and their contacts.

Monoclonal antibodies MLO4, MLO6 and ML34 which react with 35 KD, 12 KD (proteins) and 40-50 KD (Polysacchride) antigens respectively of M.leprae have been used in the assay. It is observed that the polysacchride antigen (40-50 KD cross reactive) is degraded slowly compared to the protein ones. The present study indicates that 35 KD and 12 KD based specific assays for M.leprae are important in distinguishing leprosy from tuberculosis infection.

The efficacy of the assay and its use in the serodiagnosis of leprosy will be discussed.

FP 002

A TRIAL TO COMPARE SERODIAGNOSTIC TESTS FOR LEPROSY

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Six kinds of serological tests for leprosy, i.e. fluorescent leprosy antibody absorption test (FT), enzyme-linked immunosorbent assay (ELISA) using synthetic disaccharide-BSA antigen (NDH) or synthetic trisaccharide-BSA (NTH) or deacylated (ES) or sonicated (WMT) phenolic glycolipid-1 of M. leprae and passive hemagglutination test (HAT) using NDH, were independently carried out at 3 laboratories by using the same set of coded sera which were collected from 6 Asian countries and USA. The sensitivity of FT and HAT was significantly higher than that of the other tests in 43 sera from paucibacillary leprosy patients. FT and NDH showed significantly lower sensitivity than ES and HAT in 154 sera from multibacillary leprosy patients. Treatment of these patients for 2 years or longer reduced the sensitivity of every ELISA tests and HAT, while that of FT was elevated by the treatment for 6 months to 2 years. The percentages of positive reactions in FT and HAT were significantly higher than those in the other tests with 81 sera from contacts and 135 sera from non-leprosy cases, suggesting that the former two tests are useful for detecting subclinical infection with M. leprae.

FP 003

Serology During the Clinical Course of Treated Leprosy

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Serum antibodies to a synthetic version of the M. leprae-specific phenolic glycolipid I (ND-O-BSA) & the common mycobacterial antigen lipoarabinomannan (LAM) were assessed in selected patients undergoing outpatient therapy for leprosy in San Francisco from 1981 to 1986. A total of 724 sera obtained sequentially from 90 patients classified clinicopathologically as LL (54), BL (12), or BT (24) are included in these analyses. Patients were selected for study either because therapy was initiated in 1981-82 or because they underwent a significant reaction. Antibody titers were considered positive when ELISA optical density values were >3 s.d. from the mean of a healthy population in a leprosy non-endemic locale, >0.10 for ND-O-BSA & >0.40 for LAM. Antibody to ND-O-BSA was more commonly positive (85% initially & falling to 77%) in sera obtained in each of the six initial years of therapy than antibody to LAM (67% to 33%). An analysis of variance of paired determinations revealed that the average antibody to both ND-O-BSA and LAM fell significantly in all 3 forms of leprosy between years 1-2 & 1-3 ($P \leq 0.02$). Average yearly antibody responses to LAM consistently fell over all yearly intervals up to 4 years, but antibody to ND-O-BSA fell significantly only during the first year of therapy. Neither intervening lepra type 1 or lepra type 2 reactions significantly affected the overall course of antibodies to either moiety over intervals between 1 & 4 years. Additionally, single antibody determinations were made on a further 45 BL & LL patients who had been on treatment for 6 to 36 years (average 10.5 years) and who were skin smear negative in 6 disparate sites. Significant antibody to ND-O-BSA and LAM was detected commonly: 19 had antibodies to both moieties; 11 to only ND-O-BSA, 5 to only LAM, while 10 had antibodies to neither. The implications to clinicians of these results will be discussed.

FP 004

Detection of phenolic glycolipid I of Mycobacterium leprae for monitoring the chemotherapy of leprosy.

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Phenolic glycolipid I (PGL-I) is a Mycobacterium leprae-specific antigen and has been used widely for the serodiagnosis of leprosy. The presence of PGL-I in sera of untreated lepromatous patients and the absence of the antigen in long-term treated patients have suggested

that PGL-I might be useful for a monitoring tool for the effectiveness of the chemotherapy of leprosy. In this study, a rather simple PGL-I detection tool was developed, and 21 new patients classified as BB, BL, or LL were examined for the presence of PGL-I and its antibodies before and after the chemotherapy was initiated. Among the 21 patients, 19 (90.5%) had detectable PGL-I in their sera or were seropositive to the antigen. Of 14 patients with BI 5+ or higher, 12 (85.7%) were PGL-I positive and 13 (92.9%) were seropositive to PGL-I. However, only 1 (14.3%) of 7 patients with BI 4+ or less were PGL-I positive and 6 (85.7%) were seropositive. When patients with PGL-I in sera were monitored with regular intervals after chemotherapy, PGL-I titer declined as early as one week after chemotherapy. The geometric mean titer of PGL-I among 8 patients who had been followed more than 3 months were 54.3 at day 0, 42.3 at week 1, 25.3 at week 2, 17.4 at week 3, 9.1 at week 4, 3.3 at week 8, and 1.0 at week 22, respectively. During the same period, however, there were no appreciable changes in anti-PGL-I antibody levels and bacterial indices. This study thus showed clearly that PGL-I in serum might be the most reliable parameter to monitor early responses of leprosy patients to the chemotherapy.

FP 005

COMPARATIVE STUDIES OF SERUM IgA1, IgA2 AND IgM AGAINST PHENOLIC GLYCOLIPID I IN LEPROSY PATIENTS AND CONTACTS

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Since infection with Mycobacterium leprae takes place through dermal and mucosal surfaces, where IgA plays a major role in immunological defence, we characterized serum IgA antibodies against Phenolic Glycolipid I (PGI) with respect to subclass distribution in leprosy patients, contacts and controls by an enzyme-linked immunosorbent assay. Our results show that serum anti-PG IgA in patients and contacts are essentially of the IgA1 subclass. Anti-PG IgA1 titers correlate with anti-PG IgM titers in leprosy patients, IgM predominating over IgA1. Both anti-PG IgA1 and anti-PG IgM mean levels decrease from the lepromatous towards the tuberculoid pole of the disease spectrum. Although anti-PG IgA1 as well as anti-PG IgM levels generally increase with increasing bacillary index (BI), a number of BI-negative patients show elevated anti-PG IgA1 and/or anti-PG IgM titers, indicating a persistent immune reaction against PGI. Interestingly, a number of contacts were detected with elevated anti-PG IgA1, but not with anti-PG IgM, suggesting that appearance particularly of serum anti-PG IgA1 might be an early event in leprosy. The determination of anti-PG IgA1 therefore may be considered as a possible tool for the detection of leprosy in its incubating subclinical stage.

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FP 006

AN ENZYME IMMUNOASSAY (EIA) BASED ON ANTIBODIES AGAINST HUMAN NERVE ANTIGEN FOR DIAGNOSIS OF ALL CATEGORIES OF LEPROSY PATIENTS

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EIA's based on IgM class of antibodies against the phenolic glycolipid unique to M.leprae detect primarily multibacillary leprosy patients, & are limited for diagnosis of other forms of leprosy. A new EIA has been developed which measures antibodies against the human peripheral nerve antigen(s). Sera from 220 patients belonging to LL (77), BL (43), BB (39), BT (48), TT (11) were correctly diagnosed by this assay. It was negative for 95 normal healthy laboratory personnel. Sera of 80 apparently healthy subjects from the endemic areas of Madras and Chingelpattu were screened, 59 were negative and 21 gave a weak reaction. The assay was discriminatory for Tuberculosis. Sera of 112 active pulmonary tuberculosis patients did not give any reaction. The assay was also negative with sera from patients suffering from various dermatological disorders such as psoriasis and scabies. However, patients of systemic lupus erythematosus, and Guillan-Barre syndrome gave a relatively weak reaction.

Inter and intra-lab validations confirmed the reproducibility of the assay. Third party validation trials are being carried out at the Central Leprosy Training and Research Institute, Chingelpattu. Results on 106 patients, 18 controls and 62 apparently healthy controls are available. The test was able to diagnose clearly 104 out of 106 leprosy patients.

FP 007

GELATIN PARTICLE AGGLUTINATION TEST FOR SERODIAGNOSIS OF LEPROSY--A NEW SIMPLE TEST USEFUL FOR FIELD APPLICATION.

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4) Central Research Laboratory, Fuji Rebio, Inc.

The discovery of M. leprae specific phenolic glycolipid antigen (PGL) and the successful synthesis of antigenic trisaccharide moety of PGL opened a new horizon to serodiagnosis of leprosy. We have synthesized a new semi-synthetic antigen, NT-P-BSA, useful for serodiagnosis of leprosy by conjugation of synthetic trisaccharide to BSA via phenyl propionate as the linker arm. Then we sensitized artificial gelatin particles with NT-P-BSA and developed a new diagnostic kit named "MLPA".

MLPA can detect mainly IgM class of anti-PGL antibody which plays an important role in humoral immune response to M. leprae infection. The possible fields of application of the test are:

1. Monitoring of MDT: Through the follow-up study, we found that the antibody level decline by the effective chemotherapy showing the possibility to use the test for monitoring of Multi-drug therapy.
2. Prediction of relapse: We experienced a case to show the elevation of antibody level six months prior to the clinical relapse.
3. Detection of high risk group: Preliminary results of contact survey in endemic area proved that about 40% of them are positive to MLPA showing the possibility to detect high risk group in the contacts by this test.

FP 008

FREQUENCY AND POLYREACTIVITY OF HUMAN ANTIBODIES TO PHEN GL-1 FROM LEPROSY PATIENTS DEFINED BY ANTI IDIOTYPES

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Two human monoclonal antibodies (MAb), PR4 and TH3 were produced by fusion of peripheral blood cells from two lepromatous patients with the human lymphoblastoid cell line GM 4672, and selected on the basis of binding to M. leprae, Phen GL-1 and ssDNA, but not RNA by ELISA. Although binding profiles of these two IgM Kappa MAb were similar, only PR4 bound to basal keratinocytes of normal human interfollicular epidermis and astrocyte cytoplasm in normal brain tissue. Rabbit anti idiotypes produced against these MAbs were specific for their respective idiotype, and id-anti id binding was inhibitable by both Phen GL-1 and ssDNA. The PR 4 idiotype was detected on IgM and IgG and was elevated more than 3SD above the mean of 30 local controls in 48% LL, 56% BL, 40% BT, 33% TT in 187 highland Papua New Guinean leprosy patients. Skin binding and fluctuating concentrations during ENL reactions suggest a pathologic role for these germ line encoded antibodies, which bind not only mycobacteria but also auto antigens.

FP 009

A PASSIVE HEMAGGLUTINATION TEST FOR LEPROSY USING A SYNTHETIC DISACCHARIDE ANTIGEN

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There is need for simple, sensitive, specific and reproducible test for serodiagnosis of leprosy. A passive hemagglutination (PHA) for leprosy was developed to meet these requirements. A synthetic disaccharide , conjugated to bovine serum albumin and specific for the phenolic glycolipid of M. leprae, was synthesized as described by Chatterjee , Cho, Brennan and Aspinall. The antigen was optimally sensitized, in 0.1 M acetate buffer pH 4, to sheep erythrocytes (SRBC) already preserved with pyruvic aldehyde, tanned and treated with glutaraldehyde. The sensitized SRBC were suspended in 0.15 M PBS pH 7.2 containing 0.5% bovine serum albumin, 0.1% sodium azide, lyophilized and used for testing sera from leprosy, tuberculosis and normal control, at 1:64 and 1:128 serum dilutions. It was found that if the hemagglutination reaction with specimens at $\geq$ 1:128 are considered positive, the test were positive in 84.2% of 38 cases of multibacillary leprosy, 16.7 % of 24 cases of paucibacillary leprosy, 16.7 % of 6 contacts of multibacillary leprosy, 11.8% of 51 cases of tuberculosis and 3.7% of 54 blood donors more sensitive but less specific. The results was similar to that of ELISA test for IgM antibody to the same synthetic antigen. The present PHA is simple sensitive, but moderately specific. Its simplicity, specificity and sensitivity make it highly suitable for large scale screening of contacts in leprosy endemic areas.

FP 010

Evaluation of chemotherapy in leprosy by monitoring Mycobacterium leprae specific antibody titres in patients.

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Although good treatment is available for leprosy, one is often faced with the problems like selecting a suitable drug regimen, prospective evaluation of disease activity,emergence of drug resistance and relapses etc. This study was initiated to observe whether periodical assessment of M.leprae specific antibody titres in patients undergoing treatment would help in solving these problems.

So far 110 LL/BL patients, who were either untreated or undergoing treatment for various time durations, have been subjected to this study. The M.leprae specific antibody titres were measured by applying two methods: An ELISA for antibodies to phenolic glycolipid I and an RIA (serum antibody competition test or SACT) for antibodies to an epitope on 35 kd antigen of M.leprae. Correlation between antibody titres, bacteriological indices and durations of treatment were sought.

The antibody titres tended to decrease with increasing durations of treatment or decreasing BI, but there were large individual variations. Of particular interest was the observation that even after attainment of smear negativity for AFB, some of the patients continued to show high antibody titres. Significance of these observations will be discussed.

FP 011

EVALUATION OF NATURAL PHENOLIC GLYCOLIPID (GPI) AND ARTIFICIAL ANTIGEN IN THE SERODIAGNOSIS OF LEPROSY

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We compared ML with PGl, ND-O-BSA,ND-P-BSA,NT-O-BSA, and NT-P-BSA angigens by ELISA determinations. The sera were collected from patients with leprosy(136),active tuberculosis (TB) (20),autoimmune skin disease (ASD)(10) and normal controls (NC) (30). The main results are as follows:

1. The six types of antigen used all showed very strong reactivity to sera from leprosy patients with their MOD being: PG1 0.76,ML 0.69,ND-O-BSA 0.52,NT-O-BSA 0.45,ND-P-BSA 0.40 and NT-P-BSA 0.28.In the TB sera,except for PG1(Mod=0.11) and ML (Mod=0.24), the other values were all 0.10 in the ASD sera, the values of MOD were all <0.10 (0.03-0.08). Interestingly, in NC's sera, the reactivity was negligible (MOD:0.02 with ML, 0.01 with the others). The results of quantitative analysis showed that, except for the sensitivity of ND-P-BSA-ELISA which is lower, the other ELISA's are highly sensitive and their positive rates were 96-100% in multibacillary patients (MB). The ML-ELISA, PG1-ELISA, NT-O-BSA-ELISA showed higher cross-reactivity with TB sera (40-45%),however, the specificity of ND-O-BSA-,ND-P-BSA-,and NT-O-FSA-ELISA maintained higher positive rates (75-79%) in leprosy patients, especially in the MB (91-96.4%).

2. There are highly significant positive correlations (R-values: 0.82-0.965) between the antigens used, and individual agreement (77.2-88%).

3. IgA, IgG and IgM antibodies are all found in leprosy patients' sera.Their content are at different levels and orders. In ML-ELISA, IgG)IgM)IgA; in PG1-ELISA IgG)IgM)igA;in paucibacillary patients (PB),however,IgM>igG)IgA in MB. The same results were obtained with ND-O-BSA,ND-P-BSA-,NT-O-BSA- and NT-P-BSA-ELISA, naaely, IgM)IgG)IgA. From these values the authors regard all ELISA (except NT-P-BSA-ELISA) compared to each other are useful for preliminary screening of leprosy infection.Furthermore, ND-O-BSA-(1st), PG1- (2nd),ND-P-BSA-(3rd) and NT-O-BSA-ELISA (4th) will be more useful for serodiagnosis of leprosy, detecting subclinical infection with M. leprae. In studying relevant leprosy epidemiology, especially ND-O-BSA- and PG1-ELISA are useful.

FP 012

EVALUATION OF FLA-ABS.T/PG1-ELISA AND THEIR USES IN IMMUNOEPIDEMIOLOGIC STUDIES ON LEPROSY

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We have systematically conducted comparison studies of FLA-ABS.T/PG1-ELISA for validity, reliability and practicality in large sample of 284 cases of leprosy,20 cases of tuberculosis,172 normal controls (from a non-endemic area of leprosy), 425 cases of leprosy household contacts (HC) and 2573 cases of random population (RP). The results indicated that FLA-ABS.T/PG1-ELISA are highly sensitive and specific for detecting antibodies against M.leprae. Their correct index (CI) are all higher than 90%, and the positive predictive value and negative value are all higher than 90% as well. Additionally several agreements were found in leprosy immuno-epidemiological studies:

1. The positive rates increased gradually from TT to LL in leprosy patients in FLA-ABS.T/ELISA (in HC, the positive rates of PG1-ELISA are much higher with multibacillary patients than with paucibacillary patient contacts);
2. The positive rates detected by FLA-ABS.T are identical with those in PG1-ELISA either in HC or in RP;
3. In RP, the positive rates detected with FLA-ABS.T/PG1-ELISA are all similar in each district and in concordance with the general trend of prevalence rates.

On these bases the FLA-ABS.T/PG1-ELISA tests may be regarded as useful tools in the diagnosis of leprosy, detecting subclinical infection with M.leprae and relevant immuno-epidemiological studies. However, because the PG1-ELISA is simpler, rapid, cheaper and easier to use, this may be more practical than FLA-ABS.T in future.

On the other hand, it is emphasized that the methodology of dried blood from ear lobes is very important in achieving leprosy field immuno-epidemiological studies on a large scale. Meanwhile,the authors still hold the two preliminary concepts of "subclinical infection zone" and "diagnosis line".

FP 013

INDETERMINATE LEPROSY IN A POPULATION SURVEY AND IN THE SUBSEQUENT FOLLOW-UP OF CHILDREN*

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The paper discusses various aspects of indeterminate (I) leprosy in the initial survey undertaken in the Burma BCG trial (69 242 inhabitants), and in the annual examinations of 28 220 children in the trial followed up over periods of five to eight years.

Age-specific rates in the initial mass survey are presented. In total 1914 cases were detected (6.2% I, 76% T, 16% L and 1.8 B.) Among the children in the BCG trial 768 cases were detected: 255 of them had the I form and their proportion (33%) was much higher than in the population survey. Of these 255 I cases only 4.3% had a negative or doubtful lepromin reaction. Two-thirds of these 255 cases evolved to the tuberculoid pole in less than one year. No L cases appeared in the trial population until ten and eleven years after the start of the trial.

It is concluded that whereas a high proportion of indeterminate cases regress spontaneously or evolve towards the T pole, the indeterminate lepromin negative cases are important in the dynamics of the disease, because a proportion of them, if untreated, tend to evolve towards the L form. This stresses the importance of detection and treatment of I cases at an early stage in an effective strategy for controlling leprosy.

* The data are reported with WHO approval.

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FP 014

A NEW CONCEPT OF STAGING PAUCIBACILLARY LEPROSY AND ITS APPLICATION TO THE ANALYSIS OF POST-TREATMENT RESULTS OF A MDT STUDY IN MALAWI

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Paucibacillary leprosy patients differ not only by age, sex, and classification but also by the degree to which the disease has advanced. For the analysis of leprosy field research data the latter heterogeneity creates difficulties which have been insufficiently addressed so far. As one way to overcome these difficulties we have developed a five point staging system for paucibacillary leprosy. Essentially the extent of sensory loss in skin lesions, peripheral nerve enlargement and extent of functional loss were used for this staging system, stage-1-patients being those with definite histopathological evidence of leprosy but non-anaesthetic skin lesions only and stage-5-patients being those with definite disabilities typical for leprosy neuropathy.

When applying this staging to various outcome data in patients recruited into an ongoing MDT study in Malawi, a strong association between outcome after treatment and stage at intake became apparent. This association is particularly marked for the development of disabilities, late Type-I reactions, incidence rates and the disappearance of skin lesions. No patients with stage-1 or stage-2 disease at intake developed disabilities, while 4.7 % and 18.2 % of patients with stage-3 and stage-4 disease respectively had developed disabilities two years after completion of treatment.

FP 015

SENSORY EVALUATION IN LEPROSY PATIENTS USING NYLON FILAMENTS

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If early detection of nerve function loss is important for timely medical/surgical intervention to prevent progressive and permanent nerve function loss, then it is mandatory to have a reliable sensory testing instrument. This is very important in leprosy patients where decreased sensory function may preceed motor function loss.
Sensory testing using a ballpoint pen is practised in most leprosy control programs. Bell and Tomancik have shown that this is not a reliable testing instrument.
Sensory testing instruments that use nylon filaments are available commercially but the cost will be prohibitive for universal acceptance by field workers in most leprosy control programs.
When nylon filaments are available a simple testing instrument can be made from a bicycle spoke or discarded syringes and needles.
The authors have used surgical nylon and by attaching different grades of surgical nylon at different lengths to a handle were able to get a range from 0.03-10 gms. It is suggested that when it is only practical to use one filament to use the one that indicates loss of protective sensation.
Seven filaments with different buckling forces (0.5-50 gms) have been applied to the palm of the right hand and the sole of the right foot of controls and a group of leprosy patients. The results will be presented.

FP 016

3299 CASES OF CHILDREN LEPROSY IN FUJIAN

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The data of 3299 cases of leprosy in children, up to the age of 14 in Fujian Province, china, are analysed. In general the first lesions appeared in lower extremities in 34.7% and in upper limbs in 25.1%. In multibacillary patients , however , lesions mostly appeared on the faces and necks as infiltrations and maculae. In paucibacillary patients the lesions appeared as erytheaas and plaques. Depigaentation and anesthesia were more evident in paucibacillary patients.

The incidence rate and the prevalence in child cases were parallel to those of the population at large, so that childhood leprosy reflected the overall severity of the disease in the whole population.

At the time of confirming the diagnosis, the percentage of cases with a single skin lesion was 32.5%, and with a two year history of disease in 42.95% of the cases. Both percentages were larger than those comparable in the adult patients.

The mean time needed for a clinical cure in multibacillary children was 86 months and in paucibacillary cases it was 54 months. The relapse rate was 1.8% which was significantly lower than that of the adult patients.

FP 017

SITE OF EARLY LESIONS IN LEPROSY.

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The mode of Transmission of Leprosy is still not clear. In order to find out weather the site of Lesion and its nature could reflect on the pathogenesis of Leprosy, we analysed our clinical material.

209 cases, out of 2800 attending our Leprosy clinic, of Paucibacillary Leprosy were subjected to clinical charting, smear & Histopathological examination. It was observed that 166 had solitary lesion, 38 presented with two lesion while only 5 were having three lesion. Histologically 102 cases were of TT, 97 of Indeterminate and 10 of BT. It was interesting to note that in 186 (88.99%) cases lesions were present on uncovered parts of body while only in 13 (6.22%) patients they were on covered areas. In remaining 10 cases (4.78%) lesions were present on both the areas. Site of lesion did not show any co-relation with age & sex of patient & duration of illness.

We are of the opinion that if bacilli enters through epidermal route where it is exposed to skin associated lymphoid tissue(SALT), it probely generates sensitization & can end up either in no disease or indeterminate leprosy or tuberculoid spectrum. This observation might strengthen the concept that mode of entry could be a deciding factor in the development of the disease spectrum.

FP 018

PREVALENCE ET EVOLUTION DE L'INFECTION AU VIRUS HUMAIN D'IMMUNODEFICIENCE (VIH) CHEZ LES LEPREUX EN HAITI

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De Avril 1985 à Décembre 1987, 275 lépreux de 5 à 90 ans (200 tuberculoides, 75 lépromateux, soit 135 femmes, 140 hommes) ont été testés pour VIH par la méthode Elisa. Le taux de positivité est de 6.5% (13/200) chez les tuberculoides, et 6.6% (5/75) chez les lépromateux.
Des 18 lépreux séropositifs préalablement asymptomatiques, 14 (78%) ont développé un ou plusieurs symptômes associésau VIH après une pé-

riode de 6.3 mois (2-15 mois). 4/18 (22%) ont récidivé de leur lèpre sous traitement comparés à 2/257 séronégatifs (0.7%).
Parmi les lépreux préalablement séronégatifs, 75 suivis sur une période moyenne de 22.8 mois ont été retestés, 7/75 (9.3%) ont séroconverti: 6 hommes et 1 femme, tous symptomatiques de l'infection par le VIH.
Conclusion:
- Chez les lépreux, la séroprévalence de l'infection par le VIH est de 6.5%
- 78% des lépreux séropositifs ont développé une symptomatologie associée au VIH
- 22% des lépreux séropositifs ont récidivé de leur lèpre sous traitement
- 9.3% des lépreux séronégatifs ont séroconverti sur une période moyenne de 22.8 mois.

FP 019

THE ANATOMICAL DISTRIBUTION OF SINGLE LEPROSY LESIONS IN AN AFRICAN POPULATION, AND ITS IMPLICATIONS FOR THE PATHOGENESIS OF LEPROSY.

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Detailed data on the anatomical sites of single leprosy lesions found on 632 confirmed leprosy cases newly ascertained during total population surveys carried out by the LEPRA Evaluation Project in Northern Malawi will be presented and discussed. The data reveal a remarkable predilection of single lesions for the face (28.2%) and the extensor surfaces of the arms (25.0%). On the other hand, there is a scarcity of single leprosy lesions on the legs (10.1%) and on the chest and upper abdomen. This distribution is very different to the distribution of lesions reported for populations in India, Burma and the Philippines. Data will be analyzed by age, sex and mode of detection, and the implications of the findings will be discussed with reference to completeness of examination, potential skin entry of M leprae, temperature gradients on the skin and the pathogenesis of disease.

FP 020

DIAGNOSTIC VALUE OF CARDINAL SIGNS/SYMPTOMS IN PAUCIBACILLARY LEPROSY.

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With the help of sensitivity and specificity criteria, an attempt is made to quantify the gain in certainty in diagnosis with the use of various cardinal signs/symptoms (S/s) of leprosy in order to study their predictive value in correct diagnosis of paucibacillary leprosy (PB) by the Paramedical workers. The study was based on the findings in 326 new cases of paucibacillary leprosy detected by 10 paramedical workers during a recent field survey. Observations in the present study confirm the scientific basis of presently used combinations of cardinal S/s for correct diagnosis of leprosy especially the combination of (skin) patch with loss/impairment of sensation. The detailed observations made in the study will be discussed.

FP 021

CASE STUDY OF PATIENTS RELEASED FROM OBSERVATION

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Objective of study: MDT was introduced in the leprosy control programme in Nepal in April 1982. The programme in the Western and Mid-Western regions has now reached the stage of releasing paucibacillary patients from a 4 year period of observation.

Since there are only a few guidelines/recommendations given concerning the minimum on-going care for this group, it has been the objective of this study to reveiw the general condition of those cases and give appropriate recommendations in order to meet their minimum needs eg. foot ware, ulcer care, etc. In addition this study reflects also on the necessity/benefits of the observation period. It covers the following aspects:

1. Patients compliance with the observation period after release from treatment.
2. Post treatment observation to:
   - determine progress or regress of clinical features of leprosy;
   - to record patients faith in the reliability in the treatment regime.
3. Evidence of relapse.
4. Social aspects - social acceptance of the cured in their society after release from treatment.
5. Need for continuous minimal care for those suffering from disabilities, social problems and others.
6. Conclusion: findings and recommendations.

FP 022

Tetanus in leprosy patients: report of 5 cases

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Five cases of tetanus in Ethiopian leprosy patients are reported. There were 4 males and 1 female; 2 TT, 1 BL, 1 LL, 1 unknown; 4 had no history of trauma, 1 had a nail wound.

It might be expected for leprosy patients to have an increased incidence of tetanus. Studies from Africa and Asia indicate that tetanus is rare in leprosy patients. A series of 503 tetanus cases in adult Nigerians found no patient with leprosy.

Significant levels of anti-tetanus antibodies have been found in non-immunized populations. 197 of 200 Ethiopian falashas arriving in Israel had antibodies detected, 30% having protective levels. Antibody levels are increased in unimmunized lepromatous leprosy patients, with up to 45% having protective levels, possibly due to bowel clostridium stimulating the lymphoid system. Furthermore, clostridium appears to be rare in the foot ulcers of Ethiopian leprosy patients.

The finding of these 5 cases, the first from Africa, is quite significant, and indicates that protection against tetanus is incomplete. Single-dose vaccination is recommended.

FP 023

TUBERCULOID RELAPSE IN LEPROMATOUS LEPROSY

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In 1978, we presented 3 patients who, having commenced dapsone therapy when they were undoubtedly suffering from advanced lepromatous (LLs) leprosy, subsequently

relapsed, after several years of smear negativity, with tuberculoid leprosy, which was clinically and histologically BT. The two who were tested were Mitsuda positive.

We now extend our observations, comparing this rare syndrome with that of the development of BT l esions in apparently-quiescent MBL patients shortly after their commencing the 2-year course of MDT. Its relevence to immunotherapy, and the attempted induction of positive lepromin skin tests, will be discussed.

FP 024

Is the Proportion of New Indeterminate Leprosy Cases Dependent on the Screening Interval?

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It is often suggested that many new leprosy cases classified as TT, BT, BB, BL, or LL have previously passed through a transient, unnoticed Indeterminate stage prior to diagnosis. The implication of this hypothesis is that the shorter the screening interval in an exposed population, the more likely that the new cases found will be in the Indeterminate stage. To test this hypothesis, we present distributions of new cases found in two ethnically different high-risk populations in Pohnpei, Micronesia, by screening interval, age group, and disease classification. The implications of these findings for disease control strategy are discussed.

FP 025

MOUSE FOOTPAD PATHOGENICITY OF THE CHEMOAUTOTROPHIC NOCARDIOFORM ISOLATES FROM HUMAN AND MOUSE FOOTPAD LEPROSY TISSUES.

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and

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Pathogenicity was studied of the acid-fast chemoautotrophic nocardioform isolates from infectious leprous tissues from 2 humans, 2 mouse footpad (MFP) and one armadillo isolates, in the mouse footpad, with respect to the granules produced by these bacteria in vitro, as well as that of the free bacilli derived from these granules. The granular pathogenesis was characterised by local inflammation and swelling by 4-6 weeks, which subsided ; there was typical granuloma formation around these granules with gradual disintegration of the granules and infiltration of the mycelial mass into the muscles, connective tissue, epithelial cells and nerve bundles ; large number of macrophage globi were present from which plenty of mycelial tufts were seen to emanate. By 6-9 months these granules got completely disintegrated into large number of free bacillary bodies, small single-layered rings, small globi and some residual mycelium. The free bacillary forms from the MFP resembled the leprosy bacilli found in the original specimens, in morphology, in acid-fastness and its pyridine extractibility, metabolism and in exhibiting DOPA oxidase and catalase and in respect of multiplication in the MFP.

FP 026

ARMADILLOS IN LEPROSY RESEARCH: CURRENT STATUS.

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Although the nine-banded armadillo (Dasypus novemcinctus) has been the major source of M. leprae for use in research and vaccine production since 1971, we still must use wild caught animals and young born to dams that were pregnant when captured because of failure to breed them routinely in captivity.

A major problem in breeding was solved when it was found that females, under conditions of stress, often retain dormant embryos (or gametes) for 12 months (and in one case, 24 months) beyond the normal date for bearing young. This phenomenon, unique among mammals, had made it impossible to distinguish between delayed parturition and successful breeding.

Four of nine females have now produced young in captivity under conditions that preclude their being pregnant when captured. Three of the females were housed in outdoor pens and one in an indoor concrete and cement block pen. It is believed that the major problems preventing successful breeding in captivity have now been solved, although considerable work remains to be done before this can be accomplished routinely.

FP 027

Skin Lesion in Strain 13 Guinea Pigs Induced by a Human Non - Myelin Antigen in Dorsal Roots.

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Systemic skin lesions have previously been produced in Dutch Bantam rabbits using sensory peripheral nerve as antigen. In order to develop this model in an inbred strain we injected 4 Strain 13 guinea pigs with a suspension of the nuclear fraction of human dorsal roots plus Freund's Complete Adjuvant into the footpads. Two weeks after injection, skin lesions with hair loss appeared on the back in 3 of 4 guinea pigs, the fourth developing a lesion after 6 weeks. After 7 months observation, 7 lesions had appeared, one lasting 5 months. Three Strain 2 guinea pigs injected with the same antigen have not developed any skin lesions after 3 months observation. Biopsy of the skin lesions in Strain 13 guinea pigs showed degeneration of unmyelinated fibres in dermal nerves. Myelinated axons were enlarged with increase in neurofilaments. These results in myelinated axons are similar to those in various human and experimental dying - back neuropathies or axonopathies. These experiments also provide further evidence that the skin lesions in nonlepromatous leprosy are due to an autoimmune response to a non - myelin antigen in sensory peripheral nerve rather than being directly due to M. leprae. The antigen may be a component of the axoplasm or axolemma.

FP 028

THE ROLE OF $CD8^+$ CELLS IN RESISTANCE AND DELAYED HYPERSENSITIVITY REACTIONS IN MYCOBACTERIUM LEPRAEMURIUM INFECTION

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T cell lines and clones were used for studies on the adoptive transfer of resistance to Mycobacterium lepraemurium and delayed hypersensitivity reactions to soluble mycobacterial antigens. Cells were propagated in vitro in the presence of whole autoclaved M. lepraemurium organisms as antigen and supernatants containing Interleukin-2. It appears that $CD4^+$ cells alone mediate delayed hypersensitivity responses and $CD8^+$ cells can regulate this response. Adoptive transfer of resistance demonstrated that both $CD8^+$ and $CD4^+$ cells are necessary for mediating resistance to infection.

FP 029

An experimental model of chronic nerve compression and the effect of M.leprae infection on a nerve with chronic compression neuropathy.

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The ulnar nerve at the elbow is one of the common sites of nerve involvement in leprosy and entrapment neuropathies. An experimental model of chronic compression peripheral neuropathy, resembling the ulnar nerve at the elbow was produced by angulating the right sciatic nerve of a mouse, using a monofilament polyamide thread. The left sciatic nerve acted as a normal control. In a controlled study of 80 such animals half of them were inoculated with $4x10^4$ M.leprae in both their hind foot-pads. Preliminary observations will be presented of clinical findings and ultra structural changes within the sciatic nerves of both infected and non infected animals.

FP 030

SEROLOGIC RESPONSES TO MYCOBACTERIUM LEPRAE-SPECIFIC PHENOLIC GLYCOLIPID-I ANTIGEN IN SOOTY MANGABEY MONKEYS WITH EXPERIMENTAL LEPROSY. Bobby J. Gormus, David K. Ohashi, Gerald P. Walsh, Wayne M. Meyers and Cynthia B. Trygg, Delta Regional Primate Research Center, Tulane University, Three Rivers Road, Covington, LA 70433 and the Armed Forces Institute of Pathology, Washington, DC 20306, USA.

We inoculated 4 pairs of sooty mangabey monkeys (Cercocebus atys) with serial, 10-fold dilutions of mangabey-origin Mycobacterium leprae. The high dose pair received 4.8×10^{10} M. leprae. Animals were closely monitored for symptoms of leprosy and serum samples obtained at intervals for 35 months. Longitudinal serum samples were assayed by an ELISA method for IgG and IgM antibodies to the M. leprae-specific phenolic glycolipid (PG-I) antigen.

In general, the onset of symptoms paralleled the dose of M. leprae, but the ultimate course of disease depended upon individual animal susceptibility. Both IgG and IgM anti-PG-I isotypes were observed in variable levels and patterns, related to the disease stage, among the 8 mangabeys.

High IgG and low IgM anti-PG-I titers correlated with less severe disease, whereas, initial high IgM titers and/or rising or sustained high IgM titers, especially along with low IgG anti-PG-I titers, preceeded or corresponded to periods of progressive leprosy.

The results show that both IgG and IgM anti-PG-I antibody isotypes can be present in significant titers among mangabeys early after infection with M. leprae. The relative levels of these anti-PG-I isotypes appear to be correlated with the susceptibility of individual animals to the development of lepromatous leprosy.

FP 031

PGL-1 INDEPENDENCE OF THE LEPROMIN (MITSUDA) REACTION IN PRE-SENSITIZED GUINEA PIGS.

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PGL-1, the principal, phthiocerol-containing glycolipid of Mycobacterium leprae, has been demonstrated to be species-specific and of major significance in the serologic responses of patients and experimental animals with multibacillary Hansen's disease (HD). Because of suspicions that PGL-1 may be a specific factor in pathogenesis of the characteristic lesions of HD, it was suggested that this unique substance could also be of importance in the development of skin-test reactivity to lepromin, particularly of the Mitsuda type. In fact, Job et al reported being able to produce delayed-type hypersensitivity granulomas, with lepromin-compatible histology, by intradermal inoculation of large quantities of extracted PGL-1 into lepromin-positive, but not lepromin-negative armadillos. However, because the quantity employed (100 µg) was 25-100 times that found in standard lepromin doses by high performance liquid chromatography (HPLC), questions of etiology in lepromin responsiveness in the armadillo model remained.

In order to explore further the role of PGL-1 in the lepromin reaction, guinea pigs pre-sensitized with armadillo-derived lepromins or BCG were skin-tested with doses of 5-100 µg of the purified glycolipid in comparison with standardized lepromin A, Dharmendra lepromin, sham lepromins and controls. Erythema and induration were measured over 4 weeks, and groups compared.

The results indicated a rapid disappearance of initial, mild reactivity to intradermal injections of PGL-1 preparations, in contrast to observed, delayed-positive (Mitsuda) reactions to either lepromin A or Dharmendra lepromin at 2-3 weeks. These observations indicate that PGL-1 is not, itself, responsible for lepromin reactivity in the guinea pig model, and raise the possibility that previously reported reactivity to PGL-1 in armadillos could have been due to other, co-extracted components of the leprosy bacillus.

FP 032

COMPARISON OF CELL-MEDIATED IMMUNE RESPONSES TO M. LEPRAE IN MICE FOLLOWING SUCCESSFUL INFECTION WITH M. LEPRAE OR IMMUNIZATION WITH KILLED M. LEPRAE.

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Spleen cells from Balb/c mice infected with M. leprae 6-8 months previously, responded in vitro to various mycobacterial preparations. The response to freshly isolated, Percoll-purified M. leprae (pp-ML) was, however, consistently higher than the response to irradiated M. leprae (gamma-ML), heat-killed BCG (HK-BCG) or heat-killed M. kansasii (HK-MK). The in vitro response to mycobacteria could only be detected in mice with at least 1×10^5 acid-fast bacilli in the foot pads. Kinetic studies of the in vitro response of popliteal lymph node cells following subcutaneous immunization with gamma-ML showed that the response was biphasic. One week after immunization there was a marked lymphoproliferative response to all killed mycobacterial preparations as well as to tetanus toxoid and medium alone. This non-specific phase declined rapidly coincident with emergence of mycobacterial specific response. By 21 days post-immunization, the response of lymph node cells was significantly higher when tested against mycobacterial antigens than when non-mycobacterial antigens were used. Spleen cells from immunized animals showed a short-lived monophasic response being detectable 2 weeks after immunization and falling to undetectable levels 5-6 weeks post-immunization. The spleen cell response was always lower than the corresponding regional lymph node response.

Our results show that there is a difference between the immune response following successful infection with M. leprae and that which follows immunization with killed M. leprae. The former is a moderate but systemic, long-lived response, elicited most strongly with viable M. leprae while the latter is a rapidly acquired, strong but localized, short-lived immune response directed mainly to antigens of dead mycobacteria. Whether the two immune responses are mediated by the same cells or whether these responses reflect similar or divergent mechanisms with regard to protective immunity is currently under investigation. Because mice successfully infected with M. leprae are considered immune to reinfection, our results suggest that these animals should prove very useful in studies of acquired immunity to M. leprae.

FP 033

ONTOGENESIS OF ANTIBODIES IN RHESUS MONKEYS INFECTED WITH M.LEPRAE

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Adult healthy Rhesus monkeys (Macacca Mulatta) selected on the basis of their negativity to Mitsuda lepromin were inoculated with M.leprae by both the intravenous and subcutaneous routes. Sera were collected at regular intervals over a period of one year. In microtitre plate ELISA, sera were screened using ND-BSA, M.w sonicate antigens and monkey peripheral nerve antigens. The results of the study revealed that antineural antibodies appeared at significantly high level first, followed by antibodies reactive with M.w antigens, and finally antibodies to phenolic glycolipid. After one year, the antibody titres against all the three antigens tested were significantly high. At the time of sera collections, there

were no visible signs of nerve damage as evidenced by dryness, scaling, resorption of terminal phalanges, deformities and ulceration. These observations suggest that on infection with M.leprae, antibodies directed to host peripherel nerve and Mycobacteria appear before overt signs of the disease. It is also indicated that in primates, nerve damage precedes the appearance of typical leprous lesions. Infected animals are currently under observation.

FP 034

Macrophage mediated immune responses in the sciatic nerves of M.leprae infected nude mice with possible bystander and autoimmune demyelination - an electron microscopic study.

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The pathological changes within the sciatic nerves of nude mice were observed ultrastructurally. The progression of these changes were observed at various intervals ranging from 3 to 22 months post-inoculation. Vascular changes were observed in the early stages, even in the absence of detectable infection. Endoneurial explosion of infection was observed in the later stages. Mycobacteria, myelin and cellular debris were found extracellularly and within macrophage phagolysosomes. Active macrophage processes appeared to encircle normal looking myelinated fibers without any bacilli within them. The Schwann cell cytoplasm of these fibers appeared to flow towards these processes suggesting some form of affinity between them. In the vicinity of these active phagocytic processes there was disruption of myelin suggesting an extracellular enzymatic mechanism in play. Macrophages also invaded myelinated fibres and their 'foot-like' cytoplasmic processes were actively stripping myelin. Extracellular disruption of myelin was also observed close to mast cells and plasma cells. It is known that macrophage-mediated immune mechanisms are operational when severe infections with intracellular pathogens occur, and the role of such mechanisms in nerve damage will be discussed.

FP 035

IMMUNO-ELECTRON MICROSCOPY OF MYCOBACTERIAL GRANULOMAS IN THE SCIATIC NERVES OF GUINEA PIGS

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A model of nerve damage in leprosy has been developed in the sciatic nerve of the guinea pig. Intraneural injection of 10^7 BCG organisms induces an epithelioid cell granuloma in two weeks, similar to those found in tuberculoid leprosy patients. In contrast, intraneural injection of 10^9 cobalt-irradiated M. leprae organisms induces a macrophage granuloma in five weeks, similar to those found in lepromatous leprosy patients. The experimental lesions show many of the features documented in studies of nerve damage in leprosy patients, such as demyelination with axonal sparing, perineurial thickening and increased fibroblast activity. Functional deficit has been demonstrated by electrophysiological techniques.

The phenotype of cells and distribution of Major Histocompatibility Complex Class II antigens within the experimental lesions has been investigated using an electron microscopic immunocytochemical technique on post-fixed, pre-embedded tissue. This procedure yields much more information regarding phenotype and cellular interactions than does conventional light-microscopic immunocytochemistry. Class II antigens are expressed on infiltrating leucocytes, endothelial cells and neurofibroblasts, but not on Schwann cells, in contrast to apparent findings at the light microscopic level.

FP 036

LEPROSY IN THREE SPECIES OF MONKEYS—AN OVERVIEW

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Nonhuman primates show great promise as models for studying the pathologic changes associated with leprosy as well as evaluating experimental vaccines.

We have experimentally infected three species of monkeys with Mycobacterium leprae. Of 33 mangabeys inoculated, 23 (70%) developed infection. Twenty-two mangabeys developed BL-LL disease, and one had a neuritic form of leprosy with evidence of erythema nodosum leprosum (ENL) in the ulnar nerve. Mangabeys with disseminated disease responded well to treatment with antileprosy drugs. A second mangabey was recently diagnosed with naturally-acquired leprosy. Seven rhesus monkeys inoculated with M. leprae have developed active leprosy and this species shows promise as an alternate model for laboratory studies in leprosy. African green monkeys inoculated with M. leprae developed polyneuritic leprosy; this species may be of great value in studies of the nerve damage associated with leprosy.

FP 037

SERODIAGNOSIS OF LEPROSY INFECTION IN 9 BANDED ARMADILLOS.

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Blood samples, collected with 3 months intervals after inocculation with 5.10^8 M.leprae bacilli, from armadillos were tested for the presence of anti-mycobacterial and M.leprae specific antibodies with : 1. an ELISA test using a BCG sonicate antigen. 2. Haemagglutination and ELISA tests using a synthetic antigen based on the structure of the 3,6-di-O-methyl-glucose epitope of PGL I of M.leprae. 3. 36 kd ELISA inhibition test. Binding of armadillo antibody was detected using peroxidase labeled anti-armadillo and/or anti-human IgM(μ). In most animals a rise in seroreactivity was observed after 6-9 months after inocculation. Sera from natural infected armadillos were also tested for presence of M.Leprae specific antibodies. Using a dot-ELISA sera from infected armadillos were also investigated for the presence of phenolic glycolipid I.

FP 038

INDUCTION OF THE LATE HIPERSENSITIVITY REACTION TO DNCB IN PATIENTS WITH DIFFERENT CLINICAL FORMS OF HANSENIASIS IN BRAZIL.

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One hundred and twenty Brazilian patients with several forms of hanseniasis were tested with DNCB.

1 - The sensitization of patients with hanseniasis to DNCB was lower than seen in the general population.
2 - The sensitization of the borderline and virchowian forms of hanseniasis was lower than seen in the indeterminate and tuberculoid forms.

Conclusion: There is a deficiency of the late immunity in the borderline and virchowian forms of hanseniasis.

FP 039

SOLUBILIZATION OF PREFORMED IMMUNE COMPLEXES IN SERA OF LEPROMATOUS PATIENTS WITH ERYTHEMA NODOSUM LEPROSUM

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Significant immunologic alterations inthe lepromatous patients with ENL,particularly with respect to serum complement have been reported earlier(Scan.J.Immunol.17,37,1983).Increased complement utilization appears tobe an important event in the reactional states in the ENL patients, when massive quantity of M.leprae alongwith its breakdown products from the bacilli-loaded macrophages is thought to be released into circulation and immune aggregates,thus formed may eventually initiate the inflammatory processes. To unfold the role of complement in the ENL episode,serum complement activity in leprosy patients has been studied,using solubilization of preformed immune complexes as an index.Solubilization capacity of sera from the lepromatous patients with or without ENL was found markedly reduced as compared to controls.After clinical remission of the lepra reaction,the patients showed no appreciable increase in the IC solubilization. Addition of fresh normal sera to the sera of these patients failed to restore this defective solubilization capacity.Further experiments revealed that M.leprae sonicate that is known to consume complement,interfered with the solubilizing capacity of sera.It is suggested that the presence of large quantity of circulatory bacterial products in the sera of these patients could possibly abrogate the IC solubilization.

FP 040

LYMPHOCYTE BLASTOGENESIS AND LEPROMIN REACTIVITY IN LEPROSY PATIENTS AND THEIR PARENTS.

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To determine whether there is an inherited familiar trait linked to the LTT, under stimulation with PHA, lepromin and M.leprae in culture medium containing autologous plasma, this test was studied in patients with the polar forms of leprosy and their parents. The lepromin reacting was also studied in the patients and their parents because, since the test is negative in L patients and a greater proportion of negativity is detected among their relatives, it may be assumed that the lymphocytes of these individuals could have a lower tendency towards blastogenesis than lymphocytes of T patients and their relatives.

Thirty individuals were studied, ten of them were patients (4 L and 6 T) and the remaining were their parents.115 LTTs, including control and stimulated cultures, were performed.

The results showed that in contrast to te patients and their fathers and mothers, L patients and their parents had a decreased blastogenic response.

Parents mainly the mothers and their L descendants tended to respond to LTT and lepromin test in a similar way, a fact that could favor the hypotesis of a inherited familiar trait of susceptibility to leprosy.

Fathers and their T descendants were lepromin positive and there was a relationship between this reactivity and blastogenesis. This could suggest a possible inherited familiar trait related to a relative degree of resistance.

FP 041

Immunological heterogeneity in type I reactions.

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Both peripheral blood related and lesional T cell perturbations have been studied in type I reactions of leprosy using in vitro correlates of cell mediated immunity and monoclonal antibody based in situ phenotypic identification of cells. Our results indicate a dichotomy in T cell perturbations occuring in borderline tuberculoid (BTR) and borderline lepromatous (BLR) type I reaction patients. Whereas ninety per cent of the BTR patients showed deterioration of lymphoproliferative responses and 40% of lymphokine production, 60-86% of the BLR patients showed emergence of antigen reactive T cells. In addition, the lesional granulomas of BTR patients showed a reduction, and BLR patients an increase in the CD4/CD8 ratios. However, these patients continued to reflect the background leprosy type in delayed type hypersensitivity testing with M. leprae antigens. In addition, 3/3 of the BTR and 4/7 of the BLR lesions showed keratinocyte Ia expression indicating local production of interferon- γ. It appears that the nomenclature of type I reaction does not adequately reflect the dichotomy of immunological perturbations that occur during these episodes.

FP 042

HUMAN MONOCLONAL AUTO ANTIBODIES FROM LEPROMATOUS LEPROSY

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The origin of auto antibodies in patients with leprosy was investigated by preparing human hybridomas from peripheral blood lymphocytes of a lepromatous patient fused to the human lymphoblastoid cell line BM 4672. Hybridomas were tested for binding to a DNAse treated sonicate of M. leprae and a panel of autoantigens in solid phase ELISAs. Of the 92 primary (uncloned) cultures, 14% bound ss DNA, 35% bound M. leprae, 11% bound both M. leprae and DNA and 16% bound to mitochondria. Several also bound to the acetylcholine receptor (AChR) of Torpedo mormorata. Monoclonal antibodies (MAb) derived from separate primary cultures revealed cross reactions between autoantigens and M. leprae, including one which bound mitochondria and the AChR. This MAb was recognised by an anti idiotypic antibody bearing the internal image of the AChR. These data suggest antigenic mimicry by M. leprae elicits autoantibody expression from the immune repertoire.

FP 043

Killing of human monocytes by specific cytotoxic T cells and nonspecific, MHC unrestricted killer cells after activation by mycobacterial antigens

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Little is known about the nature of the cytotoxic cells that eliminate human monocytes/macrophages infected with mycobacteria. We developed a cytotoxicity assay in which infected and ^{51}Cr. labelled monocytes were used as targets. As effector cells, PBL from healthy immune donors or leprosy patients were educated by antigen for seven days. Results indicate that efficient cell killing of autologous monocytes was induced by both BCG and M. leprae. Killing was generally higher against infected v/s non-infected targets, although there was still significant killing of the latter as well. Cytotoxity could be generated only with PBL from good LTT responders. Crossreactivity was observed between BCG and M. leprae but not with an unrelated antigen (tetanus toxoid). Killing of infected and non-infected allogeneic monocytes was as high as that of non-infected autologous ones. Parallel assays for natural killer (NK) cells showed that high NK-activity was generated both by BCG and M.leprae. Recombinant IL-2 alone also generated cytotoxic effector cells (so called lymphokine activated killer cells, LAK-cells) which equally lysed both infected and non-infected

monocytes. Cytotoxicity was reduced most by the depletion of Leu-1 (Pan-T) follwed by Leu-2 (CD-8) and Leu-19 (NK-cell) surface marker positive cells in that order. These findings show that mycobacteria have the ability to induce both antigen specific cytotoxic T-cells as well as non-specific "MHC non-restricted" killing, probably generated by activated NK cells.

FP 044

PERSISTENT REDUCED SOLUBILIZATION OF IMMUNE COMPLEXES IN LEPROSY PATIENTS WITH REACTIONS

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It is held that immune complexes(IC) play a vital role in the pathogenesis of some of the reactions in leprosy. The complement system is known to solubilize and render IC innocuous. We have previously shown that patients undergoing lepra reactions had lowered complement mediated IC solubilization (CMS).

We,therefore, undertook a prospective study of untreated patients and monitored their CMS sequentially while on therapy. In addition, the levels of complement component C3d, immunoglobulins G, A and M and circulating immune complexes were also estimated. A total of 26 patients were included in the study and were investigated at 3 monthly intervals for 2 years and clinically followed up for a total of 4 years.

It was found that the 14 patients who did not develop reactions at all had CMS values which were normal although they had elevated levels of CIC. The 12 patients who developed lepra reaction had low CMS values right from the inception of treatment. This remained below normal levels even after evidence of complement activation disappeared and long after the subsidence of reaction. The possibility of this defective CMS being a predisposing cause of lepra reactions will be discussed.

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FP 045

CHANGES IN CIRCULATING LEVELS OF AGALACTOSYL IgG DURING EPISODES OF ERYTHEMA NODOSUM LEPROSUM

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There is a biantennary oligosaccharide on a conserved N-glycosylation site on the CH2 domain of the IgG heavy chain. It has recently been observed that in several disease states (rheumatoid arthritis, Crohn's disease and tuberculosis) there is an increase in the circulating level of IgG molecules on which this oligosaccharide lacks terminal galactose, and so terminate with N-acetylglucosamine (agalactosyl IgG).

In contrast to the situation in Tuberculosis, levels of agalactosyl IgG are not raised above normal in any part of the spectrum of leprosy (Parekh et al, submitted). However, using a novel "dipstick" assay for agalactosyl IgG based on a monocloncal antibody to terminal N-acetylglucosamine, we now report that there is a brief peak of agalactosyl IgG during ENL episodes. Other studies have shown that levels of this glycoform of IgG may be regulated by T cells, and that it is involved in cytokine release from macrophages. Its production during ENL therefore casts some light on the pathogenesis of this reaction.

FP 046

INTRALESIONAL CELLULAR AND SOLUBLE IMMUNOREGULATORY EVENTS IN TYPE I ("REVERSAL") REACTIONS.

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Type I reactions in leprosy reflect a marked shift in the cellular immunity of borderline patients, away from the immunologic steady-state of typical, non-reacting lesions. They thus provide a valuable natural, human model of immunoregulation in leprosy. To examine the natural immunoregulatory events within human skin lesions, we have quantitated cell subsets and soluble immunoregulatory substances within multiple cutaneous blisters, induced by suction directly over reacting and non-reacting lesions.

In over 50% of reacting lesions, increases were observed in the total number of mononuclear cells, and of both T-helper and T-suppressor phenotypes, as well as in the H:S ratio. An absolute increase in the number of T-helper cells in reacting lesions is correlated with an increase in the level of Tac peptide (soluble IL-2 receptor) ($p < 0.01$). Increased Tac peptide is also associated with increased numbers of T-suppressor cells, but not to a statistically significant degree. Prednisone treatment results in a dissociation of these two parameters; cell numbers are reduced with or without reductions in Tac peptide.

These findings indicate that the likely mechanism for Type I reactions involves transient or intermittant activation of T-helper cells, together with their recruitment and proliferation within the lesion. Lesions without elevations in cellularity or Tac peptide are probably resolving reactions. The associated levels of gamma-interferon and prostaglandin E_2 in all of these types of lesions are under investigation.

FP 047

IMMUNOREGULATORY MECHANISM OF ENDOGENOUS GLUCOCORTICOID IN LEPROSY

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Serum levels hydrocortisone,glucocorticoid receptors in lymphocytes, enumeration of T-lymphocytes and lymphocyte transformation test (LTT) to PHA-P and M.leprae were studied in 18 lepromatous patients, 17 tuberculoid and 15 healthy controls. It was observed that an increase in glucocorticoid level in lepromatous patients was related to the activity of the disease process. Interestingly most of these patients ($P<0.005$) show an increase in glucocorticoid receptor content in lymphocytes.These patients further showed a depressed lymphocytic response to M.leprae than PHA-P. Low values of LTT to M.leprae and decrease in T-cell number were accompanied by high levels of glucocorticoid and increase in glucocorticoid receptor in lepromatous patients. Surprisingly the lymphocytes treated with cortisol-21-mesylate (a glucocorticoid antagonist) were showing an augmentation in the lymphocytic response to M.leprae.

Findings of these study indicate the role of endogenous glucocorticoid as regulator of circulating T-cell function. The increase in glucocorticoid level and glucocorticoid receptor content in lepromatous patients reflect the possible involvement of endogenous glucocorticoid in T-cell suppression.

FP 048

Tumor necrosis factor in leprosy patients.

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Tumor necrosis factor (TNF) is a cytokine with a broad range of biological activities. By means of cytotoxic activity for L929 tumor cells, we have assessed the levels of TNF in the serum and in supernatants of cultures of peripheral blood mononuclear cells (PBMC) from a group of patients with the polar forms of leprosy (T and L patients) and from healthy controls. Of the 6 T leprosy serum samples tested, 5 contained between 280 to 340 TNF units/ml. The levels of TNF were within the normal limits (less than 60 units/ml) in 6 L leprosy patients and in 20 healthy individuals sera tested.

PBMC from T patients stimulated with S. typhymurium lipopolysaccharide (PPS, 10ug/ml) or with lepromin (1x10^6 bacilli/ml) released high levels of TNF in vitro assay (220±22 units/ml). In contrast, L patients showed depressed production of TNF in cultures of PBMC stimulated with LPS or lepromin (65±28 units/ml). Spontaneous TNF synthesis in unstimulated cultures of PBMC from T patients was significantly increased when compared with that observed for healty individuals and for L patients.

The data presented here permitted us to speculate that the increased TNF synthesis by PBMC from T leprosy patients could be related with the control of the host response in leprosy.

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FP 049

GLUCOCORTICOID RECEPTOR AND LYMPHOCYTES IN LEPROSY

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Quantitation study on glucocorticoid receptors was made in 56 lepromatous patients, 27 patients suffered from Tuberculoid leprosy, 9 reactional patients and 30 Healthy controls. Radioreceptor assay for glucocorticoid was employed while using ^{3}H-Dexamethasone as a ligand in the whole cell assay of lymphocytes from the groups studied. More than two-fold increase in glucocorticoid receptor content in lymphocytes was noticed in lepromatous patients. Lymphocyte transformation study also shows that M.leprae were able to increase the glucocorticoid receptor expression when lymphocytes were stimulated with. Evaluation of glucocorticoid receptor content in purified T-cells on nylon wool column indicate that the increase in receptor content in lepromatous patient is mainly confined to T-cells. Cell sensitivity assay to Dexamethasone shows that the lymphocytes of the lepromatous patients are more susceptible to steroid induced cytolysis. The emerging hypothesis from this study indicates the possibility of endogenous glucocorticoid involvement in T-cell lymphopenia, inhibition of IL-2 synthesis, suppression of IL-2R expression and inhibition of clonal expansion of M.leprae reactive T-cells in lepromatous patients. However, it needs further confirmation.

FP 050

LEPRA REACTIONS AND DISABILITIES IN PATIENTS TREATED WITH DAILY MDT IN NEW CALEDONIA, FRENCH POLYNESIA AND GUADELOUPE.

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Since january 1980, in New-Caledonia, French Polynesia and Guadeloupe, the incidence of disabilities before and during daily multidrug therapy (MDT) was studied in 832 leprosy patients, 369 multibacillary (MB) and 463 paucibacillary (PB). The MDT consisted for PB patients of daily 10 mg/kg rifampicin (RMP) and 100 mg dapsone (DDS) during 6 months and for MB patients of daily RMP and DDS at the same dose during 24 months supplemented by 10 mg/kg of a thioamide during the first two months (Polynesia) or 12 months (Guadeloupe). Before treatment, two groups were distinguished : patients with disability and patients without disability. During treatment the incidence of new disabilities or the worsening of previous disabilities were studied in these two groups, year by year, in relation with the occurrence of lepra reactions (type 1 and type 2). The risk of neuritic complication is assessed in all groups of patients and is compared to the risk of neuritic complication in patients receiving WHO-MDT.

FP 051

REACTIONS IN LEPROSY : A STUDY OF 250 PATIENTS IN MDT PROJECT, BARODA DISTRICT (GUJARAT).

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The behavious of reactions in leprosy, (erythema nodosum leprosum and reversal reaction) was studied in 250 patients in this clinical picture in MDT project under operation since 5 years with assistance of the WHO and the SIDA.

The following data were collected : Age, Sex, Colour of the skin, type of reaction, number of erythama nodosum leprosum reactions, symptoms of first ENL and its development and symptoms of the reversal reactions. 17897 cases of leprosy registered for treatment between commencement of MDT and till January 1988. Out of which 17098 are MB cases and 10799 are PB cases. 235 MB cases and 15 PB cases developed reaction within period of 2 years treatment.

It was observed that all patients showed ENL were LL and those that showed reversal reaction were BB, BT and BL. The ENL appeared in majority of patients between 6 months to 2 years of treatment and reversal reaction between 6 months and 1 year of treatment. 33 patients required hospitilization, out of which 31 were MB and 2 PB cases. 57 cases required temporary interruption of treatment, out of which 54 were MB and remaining 3 PB.

The ENL was treated with high dossage of corticosteroids and analgesics, the reversal reaction with chloroquine, analgesic and steroids. The improvement in all cases was satisfactory.

FP 052

MALE HORMONAL INSUFFICIENCY IN MULTIBACILLARY HANSEN'S DISEASE--PREVALENCE AND CLINICAL MANIFESTATIONS

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Orchitis is well-recognized as a problem in patients with multibacillary leprosy. This may result from two distinct pathologic processes. There may be direct infection of the testis by Mycobacterium leprae with testicular damage produced by the associated inflammatory reaction. Alternatively, orchitis may be a part of a Type 2 reaction (Erythema Nodosum Leprosum) with destruction of testicular tissue resulting from immunologically-mediated inflammation.

Clinically, orchitis may be manifest as an inflammatory disease characterized by acute or chronic inflammation of the testes. Alternately, the primary manifestations may be those produced by a deficiency of male hormones due to testicular atrophy and destruction of the Leydig cells which produce testosterone.

Most of the clinical data available is derived from studies of men known to have testicular insufficiency, for example those with gynecomastia. There has been little or no correlation with clinical characteristics of the Hansen's disease of the patients studied. In this study, testicular function was assayed in a group of men with multibacillary leprosy. Serum levels of testosterone, luteinizing hormone (LH), and follicle stimulating hormone (FSH) were assayed. Clinical evaluation of those with abnormal results is presented. In addition, characteristics of Hansen's disease in terms of duration of disease, bacillary status, treatment, and Hansen's disease complications other than gonadal insufficiency are presented.

FP 053

ETUDE EPIDEMIOLOGIQUE DES DEFORMATIONS CHIRURGICALEMENT CURABLES DE 1059 PATIENTS HANSENIENS EN ZONE RURALE.

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Avec une prévalence globale de 19% , le Tanil Nadu en Inde du Sud est un des états les plus endémiques. Au Hemerijckx Rural Centre, près de Pondicherry nous avons revu un échantillon de 1059 patients dans le but d'apprécier l'importance des déformations chirurgicalement curables et les obstacles rencontrés par cette chirurgie.
Les déformations des mains, des pieds, de la face ont été particulièrement étudiées en fonction du sexe, de l'âge, du type lépreux, de l'activité et de la durée enregistrée de la maladie, de la nature du traitement et sa régularité, enfin de la nature du travail.
2% des sujets ont été opérés, les résultats sont discutés. 87% des patients qui auraient pu se faire opérer ne l'ont pas été. L'obstacle principal tenant du fait que le patient peu motivé, insuffisamment informé, ne peut arrêter son travail sans perturber gravement les conditions de vie de son entourage. Tous les résultats sont discutés.

FP 054

THE SIGNIFICANCE OF FACIAL PATCHES IN RELATION TO FACIAL NERVE DAMAGE IN PAUCIBACILLARY LEPROSY.

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Paucibacillary Leprosy patients numbering 1073 registered between 1982 and 1987 at Dhoolpet Leprosy Research Centre were reviewed for facial patches and facial nerve damage if any. Patients were divided in three groups for this study, depending on their status at the time of registration:

A: Patients with recent nerve damage, with or without involvement of the facial nerve.

B: Patients with type I reaction without nerve damage.

C: Patients without recent nerve damage or type I reaction.

The relation between large reactive patches in the face, especially if surrounding the eye or covering a large area of the cheek became very obvious. It was observed that early recognition and treatment of facial nerve damage with steriods and physiotherapy usually will lead to good recovery. We therefore recommend to monitor large reactive patches in the face carefully for the possible onset of facial nerve damage or even to treat such patches with a course of steroids as in case of recent nerve damage.

FP 055

The Reactional Tuberculoid - its Position in the Classification of Leprosy

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Forty reactional tuberculoid cases have been studied as stated by the classification of Madrid, according to the clinical, bacteriological, hystopathological, immunological and evolutive criteria.

The skin lesions have been analysed from the clinical point of view according to their manner of starting, their pattern, number, color, size, disposition, limits with the normal skin, edema of the extremities and also the presence or not of nervous impairment and lesions in other sites such as mucous membrane, lymphnodes and viscera.

The bacteriology has been studied by collecting six smears of the more active lesions at the start of the episode and others during their retrogression and an accurate histopathological examination has been performed.

The Mitsuda reaction has been investigated in all cases, during the episode and after its disappearance and in many of them a histopathological study has also been performed.

Finally all patients have been re-examined from two until five years after the starting of the clinical picture and verified for the presence of lesions in activity, presence of residual lesions, great atrophy and neurological sequelas. The bacteriology has been repeated in all of them, as the histopathological examinations and the Mitsuda reaction.

FP 056

DISABILITIES IN LEPROSY PATIENTS ASCERTAINED IN A TOTAL POPULATION SURVEY IN KARONGA DISTRICT, NORTHERN MALAWI

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This paper will present data on the disability status of more than 1700 new leprosy patients ascertained during the course of a total population survey (the Lepra Evaluation Project, LEP) in Karonga District, Northern Malawi. Relevant clinical details were extracted from field examination forms, coded, and entered onto microcomputers for analysis in conjunction with main LEP data files. Frequency distributions of disabilities will be presented by severity and anatomical site, for different groups defined by age, sex, mode of ascertainment and classification on registration. Approximately 15% of patients were considered to have some disability at time of registration. Of these, the disability was considered insignificant in 22%, moderately severe in 72%, and severe enough to interfere with daily activities in 6%. The incidence rates of disabilities developing during and after treatment of individuals initially without disabilities will be presented. The appropriateness of the WHO Disability Scale for such analyses will be discussed.

FP 057

Relationship of paralysis to age in leprosy patients in Ethiopia

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The extent of paralysis in leprosy varies from patient to patient. Many different factors are involved. Because it appeared that severe paralysis was much more prevalent in younger patients a survey of all reconstructive surgical cases in ALERT over a three year period has been carried out to determine differences and patterns of paralysis in different age groups.

FP 058

Maxillary Antrum in Lepromatous Leprosy (Antroscopic study)

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Lepromatious leprosy affects the nasal mucosa in about 90% of the patients and disease is liable to spread into the maxillary antrum. Antroscopy is the only

procedure helpful in accurate diagnosis of maxillary antral diseases. The present study consists of antroscopic observations in 20 untreated lepromatous leprosy patients. Various types of lesions starting from scattered areas of mild hyperaemia to frank ulceration or granuloma were seen. It has been found that the antero-inferior part of the maxillary antrum is most commonly affected site. The importance of maxillary antrum involvement in lepromatous leprosy with salient features are displayed in the light of available literature.

FP 059

FACIES LEPROSA: SOME RECENT OBSERVATIONS IN PATIENTS WITH LEPROMATOUS LEPROSY IN MALAYSIA

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The tripartite resorption of osseous projections of the maxilla, Facies Leprosa, was first reported by Hansen and subsequently confirmed in several contemporary studies. The purpose of the present study was to evaluate resorption of the anterior nasal spine (ANS) and the anterior maxillary alveolar process (AMAP) and ascertain whether these two events were dependent or independent of each other.
76 patients with lepromatous leprosy were evaluated. The prominence of the ANS was evaluated clinically by palpation using the scale of 0-not palpable, 1-barely palpable or 2-easily palpable. Observations were reconfirmed on lateral maxillary radiographs. Loss of AMAP was evaluated radiographically and quantified using previously established criteria.
The results showed that resorption of both osseous projections was a characteristic feature in lepromatous patients in Malaysia. However, there was no significant correlation between resorption in the two areas, suggesting that these may be independent events. These observations differ from other studies.
The resorption of AMAP is believed to be mediated by osteoclasts and by inference to the presence of the leprosy bacillus. Whether resorption of the ANS is by similar mechanisms or results from secondary infections of cartilage and bone in the nasal septum is not known.

This study was supported by a grant from the University of Malaya and an Investigators Award from the Heiser Program for Research in Leprosy. The study was carried out at the National Leprosy Control Centre, Malaysia

FP 060

TYPE I REACTION IN BORDERLINE LEPROSY - A DHOOLPET EXPERIENCE

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Among the 1269 borderline leprosy patients (BT,BB,BL), registered at Dhoolpet Leprosy Research Centre during the period 1982-87, the 215 cases that had clinical signs of Type I reaction in the skin were the focus of this study. Skin biopsy was done in 142 of these cases and histological evidence of Type I reaction was seen in two-third of these cases.

In this study it was observed that a majority of the cases(72%), presented with Type I reaction at the time of registration at the clinic and 28% developed reaction after start of anti-leprosy therapy. The frequency of patients developing Type I reaction among Borderline patients and the variations with regard to classification will be discussed.

Voluntary Muscle Testing was done in all cases. Among the 215 cases, 128 of them had associated loss of nerve function. Involvement of nerve function was slightly higher in the BT group as compared to the BL group.

All the 215 cases (with or without loss of nerve function), were treated by similar steriod regimens, with good response. The results will be presented. Results indicate that a similar steriod regimen could be used safely and effectively in Type I reaction with or without associated nerve damage. Colour slides of few patients before and after treatment will be shown.

FP 06.

DISABILITY SURVEY IN 1480 CASES OF LEPROSY

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In order to obtain some basic data on disability in leprosy,disability surveys were carried out in two leprosy hospitals,in one city and in one county in 1987. WHO Disability Grading (with minor modifications) was used for the survey. The causes of the disabilities were investigated.

A total of 1480 cases,females 372,males 1108,aged 8-92 years (mean age of 49.45 years) including active patients and cured leprosy patients, were examined. Among them there were 999 disabled patients, (the disability rate was 67.5%). Among the 999 there were 241 (73.48%) active and 753 (65.88%) cured patients. The percentage in the disabled cases whose anti-leprosy treatment had not yet begun was 55.8% (340/609). the number of patients, who suffer from deformity within four years after leprosy was diagnosed,was 36.5% (365/999). The number of patients with WHO Disability Grade 3 reached 418 (41.8%) though in Grade 1 there were only 120(12.0%).Leprosy reaction and nerve pain were the most common causes of disability.

The authors note that all the above-mentioned factors showed the severity of the leprosy disability problem in China today.It should be emphasized that arrested disease is not synonymous with the arrest of disability. Therefore objectives of leprosy control should have the following precedence: (1)to reduce the incidence, (2) to cure patients and attain complete rehebilitation and (3) to prevent deformities. Finally, the problems involved in disability surveys are discussed.

FP 062

DFS, AN ANTI-LEPROSY DRUG WITHOUT SIDE EFFECTS

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Deoxyfructose serotonin (DFS) has shown good results in two clinical trials of LL patients including early response. Pre-clinical pharmacology had shown absence of side effects and toxicity up to 200X clinical dose.

In vitro tests show that DFS enhances cellular immune response. Receptors for anti-erythrocyte anti-body on LL macrophages are demonstrated by erythrocyte rosetting. Infection with M. leprae markedly reduces rosetting. But in the presence of DFS this reduction in rosetting is not observed. Patient's peripheral blood lymphocytes, sensitised with leprosy antigen, show a low level of rosetting with patients' macrophages. DFS greatly enhances the lymphocyte-macrophage interaction.

The capacity of peripheral blood lymphocytes to respond to PHA is depressed in volunteers who have taken DDS for 7 days (Sengupta et al). This we have confirmed. A similar treatment with DFS shows, in preliminary tests, no reduction in PHA response. The evidence that MDT has some depressing effect on immune response, together with the failure of BI to fall to zero with prolonged treatment in some cases, suggests that DFS, perhaps with improved nutrition, will have a major role in MDT. It has anti-stress activity. Das Neves et al showed that gastric ulcers induced in rats by restraint were reduced by 50% by DFS.

We are making DFS analogues to further develop the range of these important drugs.

FP 063

THE EFFECT OF CLOFAZIMINE IN CELL MEDIATED IMMUNITY: INTERFERENCE WITH ANTIGEN PROCESSING AND PRESENTATION BY MACROPHAGES.

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The effectiveness of clofazimine in the treatment of leprosy as well as in erythema nodosum leprosum (ENL) is well documented. The mechanism by which clofazimine exerts its effectiveness in ENL is, however, unclear. Recent data suggest that the pathogenesis of ENL may involve cell-mediated immune responses. The study presented here examined in vitro T&B cell responses of clofazimine-fed Balb/c mice. In addition, we examined macrophage functions and T-cell subsets in the same animals. Our data show that clofazimine did not reduce antibody-producing cells, measured by PFC assay, in response to sheep red blood cells (SRBC's). Phenotypic analysis of both spleen cells and peripheral blood did not show any differences in T-cell subsets (Thy 1.2, L3T4, Lyt 2) when comparing clofazimine-

treated and control animals. We found that T-cells, from clofazimine-treated, BCG-immunized mice, respond normally, as compared to controls, in standard lymphoproliferative assays, using Con-A and BCG as stimuli. In crossover lymphoproliferative assays, using macrophages from clofazimine-treated mice in co-culture with normal lymph node cells (LNC's), our studies showed a marked decrease in lymphoproliferation, suggesting a defect at the macrophage level. Interleukin-1 (IL-1) production by peritoneal exudate cells in response to stimulation with BCG or lipopolysaccharide (LPS), was measured by using a modified C3H mouse thymocyte assay. There was a reduction in IL-1 production by cells from clofazimine-treated mice. On the other hand, interleukin-2 (IL-2) production by spleen cells in response to Con-A did not show any difference between the two groups of animals. IL-2 production in response to BCG was, however, reduced in clofazimine-treated, BCG-immunized mice. Macrophage phagocytic activity was enhanced in colloidal carbon clearance studies as well as in studies where macrophages were challenged with Candida tropicalis after in vitro feeding with clofazimine. We conclude, therefore, that clofazimine accumulates in macrophages and disturbs antigen processing and presentation which ultimately depresses lymphoproliferation and IL-2 production by T-lymphocytes.

FP 064

IN VITRO AND IN VIVO ACTIVITY OF MACROLIDES AGAINST MYCOBACTERIUM LEPRAE.

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We have rapidly assessed the in vitro activity of over 40 antimicrobial agents against intracellular and/or extracellular M. leprae by measuring the net energy level (ATP), catabolic (palmitate oxidation) and anabolic (PGL-I synthesis) capacity of the bacillus. Erythromycin was exceptionally active in these systems while two new macrolides possessing superior pharmacokinetic properties in man, roxithromycin and clarithromycin, demonstrated even higher activity against extracellular M. leprae. When administered in the feed of mice at 0.01 and 0.1% (w/w), erythromycin was undetectable (< 200 ng/ml) in the serum, roxithromycin was detectable only in mice receiving the higher dosage whereas clarithromycin was easily detectable at both dosages. When administered at 0.01% (w/w) in a modified kinetic mouse foot pad test, erythromycin was completely inactive, roxithromycin was inactive or partially active and clarithromycin was highly active. Clarithromycin is currently in clinical trials for other infections and its in vitro and in vivo activity against M. leprae warrant a clinical evaluation in leprosy as well.

FP 065

PEFLOXACIN OR OFLOXACIN IN LEPROMATOUS LEPROSY AT ADZOPE (IVORY COAST) : II BIOLOGICAL RESULTS.

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To assess the killing activity of a daily treatment with pefloxacin against M.leprae 10 lepromatous leprosy patients, previously untreated, were given orally 400 mg pefloxacin twice daily for 6 months. The killing activity was assessed by inoculating into the foot-pad of normal and nude mice serial dilutions of bacilli harvested from biopsies taken at regular intervals : before the start of treatment and after 2, 4 and 6 months of treatment. The proportion of viable organisms recovered from the pre-treatment biopsy varies from 0.06 per cent to 5 per cent. The M.leprae recovered in mice from biopsies taken after 2 months of treatment from 9 patients multiplied neither in normal nor in nude mice. One biopsy yielded organisms which multiplied in 4 out of 10 normal mice but in none out of the 10 nude mice inoculated. After 4 months of treatment no biopsy contained M.leprae capable of multiplying neither in normal nor in nude mice. Loss of viability studied with normal mice can be assumed to be between 60.32 to 99.58 per cent and when studied with nude mice between 96.6 to 99.999 per cent. Such an important killing activity led us to perform another trial with ofloxacin, another fluoroquinolone which activity in mice was better than that of pefloxacin. Twenty patients were randomly allocated in two equal groups and were treated either with pefloxacin or with ofloxacin. Treatment started with a single loading dose of 800 mg of one of the two drugs followed with no treatment for the next 7 days and then 56 days of daily treatment with 800 mg pefloxacin alone or with 400 mg ofloxacin alone. The study is still in progress.

FP 066

PEFLOXACIN AND OFLOXACIN ACTIVITIES AGAINST M.LEPRAE IN THE MOUSE.

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To compare the experimental activity of ofloxacin, pefloxacin and dapsone, 600 normal mice were infected with 5,000 dapsone-sensitive M.leprae and were randomly allocated in five treatment groups. Two months later, 4 groups of 120 mice were treated for 3 months either with 50 or 150 mg ofloxacin per kg body weight, or 150 mg pefloxacin per kg body weight or 0.01 g per 100 g diet with dapsone. The fifth group was left untreated to act as a control. Multiplication of M.leprae in the treated mice and in untreated controls was assessed by monthly harvests of 10 mice. The treatment of mice with 50 mg/kg ofloxacin, pefloxacin or dapsone resulted in a delay of multiplication of 4 months compared to the multiplication of M.leprae in the untreated controls. The delay of multiplication being one month longer than the duration of drug administration all of these treatments may be considered as bacteriopausal or slightly bactericidal (75 % killing). The treatment of mice with 150 mg ofloxacin per kg resulted in no growth of the organisms as late as 24 months after inoculation. Because as few as 5 viable M.leprae can give rise to multiplication in the mouse foot-pad, ofloxacin must have killed a large amount of M.leprae, may be all of the viable organisms. Such a profound killing activity has been observed only with rifampicin.

FP 067

THE DESIGN AND DEVELOPMENT OF NOVEL BROAD SPECTRUM ANTI-MYCOBACTERIAL COMPOUNDS FROM THIOUREAS.

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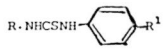
An initial[1] quantitative structure-activity relationship (QSAR) derived from a series of N,N[1]-diarylthioureas (1; R = aryl) indicated that the length of the substituent, R^1, correlated with activity against Mycobacterium tuberculosis. The optimal length of R^1 corresponded to O-n-C_4H_9 to O-n-C_6H_{13}. The poor pharmacokinetic properties of the current thioureas, their limited bacteriostatic properties, and the toxicity associated with the thiourea moiety all militate against their use as drugs to treat mycobacterial disease. We have addressed all these problems in designing new molecules in which both the groups R and R^1 have been manipulated to provide active compounds with better pharmacokinetic compounds and/or possible bactericidal properties. Additionally we have identified an alternative molecular fragment to replace the thiourea moiety. The design strategy, compound synthesis and testing results will be reported.



(1)

1. Hooper, M. and Kulkarni S.N. Br. J. Pharmac. 1982, 77, 584P.

FP 068

EFFECT OF OFLOXACIN ON EXPERIMENTAL LEPROSY

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Ofloxacin, a quinolone compound and a synthetic antibiotics which has a wide spectrum and its anti-mycobacterial activity in vitro and in vivo has been reported. The effect of ofloxacin on experimental leprosy with nude and normal mice was examined.

M. leprae originated from a LL patient and serially passaged through nude mouse foot pad were inoculated into right hind foot pads of nude and/or normal mice. The infected mice were treated with ofloxacin by giving the

drug containing diet or administrating the drug by gavage once daily.

The results suggest that ofloxacin is effective to suppress the growth of M. leprae in both of the nude and normal mice. In nude mice, ofloxacin treatment with drug containing diet in concentration of 0.025% for 100 days was slightly effective, and with 0.05% or 0.075% drug containing diet for 100 days showed suppressive effect in the growth of M. leprae. Dose response of the drug was observed in sub-groups of the treated mice. In normal mice, however, even in the group treated with 0.075% drug containing diet showed no effect. On the other hand, normal mice treated with ofloxacin 1 mg by gavage 6 times a week for 100 days (equivalent to 0.025% in diet) showed significant effect to suppress the growth of M. leprae.

FP 069

THE ACTIVITY OF MINOCYCLINE AGAINST M. LEPRAE-INFECTED MICE.

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Previously tetracycline itself was found in mice by others to be inactive for M. leprae. However certain tetracyclines, doxycycline & especially minocycline, are active in vitro against cultivable mycobacteria & have been for some of these infections demonstrated to be effective in man. In our first study with these tetracycline derivatives, groups of M. leprae-infected mice were treated by the kinetic technique (therapy from day 60 to 150 following foot pad infection) with doxycycline (0.02%) & minocycline (0.04%). Doxycycline was inactive but minocycline delayed multiplication for 270 days after discontinuation of therapy, which suggests that minocycline is bactericidal for M. leprae. In our second study by the kinetic technique we found that dietary minocycline 0.02%, 0.03% & 0.04% were bactericidal & even minocycline 0.004% & 0.01% were active. By an agar disk diffusion method utilizing the minocycline-sensitive Bacillus cereus strain, ATCC 11718, we established in this study that the mouse minimal inhibitory serum concentration for minocycline is <0.2 μg/ml, which is exceeded several fold by standard oral therapy with this commercially available tetracycline. Further in this study minocycline's activity against M. leprae was found additive with dapsone, kanamycin & rifampin. In our final study, conducted utilizing the proportional bactericidal technique, minocycline was found impressively bactericidal, 99.2 ± 0.7% alone & 99.7 ± 0.2% when combined with dapsone. This profound bactericidal activity is likely a result of minocycline's unique lipophilicity amongst the tetracyclines, & hence its ability to penetrate the largely lipid outer capsule & cell wall of M. leprae. Of particular importance to its possible application in therapy of leprosy, minocycline appreciably penetrates skin & neural tissue.

FP 070

PEFLOXACIN OR OFLOXACIN IN LEPROMATOUS LEPROSY AT ADZOPE (IVORY COAST) : I CLINICAL RESULTS.

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To assess in man, the activity of pefloxacin, a new fluoroquinolone, against M.leprae, 10 lepromatous leprosy patients, previously untreated, received orally 400 mg pefloxacin twice daily for 6 months. The therapeutic activity was assessed at regular intervals by clinical examinations, blood, urine samples, skin-smears and biopsies for mouse foot-pad inoculation. The clinical response was good with improvement of lesions, flattening of infiltration as early as within 2 months of treatment. Tolerance was satisfactory with 1 case of joint pain, 1 case of pruritis, 2 cases of dizziness and another 2 cases of abdominal pain without leading to the withdrawal of the drug. Bacterial index (BI) remained stable with mean values before treatment of 4.77 and at the end of treatment of 4.57. Morphological index (MI) decreased from a mean value of 38 % before treatment to 5.7 % within 2 months and no further change. Because another fluoroquinolone, ofloxacin, had an activity against M.leprae in mice better than that of pefloxacin, the activity of ofloxacin and pefloxacin in man was compared. Twenty patients were randomly allocated in two equal groups and were treated either with one daily 800 mg pefloxacin or 400 mg ofloxacin for 56 days. The clinical response was good for all patients with no difference observed between the two therapeutical groups. Tolerance was satisfactory except one episode of mental disorder in a female patient treated for 40 days with pefloxacin. The patient recovered within two days after the withdrawal of the drug. BI remained stable. MI fell significantly from 19 % before treatment to 5 % within 28 days for both therapeutical groups and no further change till day 56.

FP 071

POSSIBLE USE OF β-LACTAM ANTIBIOTICS IN THE TREATMENT OF HANSEN'S DISEASE

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We demonstrated that Mycobacterium leprae exposed in vivo to a β-lactam antibiotic synthesizes β-lactamase. The bacteria retained the ability to produce β-lactamase even when passaged in armadillos untreated with the drug, indicating that what is involved is de-repression and not simple induction. The enzyme could not be induced in vitro; the bacteria had to multiply for any biosynthesis to take place. The bacilli used in the study were separated from aseptically-collected tissues and all the preparative procedures were done at 0-4°C to exclude contaminant organisms. β-lactamase synthesis is the major mechanism of β-lactam-resistance in most bacteria. Infections caused by many β-lactamase-producing organisms are now being treated successfully by combinations of β-lactams with β-lactamase inhibitors. The enzyme in M. leprae was almost completely inhibited by sulbactam, but clavulanate showed only about 50% inhibition. Another effective compound we tested was YTR-830H (TAIHO). Combinations of β-lactamase inhibitors with penicillins or cephalosporins could provide an alternative treatment mechanism for Hansen's Disease, and parenteral administration of the drugs (e.g., intravenously or intramuscularly) would minimize their inactivation.

FP 072

GANGLIOSIDES(Cronassial)& NERVE REGENERATION IN LEPROSY.A MULTICENTRE TRIAL.PRELIMINARY REPORT.

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Gangliosides have been used successfully in various forms of Peripheral Neuropathies.We have conducted a clinical trial of Cronassial(a cocktail of 4 Gangliosides) in 226 leprosy-patients who had sensory/motor/sympathetic changes,in a dosage schedule of 40 mgs.I.M. daily for 35 consecutive days.The trial was conducted at 6 centres in 4 cities in India.The data collected, circa 350.000,are still under evaluation.
Though all symptoms and signs of neuritis have been recorded,as well as motor and sympathetic changes,in this preliminary report the evaluation of the results and the score are based on sensory changes and its modalities:touch,temperature,pin prick.The patients were assessed at weekly intervals.A random sample of 10% were assessed,once again,after 2 years and the results were found to be consistent in time.
The results,very encouraging,will be presented in details. The discussion will deal with nerve regeneration(based on the theory of Nobel Laureate Rita Levi-Montalcini),the role of Nerve Growth Factor & Gangliosides(Cronassial in particular)in the process of nerve regeneration.

FP 073

Structure Pharmacokinetic Relationship in a Series of Dapsone Derivatives

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The pharmacokinetic constants (elimination rate constant, volume of distribution, clearance) of 13

dapsone derivatives with potential antileprotic activity were derived from experiments with rats.
Under "in vivo" conditions the pharmacokinetic properties of a drug determine its concentration at the appropriate receptor site. These properties might be different from those leading to pharmacodynamic response. In this case it should be possible to synthesize drugs with optimal pharmacokinetic behaviour without loss of activity. Data analysis was carried out using multiple linear regression- and principal component analysis. The results showed that the lipophilicity (log P) of those compounds which were glomerularly filtered gave a good correlation with several pharmacokinetic parameters.

FP 074

CORRECTION OF SEVERE FOOT DEFORMITIES BY A SIMPLE TECHNIQUE.

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Dr. H.S.M. Raat, Orthopaedic Surgeon, is well known for his many interventions in reconstructive surgery for polio and leprosy patients around the world. It was through a mutual acquaintance, Dr. J.A. Warndorff, that we were able to get Dr. Raat to come to Ghana. After many successful operations in foot reconstruction we thought it would be helpful to put his experience into writing.
The purpose of this paper is to outline an operation he has performed many times over the past fifteen years to correct severe fixed equino-varus deformities mainly in post-traumatic cases.
The same technique has also been used for leprosy patients who were on the list for amputation because of severe stiff equino-varus feet with recurring ulcers. The results in all cases were very satisfactory and encouraging.
The technique of the operation is presented and discussed here together with the results in more than fifty cases.

FP 075

GENOMIC AND AMINO ACID SEQUENCE OF THE M.LEPRAE 70 KD ANTIGEN IS HOMOLOGOUS TO THE HIGHLY CONSERVED 70 KD HEAT SHOCK PROTEIN (hsp70) OF EUKARYOTES

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The 70 KD antigen of M.leprae defined by Mab L7 has a homologue in M.bovis, M.tuberculosis and M.scrofulaceum. The M.bovis BCG 70 KD antigen is a potent stimulator of immune human T cells in vivo and in vitro. Using L7 we have isolated clones JKL2 and JKL15 from the M.leprae-λgt11 library of R. Young. The DNA insert from the largest of these, JKL2, was mapped and the coding region sequenced and found to contain a 1037bp open reading frame encoding the 344 amino acid COOH region of the M.leprae 70kd proteiη. There is extensive homology at both nucleotide and amino acid level between this coding region and that of the dnaK gene of E.coli (55% and 51%) and slightly less homology with other members of the hsp70 family such as those in the malarial parasite Ag63 and in man. This nucleotide sequence data complements N terminal amino acid sequencing data which showed homology between the N terminus of M.bovis BCG affinity purified 70KD antigen and the consensus sequence of the eukaryotic and prokaryotic hsp70 proteins. The JKL2 insert DNA also has extensive homology with the M.tuberculosis 71KD protein antigen gene as shown by hybridisation under stringent conditions.
T cell epitope analysis algorithms have located numerous regions within the amino acid sequence of JKL2 which can form amphipathic structures predicted to be candidate "T cell epitopes" and these include regions of the sequence which are not highly conserved.

FP 076

MUCOSAL IMMUNITY IN LEPROSY

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While there have been many studies of systemic humoral and cell-mediated immune responses in leprosy patients, there have been few investigations of mucosal immune responses. In this study, we have estimated the IgA responses to whole γ-irradiated M. leprae by ELISA in saliva from 253 subjects living in North East Bangladesh, including 52 untreated patients and 53 treated patients. Three groups of healthy subjects were studied: 78 household contacts of untreated patients, 50 indigenous subjects with no known leprosy exposure, and 20 leprosy hospital workers. The results show substantially lower levels of IgA against M. leprae in household contacts of untreated patients than indigenous subjects and hospital workers, who had the highest rate of response. The IgA responses were similar in household contacts of untreated paucibacillary and multibacillary patients. IgA responses were common amongst treated patients than untreated patients, matching their skin test responses. This suggests that mucosal immunity to M. leprae may be part of a protective immune response, since our results match closely the risk of leprosy in the subject groups studied. The results of a follow-up study of the subjects (currently in progress) two years after the initial one will be discussed, together with the implications of these findings.

FP 077

T CELL REACTIVITY OF LEPROSY PATIENTS AND THEIR HOUSEHOLD CONTACTS TO MYCOBACTERIAL SONICATES AND AFFINITY PURIFIED ANTIGENS.

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T cell reactivity to mycobacterial sonicates and affinity purified antigens, p65 and p70 from BCG, was measured in 9 cases of leprosy (4LL, IBL, INT, 3TT) and 35 household contacts from 6 interrelated aboriginal families as well as a control family. Negligible proliferative and DTH responses to M. leprae sonicate and the two purified antigens were obtained in the LL patients. Of the 3 TT cases two had good responses to sonicates, p65 and p70, while the third was a low responder. When the data was analysed in the context of household contacts, the families could be ranked into high (2) moderate (2) and low (2) responders. High responders to BCG and M. leprae sonicates reacted equally well to p65 and p70, whereas in moderate responders p70 was more immunogenic than p65 which was unexpected in view of the more restricted species distribution of p70. By contrast a low response to sonicates correlated with a lack of or low response to purified antigens, particularly p65. Serum antibody levels to dBSA were inversely related to T cell reactivity in the families with index cases. Controls with no household exposure displayed high proliferative responses to all antigen preparations and relatively low dBSA antibody levels. At present responder status is being correlated with precursor cell frequency and HLA.

FP 078

TRIAL TO DETERMINE THE CAPACITY OF SEVERAL VACCINES TO PRODUCE SKIN-TEST REACTIVITY TO A SOLUBLE M. LEPRAE ANTIGEN IN TREATED SMEAR-NEGATIVE PATIENTS WITH LEPROMATOUS LEPROSY.

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The objective of this controlled blind study is to determine and compare the capacity of BCG, HKML and combination of BCG and HKML in inducing sensitivity to soluble M. Leprae antigen (SMLA) among previously treated smear-negative post-lepromatous patients, and to monitor untoward reactions and side-effects.

The study was started in April 1986. A total of 346 post-lepromatous patients, mostly residing in satellite communities around the Eversley Childs Leprosarium were sequentially admitted and assigned at random to the four vaccine regimens: Group A (placebo), Group B (BCG), Group C (HKML, $6x10^8$ AFB), and Group D (BCG + HKML). Vaccinations were done every three months for a total of eight vaccinations. Total vaccine dose per vaccination, was equally divided into three parts and intradermally injected to three skin sites. Skin testing with SMLA was done every three months, three days prior to the vaccinations. Reactions to SMLA were evaluated at 72 hrs. The patients were regularly observed for the occurrence of untoward reactions and side-effects.

Preliminary results of the trial will be presented and discussed, as well as the observed side-effects and acceptability of the procedure.

This investigation received financial support from the UNDP/WORLD BANK/WHO Special Program for Training in Tropical Diseases.

FP 079

Evidence that Mycobacterium leprae specific helper T cells exist in lepromatous leprosy patients

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A study of the proliferative responses of peripheral blood monocytes taken from long-treated (> 20 years) and untreated lepromatous leprosy (LL) patients revealed that while 3 of the 16 untreated LL patients and 5 of the 10 treated LL patients responded to M. leprae, 7 of the 16 untreated LL patients and all of the 10 treated patients responded to BCG. T cell clones against M. leprae were raised from 2 of these long-treated LL patients, using standard techniques. For comparison, such clones were also raised from 2 Tuberculoid (TT) patients. All of the 5 T cell clones from the TT patients and 6 of the 13 T cell clones from the long-treated LL patients responded to M. leprae but not to BCG in proliferation assays. Seven of these CD4+ CD8- clones were further screened for reactivity to other Mycobacteria and to the 5 recombinant protein antigens. Five clones (3 from TT patients and 2 from an LL patient) responded only to M. leprae while 2 clones (from an LL patient) responded to various other mycobacterial antigens. None of the clones responded to any of the recombinant antigens.

FP 080

T-CELL RESPONSES TO THE *MYCOBACTERIUM LEPRAE* 18kD ANTIGEN

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The helper T-lymphocyte plays a fundamental role in providing protective immunity against *Mycobacterium leprae*, the causative agent of leprosy. *M.leprae* is an antigenically complex pathogen. However, the identification of potentially protective antigens has been greatly facilitated by the cloning and expression of a number of *M.leprae* genes. Of particular interest to this laboratory is the immunological responsiveness of T-cells to an 18,000MW recombinant *M.leprae* antigen. The presence of T-cell epitopes have been investigated with polyclonal and monoclonal T-cell response assays. Polyclonal responses have been generated with T-lymphocytes from mice immunised in vivo with recombinant 18kD protein and subsequently challenged in vitro with whole *M.leprae* antigen. Human and murine T-cell clones reactive with *M.leprae* have also been assayed with recombinant antigen. Our results indicate the 18kD antigen possesses epitopes which may be important in the immune response to *M.leprae*. Computer analysis of the 18kD protein amino acid sequence has identified a number of regions which may contribute significantly to the molecules overall antigenicity. Synthetic peptides corresponding to these potentially immunologically reactive regions have been generated and we are currently testing these peptides in a variety of T-cell response assays. Preliminary results show that some peptides do contain epitopes recognised by T-cells. These peptides from the *M.leprae* 18kD protein may therefore form the basis of an effective leprosy vaccine.

FP 081

Screening for T cell reactivity of recombinant M. Leprae peptides

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Peripheral blood mononuclear cells (PBMC) and T Cell lines derived from leprosy patients were used to assess the efficacy of E. Coli lysate antigens (M. leprae genomic library obtained from R.A. Young) for their ability to stimulate T cells. Each lysate was made with a random pool of about 5000 plaque forming units. Since E. coli lysates are known to be either toxic or stimulatory, various concentrations have been used in the proliferative assay. Of the six tuberculoid patients tested, preliminary results indicate that lysate P_1 was stimulatory in four patients (stimulation index of more than 2) whereas P_2, P_4 and P_5 were stimulatory in three patients each. Significantly four out of five healthy subjects responded to P_4 lysate antigen, whereas lysates P_1 and P_5 had no effect on any of the healthy individuals. Screening of these antigens for T cell reactivity may be useful in elucidating the immunodominant T cell epitopes of M. leprae.

FP 082

MOLECULAR PATTERN OF THE T-CELL REPERTOIRE IN LEPROSY PATIENTS AND THEIR RELATIVES.

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The diversity of antigen recognition by the T-cell repertoire in leprosy was investigated using antigen-bearing nitrocellulose particles from SDS-polyacrylamide gel electrophoresis blots. Twenty fractions from soluble extracts of M.leprae and M.tuberculosis covering the 10-100 kDa molecular weight range were produced in batches which sustained the proliferative assay (triplicates at two concentrations) of peripheral blood mononuclear cells from 15 donors. Reproducibility of the technique with satisfactory resolution has been demonstrated by repeated analysis of representative samples. Individual patterns of specificity were observed when comparing the responses to fractionated or whole M.leprae and M.tuberculosis. Dissimilar patterns were obtained when comparing the source case with the family contacts. At least in one case, the response to fractionated antigens was profoundly above the stimulation by whole mycobacterial extracts. The most frequent stimulatory antigens of M.leprae appeared with the molecular weight of 35 kDa (58%), 20-24 kDa (50%), 12-15 kDa (42%) or 60-65 kDa (25%). Moreover, the stimulatory fractions from M.leprae and M.tuberculosis did not overlap in the majority of cases, thus indicating the immunodominant role of species-specific T-cell epitopes.

FP 083

IIC8 HYBRIDOMA B CELLS CAN PRESENT RECOMBINANT 65-KDA MYCOBACTERIAL ANTIGEN TO T CELLS.

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Using in vitro lymphoproliferative assays as well as assays for interleukin-2 production, IIC8 hybridoma B cells producing antibodies to the 65-kDa protein of mycobacteria, were examined for their ability to present both recombinant 65-kDa (r65-kDa) protein as well as other mycobacterial antigens to mycobacteria reactive murine T-cell lines. Irradiated IIC8 cells were found to be very efficient at inducing T-cell line proliferation in response to r65-kDa protein. When using whole mycobacterial preparations, IIC8 cells were slightly less efficient than irradiated spleen cells. T-cell proliferation in response to sonicated mycobacteria were similar when using IIC8 or spleen cells as antigen presenting cells. T cells were shown to produce IL-2 in response to r65-kDa protein presented by IIC8. The amount of r65-kDa

procein required to induce similar amounts of IL-2 when using spleen cells as antigen presenting cells was significantly higher than that required when using IIC8 cells. IIC8 cells were unable to efficiently present non-mycobacterial antigens. Our findings suggest that one could utilize antigen-specific hybridoma B cells as antigen presenting cells to generate and propagate T-cell clones of desired specificity. Such an approach should be useful in the development of vaccines designed to induce T-cell mediated immunity.

FP 084

INYECCIONES DE MICOBACTERIUM VACCAE MUERTAS INDUCEN RESPUESTAS INTRADERMICAS FRENTE ANTIGENOS SOLUBLES DEL M.LEPRAE EN 50% DE PACIENTES LEPROMATOSOS

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La ausencia de respuestas mediadas por celulas frente al M.leprae,en lepra multibacilar no se recupera al finalizar la quimioterapia y conseguir la negativizacion bacteriologica.Hemos investigado 124 de estos pacientes por inyecciones intradermicas anuales de Tuberculina,Leprosina A, Scrofulina yVaccina durante un periodo de 5-6 años.Se describen los efectos de la administracion de dosis unicas de 10^7,10^8 o 10^9 M.vaccae muertas por irradiacion durante este periodo.Seguidamente se observa una conversion positiva a Leprosina A en 3/29,0/6 y12/32 pacientes respectivamente.En el grupo control sin M.vaccae la conversion fue de 1/29.Añadir 0.02ug. de Tuberculina a 10^9 M.vaccae produjo conversiones en 12/23 pacientes.La tuberculina redujo de manera significativa la respuesta local a la inyeccion y se encontró una correlacion entre la respuesta local 7 dias despues de la inyeccion y respuesta al Leprosina A.

Se describirán futuras modificaciones y la introduccion de un sistema como metodo de inmunoterapia.

FP 085

DO ENVIRONMENTAL MYCOBACTERIA INFLUENCE THE DISTRIBUTION OF DISEASE IN THE LEPROSY SPECTRUM? BACTERIOLOGICAL AND SKIN TEST STUDIES CARRIED OUT IN IRAN.

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Close to the town of Rasht in the province of Gilan at the south west corner of the Caspian sea are 2 small areas endemic for leprosy. One of these is mountainous and the majority of cases are lepromatous; the other is of lowland rice paddy and a proportion of the cases are tuberculoid. We have cultured many soil samples from both of these areas and have found marked differences in numbers of cultivable mycobacteria isolated, and in the species identified. We have extended our studies to skin test surveys of children attending schools in the 2 regions and have found some interesting differences suggesting that those with different patterns of cell mediated response to cultivable mycobacteria may have susceptibilities to different forms of leprosy.

Studies of the families of patients in the 2 areas are in progress and an up to date report will be presented.

FP 086

Comparative biochemical analysis of the genomes of leprosy associated bacteria (M. leprae, LDC and ADM).

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The genomes of leprosy-associated microorganisms (LAM) : M. leprae (ML), leprosy-derived corynebacteria (LDC), and armadillo-derived mycobacteria (ADM), were analyzed by newly developed microanalytical techniques and compared with reference organisms of the CMN (Corynebacterium, Mycobacterium, Nocardia) group. The guanine-plus-cytosine content (% GC) of DNA, as determined by a double-labelling procedure (1), was found to be : 54.8 ± 0.9 for ML (2), 54-56 for LDC (2), 62.2 to 67.1 for ADM (3), and 62 to 71 for reference mycobacteria (2,3). Restriction patterns disclosed no methylated cytosine (Me^5C) in DNA of LAM. A specific genetic marker, N^6methyladenine (Me^6A), was found in all the GATC sequences of LDC-DNA (2) : the other CMN organisms missed it (2,3). Hybridization experiments yielded homology levels higher than 60 %, with 4 of 7 LDC strains analyzed, but 40 % or less with 3 of them (4). ADM strains, previously classed into 5 subgroups according to phenetic traits, showed high homology within single subgroups, but low homology outside (3). Low hybridization (less than 18 %) was observed between : ML and LDC, LDC and reference CMN organisms, ADM and ML. The genome sizes of 3 LDC strains were 1.2 to 2.5 x 10^6 base pairs (bp) (4); that of ML was shown to be 2.7 to 3.5 x 10^6 bp (E. coli genome has 4.2 x 10^6 bp). The smaller size of ML and LDC DNA might account for their inability to axenic growth. In conclusion, ML, LDC and ADM are genetically unrelated; genetic heterogeneity is observed for LDC and ADM. In addition, LDC are genetically unrelated to reference CMN organisms, but immunologically related to ML. Ref. : (1) Coene M. & al., Eur. J. Biochem., 1985, 150, 475-479; (2) Hottat F. & al., Med. Microb. Imm., 1988, 177, 33-45; (3) De Kesel M. & al., Int. J. Syst. Bact., 1987, 37, 317-322; (4) Antoine I. & al., J. Med. Microb., 1988, in press.

FP 087

THE LARGE MOLECULAR MASS CELL WALL PROTEIN OF M. LEPRAE.

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Cell walls of M. leprae prepared by solvent extraction contain protein that stimulates proliferation of T cells from tuberculoid leprosy patients and elicits delayed-type hypersensitivity skin reactions in guinea pigs and patients sensitized to M. leprae (Melancon-Kaplan et al., Proc. Natl. Acad. Sci. USA 85: 1917-1921, 1988). Sequential removal from cell wall preparations of mycolates and arabinogalactan by chemical degradations and peptidoglycan by digestion with muramidase results in a large molecular mass, highly immunogenic protein (cell wall protein; CW-P) (Mr =1.5 x 10^6) resistant to trypsinization, insoluble in a variety of aqueous and detergent-containing buffers, non-electrophoresable under conventional conditions, and resistant to urea-mediated dissociation/disaggregation. Yet CW-P reacts with those anti-65 kD monoclonal antibodies (C1.1, IIIE9, IIC8, IIIC8, and others) that recognize epitopes throughout the span of the polypeptide. Likewise, many monoclonal antibodies raised to CW-P recognize soluble 65 kD protein. However, CW-P also reacts with monoclonal antibodies and T cell clones to other monomeric proteins, thus pointing to a highly stable, protein heteroligomer endowed with much of the immunogenic activity associated with the whole leprosy bacillus.

FP 088

LIMITED IN VITRO MULTIPLICATION OF MYCOBACTERIUM LEPRAE.

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Inability to cultivate M. leprae in vitro has been a major bottleneck in leprosy research. Today, leprosy bacillus remains the only bacterium causing disease in man that has not been cultured in vitro, and until this is achieved, all studies on leprosy will remain at a serious disadvantage compared with other human bacterial infections.

Studies have been initiated to achieve in vitro growth of M. leprae. Three biochemical parameters were used to follow the fate of M. leprae incubated in a given medium and they are intracellular levels of adenosine triphosphate (ATP) and deoxyribonucleic acid (DNA) and uptake of (^{3}H)-thymidine. Among the various growth media tried only two supported the growth of M. leprae to a limited extent and these are (1) modified Nakamura medium in which Dhople and Hanks achieved primary and also sub-cultures of M. lepraemurium, and (2) Mahadevan's conditioned medium. After an initial lag of 4-6 weeks, maximum growth, as judged by all the three criteria, was obtained between 14 and 16 weeks. The cells harvested at 16 weeks exhibited several criteria typical of M. leprae including DOPA oxidase, mouse foot

pad inoculation and presence of phenolic glycolipid I. However, these cells, when inoculated into fresh medium failed to grow and also lost metabolic activity and viability.

The initial lag period was reduced to 3-4 weeks and the yield of cells at 16 weeks was improved by incorporating several new nutrients such as galacturonic acid, yeast extract, trypticase, nucleotides, cholesterol:lecithin and replacing fetal bovine serum with fatty acid-free fraction V of bovine serum albumin. The in vitro grown cells exhibit microaerophilic character and incorporate radio-labelled acetate and palmitate into their phenolic glycolipid I fraction. These cells further demonstrate the susceptibility to DDS and rifampicin, suggesting the feasibility of this in vitro model in screening potential anti-leprosy compounds.

FP 089

Further evidence for an extended capsule of pathogenic mycobacteria.

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In ultrathin sections of embedded mycobacteria the peptidoglycan (inner) and lipopolysaccharide (outer) layers of the wall are readily visualized. Using special stains, others have demonstrated that additional material, probably carbohydrate in nature, is attached to the outside of the wall. Using antisera raised against intact mycobacterial cells, I have now observed an extended (60nm) layer of material in this position in M.microti cells, able to react with antisera. The presence of similar material on other pathogenic species will be studied, and its nature investigated.

The same experimental technique gives indirect evidence for the shrinkage of the lipopolysaccharide layer during processing for electron microscopy. This shrinkage probably contributes to the formation of the 'electron transparent zone' of pathogenic mycobacteria, though capsular lipids are clearly also involved in several species.

FP 090

LIPOARABINOMANNAN AND LIPOMANNAN.

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Lipoarabinomannan (LAM) and lipomannan (LM) are two prominent lipopolysaccharides present in M. leprae and M. tuberculosis (Hunter et al., J. Biol. Chem. 261: 12345-12351, 1986) and other mycobacteria, which, on conventional electrophoresis, appear to have Mr values of ca. 35 kD and appear to be glycoprotein due to tenacious association with highly lipophilic, immunogenic proteins of Mr ca. 35 kD. However, biphasic solvent extraction and DEAE-Sephacel chromatography in detergent will yield pure LAM and LM devoid of appreciable protein. Sugar analysis of LAM points to a core of α1→6-linked Man units to which are attached α1→2 Man residues and substantial amounts of Araf oligoglycosyl units; on average, each LAM molecule contains $(Araf)_{80}$-$(Manp)_{20}$. Hydrolysis of alkali-treated LAM with CF_3COOH released inositol-1-P and α- and β-glycerophosphate, and HF hydrolysis produced a diacylglycerol. Acetolysis released a fragment, $(Man)_x$-inositol. Thus, both LAM and LM apparently are anchored on a phosphatidylinositol residue. LM, in essence, is LAM devoid of the Araf residues. Immunogold-labelling demonstrates the prominence of LAM on the outer surface of M. leprae. LAM is highly immunogenic with the presence of high titre IgG antibodies in sera of LL patients; LM is not antigenic. Work with others has implicated LAM as the key ingredient in the initial association of bacillus and macrophage. LAM also inhibits γ-interferon mediated activation of macrophages. It appears that the phosphatidylinositol terminal unit of LAM is the essential component in these interactions.

FP 091

IN VITRO CULTIVATION OF MYCOBACTERIUM LEPRAE UNDER MICROAEROPHILIC CONDITIONS.

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Although numerous attempts for the in vitro cultivation of Mycobacterium leprae have been made, this mycobacterium has not yet been cultivated outside the host tissues. Both murine and human leprosy bacilli are considered as microaerophilic. Cultivation of M. leprae in an artificial medium under different oxygen tensions was investigated. Bacilli were isolated from non-irradiated armadillo M. leprae infected tissues. Several slants containing synthetic solid medium were heavily inoculated and incubated at 34°C under different oxygen tensions varying from 1 to 20% oxygen. No growth occurred in tubes incubated under 1, 5 and 20% oxygen tension while primary as well as successive subcultures were obtained on the medium incubated at 2.5% oxygen and 5 or 10% CO_2. These results suggest that M. leprae is probably a microaerophilic organism and its in vitro cultivation may possibly be achieved at low oxygen tension. These in vitro grown cultures showed no growth on the usual media used for cultivable mycobacteria. The pathogenicity in animals of the cultivated cultures is under investigation.

FP 092

COMPARISON OF IN VITRO Fc RECEPTOR ASSAY WITH OTHER METHODS INCLUDING MOUSE FOOT PAD METHOD

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Chemotherapy of leprosy is the only tool available to eliminate the disease completely. Drug susceptibility pattern of M. leprae from a patient assumes a great significance while treating him. Fc receptor assay which is an in vitro method and takes 10 days to yield results has been developed to determine if M. leprae is becoming resistant to drugs. The method is based on the fact that only viable M. leprae can down-regulate the Fc receptor expression of mouse peritoneal macrophages whereas dead bacilli are not able to do the same.

The Fc receptor assay has been correlated with the reliable mouse foot pad method. The bacilli were derived from patient biopsies and were simultaneously tested by the in vitro and the in vivo methods in a blind trial. The results of the in vitro method were not revealed to the personnel doing the in vivo method. A good correlation was observed when the results of the two methods were compared.

Data will be presented to show the correlation between the two methods. The Fc receptor assay was also seen to concur with other in vitro methods like FDA/EB & ATP estimation which will also be discussed.

This in vitro method is therefore now available for doing a quick assay of the status of a patient and also to shortlist the candidate drugs before mouse foot pad tests.

FP 093

MEASUREMENT OF ATP CONTENT OF M.LEPRAE-ITS APPLICATION TO THE DETERMINATION OF VIABILITY AND DRUGS SENSITIVITY SCREENING.

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Measurement of ATP content has been earlier reported to correlate with viability. In the present study, biopsies from multibacillary patients-40 untreated and 32 after 2 years of Multidrug therapy were obtained. ATP content was measured by a modified purification-extraction-assay procedure standardised at this

laboratory which can detect very small number of colony forming units of cultivable mycobacteria. By this assay, all the untreated patients had viable bacillary population ranging from 0.01-9% in different biopsies. After 2 years of MDT, 16% patients had significant viable bacilli ranging from 0.0001-0.001%. Bacilli from different untreated patients were inoculated into different media viz. Dhople & Hanks, Modified Sauton's, Modified Dubos, RPMI, Dubos and Sauton's. The incubation was done in the absence and presence of different concentrations of drugs like, dapsone, rifampicin, clofazimine, ethionamide, cycloserine, ethambutol, tetracycline, erythromycin. It was observed that spontaneous ATP decay was faster in Sauton's and Dubos media whereas these levels were relatively maintained in other media. ATP decay was accelerated by drugs like rifampicin, clofazimine, ethionamide, cycloserine, dapsone, whereas others were relatively inactive. ATP measurements from M.leprae appear to be useful for monitoring the chemotherapy and also for possible sensitivity screening.

FP 094

The influence of associated mycobacteria on the growth and pathogenicity of M.leprae.

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Mycobacteria other than M.leprae have often been isolated from human and animal leprosy tissue. Cultivable mycobacteria resembling M.intracellulare serotype 19 (MI19) were found together with M.leprae in soil of leprosy endemic regions. When inoculated together in cultivation media, MI19 and some other associated mycobacteria enhanced significantly the multiplication of M.leprae in vitro. These cultures retained their pathogenicity in nude mice and in nine-banded armadillos. Furthermore, some of the associated strains enhanced considerably the pathogenicity of M.leprae in nude mice. It resembles in excelleration of foot pad swelling and especially in development of cutaneous leproma after intraplantar inoculation. The associated strains alone were not pathogenic for experimental animals.

FP 095

USE OF MONOCLONAL ANTIBODIES IN THE IDENTIFICATION OF MYCOBACTERIAL ANTIGENS.

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Specific and cross-reactive monoclonal antibodies against M.leprae, M.tuberculosis, M.kansasii and M.avium are described including a monoclonal antibody reactive with a shared determinant on M.avium, M.intracellulare, and M.scrofulaceum. Glycopeptidolipids of M.avium could be identified using an immuno thin layer chromatography technique. Eighty percent of the isolates of M.tuberculosis and M.avium cultured from patient material could be identified with a panel of monoclonal antibodies using immuno-fluorescence. Isolates from M.leprae, M.tuberculosis, M.avium and M.kansasii could be identified using a Western blot technique and a panel of monoclonal antibodies against these mycobacterial species. The method proved to be useful for the classification of mycobacteria. Monoclonal antibodies against M.leprae antigens and armadillo tissue could be used for monitoring the purification of M.leprae from armadillo tissue.

FP 096

FLUORESCENT STAINING PROCEDURE (FDA/EB) FOR DETERMINING THE VIABILITY OF MYCOBACTERIUM LERPAE

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A fluorescent staining procedure (FDA/EB) for determining the viability of M. leprae was used on skin smears of 58 cases of multibacillary leprosy patients. The final concentration of fluorescein diacetate (FDA) was 10 ug per ml and ethidium bromide (EB) 8 ug per ml. The esterase in viable mycobacterial organisms can hydrolyze FDA to free fluorescein and appears green while EB can not penetrate the cell wall of the viable bacillus. Nonviable mycobacteria can not hydrolyze FDA but can absorb the EB counterstain and appear orange. Our results show that the average percentage of green-stained M.leprae in 8-12, 13-24,25-48 and more than 48 months of therapy was 8.7%, 9.4%, 6.0% and 4.0% respectively. The percentage of green-stained M.leprae in four patients treated by MDT (WHO 1982) for 16.6 months only was 14.6%. These results indicate that viable bacilli decreased during therapy. No green-stained M.leprae could be seen in 8 cases among 55 cases with treatment periods longer than 13 months. This indicates that in a few patients only nonviable bacilli remained. The green stained bacilli nearly disappeared from the smears after storage at room temperature for 24 hours while the orange-stained bacteria persisted. The viable bacilli decreased to about 1% when the smears were incubated at 60 degree centigrade for 30-40 min. There was no significant change in the percentage of viable bacilli when the smears were stored at -20 degree centigrade for two weeks.

These data are encouraging and suggest that the FDA/EB staining method provides a sensitive measure of the viability of M.leprae, that it is objective and simple to perform.

FP 097

PYRIMIDINE SCAVENGING IN MYCOBACTERIUM LEPRAE

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Substrates including the pyrimidine ring would be expected to be available to intracellular *M. leprae* organisms. When isolated from host tissue, leprosy bacilli take up a wide range of pyrimidines and incorporate them into nucleic acids at differing rates. Interestingly, thymidine is incorporated relatively slowly - for instance, thymine is incorporated 3-4 times more rapidly than thymidine. Since this suggests that incorporation of labelled thymine might be more suitable for estimating viability of *M. leprae* than thymidine, rates of their incorporation into intracellular *M. leprae* were also compared.

Evidence will also be presented briefly to indicate whether the pyrimidine ring is a growth requirement for *M. leprae*, or whether, like microbes that can be cultured in simple growth media, *M. leprae* can synthesise pyrimidines *de novo* itself.

FP 098

THE ROLE OF A GEOGRAPHER IN LEPROSY RESEARCH AND CONTROL: CASE STUDY FROM NIGERIA

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Medical Geography has two functions, both relevant to the fight against leprosy: the study of disease ecology, and the study of the geographical pattern of health care delivery.

The distribution of leprosy at any scale is characteristically uneven, with prevalence rates showing marked variations between adjacent areas, which cannot all be accounted for by different methodologies in data collection. The geographical approach in analysis begins by mapping prevalence and incidence rates of disease, and examining possible relationships with distribution patterns of environmental and/or socio-economic features.

Health care provision is known to influence the reporting rate of disease. The distribution of leprosy control treatment centres past and present

may be a cause or an effect of reported disease prevalence.

The papér will address the characteristics of the contemporary uneven distribution of leprosy in a state in S.E. Nigeria, and will consider some of the factors which may have contributed to the prevalence and incidence rates. The role of the distribution of treatment centres in both the pre-sulphone and immediate post-sulphone eras, and the collapse of effective control during the Nigerian Civil War will all be assessed.

See also Lep. Rev. (1987), 58.1, 60-78

FP 099

ANALISIS DE LOS REGISTROS DE LEPRA EN ESPANA

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En este estudio se pretende tener una visión de los datos actuales existentes sobre la endemia de la lepra en Espana y su distribución por las diferentes regiones del país. Así mismo, se pretende llegar a conseguir una aprosimación--real al número de enfermos existentes en nuestro país mediante la elaboración- de procedimientos para la adquisición y trantamiento de la información, determinación de procedimientos para la recuperación, organización y difusión de la misma, así como de su evaluación, y resolver los problemas de estandarización de los registros. Todo esto dentro del marco--del actuel Sistema Sanitario en los tres niveles de actuación: Local, Regional y Central, con su registro centralizado de los datos.

FP 100

VIABILITY OF M. LEPRAE IN SOIL AND DEAD ARMADILLO TISSUE AND ITS SIGNIFICANCE. Eugene B. Harris, Maggie Landry, Rita Sanchez, C. K. Job and Robert C. Hastings. Gillis W. Long Hansen's Disease Center, Carville, LA.

According to a recent study of armadillos killed on the roads of Louisiana, 2% of them showed evidence of lepromatous disease. Up to 10^{12} organisms can be present in an armadillo with established lepromatous leprosy. The viability of these organisms and the effect of their entry into the environment needs careful study, especially after reports that some individuals with leprosy have reported a history of handling armadillos.

In this study it was planned to test the viability of M. leprae left in the soil and in the organs from dead armadillos exposed to ordinary room temperature and humidity, but protected from any light sources.

A random soil sample was taken from an area recognized as having a high armadillo population. After autoclaving the sample was inoculated with a homogenate prepared from the infected liver of an armadillo previously experimentally infected with M. leprae. A concomitant experiment included placing 100 mg each of M. leprae-infected armadillo liver and skin nodule in sterile culture tubes and storing in the dark at ambient temperature. The viability of the organisms in the soil and tissue samples was then determined at different time intervals by using the mouse foot pad technique.

M. leprae were found viable in liver specimens up to 48 hrs. and in skin nodule up to 3 weeks. Organisms from soil samples were found in footpad isolates up to 33 days.

It is clear from this study that the M. leprae discharged from lepromatous armadillos remain viable in the tissues of dead animals and in the soil. The transmission of leprosy from organisms in the soil is a distinct possibility.

FP 101

INTEGRATED LEPROSY CONTROL IN THE GAMBIA

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Leprosy and Tuberculosis are community health problems which require cooperation of the communities for control of these chronic diseases, which need motivation for their long treatment. In 1957 a vertical leprosy control was effected with many patients registered. There were no record cards for individual patients and no laboratory diagnosis. The work suffered from changes of project leaders and economic problems. In 1979 the country opted for primary health care. The PHC programme is based on "self reliance" for most of its operation. A decentralized regional structure with administrative autonomy from the main health services, provides villages of more than 400 population with a health worker and a TBA, whose six weeks training includes leprosy and TB. Medicines are bought from proceeds from sale of drugs to villagers, which serves as a revolving fund. The PHC programme now covers 289 villages. In 1984 leprosy and TB were combined and started to be integrated into the PHC system. Structurally the control programme knows three layers:
- peripheral PHC staff, who do case finding, case holding and supervised drug taking.
- technical staff: leprosy TB Inspectors in 15 health facilities, who diagnose-also microscopically and manage patients. They are supervised by regional control officers.
Central level: referral and coordination at ministry level.
The programme uses MDT for both diseases which is issued in prepacked form for supervised taking.
Individual record cards are used to enhance close monitoring.

FP 102

ENQUETES D'EVALUATION PAR SONDAGE DE LA PREVALENCE DE L'ENDEMIE LEPREUSE EN AFRIQUE CENTRALE.

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1) OCEAC, 2) Ministère Santé Publique Cameroun, 3)Ministère de la Santé Publique, Centrafrique, 4) Ministère de la Santé Publique Guinée Equatoriale, 5) Ministère de la Santé Publique et de la Population Gabon, 6) Hôpital Saint-Louis Paris.

Après une enquête préliminaire destinée à tester la méthode et réalisée dans l'Île de Bioco (Guinée Equatoriale), le Service d'Epidémiologie et de Statistique de l'OCEAC a mené en étroite collaboration avec les Services Nationaux concernés , 3 enquêtes d'évaluaton de la prévalence de l'endémie lèpreuse au Cameroun (1985, zone rurale) en République Centrafricaine (1986, zone rurale et urbaine) et au Gabon (1988, zone rurale et urbaine).

La méthodologie retenue a été celle du sondage en trente grappes. Selon la prévalence officiellement déclarée par chacun des Etats, l'effectif des échantillons a varié de 6500 à 12000 personnes.

Au total près de 25000 sujets ont été examinés. Les résultats obtenus sont supérieurs aux chiffres officiellement calculés jusqu'à là par les Services de lutte contre la lèpre.

FP 103

SELECTION OF MDT STRATEGIES THROUGH EPIDEMIOMETRIC MODELLING

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The emergence of sulfone resistant strains of M.leprae and the rapid spread of primary resistance has made multidrug therapy (MDT) the backbone of leprosy control. Its introduction is however slow, due to logistic constraints and limited resources.
In spite of recommendations by WHO, the selection of target groups to be treated by priority with MDT has been the subject of controversy.

Epidemiometric models are useful to predict the effects of various strategies on the long-term incidence of the

disease. Using the model developed from the Polambakkam database, the effects of MDT and dapsone monotherapy on incidence have been simulated.

The reduction of incidence has been studied when MDT is given exclusively either to the multibacillary or to the paucibacillary cases.

The simulations show that treatment of all patients with MDT results in a reduction of incidence of about 90 % after 10 years, compared to 55 % for patients treated with dapsone monotherapy. They also show the benefit that could be drawn from treating not only multi-, but also paucibacillary cases with MDT.

Besides helping in designing the optimal strategy for reducing the incidence, these results are also used to make a cost-effectiveness analysis of strategies restricted to specific groups of patients.

FP 104

THE GLOBAL LEPROSY SITUATION AND THE IMPLEMENTATION OF LEPROSY CONTROL THROUGH MULTI-DRUG THERAPY

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The current global situation with regard to leprosy remains serious. While the availability of better technology for leprosy control through multi-drug therapy, as recommended by WHO, has resulted in marked reductions in the prevalence of leprosy, at least in parts of some countries, in others the situation remains unchanged. However, the overall global figures for registered cases, the number of cases currently under multi-drug therapy and the number of cases who have completed multi-drug therapy, show that the situation is improving and that for the first time a downward trend with regard to registered cases is being seen. As demonstrated by a number of multi-drug therapy programmes, it is now possible to reduce the prevalence of leprosy by as much as 50% to 80% in a period of three to five years.

Notwithstanding reductions in prevalence, it should be recognized that other problems will remain for a long time such as disabilities among cured patients and a continued, albeit reduced, incidence of new disease arising from infections caught several years earlier. Hence the need to concentrate on activities such as disability prevention and early detection and treatment through primary health care.

FP 105

TECHNICAL PROBLEMS RELATED TO MULTI-DRUG THERAPY IN LEPROSY CONTROL

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The WHO multi-drug standard regimens for leprosy control have been, or are being, applied to about 1 800 000 patients. The main technical problems faced will be discussed.

- The WHO MDT regimens have proved to be well-accepted and non-toxic
- With regard to their efficacy, post-therapeutic relapses in both MB and PB patients have been negligible when observed over periods of one to three years
- To avoid some MB patients being mis-classified as PB patients, it is now recommended that, for the purpose of MDT, all smear positive cases be included in the MB group
- Whenever new lesions appear in PB patients who have completed MDT, it is often difficult to distinguish between late reversal reaction and relapse. It is now important to elucidate the length of treatment needed to eliminate all drug resistant mutants and the relationship between the presence and number of persisters and the risk of relapse after stopping treatment. Based on the answers to these questions, the currently recommended MDT regimens might be modified. However, as long as these points need clarifying, MDT for leprosy control must continue to be applied in accordance with the present WHO recommendations.

FP 106

THE CHARACTERISTICS AND MODE OF DETECTION OF THE NEW PATIENTS ENCOUNTERED IN THE LEPROSY ENDEMIC PROVINCE OF VAN WITHIN THE LAST FIVE YEARS

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Between 1983-1987, the Istanbul Leprosy Center team organized in Van initially a leprosy education program for medical personnel and the local population, subsequently whole population surveys and Contact-case surveys were carried out independently in different regions.

There were 366 (100%) registered patients in the province. 66(20%) of these patients were found during the activities we undertook between 1983-1987. The sex ratio of the 66 is 41 male (62%), 25 female (38%); the disease type is 45 MB (68%), 21 PB (32%). Of the 66 patients 13 (20%) were detected in 1983, 25 (38%) in 1984, 11 (17%) in 1985, 9 (13%) in 1986 and 8 (12%) in 1987.

10 (15%) of the 66 new cases were diagnosed by the local medical authorities after our education program and 56 (85%) by our ILC team. 18 (27%) patients were sent to our Center by local centers as leprosy-suspected cases where upon the diagnoses were verified, 20 (31%) cases were detected in contact-case surveys and 18 (27%) in mass population surveys of 33458 persons. In 49 (74%) of the 66 there was one or more close contact within the family, in 17 (26%) there was none, but old patients in the village.

We can conclude that the education of the local medical personnel and the population is of utmost importance in the early diagnosis of leprosy. The probability of finding new cases in close contact with old cases is very high. Therefore, we believe that patient-close contact surveys will be the best leprosy control program for our country.

FP 107

Bilan de Sept Années d'Enquêtes Systématiques de la Lèpre au Maroc.

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De 1980 à 1987, 12 enquêtes de dépistage systématiques ont été réalisées, intéressant une population de 254.979 personnes dont 236.868 ont été effectivement examinées, soit une participation de 92,61 % de moyenne.

422 suspects ont été dépistés, soit un taux de détection global de 1,66 %. et dont seuls 241 se sont présentés à l'hôpital Aïn Chock pour y être confirmés (soit 55 %).

Sur ces 241 suspects, 217 se sont révélés positifs, soit une proportion de 90 % de concordance entre la suspicion clinique et la confrontation biologique.

181 suspects qui n'ont donc jamais rejoint l'hôpital et 16 lépreux perdus de vue forment 46,68 % de l'ensemble des suspects détectés activement, ce qui dénote un manque de coordination flagrant entre les autorités locales et les services sanitaires.

Les 185 cas de lèpre confirmés sont présentés dans le tableau ci-après et comparés à ceux du fichier central

	Enquêtes		Fichier Central
65 cas	Multibacillaires	36,15 %	57,37 %
88 cas	Paucibacillaires	47,57 %	30,33 %
32 cas	Indéterminés	17,28 %	8,99 %

Le dépistage actif met surtout en évidence les formes paucibacillaires discrètes par leurs caractères peu affichants leur évolution peu bruyante et n'incitant donc pas le malade à consulter.

La répartition par sexe et âge ne montre pas de différence notable avec le fichier central.

Enfin l'efficacité des équipes, bien que remarquable et satisfaisante, pourrait être améliorée encore en réduisant le nombre de sujets à examiner par jour, lors de chaque enquête.

FP 108

AN EVALUATION OF 35 YEARS OF LEPROSY CONTROL IN NORTHERN NIGERIA AS DEMONSTRATED IN THE ORIGINAL PILOT PROJECT KATSINA

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During a complete review of all the 185 leprosy clinics from Octobre 1984 throughout March 1987, only 2,323 real leprosy patients (8.4‰) were found among the 27,675 persons registered, and 25,352 persons (91.6%) could be stricken off the registers as they did not show any sign of leprosy. This shows that leprosy control in Northern Nigeria is completely out of control which is blamed mainly on the poor documentation and the complete lack of supervision.
However, there seems to be a tremendous decline in the leprosy epidemic as the prevalence came down from 39‰ in 1952 to 1.5-2‰ in 1987 which in the auther's opinion is caused by the natural course of the epidemic and by a change in the sociohygieeconomic conditions. So, is leprosy under control? Nobody knows, and this question still has to be solved.
But even with this low prevalence there are thousands of leprosy patients who need some kind of help. An outline is given of what should be done whereby it is stressed that MDT can be implemented only following a total and complete upgrading of the leprosy control service, especially the documentation and the supervision in the field.

FP 109

M.leprae induced suppressor cells in the polar clinical forms of leprosy.María del C.Sasiain,Silvia de la Barrera, R.Valdez ,L.M.Baliña.I.I.Hema,Academia Nacional de Medicina,Hospital Argerich.Buenos Aires.Argentina.

M.leprae induced suppression of T cell proliferation was assayed in peripheral blood mononuclear cells (PBMC) from leprosy patients belonging to the different clinical forms,patients were clasified according to Ridley and Jopling:TT (n=12),BT (n=7),BB (n=4),BL(n=9),LL(n=23),LL with ENL (n=9) and BCG-immunized normal controls (N, n=23). Suppressor cell function was evaluated using a two step assay. In the first astge peripheral blood mononuclear cells (PBMC) were cultured for five days with gamma irradiated M.leprae ,to induced suppressor cells (S) or with tssue culture medium as controls (C).In the second stage mitomycin-C treated S or C were added to autologous PBMC that had been frozen at -80°C.PHA or Con A were used as T lymphocyte stimuli.The percentage of suppression obtained in the presence of a) PHA:(LL,8+4; ENL,13+10; BL,22+11; BB, 19+8; BT,26+10; TT,17+6; N,13+5) or b) Con A:(LL,-2+5; ENL,15+4; BL,28+9; BB,27+10; BT,15+9; TT,38+7; N,24+5). Statistical differences were found (Wilcoxon rank test) between LL vs N $p < 0.001$ and LL vs TT $p < 0.001$,for Con A proliferation.The results indicate that the ability of LL-PBMC to develop suppression upon M.leprae challenge was lower in LL patients than in the other clinical groups and normal controls.Suppressor cell function in ENL patients was intermediate to that of TT and LL.

In conclusion,M.leprae-induced suppressor cells are not specifically associated to the generalized lack of response observed in LL patients.On the contrary,they appear to be part of the normal immune response in individuals sensitized to M.leprae or M.leprae related antigens (TT and N).

FP 110

MONITORING OF PGLI ANTIGEN AND ANTIBODIES LEVELS IN MULTIBACILLARY LEPROSY PATIENTS TREATED WITH OFLOXACIN OR PEFLOXACIN

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Recent studies, confirmed by our personnel data, showed that conversely to antibody level, the concentration of PGLI antigen in the sera of MB patients decreased rapidly after multidrug therapy (about 90 % in two months). These results suggest the usefulness of this test to assess the bacterial viability and the effectiveness of a chemotherapy. Among the new fluoroquinolones, Ofloxacin (OFLO) and Pefloxacin (PEFLO) are effective against Mycobacterium leprae in the mouse model, and first trial on MB patients using PEFLO was promising. Consequently, a pilot trial to compare the activity of PEFLO and OFLO is conducted in Ivory Coast under the WHOThelep auspices : 16 previously untreated MB patients are orally treated at day 0 with a loading dose of 800 mg OFLO or PEFLO, then either with 400 mg/day OFLO or with 800 mg/day PEFLO from day 7 to day 60. Sera and biopsies are collected at day 0, 7, 14, 28 and 56. Viable M. leprae, and PGLI antigen and antibodies are quantitated and the morphological index MI determined. Antigen and antibodies clearance are compared in the two groups of patients treated either with PEFLO or OFLO. Correlations between the variation of PGLI concentration and the MI are studied.

FP 111

Intradermal IL-2 injections enhance in vitro responses to mycobacterial antigens in lepromatous leprosy patients.

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Armauer Hansen Research Institute, Addis Ababa, Ethiopia, and Rockefeller University, New York, U.S.A.

Twenty lepromatous leprosy patients were injected intradermally with 10-25 ug recombinant interleukin-2 (rIL-2; Cetus). Blood was taken from patients prior to injection and again 2 to 7 days after administration of rIL-2. Peripheral blood cells obtained from patients 4 days or longer but not less than 3 days after rIL-2 injection had significantly enhanced lymphoproliferative responses to PHA, M. bovis BCG, PPD, and to a mixture of BCG and M. leprae in vitro. The anergy observed in these patients to M. leprae antigens in vitro was not reversed following rIl-2 injection. However, some appeared to have higher responses after IL-2 injection when their cells were cultured in the presence of M. leprae antigen and 2-3 U/ml exogenous rIl-2. No effect of rIL2 injection was seen in response to tetanus toxoid, an antigen the patients did not respond to previously. These results indicate that a small amount of rIl-2 injected in the skin is capable of exerting a systemic effect on the immune system of lepromatous leprosy patients as measured by the in vitro T cell responses to mitogens and mycobacterial antigens.

These studies are endebted to the efforts of Sister Genet Amare, AHRI, Sister Ethiopia GebreYesus, ALERT Leprosy Control, Dr. Keith Surtees and the ALERT Hospital staff.

FP 112

The role of the 65kDal Protein in the immune response to Mycobacterium leprae

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Considerable progress has been made in expressing mycobacterial genes in E.coli. We have concentrated on one such gene, that encoding for the 65kDal protein of M.leprae. The gene has been subcloned into a high expression system in E.coli and Strep. lividans and the mycobacterial protein isolated and purified.

Using these recombinant products we have studied T-cell mediated responses of M.leprae-immune mice, and confirmed that the 65kDal protein is a major immunogenic protein in such mice. We have also studied the role of the protein in protective immunity against M.leprae footpad infection. Finally we have constructed suitable restriction fragments of the gene and cloned these such that they are expressing a series of overlapping peptides; these constructs are being used to map both T-cell and protective epitopes on the 65kDal protein.

FP 113

Reduced numbers of Leu 8(+) cells in peripheral blood of lepromatous leprosy patients (LL).María del C.Sasiain,Silvia de la Barrera,R.Valdez,L.M.Baliña.I.I.Hema,Academia Nacional de Medicina and Hospital Argerich.Buenos Aires, Argentina.

We have shown that suppressor cell function is poorly induced in LL peripheral blood mononuclear cells (PBMC). Recently,the role of suppressor inducer cells in the generation of effective suppressor cell function was recognized and these cells were shown to react with the Leu 8

monoclonal antibody (MAb).We evaluated Leu 8(+) cells in LL patients,tuberculoid leprosy patients (TT) and in BCG-immunized normal controls (N).

The proportion of Leu 8(+) cells was 51+3 % in TT;51+2% in N and only 19+7 % in LL-PBMC.The proportion of Leu 8(+) cells did not change in TT/LL or N-PBMC that were culture with M.leprae for five days,with PHA (72 hr) or Con A(96 hr).In LL patients undergoing the erithema nodosum (ENL) the number of Leu 8(+) approached that of TT an N individuals,suggesting that their had may be modulated by the inflammatory process.Fractionation of T and non-T lymphocytes by E-rosette formation revealed that the defect of Leu 8(+) cells was restricted to Leu 8(+) T cells in LL (6+2 %,LL; 54+7 %,TT; 54+6 %, N) ,as the proportion of Leu 8(+) non-T cells in this group was similar to TT and N (61+11 %,LL; 56+5 %,TT; 58+4 %,N).

We suggest that the inability of M.leprae antigens to induced suppressor cell function in LL patients is related to the low numbers of Leu 8(+) T cells and may be an important factor involved in their inability to cope with the microbial agent.

FP 114

The contribution of IMMLEP to recent advances in immunology and molecular biology of M. leprae

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The goal-oriented collaborative research programme of the Scientific Working Group on Immunology of Leprosy (IMMLEP) under the UNDP/World Bank/WHO Programme for Research and Training in Tropical Diseases (TDR) continues to make progress. The IMMLEP programme is directed towards 3 major objectives: 1) development of an anti-leprosy vaccine as a means of primary prevention, 2) development of improved methods for monitoring specific cellular and humoral immune responses to M. leprae and 3) deliniation of the immunopathological mechanisms underlying tissue damage in leprosy, including nerve damage.The IMMLEP strategic workplan has provided a basis for the global distribution of armadillo-derived M.leprae for laboratory studies and use in man; for the development, characterization and distribution of monoclonal antibodies used for the identification of M.leprae - specific antigenic determinants; and the establishment and worldwide distribution of an IMMLEP M.leprae gene bank.

A major development in leprosy epidemiology has been the organization of vaccine trials in Venezuela and Malawi, both using heat-killed M. leprae vaccine provided by IMMLEP. In addition to investigating the possibility of leprosy control by vaccination, these trials provide important population laboratories for a broad range of epidemiological studies, including the development and field application of tools for elucidating the pattern and determinants of M. leprae-induced infection and disease.

The development of a second generation leprosy vaccine will depend upon ongoing structural studies, success in genetic manipulation of mycobacteria and intensive work on animal experimental models. Additional advances in immuno-biology, including the deliniation of T-cell subsets, lymphokines and MHC-genes will also contribute to a better understanding of the immunopathogenesis of leprosy.

FP 115

THE COMPLEMENT PROFILE IN LEPROSY

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The results of the determination of C3, C4 and B factor and the hemolytic assay of the alternative complement pathway (AP-CH50) in 47 (LL 14, BL 16, BT 9, TT 8) leprosy patients' sera are presented.

The C3, C4 and B factor were quantitated with radial immunodiffusion, while AP-CH50 was detected with nonsensitized rabbit red blood cells.

The findings suggests that the level of the complement componant depends upon the type of leprosy. Serum concentration of C3,C4 and B factor are significantly lower, but AP-CH50 is higher in LL and BL patients. In these cases the depressed levels of complement components reflected the activation of classical and alternative complement pathway. The elevation of AP-CH50 may be the result of acute phase reaction. It is postulated that complement level may be used as an indicator of clinical type, treatment and prognosis in leprosy.

FP 116

DETECTION OF A SPECIFIC MYCOBACTERIUM LEPRAE ANTIGEN IN THE URINE OF LEPROSY PATIENTS

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A dot-ELISA test for detection of the M. leprae antigen, phenolic glycolipid-1 (PGL-1) has been previously reported. We have tested the assay in a population of patients who report to ALERT leprosy control field clinics and to the ALERT hospital in Addis Ababa, Ethiopia, to determine if the test accurately reflects the disease state of leprosy patients. The urine from more than 200 individuals was assayed, and the PGL-1 content was determined by comparison to PGL-1 standards of known quantity. Our results show that the PGL-1 dot-ELISA can detect as little as 5 ng of PGL-1 in the urine. There is a correlation in the levels of PGL-1 with disease status, with multibacillary (BL and LL on the Ridley-Jopling scale) patients having the highest levels of PGL-1 in the urine. Approximately 90% of the LL patients tested are positive in the dot-ELISA, while 55% of BL patients are positive and less than 10% of BT patients are positive. After the onset of multidrug therapy, there is a rapid decrease in the levels of PGL-1 in the urine with PGL-1 levels in highly positive individuals becoming undetectable after three to six months chemotherapy. The usefulness of this assay to monitor treatment of leprosy in multibacillary patients and for early case detection is being investigated.

FP 117

T cell responses to fractionated Mycobacterium leprae antigens in leprosy. The lepromatous nonresponder defect can be overcome in vitro by stimulation with high molecular weight M. leprae components.

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M. leprae directed T cell reactivity is high in tuberculoid but specifically absent in lepromaotus leprosy. In order to investigate (i) which antigenic determinants trigger T cell responses in tuberculoid patients and thus protect these individuals from developing lepromatous leprosy, and (ii) if it is possible to restore T cell responsiveness to M. leprae in lepromatous patients by rechallenging the immune system with selected antigenic determinants that will trigger help but not suppression, we have probed directly the peripheral T cell repertoire of 10 tuberculoid and 8 lepromatous patients with large numbers of different M. leprae and BCG antigenic components that had been separated on the basis of their m.w. by SDS-PAGE and electroblotted onto nitrocellulose. This technique allows the identification of T cell stimulating antigens independent of the expression of B cell epitopes by these antigens.

Our results show that: (i) tuberculoid patients' T cells responded preferentially to M. leprae and BCG antigens in the lower (i.e. < 70K)m.w. range with a peak in the 10-25K range; (ii) 3 out of 8 lepromatous patients which did not respond to whole M. leprae responded strongly to isolated M. leprae components, with a preference for the higher (>70K) m.w. range with most intense reactivity >160K, and (iii) the T and B cell repertoires in these patients are skewed towards different antigenic fractions.

FP 118

Selective coating of Mycobacterium leprae surface antigens by species and genus-specific mycobacterial antibodies and its effect on phagosome-lysosome fusions in M. leprae-infected macrophages.

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Mycobacterium leprae has been recently reported to inhibit phagosome-lysosome fusion (PLF) in infected macrophages, which is one of the main defense mechanisms by which both M. tuberculosis and M. avium survive intracellularly. However with M. leprae this inhibition was only evident during the early steps of infection.

We previously also established that coating of M. leprae by specific antiserum prior to phagocytosis reversed the early PLF inhibition (1). In the present

work, we investigated the effect of coating of M. leprae surface components using both the species and genus-specific mycobacterial antibodies on PLF inhibition and its reversal. The morphology of bacteria was studied by gold-immunocytochemistry techniques, whereas the PLF were quantified using acid-phosphatase cytochemistry (1, 2). These findings are briefly discussed in the light of current knowledge on effective vaccination against M. leprae.

1. Fréhel,C. and Rastogi, N. (1987) Infect. Immun.55:2916
2. Fréhel, C., de Chastellier, C., Lang, T. and Rastogi, N. (1986). Infect. Immun. 52 : 252.

FP 119

IDENTIFICATION OF SUBPOPULATIONS OF $CD4^+$ AND $CD8^+$ T CELLS IN LEPROSY GRANULOMAS.

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Because delineation of $CD4^+$ and $CD8^+$ T lymphocytes in leprosy granulomas has provided important information, we have sought data concerning the numbers and distribution of their subpopulation in tuberculoid (BT) and lepromatous (LL) granulomas. $CD4^+4B4^+$ (T-helper cells), $CD4^+2H4^+$ (T-suppressor inducer cells), $CD8^+9.3^+$ (T-cytotoxic cells) and $CD8+9.3^-$ (T-suppressor cells) were studied with monoclonal antibodies using single and double immunoperoxidase staining of frozen sections and FACS IV sorting of double stained, lesion or peripheral blood derived lymphocyte suspensions.

Of $CD4^+$ subpopulations, in BT lesions 90% were $CD4^+4B4^+$ (T-helper cells) and were most commonly admixed with epithelioid cells; only 10% were $CD4^+2H4^+$ (T-suppressor inducers) and were restricted to the lymphocytic mantle about the epithelioid tubercle, as were $CD8^+$ cells. In contrast, in LL lesions these two $CD4^+$ subsets were present in approximately equal numbers, both distributed among macrophages.

Of $CD8^+$ subpopulations, in BT lesions 75% were $CD8^+9.3^+$ (T-cytotoxic) cells and 25% $CD8^+9.3^-$ (T-suppressors); both were restricted to the lymphocytic mantle. In contrast, in LL tissues only 25% were $CD8^+9.3^+$, but 75% were $CD8^+9.3^-$.

Cells of the T-cytotoxic phenotype may be important in tissue destruction or elimination of bacilli in BT lesions. The large numbers of both T-suppressor cells and T-suppressor inducer cells emphasizes the importance of suppressive mechanisms in the immunologic unresponsiveness of LL patients.

FP 120

NATURE OF T SUPPRESSOR CELLS IN LEPROSY Salgame, P., Modlin, R.L., Brenner, M.B., Melancon-Kaplan, J., Rea, T.H., and Bloom, B.R. . A. Einstein Coll. Med. Bronx, NY 10461, USA.

We have previously reported that lepromatous patients have antigen specific suppressor CD8 cells that inhibit mitogen induced T cell proliferation in vitro and that some of these Ts cells can be activated by the unique phenolic glycolipid-I [PGL 1] of M.leprae. To test the correlation of the Ts with the clinical spectrum, we established CD8 lines from lesions and peripheral blood of lepromatous patients. Lepromin induced suppression of the Con A responses of PBMC of normal random donors was observed in 50% of the CD8 lines derived from lepromatous patients and in none hrom tuberculoid patients. To explore possible genetic restrictions on suppression, CD8 clones were derived and tested Th responses on different HLA types. Lepromin-induced suppression of responses of PBL and CD4 clones to ConA were MHC Class II restricted. Suppression of CD4 Th clones to specific M. leprae antigens was simi-larly found to be Class II (HLA-D) restricted, providing evidence on genetic restrictions on Ts suppression in man. These results are confirmed in two independent laboratories. The nature of the T cell receptor (TCR) proteins and genes in CD8 Ts clones was examined, and 10/10 were found to express TCRα,β heterodimers. Finally, possible mechanisms involved in the unresponsiveness in lepromatous leprosy will be discussed.

FP 121

Molecular relatednes among Mycobacterium leprae isolates defined using recombinant DNA probes.

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Insert fragments from 14 recombinant DNA molecules, selected from genomic libraries of Mycobacterium leprae DNA have been used as probes in Southern hybridizations with restriction endonuclease-digested total chromosomal DNA from four different isolates of M. leprae. The M. leprae isolates were from human leprosy patients in India a naturally infected armadillo from the U.S., and a naturally infected Mangabey monkey from Africa. Chromosomal DNA preparations were totally digested with six different restriction endonucleases prior to electrophoretic separation of the fragments and transfer of the fragments to nitrocellulose filters. Hybridization experiments demonstrate essentially complete identity among the genomes of the M. leprae isolates, indicating a remarkable conservation of genomic sequences.

One of the probes, pYA1065, hybridizes to at least 19 fragments of M. leprae chromosomal DNA. This probe has been used in dot-blot hybridization experiments with purified M. leprae chromosomal DNA and hybridizes at an easily detectable level with DNA from 4×10^3 cells. The probehas also been used in dot-blot experiments with biopsy material from human leprosy patients and hybridizes easily with 10^4 M. leprae cells in a dot. This probe has potential for use as a diagnostic tool for detection of leprosy and may also be useful for monitoring growth of M. leprae in mouse footpads during experiments testing the efficacy of potential drugs for the treatment of leprosy.

FP 122

EXPRESSION IN RECOMBINANT E.COLI OF BIOTINYLATED PROTEINS OF M.LEPRAE

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While screening mycobacterial gene libraries for gene expression using antibodies plus a streptavidin/biotinylated peroxidase detection system, clones are frequently encountered that react directly with the detection reagent in the absence of antibody. The products of these clones are thought to be mycobacterial proteins that are not only expressed but are successfully biotinylated in the foreign host (Collins et al, 1987). Three clones were isolated from a gt11 library of M.leprae; the insert structure of all three was the same. Western blotting showed the presence of a biotinylated protein of 85kD, the same size as that identified in BCG clones previously.

A similar phenomenon was noted with one of the clones described by Young et al (1985): gt11 clone Y3184 expresses a presumed fusion protein (>116kD) that is detected in the absence of antibody and therefore is likely to be a biotinylated protein.

References:

Collins, M.E., Moss, M.T., Wall, S. & Dale, J.W. (1987). FEMS Microbiology Letters **43**, 53-56.
Young, R.A. et al (1985). Nature **316**, 450-452.

FP 123

Analysis of Mycobacterial Ribosomal RNA

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Study of ribosomal RNA sequences provides valuable information on taxonomic classification of organisms, which can also be exploited for the construction of labelled hybridisation probes which can detect small numbers of bacteria and distinguish between genera and species. With the development of such probes in mind,

we have determined partial nucleotide sequences of the 16S rRNAs of Mycobacterium leprae and other mycobacteria by primer extension. Regions of the M.tuberculosis operon representing the 5' end of the 16S and the 3' end of the 23S rRNAs have been cloned and sequenced; completion of these data is expected in the near future. The M.leprae operon is also being cloned prior to sequence analysis. Southern blot analysis of the M.tuberculosis genome using labelled total rRNA and the two cloned regions has shown the existence of a single rRNA operon in this species, for which restriction enzyme cleavage sites have been mapped. Southern blot analysis has also shown a high degree of conservation within the rRNA operon of a number of strains of M.tuberculosis, and that M. microti is very closely related to M.tuberculosis.

The high copy number of ribosomal RNAs, and the existence within them of sequences which are specific to bacterial genera or species renders them attractive for the development of sensitive hybridisation probes for detection of bacteria within mammalian tissues. We have constructed an oligonucleotide which is complementary to one of the most widely conserved regions of the bacterial 16S molecule and demonstrated its ability to recognise this rRNA isolated from a range of bacterial genera and species including M.leprae. The probe has been shown not to recognise the equivalent rRNA of eukaryotic species. We are using the mouse footpad model to investigate the ability of this probe to detect and quantitate the presence of small numbers of bacteria in tissues.

FP 124

EXPRESSION, PURIFICATION AND IMMUNOLOGIC ACTIVITY OF RECOMBINANT 65-KILODALTON PROTEIN OF MYCOBACTERIUM LEPRAE.

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Recombinant lambda gt 11 lysogens of E. coli Y1089 and pKK223-3 and pUC18 transformants of E. coli JM105 and JM103, respectively, were developed and analyzed for production of the recombinant 65-kilodalton (r65-kDa) protein of M. leprae. Recombinant lysogens were produced in E. coli Y1089 with lambda gt 11 clone Y3178, which encodes the gene for the M. leprae 65-kDa protein. Results showed that all lysogens tested produced r65-kDa in low but detectable amounts as assessed by immunoblotting using monoclonal antibody (MCAb) against the native 65-kDa protein. Equivalent amounts of JM105 cells transformed with the expression vector pKK223-3, containing a 3.6 kilobase (kb) EcoRI fragment from Y3178, produced significantly greater amounts of r65-kDa. E. coli JM103 transformants were developed using the pUC18 vector, containing a 2.9kb NruI fragment derived from the 3.6kb EcoRI fragment of Y3178. Under optimal growth conditions the pUC-2.9 transformants produced the largest yield of r65-kDa after extraction and purification by monoclonal antibody-based affinity chromatography. The r65-kDa was purified from an SDS-soluble fraction, extracted from an insoluble bacterial fraction, harvested by centrifugation after lysozyme-EDTA treatment and fracture by high pressure. Immunologic activity of r65-kDa showed that both B-cell and T-cell epitopes were present on the purified molecule by comparing antibody and lymphoproliferative responses in Balb/c mice to the native and recombinant proteins. Further investigation of the immune response to the 65-kDa protein in other animals and humans should help define the significance of the immune response to this molecule during infection with M. leprae.

FP 125

SELECTION OF RECOMBINANT DNA CLONES EXPRESSING THE 12K AND 36K M.LEPRAE ANTIGENS IN E.COLI K12.

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Recombinant DNA libraries of M.leprae DNA in the vectors lambda gt 11 and pEX 1,2,3 have been used to express M.leprae antigens in E.coli K12. Using a pool of monoclonal antibodies recognizing several M.leprae antigens, recombinants were selected that expressed 12K and 36K antigenic determinants. Western blotting analysis revealed that all 12K recombinants were expressed as fusion proteins with beta-galactosidase. Molecular characterization and antigenic properties of the 12K and 36K recombinant proteins will be presented.

FP 126

Expression of Heterologous Genes by Lysates of Mycobacterium smegmatis.

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The proposed use of mycobacteria, in particular M.bovis BCG, as agents for the construction of multiple vaccines requires the development of cloning vectors which will express a variety of immunogenic foreign gene products in these organisms. The means by which expression of heterologous genes is achieved will depend on the ability of mycobacterial transcription and translation mechanisms to recognise the control signals present in the sequences of these genes; it is possible that mycobacterial expression vectors will need to be constructed. While other groups are involved in the construction of basic cloning vectors, we are investigating the ability of cell-free extracts of M.smegmatis to transcribe and translate heterologous cloned genes. As an aid to developing and optimising the system, we are using a number of cloned M.leprae antigen genes; one of which, the 18 kDal antigen gene, has thus far been shown to function in the system.

Since it is likely that mycobacterial expression vectors will also have to be constructed, we have embarked on the study of a candidate mycobacterial promoter. The amidase gene of M.smegmatis can be induced to express very large quantities of its gene product by cultivation in the presence of the substrate acetamide. We have purified the amidase for determination of partial amino acid sequences, and from these data we will design an oligonucleotide to identify clones containing the gene. We will then study the properties of the promoter, which has obvious potential in the design of regulatable mycobacterial expression vectors.

FP 127

CONSTRUCTION OF GENOMIC LIBRARY OF MYCOBACTERIUM LEPRAE GENE AND ITS EXPRESSION IN STREPTOMYCES LIVIDANS

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Shuttle vectors which can replicate both in Escherichia coli (E. coli) and Streptomyces lividans (S. lividans) were constructed. By using one of these vectors, pSN463, genomic library of Mycobacterium leprae (M. leprae) was constructed in E. coli. Three-thousand-five-hundred transformant colonies carrying the recombinant DNAs were picked from the selecting plates. Because the average size of the DNA ligated into pSN463 was 7 kilo base pairs (kb), the library should cover most of M. leprae genome. The recombinant plasmids were introduced into S. lividans by protoplast transformation, and the expression of the M. leprae genes in S. lividans was examined. By Western blotting experiments, extracts of 19 out of 600 S. lividans transformant colonies were stained positive with polyclonal anti-M. leprae serum. Two of these reacted with a monoclonal antibody specific to the M. leprae 65 kDa protein. These results indicate that many M. leprae genes were experessed in S. lividans. This system may be useful for cloning and the expression of M. leprae genes.

FP 128

USE OF DNA PROBES TO INVESTIGATE THE GENETICS OF MYCOBACTERIUM LEPRAE. Johnjoe McFadden, Dilip Banerjee and John Stanford. Department of Surgery, St Georges Hospital Medical School, London, UK. Dept microbiology, SGHMS, London. Dept. Pathology, Middlesex Hosp. Med. Sch., London.

M. leprae was harvested from nu/nu mice inoculated with lepromatous leprosy tissue. The bacilli were extracted into organic solvent and recovered by centrifugation. High molecular weight DNA was extracted from the bacilli after lysing the cells by incubation with subtilisin, lysozyme and protese and SDS. DNA was digested with restriction endonucleases and cloned into

plasmid vectors, and also electrophoresed, and Southern blotted onto membranes. Radiolabelled recombinant clones were hyridised to membrane bound DNA and the filters autoradiographed. M. leprae-derived clones were found to hybridise strongly to M. leprae DNA but only very weakly to DNA from a range of mcobacteria, indicating that M.leprae is only distantly related to these mycobacteria. A clone encoding an insertion sequence found in the genome of Mycobacterium paratuberculosis was found to hybridise to M. leprae DNA, indicating that M. leprae may have insertion sequences in its genome.

FP 129

Overproduction and purification of Mycobacterium leprae 65kD Protein in Escherichia coli

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To construct an antigen 65kD-overproducing subclone, recombinant phage Y4178 was digested with EcoR1 and subcloned into the EcoR1 site of the expression vector pUC8. Plasmid clones containing the 3.6kb DNA fragment for entire 65kD protein were obtained (pUC-N5 and pUC-N4, pUC-N7). The orientation of this fragment in these plasmids differed, however, an equally high level of production of the 65kD protein was observed under inducing or noninducing conditions with IPTG in both orientation in vector plasmid pUC8.

M. leprae 65kD protein from crude protein preparation of cells carrying pUC-N5 was purified by immunoaffinity chromatography on M. leprae cross reactive monoclonal antibody 3A-Sepharose.

Skin response of BALB/c mice preinoculated with M. leprae (4 months before) to purified 65kD protein was performed, and gross changes was observed not only at the skin-test sites (left-hind food-pad), but also at the preinoculation sites (right-hind foot-pad).

FP 130

EFFECTS OF FREEZING - THAWING ON MYCOBACTERIUM LEPRAE AND CULTIVABLE MYCOBACTERIA.

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Most studies on M.leprae cells use samples of tissues stored frozen. There are few quantitative studies dealing with the viability of the leprosy bacillus after repeated freezing - thawing cycles of pieces of M.leprae - infected tissues. By submitting ten M.leprae infected armadillo tissues to 1 through 5 freezing - thawing cycles (-70°,Rt°), we have found that the viability of M.leprae, evaluated by mouse footpad titration, is significantly reduced after 2 or more freezing - thawing cycles. In most samples, 3 or more freezing - thawing cycles result in the absence of multiplication of M.leprae in the mouse footpads. Electron microscopy (EM) studies have shown that one cycle of freezing and thawing affects the membranes of M.leprae, producing changes in the membrane geometry, and distribution of polysaccharides between the two membrane layers and membrane fractures. The ultrastructure studies showed that "in vivo" grown M.lepraemurium and M.avium are much less susceptible to freezing -thawing than M.leprae. These findings were confirmed by fluorescein diacetate and ethidium bromide (FDA/EB) stainings (for indirect assessment of viability) which gave no significant difference in the proportion of green - stained bacteria between fresh tissues and one or two freezing - thawing cycles. On the contrary, M.ulcerans inoculated in the mouse footpad, was found to be susceptible to one freezing - thawing cycle as evaluated by the FDA/EB staining. Several mycobacteria grown "in vitro" (M.fortuitum, M.avium, M.malmoense, M.terrae & M.gordonae) were found by CFU counts, FDA/EB stainings and EM, to be resistant to 1 freezing - thawing cycle as confirmed by previous results.

These results indicate that repeated freezing - thawing cycles of M.leprae infected tissues should be avoided when investigations require viable bacilli.

FP 131

THE 65 KILODALTON ANTIGEN OF MYCOBACTERIA.

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A 65,000-dalton protein is one of the major immunoreactive components of the pathogenic mycobacteria as well as of the vaccine strain Mycobacterium bovis BCG. The nucleotide sequence of the M. tuberculosis 65-kDa antigen gene was determined and the amino acid sequence of the protein deduced. Within the amino acid sequence, 9 T-cell epitopes and 13 antibody binding sites have been identified using chemically synthesized peptides. Some of the epitopes appear to be unique to the tubercle bacillus, while others are shared with several of the mycobacterial species. A few of the epitopes can be found on similarly sized antigens in many different bacterial species. In Pseudomonas aeruginosa, the cross-reacting protein corresponds to a 60-kDa antigen that has been called "Common Antigen". This antigen has been shown to 1) be present in most, if not all, bacteria, 2) be a major immunoreactive protein for most pathogenic bacteria, and 3) contain species-specific, genus-specific, and broadly cross-reactive epitopes. In Escherichia coli, the cross-reactive protein corresponds to the GroEL protein. Both the GroEL protein and the 65-kDa antigen are expressed as heat-shock proteins. By analogy to GroEL, the 65-kDa antigen may play a role in stabilizing or promoting the folding of other cellular proteins and thereby help maintain cell integrity during environmental stresses such as heat shock or exposure to H_2O_2.

FP 132

EXPRESSION OF THE MYCOBACTERIUM LEPRAE 18KD PROTEIN

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The gene encoding an 18kD protein from M.leprae, cloned and expressed in E.coli as a β-galactosidase fusion by Young et al. (1985), was purified for immunological studies. However, antigen-specific T cell response to the β-galactosidase portion of the fusion protein masked any response to the 18kD protein. Recloning the M.leprae DNA into the vector pUC8-2, so that the 18kD protein was fused only to a 2kD peptide, resulted in extremely low yields, presumably due to proteolysis. A new plasmid vector (pASN8+) was created to overcome this problem using the observations of Sung et al. (1986), with the foreign protein fused to a 4kD peptide containing six consecutive asparagine residues. A dramatic increase in the yield of recombinant protein resulted, and the protein has been purified for use in T cell studies. It is hoped that this vector will be of general use for genes cloned in λgt11. Experiments to secrete the authentic protein from Streptomyces lividans are in progress.

Young, R.A. et al. (1985) Nature 316:450.
Sung, W.L. et al. (1986) Proc.Natl.Acad.Sci. USA 83:561.

FP 133

IMMUNO-EPIDEMIOLOGICAL STUDIES ON SUBCLINICAL INFECTION IN LEPROSY.

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There is sufficient evidence which indicates that in leprosy, the number of persons with subclinical infection in any area are far more than overt disease. However, the most important problem is the lack of reliable information regarding the occurrence of subclinical infection. Studies in this laboratory and elsewhere on the Flourescent Leprosy Antibody Absorption (FLA--

ABS) test have shown this to be most sensitive and highly specific test for detection of M.leprae specific antibodies. A follow-up study has been carried out using FLA-ABS test in 1426 healthy contacts of multi- and paucibacillary leprosy patients. Simultaneously lepromin testing has also been done to determine their delayed type hypersensitivity. In more than 6 years of follow-up, 38 contacts have developed disease and of these 33 contacts were FLA-ABS positive and lepromin negative. Thus this test (alongwith lepromin) can be used to identify the contacts who are at higher risk of developing the disease. FLA-ABS test has also been found to be highly sensitive for detection of subclinical infection specially in younger age groups. This test could therefore serve as a very sensitive epidemiological tool for monitoring the transmission of disease especially after MDT and other intervention measures.

FP 134

An epidemiological study on leprosy in southern Taiwan.

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One hundred and fifty-seven leprosy patients of two clinics in southern Taiwan were interviewed with questionnaire and examined with disability grading scale. Their clinic charts were reviewed and summarized.

36.9% of patients had family history of leprosy. The underreporting of patient number in the family was found in interview. The disability index was increased with time. The zero bacteria index was increased from 22.3% at first diagnosis to 79.6% at present. Most patients were treated with Dapsone at first diagnosis and with multiple drug therapy at present. The proportion of irregular treatment was enhanced during 1969 to 1978. The average time lag between the clinical sign and confirm diagnosis was 3.7 years. 51.6% of patients had been diagnosed within one year. The average duration was 24 years. The reasons for interrupting treatment were "that the time is not available," "feeling much better," "busy with housework," "too far away." The Clinic charts should be improved.

With multiple logistic regression analyses, the "bacteria index" was influenced by the "drug usage" while the "regular treatment" was influenced by both the "drug usage" and "that the time is not available".

FP 135

THE RURAL - URBAN PARADOX IN LEPROSY

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There are many indications in the literature that leprosy is more common in rural than in urban environments. This is of interest insofar as Mycobacterium leprae infection is generally attributed to "contact" with infected persons and crowded conditions are generally thought to predispose to contact infections. Appropriate comparisons between rural and urban environments are made difficult by the many social, economic and demographic differences between such populations, by migration patterns between them and by the different logistical problems involved in studying them. We have explored this problem using data from a total population survey in the Lepra Evaluation Project in Karonga District, Northern Malawi. The prevalence rate of leprosy was found to be inversely related to the population density per square kilometre in this predominantly rural area, an effect which was found to be statistically highly significant ($p < 0.001$) after controlling for age, BCG scar status and ecological zone within the District. Subsequent analyses have attempted to explain whether this pattern is attributable to higher incidence rates in less populated areas, to differential migration patterns, or to longer disease duration in rural areas. Preliminary results have identified the prevalence rate of multibacillary disease as a significant risk factor for leprosy incidence, independent of population density. The implications of these findings for the natural history of leprosy will be discussed.

FP 136

OPERATIONAL EFFICIENCY OF PARAMEDICAL WORKERS IN LEPROSY SURVEY: A TIME MOTION STUDY.

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To estimate the Leprosy Survey Target and Optimal Efficiency of PMWs, this study was undertaken in two Leprosy Eradication Project Areas of Chengalpattu District. Of the total 415 families (2353 persons) surveyed by the 14 PMWs in 23 man-days, 184 families were randomly observed to study the survey efficiency of these workers.

It was noted that on an average a PMW had spent a total of 8.11 ± 0.34(Mean ± SE) minutes in different survey activities at one family, namely self-introduction (0.23±0.01 min.), briefing purpose of visit (0.25±0.02 min.),collecting family particulars (3.96±0.20 min.),family examination (2.36±0.14 min.),recording family survey results (0.50±0.04 min.), and leprosy health education (0.66±0.06 min.). It was estimated that during 4 hours of effective survey work between 6.00-10.30 AM, one PMW could conveniently cover 21 families (117 persons) and examine 71 individuals in one day. However, retrospective analysis showed that a PMW surveyed only 12 families(66 individuals)and examined 51 persons in a day, i.e. 57% & 72% of the expected efficiency in coverage and examination, respectively.

The detailed observations and various factors found to be influencing the survey efficiency of PMWs will be discussed.

FP 137

LEPROSY CONTROL THROUGH MULTI-DRUG THERAPY USING PRIMARY HEALTH CARE APPROACH

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The concepts of primary health care (PHC) and leprosy control through early case detection and treatment through specialized services have evolved independently over the years with only limited complimentarity. While multidrug therapy (MDT) in its early days was considered too complex for implementation within PHC, recent experiences suggest that this may not be true. The need to increase coverage of MDT is reinforced by possibilities of rapid reductions in the prevalence of leprosy combined with positive experiences with MDT relating to low frequency of side-effects, high levels of acceptability, increased compliance for treatment, reduced stigma, increased self-reporting by patients and low rates of relapse.

The need to make full use of PHC services to increase coverage of MDT is stressed. The approach of integration does not imply total disappearance of specialized elements but their incorporation into general health services depending on the local situation. Disease awareness in the community and community participation are very important for successful leprosy control and the PHC approach provides excellent opportunities for this. The critical element in successful integration is training of health workers at all levels and inclusion of leprosy teaching in medical and other health training schools.

FP 138

Comparative Epidemiological and Operational Assessment of a Vertical and an Integrated Leprosy Control Programme.

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The leprosy control programmes in two rural blocks of similar socio-economic and demographic character and a gross leprosy prevalence of 5 per 1,000 are supervised by the Belgaum Leprosy Hospital. The total population covered is over 500,000. In one block a vertical leprosy control programme is run whereas in the second adjacent block leprosy control is within an integrated primary health care programme. The integrated programme is strengthened by technical assistance, consultation and referral facilities by the Belgaum Leprosy Hospital.

Cost effectiveness analysis shows the vertical programme to be slightly more expensive than the integrated programme. However, case detection is better in the vertical programme with 5.3% of cases being multibacillary compared to 19.2% in the integrated programme. New cases in the integrated programme had about twice the disability rate (9.7%) of those in the vertical programme. Case holding by contrast was better in the integrated programme (98% compared with 95%).

Co-operation between voluntary organisations and primary health care, as well as the professional leprosy worker and the basic health worker are discussed. This operational study of two methods of leprosy control gives an insight to possible future developments in leprosy control.

FP 139

Multi Drug Therapy - An effective tool in Leprosy Control Programme

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Srikakulam, an hyper endomic district in India is under the shield of M.D.T since 1983 when the point prevalence is 16.2/oo (30740). With Two Million rural population, it was under Dapsone monotherapy for more than 25 years. With 37.5% 'L'Dapsone resistant cases.

23,860 (11.9/oo)cases were selected and given M.D.T during the last five years. 18,643 (83%) were released after adequate treatment reducing the case load to 3808 (2.0/oo)an achievement which was never dreampt with Dapsone monotherapy.

The results of M.D.T and an inbuilt system of delivering the therapy almost at the door steps have instilled confidence in patients and hence very high rates of attendance and drug compliance (90%)

The changed operational,epidemiological indices are adding strength to the efficacy of M.D.T in almost achieving the envisaged objectives of leprosy control within five years and also helps for integretion with general health services

Hence M.D.T is a very effective tool in Leprosy Control Programmes.

FP 140

EPIDEMIOLOGICAL IMPACT OF MULTIDRUG THERAPY IN GUDIYATHAM CONTROL AREA, KARIGIRI.

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The epidemiological impact of Multidrug Therapy (MDT) in the Leprosy Control Programme in Gudiyatham Taluk was measured in a sample of about 35,000 population through annual examinations during 1982-87. MDT was introduced in the area during 1982 for the multibacillary (MB) cases and in 1984 for the paucibacillary (PB) leprosy. The incidence rate (number of new cases arising per year out of previously examined normal population) was 1.46/1000 during 1982-84 and declined to 0.85/1000 in 1985-87, showing a 40% reduction. The profile of new cases are described. Two percent were MB and there was no deformity of grade ≥ 2. Despite annual surveys and health education activities, some cases are missed each year and detected late. Considering case detections per year, the rate was 1.90/1000 during 1982-84 which declined to 1.21/1000 in 1985-87, the quantum of reduction being the same as for incidence. The characteristics of cases missed are described. The incidence rates among household contacts of MB and PB cases under MDT are also shown. Although it is rather early to confirm the declines in incidence, there are hopeful signs of controlling transmission of leprosy through MDT much earlier than that noticed under monotherapy.

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

FP 141

COMPUTERIZED MANAGEMENT INFORMATION SYSTEM (COMIS) FOR MONITORING MDT PROGRAMME FOR LEPROSY

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In agreement with NLEP-India, a computerized monitoring system is being developed by DANIDA in order to monitor MDT activities in India.

A patient data base system based on patient cards as a basic file was developed using the dBASE III Plus package. Monthly Progress Reports and Quarterly Reports were designed for paramedical workers, Medical Officers, District Leprosy Officers and State Leprosy Officers as a quick feedback. Using the same data base a programme for both operational and epidemiological indicators was developed.

The patient data is derived from patient cards from four districts where MDT implementation is supported by DANIDA.

2 Paramedical workers, one supervisor and one Medical Officer from a leprosy control unit in each of these districts were given 3 days training in transcribing patient data from patient cards to data sheet I & II. Reports generated from this data were then sent back to the field workers to be reviewed at meetings and for their individual monitoring.

In this paper the experience gained during the development of this system and the feasibility of using such computerized system in routine leprosy control is discussed.

FP 142

MANAGING LEPROSY PATIENT CARE IN PARTNERSHIP WITH LOCAL COMMUNITIES

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Loneliness in the fieldwork has been haunting leprosy workers. To them community involvement came as tremendous job satisfaction.

Recent experiment at 5 places in Madhya Pradesh (India) meaningfully carved out dignified roles for communities. This paper seeks to explore dynamics underlying the "role taking" by them. Here, the communities managed day and night, single point camping and cost free feeding for the area-wide totalities of M.B. patients over 14-day long Intensive Therapy. In one extreme case the community action meant cutting short normally planned schedule of 10-months long drug delivery period to just 14 days. Patients too, did not grudge their wage loss, since what they received in return was close-to-heart education for arresting secondary impairments and exposure to confidence-boosting "Self-care" practicals.

Taking cues from two case studies (one on incidence and nature of secondary impairments) the paper discusses scope for integrating with the control

system deformity/disability prevention through locally organised Therapeutic Core Groups. Both in content and thrust, the paper argues, this would mean more sustained roles for "core groups."

FP 143

TREND OF LEPROSY
IN SEVAGRAM CONTROL UNIT
(MAHARASHTRA : INDIA)

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Sevagram Control Unit is the oldest Unit in India established in 1951 for control of leprosy based on annual active screening of entire population, out-patient treatment of all detected leprosy patients with monotherapy (till 1978) and multitherapy (since 1978). The population covered was initially 16,647 and presently 22,764 living in 27 villages. Health education has been conducted intensively for the community.

The Paper discusses the methodology of work, and modifications introduced based on experience gained, from time to time. The Unit had the advantage of having steady personnel: medical and paramedical during the last 35 years. Major indices for leprosy control : prevalence, case-detection rate, type-ratio, age and sex distribution, and rate of arrest have been worked out for 35 years and discussed in the paper. The change in attitude of society towards leprosy and its sufferers, as evidenced from social acceptibility, decline in social dehabilitation and vocational displacement and absence of instances social ostracism/harrasment is also discussed in the paper.

FP 144

Immuno-epidemiological studies of a hyperendemic pocket in a low endemic zone.

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Malwan a town with a steady population of about 17000 has been showing a high prevalence of leprosy over years (12 per 1000 in 1985)whereas the district PR is 1.8. MDT has brought down the PR to 3.2 in 1988. But the high incidence continues unabated. All new cases are indigenous.

Immuno-epidemiological studies have been taken up in 1985 to find out the cause of such hyperendemicity. The studies are still going on. The interim findings are given.

The stimulatory index of lepromatous group (untreated or treated for less than 6 months)shows a decrease with all the stimulants tested. This difference was in moderate value with mitogen PHA.P and antigen PPD and high with M.leprae. The lepromatous group (both treated and untreated) showed a tendency of decreased lymphocytic response when compared with healthy contacts and tuberculoid patients.

The untreated lepromatous group showed an increase in cortisol level 22 6 ug/100ml. The lepromatous patients with MDR for 3 years fail to display an increase (17.8 ug/100 ml). There is no such significant change in cortisol level in treated lepromatous, in the healthy group tested and the tuberculoid patients.

The ratio of suppressor to helper in lepromatous group is about 0.49 as against 1.29 and 1.25 in healthy contacts and tuberculoid patients tested.

FP 145

EXPERIENCES IN LEPROSY CONTROL IN A DEVELOPING COUNTRY

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After a thorough analysis of epidemiological data, social and psychological factors of the leprosy situation in Vietnam, a programme of leprosy control has been developed, which would be feasible even in difficult socio-economic conditions.

Based on a 30 year experience and an eradication trial carried out from 1974 to 1984 in the pilot district NGA SON with leprosy prevalence of 1.5 per 1000, the authors have emphasized the possibility of a programme leading to leprosy eradication in a phased manner, starting in areas where the following conditions are met :

1. awareness and determination of administrative and health authorities.
2. upgrading litteracy rate and hygiene standards of the population.
3. organizing a network of leprosy control services, priority being given to commune/village levels.
4. establishment of a multisectorial committee for promoting and supervising the programme implementation.
5. adoption of an effective and progressive method for various leprosy activities.

Preliminary results of the "Leopard-skin eradication programme" of leprosy in Vietnam has been presented in conclusion.

FP 146

SISTEMA DE LUCHA ANTILEPROSA EN REPUBLICA DOMINICANA

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Las actividades que se llevan a cabo para el control de la lepra obedecen a una línea de mando vertical. Es un programa integrado de lepra y enfermedades de la piel de caracter privado,con ayuda gubernamental e internacional. Las Unidades a nivel regional están coordinadas estrechamente con las instituciones de salud pública.

Es un programa eminentemente dinámico que abarca todo el país habiéndose sectorizado con cargo a las - Unidades dotadas de los recursos necesarios para controlar el problema.

El tratamiento a enfermos, se hace en forma ambulatoria y de acuerdo a esquemas de la O.M.S.

La pesquisa de enfermos nuevos se efectúa en forma activa por medio de exámenes a contactos intradomiciliarios, personas relacionadas y consulta a sintomáticos de dermatología.

FP 147

ANALYSES OF LEPROSY INCIDENCE IN 2261 CHILDREN OF LEPROSY PATIENTS

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The analysis of leprosy incidence in 2261 descendants of leprosy patients, indicate that the sulphone drugs had a good protective effect on the leprosy incidence in the descendants of leprosy patients.The use of combined chemotherapy should result in better achievement.The incidence in the descendants, who were born before their multibacillary (MB) parents were treated with sulphone drugs, was 3.94/1,000 person years. By contrast the incidence in the descendants, who were born after their parents with MB leprosy were treated with sulphone drugs,was 0.35/1,000 person years.This fact suggests that chemotherapy has a role in protecting from infection and it will be unnecessary to isolate the patients in leprosaria. For the descendants of leprosy patients, especially those whose patients did not take any antileprosy drug, their incidence of leprosy was significantly higher than that of the normal population. It is obvious that their high incidence related to close contact with their leprosy patients, and therefore we suggest that the descendants of leprosy patients should be checked each year for at least 5 years and if possible, for 15-20 years.

FP 148

SAMPLE SURVEYS IN LEPROSY:
MILESTONE FOR INDONESIA

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In 1975 the Department of Health of Indonesia recognized the importance of gathering and analysing reliable epidemiological information to ensure monitoring and evaluation of the leprosy situation.

For that purpose 20 sample surveys have been carried out on a nation-wide basis,using a system of clustersampling,recommended by WHO.

The results were processed by computer and identified the foci of leprosy and the potential case-load.They revealed interesting indicators as the children-proportion and disability-rate among newly detected cases, the disability-rate as a whole,and many others. It became also clear that the highly endemic province of S.Sulawesi was a main source for the spread of leprosy to other provinces.

The knowledge obtained enabled the government to build up an effective control system and to secure additional financial assistance from foreign agencies.

In S.Sulawesi an evaluation survey in 1985, as a follow-up of a sample survey,executed 10 years before,revealed a statistically significant decrease in estimated prevalence from 13.3 to 7.1 per thousand.

This paper intends to show,that sample surveys at comparatively low costs,are an important factor in the build-up and evaluation of a leprosy control programme.

FP 149

GRADUAL SETTING UP OF MULTI-DRUG THERAPY (WHO-MDT) IN BRASIL.

JUNE 1986 - JUNE 1987.

Oliveira, Maria L.W.; Penna, Gerson O.; Ledra, Jonice M.; Vieira, Lucia H.C.

The initial proposal included the gradual setting up of "demonstration areas" or pilot units in each of the political sub-divisions (states and territories) of Brazil, monitored by the National Division of Sanitary Dermatology, with financial support from the American Leprosy Mission (ALM).

At the time the pilot units were being implemented , it was decided that more than one unit would be set up in those states or territories where they would be most effective, by providing either broader coverage or the possibility of operational evaluation under different circumstances.

Recommended strategies, problems which arose during the period under consideration, and the coverage provided in twenty-one of the twenty-six states and territories contemplated in the program will be presented and discussed.

FP 150

THE POSSIBILITY OF LEPROSY ERADICATION IN SHANDONG PROVINCE BY YEAR 2000

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Shandong Province, with a population of 77 million,was one of the provinces with a relatively higher prevalence of leprosy.Since the inauguration of the leprosy control program in 1955,a total of 52,732 leprosy patients have been registered, of which 38,238 have been cured and 1,461 patients remained by the end of 1986. The detection, incidence and prevalence rates have declined by 96.3%, 94.6% and 95.05% respectively,and the incidence in the 0-14 age group has declined by 98.6%.

The average relalpse rate was 3.78 per 1,000 person years and it declined with the progress of the leprosy control program.It is estimated that the incidence will decline to <0.04/100,000 and prevalence to <0.25/100,000 by 2000 A.D.. From 1980 to 1984,the incidences of 53 counties had attained the national goal of basic leprosy elimination (incidence <0.2/100,000, county-wide).Among the total of 137 counties,the prevalence in 69 counties had declined to <1/100,000 in 1986. The prevalence of leprosy in Wulian County,which has the highest in the Province, will decline to <0.75/100,000 by the year 2000.With the implementation of multidrug therapy and other control measures,we are confident that Shandong will reach the national goal of basic elimination of leprosy by the end of the century.

FP 151

TIME TRENDS OF HANSEN'S DISEASE IN BRAZIL

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In the analysis of data, the "Register Incidence" or "Detection Rate" per 100.000 was used. It is supossed that the data analized, an operational one, could be related / with the real incidence due to the time elapsed (30 and 17 years) and no gross variation in the case finding methodology. The statistical method used was the "exponential curve fitting", the best suited from 12 equations tested. / From 1946 to 1964 there was an "average percentage decrease" of the rate of 0.4% as indicated by the regression / coefficient (slope or b) but, from 1965 to 1985 it was observed an increase of 5.3%. If this last trend is sustained the "detection rate" of the year 2.000 will be 31.47 / per 100.000 or, in a population estimated of 190.000.000 / inhabitants, 59.888 new cases. For comparision, in 1983 / there were 18.759 new cases registered. The trend analysis for each political-administrative areas (States and Territories) shows a more accentuated increase (slope) in "Center-West" and "North-West" Macroregions, a slope of 9.8% / and 10.2% respectively. In some States, like Alagoas and / Rio Grande do Norte, there was a positive slope (b) of 13% and 13.6%. The distribution of the new cases by clinical / forms, during most of the time in consideration (1962 - / 1981), confirms the trend observed. There was an increase in the "Detection Rate of the tuberculoid form - 5% annually - compared with the virchowian (summed up with bor-/ derline) 3%, and also, the increase in tuberculoid form / was greater in "Center-West" and "North-West." The conclusion is: There is a strong probability of an increase of the transmission of the disease in Brazil, a fact of great concern for the Public Health Authorities.

FP 152

CHANGES IN EPIDEMIOLOGICAL INDICES FOLLOWING INTRODUCTION OF WHO MDT INTO DOMICILIARY HD PROGRAMME:

Dr. Patricia Rose

Hansen's Disease Control Programme, Georgetown Guyana, South America.

The WHO multidrug regimen was introduced throughout the Guyana Hansen's Disease Control Programme in December 1981, when there were 719 patients on treatment. This paper studies the changes in basic epidemiological indices that have occurred over the six years 1981 to 1987 and also examines the increase in workload that resulted from the introduction of the WHO MDT:

FP 153

SURABAYA URBAN LEPROSY CONTROL PROGRAM
(SURLECOP)

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The first three and half years of SURLECOP showed encouraging results with the establishment of referal system between the Health Centers and Dr Soetomo Hospital, the involvment of all Health Centers and their Subcenters which cover the whole area of Surabaya, the improvment of the clinical and managereal skill of the H.C. Doctors as well as the intensification of M.D.T.
The program started with training for the "managereal team" of the H.C., consists of Doctors , Nurses, Field Workers and Lab Technicians, followed by a routine three monthly meetings which serve as a clinical meeting between the teams from H.C., Municipality Health Office and Dr Soetomo Hospital, where difficult cases were presented by the H.C. and discussed during the meetings.
Central registration was started by re-regis-

tration using Omslep System. The use of Omslep System with a PC is very useful for central registration, as well as for monitoring,reporting and evaluation, although the filling of Omslep is not as easy as it seems to be, especially for the multi-purpose workers in the H.C..

FP 154

leprosy control in the state of Amazonas, based on MDT (WHO/82).

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In December 1987 there were 21,973 patients registered in the central file of programme management, with a prevalence of 12. per 1,000, beeing 9,847 (44.8%) MB and 12,126 (55.2%) PB.

MDT was started in 1982 and up December 1987 some 3,276 patients were under MDT, beeing 1,345 MB and 1,931 PB.

89.2% of the patients under MDT were regular in treatment.

Problems with classification of leprosy cases, acceptability of the drugs, toxicity, reaction and training related with MDT are also discussed in the present paper.

FP 155

COMPARISON OF THE DISTRIBUTION OF INDIGENOUS HUMAN AND ARMADILLO LEPROSY IN LOUISIANA, U.S.A.

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Though the United States is not considered a leprosy endemic country, human infections have been reported among native born citizens since 1894. Primarily occurring in the states along the western Gulf of Mexico (Texas and Louisiana) these areas today also harbor large populations of nine-banded armadillos. Other than man, armadillos (Dasypus novemcinctus) are the only known natural hosts of leprosy with high rates of disease. The origins, range and risks of these infections are as yet unknown. In comparing trends in the occurrence of both human and armadillo leprosy we reviewed 521 native Louisianian cases with no history of residency outside the state, and prevalence of enzootic leprosy in more than 350 wild armadillos taken from 4 discrete regions of Louisiana. Preliminary analysis indicates similarity in geographic distributions of both human and armadillo leprosy with highest rates of disease occurring in low-lying and coastal areas tending to gradually decrease inland with elevation. Peak reported incidence of human infection was between 1910 to 1940 and has declined since armadillos first migrated to Louisiana in 1928. A slight tendency for increased geographic dispersion of human infections is noted for more recent times but could not be related with certainty to either the presence of infected armadillos or increased mobility of local populations. These data further emphasize that armadillos may represent a large and increasing reservoir of potentially infectious leprosy contacts and highlight the likely utility of these animals as models for epidemiologic studies of leprosy.

FP 156

Situación de los Programas de Control de la Lepra en las Américas.

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Al igual que para otros continentes, no hay datos precisos sobre la real prevalencia e incidencia de la lepra en la mayoría de los países de las Américas. Los hallazgos anuales solo permiten conocer una "tasa de detección" único dato disponible para evaluar el progreso de la situación endémica. La gravedad de la endemia en el continente (en cifras absolutas y en tasas) no llega a los extremos de los continentes asiático y africano, estimándose para las Américas un 6% de la totalidad del problema mundial. El análisis retrospectivo de una serie temporal de las tasas de incidencia en la Región indica que la lepra parece estar declinando o permanece estacionaria en varios países.

Pero al ser analizado en forma estratificada, observamos, en algunos países, focos de alta prevalencia e hiperendemia, donde vive significante porcentaje de la población. Esta situación es frecuente en la región amazónica y valles de otros grandes ríos. En Brazil se concentra el 70% de la prevalencia (234,560 pacientes en 1986) y el 80% de la incidencia (cerca de 20.000 casos nuevos por año) del Continente. La Organización Panamericana de la Salud y el ILEP están empeñados en colaborar con todos los países para ampliar la cobertura de la terapia multidroga recomendada por la Organización Mundial de la Salud, ya que la monoterapia con DDS es todavía el tratamiento indicado para la mayoría de los pacientes, en razón de las implicaciones operacionales del tratamiento con regímenes multidrogas supervisado.

FP 157

THE EFFECT OF LEPROSY RELAPSE ON THE BASIC ELIMINATION OF LEPROSY

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After liberation (1949), Guangdong province discovered 87,216 cases of leprosy by 1975. It had the highest prevalence in all China.During the same period 51,794 cases of leprosy were treated and cured and the actual cases were 19,925 excluding the 15,497 cases of death and migration. The incidence rate was reduced from 1.14/1000 in 1961 to 0.38/1000 in 1975.

In the past 10 years, new patients were significantly decreased in number. The number of cured patients were markedly increased, more in last 10 years than the number of new patients found in the same period. The number of counties and cities with a decreased incidence rate were apparently increased. The morbidity rate was decreased to 0.07/1000 in 1985.

The problems of the cured relapse patients with DDS are analysed also. The relapse of leprosy is the important set-back during the basic extermination of leprosy program. Their main manifestation were as follows:

1. Accumulated value of relapse rate raised.
2. Almost all the relapsed patients were of the multibacillay type.
3. The ratio between relapsed cases and new patients increased more in the later 5 years than in former 5 years.The counties and cities which the ratio was in excess of 20% were increased.
4. The ratio of relapse cases to presently symptomatic patients in 1985 was two times that of 1980.
5. The rate of decline in incidence rate was arrested.

It is emphasized that this set-back ratio must be resolved. Guangdong has been using the combined therapy (1982) Of WHO. This is an active measure for decreasing leprosy relapse and managing DDS-resistance. The acceptance rate of the combined chemical therapy has reached 77.6% since 1984. Such therapy is necessary in order to increase the therapy rate and to guarentee the quality of therapy.

This paper is the first to suggest the use of the ratio of relapse cases as compared new active cases differs from the relapse rate and should be used a parameter in future studies.

FP 158

USE OF SKIN-TESTS WITH M. LEPRAE SOLUBLE ANTIGEN FOR EPIDEMIOLOGICAL STUDIES AND VACCINATION TRIALS

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A M. leprae soluble antigen (SA) is being used in the immunoprophylaxis leprosy trial of Venezuela with the following purposes:

a) Identify the population to be vaccinated

b) Visualize the immunological changes induced by vaccination

c) Study the various risks of becoming sick (and the clinical form of the disease), according to the characteristics of previous skin-tests.

Until 1987, more than 64,000 contacts were examined and skin-tested in the intake stage of the immunoprophylaxis trial. The results further support the use of this test to delimite high risk groups: More than 86% of the detected multibacillary cases fall within the negative reactors.The average reactivity to soluble antigens is significantly lower in these cases than in paucibacillary cases: multibacillary (LL + BL + BB) 3.73 mm. and in paucibacillary 13.52 mm.

The usefulness of the intradermal test to monitor the immunological changes due to the vaccination, including the

magnitude of the modifications of the intradermal response induced by different vaccines and their persistance in time is confirmed.

The Venezuelan trial confirms that the intradermal reactivity varies according to different risk criteria involves in the incidence of the disease: thus, the cutaneous reactivity is significantly higher in household contacts than in non-household ones. In addition, significant differences were observed when comparing age groups with the cutaneous test, specially in those critical groups 6-11 years old in relation to 12-19 and 20-29 years old.

FP 159

RESULTS AFTER 5 YEARS OF MULTIDRUG THERAPY (MDT) ACCORDING WHO RECOMMENDATIONS FOR LEPROSY PATIENTS IN CURUPAITI (BRAZIL).

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From 1983's onwards multidrug therapy (MDT) was implemented in Curupaiti State Hospital in Brazil according to the recommendations of WHO. On January 31st 1988, 261 out-patients, i.e. 224 multibacillary (MB) and 37 paucibacillary (PB) were put either on treatment with daily dapsone and monthly supervised doses of rifampicin and clofazimine for 24 months or on 6 months treatment with daily dapsone and monthly rifampicin . The clinical and bacteriological evolution was recorded. The clinical response to treatment was good in both categories of patients. The attendance was acceptable, 155 patients were regular (56 % MB and 78 % PB), 63 were irregular (28 % MB and 3 % PB) and 43 were defaulters (16 % MB and 19 % PB). At now 75 MB and 23 PB have completed their treatment. Acceptability was good, only 4 % patients rejected clofazimine. Reaction episodes occurred among 127 patients from whom 97 had been previously treated. Introduction of WHO-MDT was a success in this area of Brazil and contributed to its implementation in all over Brazil.

FP 160

WHO MULTIDRUG THERAPY - A REVIEW OF 956 DOMICILIARY PATIENTS STARTING MDT BETWEEN DECEMBER 1981 AND DECEMBER 1987.

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Between December 1981 and December 1987, 956 domiciliary patients started the WHO multidrug regimen. Some of these patients had received previous treatment but all new patients from December 1981 onwards received only the WHO MDT. This paper reviews the progress of these 637 paucibacillary patients and 319 multibacillary patients from the start of MDT until the end of June 1988 with particular reference to the occurrence of reactions, relapses and drug side effects. Results so far have been satisfactory and the retreatment rate remains low.

FP 161

Results after 8 years of a daily multidrug therapy for leprosy patients in Guadeloupe, New Caledonia and Polynesia.

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From 1980's onwards a daily multidrug therapy (MDT) was implemented in Guadeloupe, New Caledonia and Polynesia. On December 31st, 1987, 832 patients were put on treatment : 359 of them were patients with multibacillary (MB) leprosy and 463 were patients with paucibacillary (PB) leprosy. The MDT consisted for PB patients of daily 10 mg/kg rifampicin (RMP) and 100 mg dapsone (DDS) during six months, and for PB patients of daily RMP and DDS at the same dose during 24 months supplemented by 10 mg/kg of a thioamide (TH) during the first 2 months (Polynesia) or 12 months (Guadeloupe). The drugs were delivered monthlyfor self administration and the compliance of the patients was assessed on their monthly visit to the Clinic . The short term efficacy of MDT was excellent : all of the patients responded favourably, the cutaneous lesions shrankled rapidly and disappeared, and neither evolution to severe peripheral neuritis nor disability of more than grade 1 were noted. In MB patients with active leprosy, the research of solid stained bacilli was negative at the end of the second year of treatment. The long term efficacy was excellent too : not a single relapse was noted in 607 patients (238 MB and 369 PB) on follow up after cessation of treatment by December 1987.
The main problem was the occurence of toxic hepatitis observed only in MB patients receiving TH with 15 % frequency in Guadeloupe and 9 % in Polynesia. All of the patients except one recovered after the intake of RMP and TH was stopped. Except in one case hepatitis did not recur when RMP was resumed. Incidence and importance of leprosy reactions are also reported.

FP 162

Double résistance RMP-Dapsone dans 12 souches de M. leprae en Martinique : étude rétrospective, analyse des causes et prospective.

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En Martinique depuis 1980, tout malade atteint d'une lèpre multibacillaire bénéficie d'une biopsie. Cette biopsie permet d'étudier la sensibilité du germe avant d'entreprendre la polychimiothérapie (PCT).

La fréquence des résistances doubles RMP-Dapsone et la qualité de notre fichier qui date de 1938 nous a poussé à faire une analyse rétrospective, car la rechute bactériologique ne peut être affirmée et étudiée qu'à l'examen direct, donc très tardivement. En pratique, il faut 10^6 B.A.A.R./mg de tissu pour pratiquer l'inoculation.

Les constatations faites lors du dépouillement de douze anciens dossiers du dispensaire E. MONTESTRUC nous incitent à faire une nouvelle proposition thérapeutique car, comme la Tuberculose, il nous semble que le succès ou l'échec de la PCT se joue dans les premiers mois de l'induction thérapeutique.

FP 163

Five years of experience with MDT in the ALERT Leprosy Control Programme.

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In January 1983 Multidrug Therapy, according to WHO-recommendations, was introduced in the ALERT Leprosy Control Programme.
After extensive preparations MDT was gradually expanded. Preparations included release from treatment of patients who, according to defined criteria, were considered of having been treated sufficiently with dapsone monotherapy. Early 1988, at the time MDT had been implemented in the whole region, over 11.000 patients had been put under the new treatment.Over 90% of the paucibacillary patients and about 80% of the multibacillary patients completed their course of MDT.
The importance of analysis of the results of the treatment with cohorts of patients will be discussed.
The compliance, which was tested with the urine spot test for the presence of dapsone, showed significantly better results during MDT compared with dapsone monotherapy.
Some relapses after MDT have been diagnosed; these will be discussed.
The occurance of reactions, mainly of Type 1, which is systematically evaluated since the introduction of out patient treatment of nerve damage, will be discussed.
A long term study on the frequency of occurence of relapses, reactions and impairment of nerve function is untertaken in part of the region.

FP 164

Myoobacterium leprae persisters in patients treated with rifampicin and acedapsone.

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Fourty-five skin smear positive lepromatous patients treated first with rifampicin and later with acedapsone were biopsied and their bacilli recovered and inoculated into the footpad of normal mice to obtain the multiplication of any survivor organisms. Growth was only observed in the animals infected with the M. leprae from 3 of the patients. The isolated strains were tested to check for susceptibility to dapsone and rifampicin. One strain was resistant to dapsone at 0.0001% concentration of the drug in the diet and susceptible to the two concentrations of rifampicin used. A second strain was fully susceptible to both drugs and the third one failed to multiply when a passage was attempted to enrich the strain. The persistence of viable organisms after the rifampicin course of the dapsone resistant strain caused the relapse of the patient, whereas the bacteriostatic effect of acedapsone seems to have been able to arrest the multiplication of persisters in the other case.

FP 165

PROGRESS IN CHEMOTHERAPY RESEARCH UNDER THELEP PROGRAMME

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The goal-oriented collaborative research of the Scientific Working Group on Chemotherapy of Leprosy (THELEP) under the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) has continued to make progress. Formal surveys on Dapsone-resistance have been completed showing that resistance is worldwide. Although primary Rifampicin (RMP)-resistance has not yet been demonstrated, a substantial amount of secondary RMP-resistance has been identified and THELEP continues to monitor for RMP-resistance.

Controlled clinical trails of various RMP-containing combined regimens have also been completed. Treatment resulted in the killing of 99.9%-99.99% of the viable M. leprae, and after only three months treatment the viable organisms were calculated to have reduced to between 50 000 - 250 000 so that the occurrence of drug-resistance mutants was unlikely. The two large-scale field trials of MDT in MB leprosy have demonstrated that the regimens were very well accepted and safe and that there was no relapse during a follow-up of more than 6000 patient-years.

Under THELEP's drug development component, the most exciting discovery has been that of fluoroquinolones which have been found to be bactericidal against M. leprae. The first clinical trial of pefloxacin monotherapy has shown that 99.9%-99.99% of the bacilli can be killed within eight weeks after starting treatment. Animal experiments have shown that ofloxacin is even more active than pefloxacin. Controlled clinical trials to compare the therapeutic effects of pefloxacin and ofloxacin have begun.

FP 166

SHORT-TERM MULTIDRUG THERAPY INJ MULTIBACILLARY LEPROSY REVIEW OF 80 CASES IN TWO PROVINCES OF CHINA

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Thirty-three active multibacillary patients from 12 counties of Weifang Prefecture, Shangdong Province and 47 active cases from Menla county, Yunnan Province were treated for 24 and 27 months with MDT(WHO 1982)respectively during 1983. Clinical assessment, smear and histopathologic examination were carried out independently by study teams from the Institutes of Dermatology of these two provinces. Re-examinations at 12-14 months and at the termination of therapy showed marked improvement and there was further improvements at the end of 18 months. Conversion of BI to negativity was 4/33, 5/47 at the time of termination of therapy and 19/33,17/47 at 18 months follow-up. Regression of specific infiltration was about 60 percent after 24-27 months of MDT with further regression at 18 months follow-up. Detailed information together with results at 30-36 months follow-up will be presented.

FP 167

MULTIPLE DRUG THERAPY IN ZIMBABWE

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Leprosy Control was disrupted during the liberation struggle which led to independence in 1980. In January 1984 the National Leprosy Control Programme initiated country-wide control measures based on the W.H.O.-recommended Multiple Drug Therapy, covering almost 100% of the 3200 detected cases. Multibacillary patients were treated for 24 months only. Patients were followed up by three- to six-monthly full clinical assessment. Investigations included a research study on the value of serum IgM Ab-levels in classification. The paper discusses the results of the control programme after 4½ years of follow-up in terms of rates of compliance, relapses, reactions and other complications, as well as the outcome of the research study.

FP 168

WHEN DO RELAPSES APPEAR AFTER TREATMENT OF MB LEPROSY WITH RIFAMPICIN CONTAINING REGIMENS ?

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The evaluation of the therapeutic value of treatment regimens in MB leprosy should be based on the incidence of relapses. To define the duration of follow-up after the end of therapy it is of primary importance to know when relapses do appear. It is sometimes said that after treatment with rifampicin (RMP) containing regimens the incubation time for relapses will be much longer than after DDS monotherapy. We have observed 52 relapses in several groups of patients who had taken RMP : (1) old MB pts BI=0 after long duration DDS treatment who had received one final dose of RMP (2) pts erroneously diagnosed as PB and treated with either a single dose of RMP followed by DDS or 10 weekly doses of RMP (3) pts who had participated in studies on combined RMP containing regimens for MB leprosy.
Results : two groups of relapses : early ones occurring within 3.5 yrs, median 2 yrs; and late relapses more than 4 yrs after stopping treatment. The first are thought to result from insufficient treatment, the second from re-multiplying persister organisms.

FP 169

WHO MDT REGIME in Molucas Province(East Indonesia), January 1982–December 1987.

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Leprosy control programme was executed in Molucas Province since 1969; Commulated cases until December 1981 are Non L.3464, L. 2313, Total cases 5777, Prevalence Rate 4,18 ‰.

Location of Treatment : Ambon municipality, Central Molucas and North Molucas.

Treatment Regime : WHO Regime for MDT, from WHO Expert Committee on leprosy, Geneva October 1981(WHO Technical Report Series 675,82)

Treatment Centres: Health Centres, sub Health Centres and outpatient clinics from leprosaria Saparua and Ternate.

Medical Doctors and Paramedical incharge. : Health Centres Doctor and medical officers from the Districts and Municipality.

Supervised : Province Leprosy Doctor and Chief Leprosy Control Division D.G.CDC Dep. of Health Jakarta.

Number of cases : Commulative Cases treated until December 1987: Non L. 921, L. 910, Total 1831.

No. of cases RFT : Until December 1987: Non L. 675,L. 441, Total 1116.

Leprosy Prevalence Rate (‰) : 1969 0,8;1974 3,6;1979 3,8;1982 4,2; 1984 3,9;1987 2,6.

Conclusions : Combined treatment with WHO MDT Regime since 1982 has reduce the Number

of cases, Number of new cases and the prevalence rate, and reduce the possibilities to get deformities/disabilities.

FP 170

FIELD TRIALS OF COMBINED THERAPY IN LEPROMATOUS LEPROSY.

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The objectives of the trial are to establish whether or not combined treatment regimens of limited duration under field conditions can:-

a) Prevent relapse during treatment.
b) After termination of treatment be followed by an acceptable relapse rate (less than 1% per annum).
c) Ensure that relapses after stopping treatment will be with dapsone sensitive M. leprae.

During the year 1982, 1067 multibacillary patients were put on two WHO recommended regimens.

This cohort of patients have now completed five years of follow-up after successful chemotherapy, for a minimum period of two years or until smear negativity in positive patients.

The acceptability of the regimens was excellent, their tolerance was good and side-effects were minimal. There is a subjective sensation of well being which becomes apparent within 1 year. The rate of clearance of bacilli is however not enhanced and remains at 0.6 to 1 unit per year.

158 patients have been deleted from the trial for various reasons, while 16 patients continue to be under treatment since they are still smear positive.

After more than 2500 person years of follow-up there has been no relapse. The drug regimens recommended are a significant advance in the chemotherapy of leprosy.

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

FP 171

INDICATIONS THAT EARLY EVENTS CAUSING NERVE DAMAGE IN LEPROSY MAY NOT BE IMMUNOLOGICALLY MEDIATED.

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It is believed that nerve damage in leprosy is initiated and sustained by immunological mechanisms. Destruction of nerves is thought to occur either as a result of DTH to bacterial antigens or through autoimmunity. These conclusions have been drawn from studies on nerves at a late/active stage of the disease which is invariably associated with the presence of inflammation. Over the years we have gathered substantial evidence that early changes in leprous nerves can occur in the absence of either inflammatory cells and overt presence of antigen. These changes were identified at theultrastructural level in both uninvolved nerves of untreated leprosy patients and in the experimental mouse model. These observations have been corroborated further in the mouse model by the study of [i]perineurial and blood nerve barriers [ii]modulation of nerve damage with anti thy1.2 [iii] adjuvant like action of M. leprae.

The features of many of these early changes do not resemble immunologically based conditions such as EAN. Rather, they mimic those of chronic nerve compression and the permanent axotomy models. Thereby they strongly implicate both physical factors and neuropeptidergic interactions as the key pathways for triggering nerve damage.

FP 172

MONITORING OF PATIENT PERIPHERAL NERVE STATUS AND DEFORMITY IN HANSEN'S DISEASE

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Even with modern chemotherapy, sensory and muscle nerve involvement and subsequent deformity continue to be a part of Hansen's disease. Most leprosy control programs monitor patients from the standpoint of immunological control, and disability grading. Few measure actual peripheral nerve status, and changes in status. Recognition and treatment of peripheral nerve problems while at an early stage hold the potential to reduce or prevent further nerve involvement, and to arrest progressive deformity and disability. A hand screen evaluation was developed to assist the physician, therapist, nurse, and health technician to recognize, classify, and refer for treatment patients with peripheral nerve involvement and changes in nerve status. It is important the health professional and health worker understand peripheral nerve involvement as the underlying cause of deformity in the disease, so that deformity can be prevented, and not just treated.

The hand screen evaluation has been used to monitor in patients and out patients at the Gillis W. Long Hansen's Disease Ctr., Carville, LA USA, for the last 3 years and in the United States Hansen's Disease Regional Care facilities. In a preliminary study, 449 patients were reviewed to identify peripheral nerve involvement in a 2 year period. Preliminary and current test results are reported. Results indicate a higher number of patients have nerve trunk involvement than is otherwise expected. More than half of the patients in the preliminary study changed in a 2 year period. Of those who changed, move patients became worse than improved. Many patients in inactive disease status changed, including those continued on antimycobacterial therapy. Results support the value of peripheral nerve status monitoring, as well as the instability of neural sensory status.

FP 173

Histology and fine structure of lepromatous nerves, before and after treatment.

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Our observations on light and electronmicroscopy of nerves from patients with untreated lepromatous (multibacillary) leprosy, revealed proliferation of Schwann cells; their very heavy bacillation by Mycobacterium leprae, predominantly of unmyelinated fibres; increased lysosomal activity and phagolysosomes with accumulated products of degradation of schwann cytoplasm and axons, and occasionally of myelin; bacillation of endothelial cells of endoneurial blood vessels; presence of macrophages with similar lysosomal accumulations in more chronically affected nerves; increasing endoneurial collagen with increasing loss of myelinated and unmyelinated fibres; and initial increase and then loss of perineurial cells with replacement fibrosis. In long treated (with DDS) lepromatous patients, pale, shrunken degenerating bacilli were seen in many Schwann cells, but with many others still containing intact osmiophilic M.leprae, despite clinical "improvement". Biopsy specimens of nerves from lepromatous leprosy provide unique material for studying phagocytic behaviour of Schwann cells; limited lysosomal digestion of M.leprae, consistent with weak CMI; and degeneration of nerve fibres in different nerves.

FP 174

OUT PATIENT TREATMENT OF NERVE DAMAGE REQUIRING CORTICOSTEROIDS IN THE ALERT LEPROSY CONTROL PROGRAMME.

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In the ALERT Leprosy Control Programme out patient treatment of nerve damage of less than six months duration was introduced in April 1987 in part of the control area.

The results of the treatment of the first 30 patients, who reside in two districts, will be discussed, as well as the advantages and contraints of treatment of nerve damage requiring corticosteroids under field conditions.

After assessment of technical and operational aspects plans have been defined for extension of the treatment to other areas.

FP 175

PRELIMINARY RESULTS ABOUT A CONTROLLED DOUBLE-BLIND STUDY WITH THREE DIFFERENT KINDS OF TREATMENT IN SEVERE NERVE DAMAGE.

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Addis Ababa, Ethiopia.

:t. While the treatment of skin reactions is almost always successful with prednisolon the treatment of severe nerve damage is still unsatisfactory. We will report the results of 3 groups of patients, each group containing 5 patients.

Treatment Regimens:

1. AZATHIOPRIN ONLY
2. AZATHIOPRIN + PREDNISOLON
3. PREDNISOLON ONLY

The patients were treated for 6 months as inpatients. The complete trial will be done on 30 patients. Improvement was assessed by voluntary muscle testing, sensory testing (by ball-point pen and Bristle test) and by Nerve conduction velocity. Since the improvement of patients treated with Prednisolon and Azathioprin is significant faster and better we will report the preliminary results in the middle of the trial.

FP 176

A clinical immunological and histological study in neuritic leprosy patients.

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Neuritic leprosy, a common disease type especially in the Indian subcontinent does not find any place in Ridley-Jopling Classification as also in the W.H.O. recommendations in control of leprosy by chemotherapy. Since all these cases are skin smear negative, arbitrarily these patients are lumped in the paucibacillary group. It thus needs to be seen if neuritic leprosy patients belong to a homogeneous group or the cases could be split across the spectrum on some clinical parameters. For this, an investigation has been undertaken to see if there is any correlation between number and distribution of clinically affected nerves with immunological, and where feasible, histological parameters.

The results indicate that neuritic leprosy patients do not belong to one immunological and/or histological type. Even the number of nerves affected do not give any idea of severity status as, in several cases with just one clinically affected nerve borderline histology with high bacillary content was found.

Detailed results will be presented and discussed.

FP 177

MULTIBACILLARY LESIONS IN NERVES OF PATIENTS WITH PRIMARY NEURITIC LEPROSY

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Ninety patients clinically suspected of primary neuritic leprosy at the Dermatology clinic of Christian Medical College Hospital, Vellore, India during 1982-1987 were subjected to nerve biopsy. Cutaneous nerve biopsies were taken from representative sites for histopathological examination. In 45 patients, the diagnosis of leprosy was confirmed. Of these, 11 (25%) were histologically classified as multibacillary; 6 (13%) as borderline lepromatous and 5 (11%) as lepromatous leprosy. Thus, multibacillary lesions in patients presenting as primary neuritic form are not so rare as is often considered.

In this paper, the profiles of patients classified as multibacillary by histology are described based on initial and followup examinations. 60% of patients had trophic ulcers as the presenting complaint. Glove and stocking anaesthesia and patchy sensory deficit were the commonest neurological deficits. There was no progression of the disease during a 3-4 year followup period. The appropriateness of WHO recommended standard regimens of MDT and the problems of monitoring the response are discussed.

FP 178

COMPREHENSIVE MANAGEMENT OF RECENT NERVE DAMAGE IN BORDERLINE LEPROSY ON AN OUTPATIENT BASIS.

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A total of 42 patients with recent (less than six months duration) loss of nerve function, who first attended Dhoolpet Leprosy Research Centre during 1982 were included in the study. These 42 cases were divided into three different groups. The first group33 cases of recent nerve damage of early onset, second group6 cases of recent nerve damage of late onset and third group3 cases of recurrent recent nerve damage.

The typical course of treatment consisted, prednisolone 30 mg. as single morning dose daily for one month, then reducing the daily dosage step wise by 5 mg. per month. The total course lasting for six months. Complications of treatment were minimal. The management of the three groups of recent nerve damage was similar. The follow-up period was more than 3 years in two-thirds of the cases. Neurological assesment was done at each visit. Majority had good end result and improvement. The end result in the three groups of recent nerve damage were equally good. The results indicate that the corticosteroid regimen used was safe and effective in all the three different groups of recent nerve damage. New methods of health education for care of anaesthetic parts and physiotherapy methods effective on an out-patient basis will be discussed.

FP 179

The endoneurial space as a channel for the spread of *M.leprae* infection and a possible mechanism of localisation at sites of entrapment.

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There have been suggestions that *Mycobacterium leprae* reach the peripheral nerves via the blood vessels or along the axons. Once inside the nerve it is not clear how the infection spreads from one segment to

another or how localisation of damage occurs at sites of entrapment. Experimental evidence to be presented suggests that the endoneurial fluid space (the extracellular compartment of the endoneurium) may act as a channel to the spread of infection and inflammatory exudate along the nerve. Obstruction to the flow of endoneurial fluid at these sites of entrapment possibly results in localisation of the nerve damage.

FP 180

Un traitement logique des névrites lépreuses tuberculoïdes et borderline aiguës ou subaiguës : La désensibilisation progressive à la lépromine.

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Les nerfs périphériques sont particulièrement atteints dans les lèpres tuberculoïde et Borderline. Des épisodes de névrite aiguë ou subaiguë surviennent aussi bien au cours de dégradations immunitaires (down grading reactions) chez les malades non traités, qu'au cours de récupérations immunitaires (reversal reactions) chez les malades traités.
Ces manifestations immunoallergiques provoquent vasodilatation et oedème inflammatoire au niveau des lésions cutanées et des nerfs périphériques. Leur mécanisme est mal connu. Nous faisons un parallèle avec les manifestations respiratoires de l'allergie aux pneumallergènes (rhinites spasmodiques, asthmes, conjonctivites allergiques) où les agents animés peuvent intervenir également (allergie à la tuberculine, à la candidine). A l'instar des allergologues qui utilisent de façon empirique des injections d'allergènes à posologie progressive, nous les avons traités avec succès par des injections progressives bihebdomadaires de lépromine à partir d'une dilution à 1/1.000, sans autre traitement. L'efficacité et la tolérance de cette thérapie sont améliorées par l'utilisation hebdomadaire de lépromine diluée-retard dans le sérum formolé de l'Institut Pasteur, additionné de carbonate de calcium ou d'hydroxyde d'aluminium. L'effet est rapide sur l'oedème violacé des extrémités des membres (15 jours), plus lent sur les douleurs spontanées (1 mois) et sur les paralysies (1 à 3 mois). Les plaques cutanées s'affaissent, se repigmentent, et des microsaillies histologiquement tuberculoïdes apparaissent en bordure chez les lépres borderline.
Le schéma thérapeutique préconisé actuellement, associe la corticothérapie à la désensibilisation progressive par la lépromine. L'antibiothérapie (rifampicine et clofazimine) sera entreprise dès l'amélioration de la névrite afin de juguler la production d'allergènes.

FP 181

IN VITRO ANALYSIS OF THE ROLE OF SCHWANN CELLS IN LEPROSY

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Mycobacterium leprae, the causative organism of leprosy, is an intracellular pathogen which preferentially lives and multiplies in nonactivated mononuclear phagocytes and in Schwann cells of peripheral nerves. We have analyzed interactions between Schwann cells, M.leprae, and antigen specific T lymphocytes in a mouse model. Schwann cell cultures virtually free of contaminating fibroblast were established. As shown by light and electron microscopy these glia cells not only phagocytosed M.leprae organisms but also possessed the lysosomal marker enzyme acidic phosphatase suggesting their degradetive ability. In vitro cultured murine Schwann cells were not only negative for class II but also for class I MHC antigens. Stimulation with recombinant interferon-y (r-IFN-y) failed to induce class II antigens but lead to the expression of class I antigens rendering these cells partially accessible for the immune system. Class I reactive T cell lines have been generated from mice immunized (s.c.) with killed M.leprae in complete Freund's adjuvant or live M.bovis. These lines were $CD3^+$, $CD4^-$, $CD8^+$ and were capable of lysing mycobacterial antigen primed, r-IFN-y stimulated Schwann cells. Lysis of infected Schwann cells could result in microbial discharge and hence be detrimental for this obligate intracellular pathogen. On the other hand, lysis of Schwann cells could lead to nerve damage and hence contribute to pathogenesis.

FP 182

LEPRE LEPROMATEUSE : ARGUMENTS CLINIQUES ET ELECTROPHYSIOLOGIQUES EN FAVEUR D'UNE MULTINEVRITE AXONALE.

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Trente patients, porteurs de la forme LL de la maladie de Hansen et jamais traités, ont bénéficié d'un examen clinique et électrophysiologique. Une évaluation clinique quantifiée a été pratiquée chez 20 d'entre eux comprenant l'examen des sensibilités tactile, discriminative, algique et thermique ainsi que de la force musculaire. Les valeurs de l'amplitude et de la vitesse de conduction nerveuse motrice des nerfs médian et cubital et sensitive des nerfs médian, cubital, radial ont été mesurées et comparées à celles d'un groupe de 22 sujets témoins. La conclusion de ce travail est que le tableau clinique et électrique est celui d'une atteinte multinévritique surtout sensitive, diffuse mais non homogène, avec comme particularités : (i) une atteinte neurologique pauci-symptomatique et souvent infra-clinique puisque 8 patients seulement (40%) se plaignaient de paresthésies, que des troubles objectifs de la sensibilité ont été notés chez 15 (75%) alors que des anomalies des VCN sont quasi-constantes (97%). (ii) Une atteinte préférentielle des sensibilités discriminative et tactile. (iii)Une atteinte particulièrement fréquente du nerf radial puisqu'il est le nerf sensitif le plus souvent atteint sur le plan clinique ($p<0.05$) et électrophysiologique ($p<0.01$). (iiii) Un tableau électrophysiologique en faveur d'une atteinte de type axonal.

FP 183

SURVEILLANCE AND RELAPSE RATES AFTER M.D.T. IN OVER 700 PAUCIBACILLARY LEPROSY CASES - A TWO YEARS FOLLOW UP AT PURULIA, INDIA.

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1550 paucibacillary cases were put on MDT-WHO Regimen since 1985 in Purulia, a town with 80,000 population. Till todate 1,250 patients were cured and discharged. A Total of 710 of the first lot who are completing two years of follow up after cure are examined at six monthly intervals. There were 8 patients who had relapsed (1.1%) giving an overall relapse rate of 5.6 per thousand person years at risk. X^2 tests conducted showed no significant difference of several factors like age, sex, classification, number of patches, duration of the disease, previous monotherapy and number of doses. 3 of the 8 cases relapsed evolved into multibacillary leprosy while others remained paucibacillary. 5 of the 8 relapses occured at the end of the first six months.

It is also observed that 9 cases (0.6%) could not improve with PB treatment and are being given MB treatment. Among the cured cases the disappearance of the lesions was subjectively assessed and found that in 85% of the cases the lesions were either disappeared or minimally visible or scarred while in 15% of the cases the lesions were still clearly visible though inactive.

This paper discusses the above factors in detail.

FP 184

JOINT CHEMOTHERAPY TRIALS IN LEPROMATOUS LEPROSY CONDUCTED IN KOREA, THE PHILIPPINES AND THAILAND (Final Report).

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The National Leprosy Hosp. (Sorokudo), the Korean Leprosy Control Assn. (Anyang) and Fatima Hosp. (Taegu) in Korea; Central Luzon Sanitarium (Tala) and Eversley Childs Sanitarium (Cebu) in the Philippines and Raj-pracha-samasai Inst. and Phrapradaeng Hosp. in Thailand.

Chemotherapy trials on lepromatous leprosy using various combinations of presently available chemotherapeutic agents were conducted jointly by the 3 countries of Korea, the Philippines and Thailand starting in 1979. The general objective was to find and select the most effective and practicable regimen or regimens for field application.

Lepromatous patients were divided into 2 groups; the first group were the new and untreated cases known as Group I and the second group were the dapsone resistant cases as proven by mouse footpad tests known as Group II. Four different treatment regimens were tried on Group I patients (IA, IB, IC and ID regimens) and another four different treatment regimens were tried on Group II patients (IIA, IIB, IIC and IID regimens), IA and IIA being common to the three countries. Comparison between the regimens was done considering, among others, their anti-leprotic efficacy, drug safety, acceptability, field practicability and economic feasibility.

A total of 234 lepromatous patients were recruited for Group I and another 178 lepromatous patients for Group II in the 3 participating countries. The trials ended March 1988 or after 9 years from the start. Results will be presented and discussed.

The trials were financially assisted by the Sasakawa Memorial Health Foundation of Tokyo, Japan.

FP 185

FIELD TRIAL OF SHORT COURSE COMBINED CHEMOTHERAPY IN PAUCIBACILLARY LEPROSY.

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Preliminary results are presented of the WHO-sponsored fieldtrial in South Sulawesi, which started in August 1985, and which will continue till 1992.
At the time of reporting, January 1988, a total of 565 new, untreated paucibacillary leprosy-patients had been selected for the trial.
Criteria for selection are presented. Concordance between clinical and histopathological classification was more than 80 %.
The treatment-regimen of rifampicine 600 mg., once a month and dapsone 100 mg., daily, over a period of 6 months, was well tolerated with minimal side-effects or toxic manifestations. A total of 41 patients (7.2 %) discontinued treatment, due to migration from the area, or other reasons, which in no case were due to adverse effects of the chemotherapy.
Out of the total of 443 patients who had completed treatment at time of reporting, 38 patients (8,6 %) still showed clinical activity. Surveillance consists of 3-monthly clinical assessment, as well as urine-testing for detection of surreptitious dapsone-consumption.
Reversal reaction during treatment occurred in 4 patients, and in 5 patients after completion of treatment. At present no relapses have been detected.
Experience so far shows that while the study closely approximates to a service programme, valuable information can be gleaned from a trial, conducted under difficult field conditions, with minimal additional inputs.

FP 186

LONG TERM FOLLOW UP OF PB PATIENTS TREATED WITH EITHER A SINGLE DOSE OF RIFAMPICIN (RMP) FOLLOWED BY ONE YEAR OF DDS (REGIMEN A) OR 10 WEEKLY DOSES OF RMP (REGIMEN B).

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Since the publication of the results of the above mentioned treatment regimens (Lepr. Rev. 1987, 58, 349) more patients have now been followed for 3-5 yrs after the end of treatment. All results are based on histopathology. Cure rates evolved as follows.

Regimen A,	-3 lesions	1986	FU4	97%	1987	FU4	97%
Regimen A,	+3 lesions	1986	FU4	89%	1987	FU4	97%
Regimen B,	-3 lesions	1986	FU4	96%	1987	FU4	98%
Regimen B,	+3 lesions	1986	FU4	98%	1987	FU4	99%
Inacessible patients		1986	FU4	91%	1987	FU4	96%

In 1986, 20 relapses had been recorded in FU2 and FU3. Of tnese, 9 healed spontaneously but 9 new cases appeared during FU4 and FU5 in 1987, the overall rate remaining the same.
On Anjouan cure rates evolved from 96% to 97.6% and the absolute number of relapses from 1 to 4.
It is concluded that (1) 1% late cures do occur between FU3 and FU4, (2) half the early relapses observed during the first 3 yrs of FU are probably type 1 reactions, (3) true relapses manifest at between 4 and 5 years after treatment.

FP 187

RELAPSE RATES IN PAUCIBACILLARY LEPROSY - WHO REGIMEN VERSUS DAPSONE MONOTHERAPY.

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WHO TRS 675 (1982) on the "Chemotherapy of Leprosy for Control Programmes", recommends that paucibacillary (PB) patients be treated with short course chemotherapy of 6 months duration, using a combination of rifampicin 600 mgm. once monthly supervised, and dapsone 100 mgm. daily unsupervised.

Approximately 2,500 PB patients from the leprosy control area of Karigiri have been put on this regimen since 1982. These patients are currently being followed up and assessed for relapse.

The relapse rates in these 2,500 patients will be compared with relapse rates in PB patients who had received dapsone monotherapy for a minimum of 4½ years, in the same area using the following parameters:-

a) Age
b) Sex
c) Type
d) Duration of treatment
e) Lepromin status
f) Prior treatment

The findings indicate that short course chemotherapy using rifampicin is superior to dapsone monotherapy per se. The drugs are well tolerated, side-effects are minimal. However, late reversal reactions are often difficult to distinguish from relapse. The risk factors will be discussed.

FP 188

EVALUATION OF THREE SHORT TERM REGIMENS CONTAINING RIFAMPIN FOR TREATMENT OF PAUCIBACILLARY LEPROSY.

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Three regimens containing Rifampin have been tried in 273 Paucibacillary leprosy patients selected by the criteria of WHO. In Regimen I, Rifampin 600mg (supervised) is given once a month for 6 months with Dapsone 100mg daily. Regimen II is same as Regimen I but is supplemented with an additional 6 months treatment with Dapsone 100mg daily. Regimen III is same as Regimen II except that Rifampin is administered daily for the first 7 days in the first month. Treatment is stopped at 6 months in Regimen I and at 12 months in Regimen II and III. At the end of the scheduled treatment period, 72.2% of patients in Regimen I, 95.5% of patients in Regimen II and 96.8% in Regimen III became inactive. All patients with residual activity of Regimen II and III regressed spontaneously after stopping treatment, whereas 18 out of 25 active cases of Regimen I worsened after stoppage of treatment and required retreatment. The relapse rates in subsided cases were 13.9% in

Regimen I; 1.2% in Regimen II and 1% in Regimen III in the two and half years of follow-up after stopping therapy. In addition, 9% of cases in Regimen I had late reaction in the first six months after stopping treatment.

FP 189

RATE AND TIME DISTRIBUTION OF RELAPSES IN MULTIBACILLARY LEPROSY

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The median delay and the rate of relapses in MB leprosy have been identified as important indicators that measure efficacy of MDT regimens. Baseline data on relapses occurring in large population of multibacillary patients treated with DDS are therefore necessary as references for valid comparison.

Of the 47068 patients registered in the Polambakkam Leprosy Centre (South-India) between 1955 and 1982, the present study includes only those who showed smear positivity (BI $\geq$ 2+) at any time during this period and reached bacteriological negativity (two consecutive years of BI = 0). These criteria were satisfied by 1886 cases, among whom 243 relapsed bacteriologically (two consecutive years of BI $\geq$ 1+).

Relapse rate was calculated at 12.7 per thousand person-years, ranging from 4.5 for patients with a regularity of treatment equal or higher to 75 % in both positive and negative periods to 24.7 for those with a regularity lower than 75 % in the two periods. Relapses spanned over 20 years after negativity, although 50 % of the cases occurred within the first 5 years.

Results of rate and time distribution of relapses are discussed with reference to different levels of regularity.

FP 190

TRAITEMENT DE LA LEPRE RURALE PAR UNE DOSE UNIQUE DE RIFAMPICINE COMPLETEE PAR L ASSOCIATION SULFONE CLOFAZIMINE EN AUTOTRAITEMENT .

MEDECIN GENERAL LANGUILLON AJACCIO FRANCE

UNE RECENTE PUBLICATION DE L ILEP INDIQUE QUE LES ASSOCIATION MEMBRES AVIENT PRIS EN CHARGE EN 1986 LE TRAITEMENT DE 637000 HANSENIENS , 22% SEULEMENT ONT BENEFICIE DE LA POLYCHIMIOTHERAPIE CLASSIQUE.
LES AUTRES MALADES RECURENT LA SULFONE AVEC LES DANGERS D4UNE SULFONORESISTANCE PRIMAIRE OU SECONDAIRE .
LA REGULARITE AU TRAITEMENT DES MALADES RURAUX EN MEME URBAINS EST DIFFICILE A OBTENIR : MANQUE DE PERSONNEL QUALIFIE , CONDITIONS GEOGRAPHIQUES ET CLIMATIQUES , MODE DE VIE , TRAITEMENT SURVEILLE TROP LONG .
A LA SUITE D ESSAIS THERAPEUTIQUES FAITS A DAKAR EN 1977, J AI PROPOSE LE TRAITEMENT SUIVANT QUI EST EFFICACE PEU COUTEUX , APPLICABLE A TOUS LES MALADES .
DES SON DEPISTAGE LE MALADE ABSORBE UNE DOSE UNIQUE DE RIFAMPICINE DE 30 MG PAR KILO CORPOREL EN EMPORTE POUR UN AUTOTRAITEMENT DE SIX MOIS LA QUANTITE DE SULFONE ET CLOFAZIMINE' . IL EST REEXAMINE TOUS LES SIX MOIS ET CONTINUE L4ASSOCIATION SULFONE ET CLOFAZIMINE JUSQU A NEGATIVATION BACILLAIRE .
LES PAUCIBACILLAIRES RECOIVENT LES TROIS MEDICAMENTS AUX MEMES DOSES PENDANT SIX MOIS .

FP 191

THE EFFECT OF TREATMENT WITH RIFAMPICIN, CLOFAZIMINE AND DAPSONE IN MULTIBACILLARY LEPROSY IN THE FIELD FOR THREE YEARS

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The feasibility and effect of treatment with rifampicin (RFP), clofazimine (B663) and dapsone in multibacillary leprosy in Yangzhou District and Dongtai county for three years (1983-1986) are reported. there were 591 cases of active multibacillary leprosy in the area in these years, 569(96.3%) being treated with this regimen. The monthly supervising rates of RFP and B663 during each of the 3 years was 96.7%, 94.04%, and 93.00% respectively. 367 cases among 569 began treatment in July-Dec.1983. Of these 33 cases (9%) interrupted their treatment continuously for over 4 months, 11 (3%) of these had toxic side effects of the drugs, such as liver damage in 6 cases (1.6%) including 2 cases with jaundice, flu-syndrome occurring in 2 cases (0.54%), severe gastrointestinal discomfort in 2 cases (0.54%) and exfoliative dermatitis due to RFP in one case (0.2%). other causes for interrupting treatment were refusal of B663 after 2 years' treatment (2 cases, 0.55%), severe complications (10 cases, 2.7%), death from other diseases (7 cases, 1.9%), etc. Among 303 cases available for the analysis of the effect of treatment, 196 cases (64.7%) showed negative skin smears and clinical inactivity. The rest showed different degrees of improvement. The bacterial index (BI) was reduced by 0.78 averagely each year. The severity and frequency of ENL and neuritis decreased markedly with the prolongation of treatment. The main toxic side effects were skin pigmentation and ichthyosiform change, but these had no influence on treatment. The preliminary results in this study indicates that the feasibility and effect of combined chemotherapy is satisfactory. Among 196 cases who showed negative skin smears, 139 cases have been released from treatment for 1 year and no relapse has occurred.

FP 192

MULTIDRUG THERAPY FOR TREATMENT OF PAUCIBACILLARY LEPROSY; THE WESTERN KENYA EXPERIENCE.

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A prospective study is being undertaken in Western Kenya to evaluate the effectiveness and tolerability of WHO-MDT, while at the same time comparing it to a modified multidrug regimen, which is rifampicin 1500mg at the onset and repeated after 3 months and dapsone 100mg daily for 6 months.

A total of 127 newly diagnosed paucibacillary cases have been admitted in to the study. The clinical cure rates observed between 0 - 24 weeks were 38/64 (59.4%) for WHO-MDT and 49/63 (77.8%) for modified - MDT ($p<0.05$). Majority of the cases on modified-MDT achieved clinical cure between 0 - 12 weeks i.e. 28/49 of those on modified - MDT as compared with 12/38 of the cases on WHO-MDT ($p<0.01$). A further follow-up of study cases for a period of 8 weeks without therapy revealed clinical cure rate of 78% for WHO-MDT and 82.5% for modified-MDT ($p>0.1$). The default rate was 6.4% and 4.8% for WHO-MDT and modified MDT respectively. Type 1 reaction was 21% and 19% for WHO-MDT and modified-MDT respectively ($p>0.1$). Only 2 cases of exfoliative dermatitis and one case of hypochromic anaemia thought to be due to dapsone were noted.

These preliminary results indicated that MDT is effective in treatment of paucibacillary leprosy and also that clinical cure can be achieved in a much shorter duration than had hitherto been supposed. These results are discused in detail.

FP 193

RELAPSE RATE IN PAUCIBACILLARY PATIENTS DURING SURVEILLANCE AFTER MULTIDRUG TREATMENT - PRELIMINARY REPORT.

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289 patients of paucibacillary leprosy (Tuberculoid and Borderline Tuberculoid), who had completed the prescribed period of treatment and are now under surveillance for varying periods are evaluated for evidence of clinical relapse of their disease. These patients are from Leprosy Control Unit, Salur, in Andhra Pradesh State, India. Paucibacillary regimen being according to Government of India was Rifampicin 600 mgm daily for 3 days and Dapsone 100 mgm daily in the first month, followed by Rifampicin 600 mgm daily for two consecutive days once in a month for 6 months and Dapsone 100 mgm daily for 6 months. The criteria applied for diagnosis of relapse after excluding Type- I reaction were extension of existing skin lesions, appearance of new skin lesions, paresis / paralysis of previously unaffected muscles and presence of acid-fast

bacilli in skin smears. The results of the study will be discussed

FP 194

MULTITERAPIA DE LA LEPRA

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Se presenta la experiencia durante 14 años con diversas asociaciones medicamentosas Rifampicina-Isoprodian,Clofazimina-Sulfonas y Rifampicina-Clofazimina-Sulfonas en 120 enfermos multibacilares.

Se expone la preferencia por el uso de las tres drogas, la buena tolerancia y la no presencia de recidivas en los enfermos tratados.

Se comenta la necesidad de unificar las pautas terapéuticas y adoptar los esquemas de tratamiento de la O.M.S. en todos los paises.

FP 195

Essai comparé randomisé de traitement des névrites hanséniennes par les corticoïdes seuls ou associés à une neurolyse.

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93 nerfs (cubital, médian, sciatique poplité externe, tibial postérieur) présentant un déficit apparu depuis moins de 6 mois ont été étudiés chez 31 patients. Tous les malades ont été traités par corticothérapie mais certains nerfs tirés au sort ont subi une neurolyse.

L'objectif de cet essai était de comparer le résultat de ces 2 traitements (médical et médico-chirurgical) avec un suivi de 2 ans au cours duquel des bilans neurologiques chiffrés ont été effectués périodiquement. Les résultats ont été traités par le test de TUKEY.

Dans le cadre de cet essai, on a observé une amélioration des fonctions sensitive et motrice dans les 2 groupes. Mais il n'a pas été noté de différence significative quels que soient la topographie du nerf, la relative ancienneté de l'atteinte nerveuse, le caractère lépromateux ou non lépromateux de l'affection, la nature du traitement antibacillaire en cours. Par contre le traitement médico chirurgical apporte une amélioration significativement supérieure si l'on considère la douleur au niveau des troncs nerveux et les déficits graves mais non complets.

Cette étude a porté sur un nombre de nerfs relativement limité ; les auteurs concluent à la nécessité de poursuivre de tels essais randomisés pour mieux définir les indications de la décompression chirurgicale.

FP 196

SURGICAL EXPLORATION OF PERIPHERAL NERVE ENLARGEMENT

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Fifty cases with a thickened nerve at a site of predilection of M.leprae infection with accompanying dysfunction as the only symptom have been surgically operated on. Enlargement of nerve trunks to varying extent and forms were observed, e. g. spindle shaped, beads,cysts or homogeneous enlargement. Such changes were seen in all cases,among which five caseous lesions, five granulomas and eighteen with thickened epineurium in addition to inflammation of surrounding tissues were found. Small size biopsies from enlarged nerves were taken in all cases for histologic examination.

Eight of 14 ulnar nerve lesions were diagnosed as leprosy,while 4 showed elbow ulnar neuritis, 1 neurofibroma and 1 amyloid deposition. Five of 6 median nerve biopsies were diagnosed as leprosy while one demonstrated hypertrophic neuritis. Two radial nerve lesions consisted of one leprosy and the other hypertrophic neuritis. Twelve peroneal nerves showed six with leprosy,five with intraneural ganglion and one with neuritis. One tibial nerve showed leprosy.Ten of fifteen cutaneous nerve biopsies were diagnosed as leprosy, two as hereditary sensory radicular neuropathy, two as great auricular neuritis, and one as superficial neuritis

Although nerve enlargement at the sites of predilection of M.leprae are a major criterion for the diagnosis of pure neuritic leprosy, similar nerve involvement is found in quite a few diseases.

Surgical exploration and biopsy may be the only tools to clarify the diagnosis. Characteristic leprous granuloma formation was found in 31 cases (62%), among which twelve cases (39%) had positive acid fast staining bacilli.

Ethical consideration of nerve biopsy may give rise to the fear of increasing nerve damage. We did not find any postoperative complication in this study group, because dysfunction had already taken place in all nerves being operated. In addition, small longitudinal specimen taken from a nerve trunk should not cause obvious side effects. On the contrary, decompression of involved nerves by operation may provide relief of symptoms, e.g. pain, numbness and paralysis.

FP 197

QUELLE ORIENTATION DU TRAITEMENT DES NEVRITES HANSENIENNES

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I - Problèmes résiduels de traitement médical
L.ENL : corticoïdes plus actifs sur les nerfs que THD
DDS action défavorable sur la réaction ENL
CLO antihansénien efficace sur la réaction et la période post-réactionnelle
RMF plus tard après la période réactionnelle
B et T.RR : 3 formules en présence :
corticoïdes + DDS (ici sans effet adverse)
corticoïdes + CLO (CLO n'agit qu'en association)
DDS à double dose quotidienne
II - Qu'en est-il de l'appoint de la chirurgie
. Indications rentables - nécroses nerveuses incipiens (limitées) extrême urgence.
- névrites hypertrophiques L-ENL, avant 10 jours récupération de la sensibilité discriminative.
- névrites des 2 catégories du nerf TP avec déficit incomplet. Résultats excellents maintenus 5 ans.
. Indications de nécessité : névrites anciennes douloureuses
. Indications à réétudier : névrites du nerf TP avec ulcère plantaire, 1ère série Van.D.ALERT, résultats maintenus. 2ème série Van.D.et alDAKAR : 19/23 rechûtes après 3 ans.
Importance cordonnerie
. A rejeter chirurgie de rattrapage, pas de résultats significatifs. Névrites récentes B et T.RR idem.
- la formule "opérer tout et de manière univoque" 10 à 15% de résultats fonctionnels.
. Sélection nécessaire.

FP 198

Evaluation of efficiency, efficacy and effectiveness of prevention and treatment of physical disabilities in leprosy control in Brazil

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Considering social difficulties for leprosy inpatients are often a result of physical disabilities, Brazil has developed methods in the last ten years to include prevention and treatment of physical disabilities by simple techniques in routine control measures, using the "Lauro de Souza Lima" Hospital as the National Reference Center, with WHO and PAHO support.

This paper evaluates the efficiency, efficacy and effectiveness of this process; using standardized procedures, 416 Health Professionals were evaluated, sanitary units visited, inpatientes examined and technical proceedings rated.

Assuming a binary scale according to the degree os satisfactoriness, efficiency and efficacy are

revealed to be satisfactory and effectiveness presented an statiscally significant differentiated behaviour indicating a satisfactory performance in services with graduated professionals and insatisfactory performance for trained personal without professional degrees.

FP 199

Measurement of shock-waves during heel strike

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Human limbs can absorb and attenuate shock-waves to a certain extent. However, arthrodeses (resulting in stiffening of kinematic chains) may affect dynamic loading of the proximal joints.
In a pilot study the transfer of dynamic loads along foot and lower leg during heel strike was studied. Input was measured directly under the heelpad by a light weight accelerometer in hard heeled shoes. Output was measured with accelerometers mounted on an aluminium miniature platform fastened with doublesided adhesive tape and clamped with two straps on the tibia. The transducers measured accelerations in axial and dorsoventral directions.
In the literature no data are found concerning accelerations in a dorsoventral direction. The results show that these cannot be ignored. Further: peak-accelerations in an axial direction at the tibia are only one tenth of those under the heelpad. At very low walking speeds this difference can increase to a factor of 18. Dorsoventral peak-accelerations seem to be less effectively absorbed over the ankle joint than axial accelerations. However, the dorsoventral acceleration decreases towards the knee. This phenomenon can be explained by comparison of the crus to a pendulum.

FP 200

TRAITEMENT PALLIATIF DE LA PARALYSIE SCIATIQUE POPLITE EXTERNE - ETUDE CRITIQUE - A PROPOS DE 30 CAS

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30 paralysies des releveurs du pied ont été traitées par transfert du jambier postérieur isolé ou associé au transfert du fléchisseur commun des orteils, selon différentes modalités :

1 - Concernant le trajet du transplant :
- La voie inter osseuse paraissait la plus séduisante : les résultats sur l'amplitude de mobilité active ont été décevants. Par ailleurs, certains sujets présentent un espace tibio-péronier étroit qui contre-indique cette technique.

- La voie sous cutanée contournant le bord interne du tibia résout ces problèmes.

2 - La fixation distale :
Initialement, suture aux tendons du jambier antérieur et de l'extenseur commun des orteils comme le préconisent CARAYON et BOURREL.

La constatation dans les résultats d'un varus constant de l'avant pied, a conduit l'auteur à modifier la technique d'insertion distale qui comporte maintenant un montage en Y sur le tendon du jambier antérieur et sur les péroniers lateraux sectionnés au dessus de la malléole externe et dont le bout distal est dérouté en sous cutané en avant du ligament frondiforme.

FP 201

UNE "CORDONNERIE MOBILE" POUR LES MALADES HANSENIENS DU SENEGAL : 4 ANNEES D'EVOLUTION.

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Institut de Léprologie Appliquée de Dakar, B.P. 11023 CD Annexe - DAKAR - SENEGAL-

Afin d'éviter l'apparition d'ulcères plantaires ou de leurs récidives, une méthode simple est le port de chaussures adaptées associé à l'éducation sanitaire des malades.
Une action sur le terrain, dite "cordonnerie mobile" est menée depuis plus de 4 ans au niveau de 12 secteurs et villages du pays, par une équipe composée d'une physiothérapeute et d'un cordonnier, à l'aide d'un véhicule équipé. Les auteurs présentent le bilan de ce projet après 4 ans d'application.
Outre le nombre plus élevé de lieux visités et celui croissant de malades traités, une amélioration des chaussures et de l'appareillage a été réalisée.
D'autre part 23 éducateurs sanitaires (1987) ont été formés pour les secteurs et villages de reclassement.
De plus, l'adaptation d'un matériel didactique simple d'éducation sanitaire et de rééducation fonctionnelle a été mis au point. L'accent est également mis sur l'adaptation des activités de la vie journalière avec du matériel local et/ou de récupération. Enfin, une décentralisation de la "cordonnerie mobile" travaillant dans le même esprit a été installée pour la région de Casamance (1985).

FP 202

SURGICAL MANAGEMENT OF ULNAR NEURITIS BY HEMICIRCUMFERENTIAL EPINEUROTOMY.

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Surgical management of neuritis of the ulnar nerve at the elbow includes a variety of one or more techniques such as (1) medical epidondylectomy, (2) external decompression by releasing of any constricting fibrous bands, (3) anterior transposition of the ulnar nerve, (4) inter and intra-fascicular decompression of the nerve. In hemi circumferential epineurotomy, the epineurium is incised longitudinally over the full length of the visibly involved segment of the nerve, and released from its attachment to the nerve fascicles for atleast half the circumference, thus effecting a decompression. No operating microscope is used.

53 nerves in 51 patients were treated by this procedure. In those cases (69.8%) where the vascular pedicle could be mobilised without jeopardising the blood supply to the nerve, an anterior transposition of the nerve and burial of the same in the depths of the common flexor origin was also performed. Nerve function was recorded objectively by voluntary muscle tests and sensory assessment.

From among those nerves analysed completely (47), results show that motor and sensory function improved in 27.7%, remained static in 63.8%, and deteriorated in 8.5%. 6 nerves were either lost to followup or had incomplete data. All patients had relief from pain, and there was clinical absence of tenderness as well. These results suggest that the procedure of hemicircumferential epineurotomy is a useful tool in the surgical management of ulnar neuritis without detriment to the patient.

FP 203

NEURITIS - SURGICAL DECOMPRESSION RELIEVES INTRACTABLE PAIN, TENDERNESS AND HYPERAESTHESIA.

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Results of decompression of nerves are presented. Nerves decompressed: Ulnar 6, Median 1, Peroneal 4, Posterior Tibial 5.

The average follow up is 1year 2 months; the longest follow up is 4 years 2 months, the shortest follow up 1½ months.

Consistently intractable pain, tenderness and hyperaesthesia were relieved; this relief is durable. This is of relevance in areas where cortisone is scarce and costly when available.

In the cases of decompression of the posterior tibial nerve, in addition to relief of pain, tenderness and hyperaesthesia, a very encouraging recovery in sensation has been noticed. An interesting finding in 3 cases has been restoration of pulsation in the posterior tibial artery (preoperatively no pulsation was felt). Not using a tourniquet is an advantage.

A modified inverted, asymetrical T shaped incision helps better decompression of the posterior tibial nerve and favours subsequent healing.

Decompression consists mainly in external neurolysis except when palpable caseation along the nerve justifies evacuation.

FP 204

New Boundaries for the Indications for Nerve Decompressions .

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Anandaban Leprosy Hospital, The Leprosy Mission Int., Nepal.

A seriesof patients with loss of sensation of the extremities ranging from a few weeks to 25 years underwent nervedecompression of the peripheral nerves. Results are discussed and new boundaries for the indication set.

FP 205

Chemical and mechanical nourolysis.

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The thickening of peripheral nerves, sequel of agression by the Hansen bacilus, with all its sensory and motor manifestations and alterations, has been one of the disturbances we must keep in mind to decide early treatment so as to avoid greater consequences. If this alteration is not resolved by traditional therapeutic measures, surgical liberation is the only alternative. The chemical and mechanical neurolysis we describe offers several advantages of the use of large incisions by assuring a greater liberation along the length of the Schwann sheath and the introduction of a steroid or other substance required under the sheath. This technique also offers the possibility of its use in other neurological situations as a therapeutic and diagnostic approach.

FP 206

Indeterminate Leprosy
Twenty Year Study - Histologic Observations

In 1968 histopathologic studies were made on biopsies taken from 52 indeterminate cases. The changes consisted mainly of round cell infiltration around blood vessels, nerves and dermal appendages; small foci of epitheloid cells were also seen in 16 cases. Nerve involvement were invariably perineural; 14 cases also showed endoneural involvement, and in 2 cases hyaline change was noted.

Acid-fast bacilli were demonstrated after careful search in nerves in all 52 cases; in 33 cases bacilli were also seen in infiltrate, and in 8 cases bacilli were noted the arrectores pilorum muscles.

Within a period of five years, 9 cases transformed to tuberculoid, one to borderline lepromatous and another one to lepromatous leprosy.

Twenty years later, 21 of the 52 original cases were re-examined. The histologic changes will be presented and their significance discussed.

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FP 207

EVOLUTION OF LEPROSY LESIONS IN MAN

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On the basis of histopathological studies carried out on early leprosy lesions at the Schieffelin Leprosy Research and Training Centre, Karigiri and follow-up of patients, an attempt has been made to reconstruct the evolution of leprosy lesions in man.

Studies of nasal mucosal biopsies from Indeterminate, Tuberculoid and Borderline leprosy reported by Chacko et al have shown nasal mucosal involvement in 65 out of 137 (47%) patients, suggesting that the disease is disseminated even when skin lesions appear localised. A further study of nasal biopsies from 96 healthy household contacts have shown presence of nerve inflammation in 40 contacts and acid fast bacilli in 4. On follow-up, one of the contacts developed peripheral nerve involvement and an indeterminate leprosy lesion in the gluteal region.

Nerve biopsy studies from Primary Neuritic leprosy patients have shown a range of host responses from Lepromatous to Tuberculoid leprosy neuritis. Six of the patients developed skin lesions on follow-up. These studies have shown that Primary Neuritic leprosy is an early stage in the evolution of the disease.

Based on the above studies a conceptual model of the evolution of leprosy lesions in man has been proposed.

FP 208

LYMPH NODE STUDIES IN 30 NECROPSIES OF LEPROSY PATIENTS.

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Lymph nodes of 7 chains (cervical, axillary, inguinal, hepatic, peri-aórtic, mesenteric and mediastinal) were studied in 30 necropsies of leprosy patients including 16 lepromatous with regressive lesions, 6 with residual lesions, 3 with reactivated lesions, and 5 non lepromatous patients. We observed:

1. The organism has a clear difficulty to eliminate residual lepromatous infiltrate from the cortical areas of limph nodes even after several years of inactivity.
2. There are preservation of paracortical areas in mediastinal, mesenteric, and in most periaortic lymph nodes in patients with extensive involvement of paracortical areas of cervical, inguinal, axillary and hepatic lymph nodes.
3. In 4 patients we found tuberculoid granulomatous reactions in paracortical areas of lymph nodes with extensive lepromatous infiltrate.
4. In reactivated lepromatous patients solid bacilli and recent specific infiltrate are limited to lymph nodes which drain cutaneous areas.

Some of those findings suggests that in lepromatous patients the organism can preserve an important contigent of thymus-dependent lymphocytes in circulation although the extense specific involvement of paracortical areas of lymph nodes of cervical, axillary, inguinal and hepatic chains.

FP 209

THE HIGH PREVALENCE OF TESTICULAR INVOLVEMENT IN LEPROMATOUS (LL) AS COMPARED TO BORDERLINE LEPROMATOUS (BL) LEPROSY PATIENTS.

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Although testicular changes are known to be common in multibacillary leprosy, details as to prevalence rates are scant, and the Ridley system of classification has not been used in addressing this problem. To study testicular involvement, serum FSH, LH and total testosterone (TT) values were determined by double antibody radioimmunoassay in 42 LL and 21 BL randomly selected male clinic patients. In 25 with low-normal TT values, free serum testosterone was also measured.

Serum FSH values were above normal (10mIU/ml) in 86% of LL and 19% of BL subjects; means 40.9 and 10.5, respectively, $p<.0001$. Serum LH values were above normal (15mIU/ml) in 79% of LL and 10% of BL subjects; means 32.5 and 11.3, respectively, $p<.0001$. Using a TT of 280ng/dl or a free testosterone of 50pg/ml as lower limits of normal, 43% of LL and 5% of BL subjects were hypogonadal, $p<.01$. These abnormalities could not be

associated with age, duration of symptoms, nor duration of therapy.

Among BL subjects, although only half were Mexican-born, the only androgen deficient patient, the only two with elevated LH, and three of the four with elevated FSH were Mexican-born.

In multibacillary leprosy the burden of testicular injury is born primarily by lepromatous subjects where the injury is extensive and occurs early. Osteoporosis is a serious health problem which may be common, but preventable, in lepromatous men. Use of Ridley's system appears to be of value in nonimmunological matters. In BL subjects testicular injury appears to be particularly common in Mexicans.

FP 210

TESTICULAR DYSFUNCTION IN LEPROSY:- RELATIONSHIPS OF FSH, LH, AND TESTOSTERONE TO DISEASE CLASSIFICATION, ACTIVITY, AND DURATION. William R. Levis, Andrew P. Lanza, Stephen Swersie, Harry C. Meeker, Georgia Schuller-Levis, and C. Wayne Bardin. Dept. of Dermatology, New York Medical College, Bayley Seton Hospital, Dept. of Immunology, NYS Institute for Basic Research, Staten Island, N.Y., and The Population Council, Rockefeller University, N.Y., N.Y. USA

The testes are known to be a favored site for focal damage in patients with leprosy. This is probably because bacillary growth is favored at the lower temperature in the scrotum, since Mycobacterium leprae grows optimally at about 30°C. There are few studies of testicular disease in men with proven leprosy. We, therefore thought it pertinent to examine men who are under treatment for leprosy for evidence of testicular failure. In the current study, 93 men classified according to the Ridley-Jopling system were evaluated for FSH, LH, and testosterone levels. The findings were correlated with two measures of disease activity, bacillary index (BI) and IgM antibody to phenolic glycolipid I (PGL-I), to determine if these were predictive of testicular failure. LH was elevated in 27 of 55 LL patients and FSH was elevated in 29 of 56 LL patients. LH and FSH were elevated in only 10% of BL, BB, and BT patients combined. Nineteen of the 93 patients examined had low testosterone levels, and 14 of these were LL. LH and FSH levels were significantly higher in LL patients compared to BL, BB, and BT ($p<0.001$). A positive correlation was seen between LH and FSH ($r=0.82$, $p<0.001$) and a negative correlation was seen between testosterone and both LH ($r=-0.41$, $p<0.001$) and FSH ($r=-0.48$, $p<0.001$). No correlation was seen between hormone levels and measures of disease activity, BI and IgM to PGL-I. A significant correlation was seen between duration of disease and FSH when age was taken into account by partial correlation analysis ($p<0.02$), indicating that testicular damage is probably cumulative and irreversible. It is recommended that LL patients be routinely screened for hypogonadism using FSH, LH, and testosterone.

FP 211

Charting of organic sites showing the presence of bacilli and scpecific infiltrate on a series of 126 necropsies from leprosy patients. Tentative of association with cause of death.

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The results from necropsies made for a series of 126 leprosy patients deceased in São Paulo State within a 10 year period (1970-80) were tabled in relation to:

1) causes (basic and associated) of death according to 9 th I.C.D.
2) Presence of bacilli in different organs
3) Presence of specific infiltrate in different organs (including amiloidosis and reactional infiltrates)

The positive organic sites for items 2 and 3 are charted and the stablishment of a relationship with the respective causes of death (item 1) is offered.

FP 212

ENDOTHELIAL CELL BACILLATION IN HUMAN LEPROSY-ULTRASTRUCTURAL ASPECTS

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The fine structure of the bacillated endothelial cell (BEC) was studied in skin biopsies from 15 LL and BL cases. The results showed presence of BEC's in all the biopsies examined. Most of the bacilli in the BEC's were uniformly contrasted and seen both singly and in clusters indicating multiplication at these sites. The bacilli were seen on the luminal and abluminal aspects and also in the subjacent tissue spaces of the BEC's indicating transcellular movement into the extra-vascular spaces. BEC's did not show any phagolysosome formations around organisms. Bacilli were also seen lying free in the lumen and in intravascular monocytes. The bacillated histiocytes in the lesion were centered around the cappillaries and showed a centrifugal increase in older cells and degenerated organisms. These observations indicate that BEC's are sites for bacillary growth and possibly influence granuloma growth through input of fresh organisms into the granuloma from the BEC's and the circulating blood.

FP 213

Leydig cells observed in autopsy cases of the national leprosarium, Okukomyoen

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In Japanese leprosaria today, the average age of patients is higher than 60 year old. Osteoporosis is common problem in orthopedic clinic as the basis of frequent fractures. Ishida carried out a survey of osteoporosis by the metacarpal index method and observed statistic significance suggesting correlation with pathologic changes of testes pointed out as one of the causes of hormonal disorder resulting gynecomasthia.

This article focuses on the pathologic change of Leydig cells in the autopsy series of Okukomyoen.

Materials

The total number is 47 of cases and 74 of testes.

L type 37	56	54 - 87	
T type 8	cases 16	testes 65 - 79	years of age
B group 2	2	49 - 76	
Average age		70.7	

Main findings of testes affected by L leprosy are

1) Degeneration and fibrosis of seminiferous tubules
2) Degeneration, nodular proliferation or fibrosis of Leydig cells and
3) Degeneration of interstitial tissue resulting vacuole formation and fibrosis.

Conclusion

Dysfunction of Leydig cells based on histopathologic changes is possiblly related to earlier start of osteoporosis in male patients with L leprosy.

FP 214

NEW FINDINGS IN THE HISTOPATHOLOGY OF INDETERMINATE LEPROSY

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Skin Biopsy was done in 100 patients who satisfied the clinical criteria for the diagnosis of indeterminate leprosy (IL) according to the Indian Association of Leprologists (IAL). The sections were stained with (1) Haematoxylin and Eosin (2) Modified Fite stain for AFB and (3) Solochrome Cyamin stain for myelin.

In addition to the histopathological features mentioned by IAL many other fea-

tures pointing to the diagnosis of leprosy were found. The criteria taken for the diagnosis of IL were finding of (1) bacilli at characteristic sites (2) significant nerve involvement and (3) granuloma at sites of election of M. Leprae.

Out of the 100 cases of IL 69% showed specific histopathological changes and 31% non specific changes. Neural changes were seen in 60% of the total cases and 85% of cases showing specific changes and granuloma in 23% of total cases. Bacilli were found only in one case. Among the inflammatory infiltrates lymphocytes were found in 62 % of cases and histocytes in 37 % of cases. Cutaneous appendages were found infiltrated by inflammatory cells in 48 % cases.

The significance of these findings is discussed.

FP 215

EFFECT OF MULTIDRUG TREATMENT (PAUCIBACILLARY REGIMEN) ON THE CLINICAL AND HISTOLOGICAL FEATURES OF TUBERCULOID AND BORDERLINE TUBERCULOID CASES.

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PHILADELPHIA LEPROSY HOSPITAL, SALUR, ANDHRA PRADESH, INDIA.

50 new cases of paucibacillary Leprosy (Tuberculoid and Borderline Tuberculoid) who are put under Multidrug treatment during 1987 from three control units of Vizianagram District, Andhra Pradesh, India, are subjected to detailed clinical and histological examination after the prescribed period of treatment and are under surveillance. Paucibacillary regimen being according to Government of India was Rifampicin 600 mgm daily for 3 days and Dapsone 100 mgm daily in the first month, followed by Rifampicin 600 mgm daily for two consecutive days once in a month for 6 months and Dapsone 100 mgm daily for six months. The clinical criteria applied for attainment of inactivity are non-occurrence of new skin lesions, non-extension of existing lesions, neuritis and bacterial negativity. An attempt is made to formulate histological criteria for inactivity in these cases by comparing histological pictures of known active cases under the same types of Leprosy.

FP 216

A quantitative study of the relationship between systemic immunity and local histopathological changes in untreated leprosy

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Skin biopsies were taken from 40 newly diagnosed untreated leprosy patients. The Ridley-Jopling classification, bacteriological index (BI) and granuloma fraction (GF) were assessed for each case. The density of apoptoses, mitoses, plasma cells, and mast cells were also measured. For comparison with the histological data, immunity to mycobacteria was assessed from the size of the 72 hours skin test reaction to Leprosin A and PPD, and by measurement of the serum antibody responses to M. leprae, M. tuberculosis, M. scrofulaceum, and a glycoconjugate which mimics the immunodominant epitope of PGL1.

Serum antibody levels and the skin test results showed the expected relationship with Ridley-Jopling classification. The delayed-type hypersensitivity (DTH) skin test reactions were inversely related to the serum antibody responses to PGL1. There was also an inverse correlation of the skin test reactions with the antibody responses to whole M. tuberculosis and M. scrofulaceum, but not to whole M. leprae. The BI showed inverse correlation with Leprosin A and PPD reactivity. None of the other histological parameters showed a significant relationship with the measurement of systemic immunity.

Our findings suggest that the inverse relationship between DTH and humoral immunity is less marked than is often thought: there may be divergent responses between humoral and cellular responses to different epitopes of M. leprae in individual patients. The lack of correlation of some histological and systemic parameters suggests that local factors may modulate systemic immunity in the pathogenesis of leprosy lesions.

FP 217

Long-term correlation between serological (PGL) and histological parameters in the control of chemotherapy in LL and BL patients.

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48 patients with histological LL and BL leprosy were treated for 3 years with either DDS monotherapy, DDS plus Rifampicin, or Isoprodian plus Rifampicin and followed up for 2 years. Clinical and bacteriological assessments were performed at 2 to 3 months intervals.Skin biopsies and serological tests (PGL-I Ab) were done every 6 months.
PGL-I Ab correlate well with histology during and after treatment. We conclude that serology, PGL-I Ab ELISA, is as effective as histology in the control of chemotherapy in LL and BL patients.

FP 218

GOVERNMENTAL RESPONSIBILITIES IN ADDRESSING THE SOCIAL STIGMA ATTACHED TO INDIVIDUALS AFFLICTED WITH HANSEN'S DISEASE

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My involvement with addressing the social stigma associated with Hansen's Disease began first as a concerned citizen and now, as a member of the Hawaii State Legislature. The perspective of governmental responsibility in addressing the social stigma associated with the disease is based upon my experience in dealing with this issue from both these viewpoints.

The key to government involvement is through its ability to provide education and to develop supportive programs designed to address not only the medical needs of the individual but also the psychological and social needs as well. Regarding the educational needs, the first area for government to address is itself, then to the individuals afflicted with the disease and finally to the general citizenry. When talking about government, we often forget that government is people and accurate information is the key to better understanding.

In dealing with the human sensitivities and needs of the individual with Hansen's Disease, Hawaii is among the forefront in establishing positive government responses to the overall needs of the individual. Through our Hawaiian experience, we can hopefully provide an innovative stimulus for other governments to consider.

FP 219

MONITORING AND EVALUATION OF TRAINING PROGRAMMES

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The effectiveness of teaching innovations remains undetermined unless evaluative research accompanies the curriculum change.

The purpose of this paper is to highlight the significance of monitoring and evaluation of training programmes, as a yardstick of performance and quality control to ensure effective learning. The Medical

Officers course being offered at the Schieffelin Leprosy Research and Training Centre, is being analysed as a proto-type for this type of monitoring and evaluation of a candidate's performance.

A brief review of this course suggests that the Pre-test is a good indicator of the candidate's performance in the Post-test as well as in the Final Assessment.

This hypothesis is being evaluated further in the two Medical Officer's course in January and July 1988.

Confirmation of this hypothesis will indicate that teaching and training methodology will have to be revised in the light of the Pre-Course test performance.

FP 220

COURSES AT A SPECIALIST LEPROSY HOSPITAL FOR THE TRAINING OF MEDICAL STUDENTS AND PARA-MEDICAL WORKERS IN NIGERIA

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New patients with advanced lepromatous leprosy frequently report to the Leprosy Hospital for diagnosis and treatment, having spent months or years attending general hospitals without receiving a correct diagnosis of their condition.

To address the urgent need for medical personnel with a basic training in leprosy, as well as a positive attitude to the disease and to clinical contacts with patients, a compulsory module in leprosy was established in 1982 at the University of Calabar Medical School. All final year students made a number of daily visits to the Leprosy Hospital 100 km away, and theory and practical exams included compulsory questions on Leprosy.

In 1987 a student hostel was opened in the hospital grounds and 2-week long residential courses for the under-graduates have now been established.

The paper will outline the nature and development of the link between the medical school and the hospital, the organisation and content of the 2-week residential module for medical undergraduates, the postgraduate programme for medical residents and the 3-month residential in-service programme for rural health personnel. The marked change in attitude of medical undergraduates will be examined.

FP 221

EXPERIENCES WITH HEALTH EDUCATION STRATEGY BEING FOLLOWED UNDER NATIONAL LEPROSY ERADICATION PROGRAMME IN INDIA.

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The existing set up of Central Leprosy Division, CHEB,StateLeprosy Divisions,SHEBs & MDT District Societies are being used for development/procurement of health education material.Many voluntary organisations and international agencies are also involved in production of effective health education material.HKNS,GMLF,TLM,UNICEF,GLRA,DANIDA are important among them.The objective of health education is to educate people about facts of leprosy and make them aware of availability of free services.Health education material generally used are films,radio,vidio,exhibition, demonstration,group talk,news paper and posters,banners, stickers,calenders,flip charts etc.The health education has been evaluated twice in the year 1986 & 1987 during the Independent Evaluation of the Programme.The findings indicate that out of 418 people interviewed in different parts of the country 88.3% knew the nearest place where treatment for leprosy was available.Knowledge of leprosy was relatively low as only over half of respondants knew that it was infectious disease.Out of 289 patients contacted in villages 98% were living with their families.Social stigma was much more in urban areas compared to the rural. The lession learned indicate that health education should be the responsibility of all the health workers.Although general awareness can be developed by any method of Mass Media & Communication but change in attitude and behaviour can be brought mainly through effective personal contact. Thus all category of health workers should be adequately trained in health education and community leadership during their basic training.

FP 222

MOTIVATING AND TRAINING FOR RECONSTRUCTIVE SURGERY AND REHABILITATION IN A SOUTH AMERICAN SETTING. Frank Duerksen, Marcos Virmond and Diltor Opromolla. Hospital Lauro de Souza Lima, Bauru, S. Paulo, Brazil.

We present our experience and methodology in motivating first and then training surgeons and allied health staff in the area of rehabilitation and reconstructive surgery for leprosy patients. Each year four courses on rehabilitation and surgery are offered at the Lauro de Souza Lima Hospital in Bauru for formal training. The goals of the courses are to show what can be done in the area of rehabilitation, teach the basic surgical procedures of the face, hand, foot and nerve surgery, indications and complications. Methodology is by lectures, patients' presentations and actual surgical procedures. Target audiences are surgeons and therapists but also everybody involved with treating leprosy patients. The technical training of the surgeons is tailored to each case. We also have a program of visiting Centres treating leprosy patients in order to assess needs, teach, motivate and assist surgeons to start a rehabilitation program. This methodology is different from the longterm training usually demanded for surgeons. In the South American medical and health system this is not possible. The training is short term and repeated or in stages. This makes it possible for many to participate. another key factor in this program is follow-up and keeping in touch with former trainees.

FP 223

FACTORS INFLUENCING VOLUNTARY REPORTING OF LEPROSY PATIENTS IN MADRAS, AN URBAN METROPOLITAN CITY IN INDIA.

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GREMALTES REFERRAL HOSPITAL & LEPROSY CENTRE, SHENOYNAGAR-MADRAS, INDIA.

Over a 15-year period of Leprosy Control work in Madras, our institution has registered 33.620 cases of Leprosy, out of which 25.91% were detected through slum survey, 26.80% through School Survey, 8.75% through Contact Survey and the MAXIMUM 38.52% through Voluntary reporting.

An analysis of various factors influencing and motivating Voluntary or self reporting is made through personal interviews with 500 self-repored patients of various age-groups and economic starta.

The role of Mass Media, group and Individual approach is analysed in detail. In Mass Media the role of various tools such as Films, Cinema, Slides, Hoardings, Exhibitions, Printed Materials etc. is Analysed. In group approach, the role of groups like Doctors, Local Leaders, Youth Clubs, etc. is analysed. In individual approach the role of satisfied patients, family members, neighbours etc. is analysed.

The relative importance of various motivating factors and the ways and means of strenghening them is discussed.

FP 224

The application of a health education model to obtain early and regular treatment of leprosy patients.

Dr. C.M.E. Matthews, Field Director, Christian Fellowship Community Health Centre, Ambilikkai, Tamil Nadu, India.

A model for bringing about behaviour change based on Cartwright's and Lionberger's theories was applied to the problem of getting

leprosy patients to take early and regular treatment. The model includes 3 stages: information, motivation, and action. Information was given using mass methods, including drama, puppet shows, films and slides. Motivation was given through leaders, group methods and individual contacts. At the action stage barriers to taking treatment were reduced as far as possible and individual reminders were given. After application of this method, the percent of known cases taking treatment increased from 43% to 88%, and the new cases found per thousand population increased from 1.0 to 1.8 indicating earlier case detection. Thus both early and regular treatment were considerably improved by using this method.

FP 225

THE PARADOXICAL STIGMA OF LEPROSY

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Instead of the current sociological interest in the origins of leprosy stigma, this study, on the contrary, focuses on the question - less investigated so far but presently more urgent - how the stigma persists in an era when medical treatment is already available and social acceptance attainable.

The research combines historical investigation (archival survey of documents covering the past 100 years) with 2½ years of empirical research (anthropological observation and interviews with 450 patients and 400 other informants - staff members, patients' relatives etc.) conducted in 20 locations throughout Thailand: leprosy hospitals, colonies, rehabilitation villages and outpatient clinics. The study examines the changes in social behaviour and attitudes towards leprosy following the progress made in leprosy control policy in Thailand.

The findings show a steady improvement as to actual reactions towards patients, but at the same time the persistence and even intensification of the theoretical negative image of leprosy. The analysis of this paradox explains the gradual process of dissociation between leprosy as a social phenomenon and leprosy as a cultural metaphor which accompanies the medical achievements.

Based upon the understanding of this process, the research presents practical recommendations for dealing with patients' social problems and a general strategy for social research on leprosy that avoids presuppositions about severe stigma, confusion between attitudes and behaviour as well as disregard of the dynamic character of the stigma.

FP 226

THE PARTICIPATION OF HANSEN'S DISEASE PATIENT IN ALL THE ACTIVITIES OF CONTROL IN BRAZIL

WAGNER ROGUEIRA and GERSON F.M. PEREIRA
MOVIMENTO DE REINTEGRAÇÃO DO HANSENIANO - MORHAN
INST. DE CIVISMO E SOLIDARIEDADE ALICE TIBIRIÇA
DIVISÃO NACIONAL DE DERMATOLOGIA SANITÁRIA - DNDS/MS

The hansen's desease control in program police en Brazil until the 80ws was implemented without any participation of the patient and the policy making.

Neverless the history register from the yeat 1980 and bey ond the inauguration of the "Sociedade Alice Tibiriça de Assistência aos Lázaros" with have development a voluntary / work based on the scientieficy knowledge of the decenium / that comanded a mandatory confinement of the patient and so making inviable of the process of has educationand promotion of social wellfair of the patient. From 1981 the Movimento/ de Reintegração do Hanseniano was inaugurated with a program designed by a hansen's desease patient wich thoughter with others patients and other persons that working in the health service, ali inagerment wichthe program ain, started their families and communities.

MORHAN was officialy creadited by the governmen and its advance was enougth to be credenciated for participation / and the 8ª Conferência Nacional de Saúde. Currently the participation of MORHAN is constant in all meeting for discu / tion and evaluation the control of the endemy trough its / 51 nuclein from 22 of the 24 states of country.

The paper ains show the MORHAN policies and strategies / included in the oficial documents of the national rules and norms.

FP 227

TRAINING NEEDS FOR LEPROSY ERADICATION THROUGH PRIMARY HEALTH CARE

Mrs.THANGARAJ, The Leprosy Mission, Salur, 532 591, A.P. India.

Definition of Primary Health Care, concepts and components. Leprosy problem is managed by vertical programme outside PHC in India. We should differentiate community participation from Community involvement.

Community should perceive the problem of morbidity. Community study and K.A.P study for making suitable efforts to bring in awareness, create interest and ensure active role in planning organising and helping in supervision and health education. Work through change agents (Nonformal leaders).

Analyse what is involved in leprosy Eradication Programme. Decide what are the tasks and responsibilities of each peripheral level health worker (CHW, PMW, TBA, MO of PHC, ANM, Malaria worker etc).

Identify teams to be trained and trainers for each group. Plan for continuing education.

Review organisational structure. Criteria for referral should be clearly specified. Referral system and channel of communication to be made clear to all category.

Intersectoral coordination with village health committees and village development committee is important.
(Details of each stage given in the paper).

FP 228

FACTORS INFLUENCING CLINIC ATTENDANCE FOR TREATMENT OF LEPROSY

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University of Oxford, OXFORD.

A review of the existing literature on patient treatment compliance in leprosy reveals inconsistencies in terms of definition, incidence, measurement of compliance and factors influencing non-compliance. Furthermore, there is a lack of explanatory models of compliance. The present prospective study takes into account the above methodological, theoretical criticisms and investigates within an inception-cohort framework the factors influencing nonattendance in two leprosy treatment projects based in Bombay (A.L.E.R.T. and B.L.P.).

Results from the analyses show that nonattendance and irregularity of attendance is widespread (i.e. 65%). It is also apparent that there is no single or simple explanation for nonattendance. However, with due attention to scientific merit, the weight of evidence leads to the isolation of a small number of factors of undoubted and considerable importance to the reasons why patients do not attend for treatment. These factors are discussed with a view to providing recommendations for the improvement of attendance and priorities for future research in this area will be outlined.

FP 229

KNOWLEDGE AND ATTITUDE OF LEPROSY WORKERS : A CASE STUDY IN STATUS ANALYSIS

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Knowledge of leprosy and sympathetic attitude of leprosy workers help in controlling leprosy. The instant study aims to gauge the status of knowledge and to assess

the attitude of leprosy workers, medical and paramedical, in Vijayanagaram district, an endemic area in Andhra Pradesh (India).

Twentyfive percent of the total of 128 workers in the district were randomly selected for the study. Open ended interview and observation were the techniques employed to collect data. Secondary data, reflecting performance and attitudinal changes, were made use of to relate individual rating.

Parameters, like perception of the disease,depth of knowledge about leprosy control programme and techniques, conviction about the programme, effect of health education and the extent of commitment on the part of the workers, were analysed.

It has been found that the educational standard and the workers'experience have little bearing on their perception of the disease, knowledge of the national programme, conviction about the effect of health education and their commitment. However, significant relation has been found between their depth of knowledge,perception of the disease, and the techniques of work adopted by them. There is also some positive association between perception of the disease, their commitment, and strong conviction of the effect of health education in controlling the disease.

FP 230

RELAPSE IN LL-PATIENTS AFTER ANTI-LEPROSY ICRC VACCINE: IT'S SIGNIFICANCE TO ANTIGENIC VARIABILITY OF M.LEPRAE.

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The antileprosy ICRC vaccine was prepared from leprosy derived mycobacteria, possessing lepromin like antigenic property. The ICRC vaccine used in LL-BL patients, since 1979, induced lepromin conversion in 60% of cases and also clinical improvement. This demonstrated the potency and efficacy of the ICRC vaccine to augment CMI against M.leprae, suggesting its prophylactic potential.

During the follow up of over 75 cases, three cases developed new LL-type lesions with 5+ AFB, 2to5 years after vaccination, despite lepromin conversion & clinical improvement. It raises the question of origin of new M.leprae and how they escaped induced persistant sensitization. The possibility of emergence of an antigenic varient of M.leprae, that may have existed, was examined by way of fresh culture isolate from new M.leprae. Surprisingly the new culture did not cross-react with the vaccine strain in 'in vitro' CMI tests in mice and man. This suggested that induced sensitization may be strain specific; and the antigen specify of the culture may be related to the M.leprae from which it was derived. If the CMI related protective antigen epitopes of M.leprae are indeed variable, it has far reaching and alarming implications in antileprosy vaccine trial, but also provides means of improved vaccine. This will also offer clues to the puzzle of spectrum of leprosy.

FP 231

NON-IMMUNE CLEARANCE OF M. LEPRAE FROM THE FOOTPADS OF M. LEPRAE-INFECTED, MULTIDRUG-TREATED NUDE MICE.

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To determine the rate of clearing of dead M. leprae in the absence of cell-mediated immunity, a group of nude mice (HSD, homozygous nu/nu (AF)) with established footpad infections [2.21(+ 1.51) x 10^9 bacilli per inoculated footpad, MI = 8.33 + 0.82] were put on multiple drug therapy consisting of 0.01% dapsone, 0.001% clofazimine and 0.01% rifampin w/w in autoclavable, powdered rodent feed. As expected, multiple drug treatment prevented enlargements (the development and enlargement of macrophage granulomas) of the inoculated footpads and prevented further multiplication of M. leprae. This was associated with a fall in morphological index to zero within 3 months of starting treatment. In the inoculated footpads there was no apparent tendency for acid-fast bacilli to clear over the course of 12 months treatment, checked at 3 month intervals. Footpad tissue samples from treated and untreated animals were collected at 3 month intervals after starting treatment for quantitating phenolic glycolipid-1 (PGL-1) antigen to determine the rate of production or clearance of PGL-1 in relation to acid-fast bacilli. A gradual clearance of PGL-1 from the treated footpad is apparent, with $t_{\frac{1}{2}}$ calculated to be approximately 117 days.

FP 232

EVALUATION OF THE EFFICACY OF CANDIDATE VACCINES AGAINST M. LEPRAE INFECTION IN MICE

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The candidate vaccines used in the trial were autoclaved M. leprae, M. vaccae, M.w., ICRC and BCG - alone or combined with live BCG. Vaccinated mice were infected with M. leprae to observe the protective value. DTH was assessed by challenging the vaccinated mice with killed M. leprae. It was found that the highest protection was afforded by M.w., followed by BCG. M. vaccae gave practically no protection. The protection by M. leprae or ICRC was not significant. Combination of BCG with M. leprae heightened the protection by the latter, while it decreased the protection afforded by M.w. There was a good correlation between protective value and DTH using autoclaved M.w., BCG, M.leprae and ICRC. On the other hand, live BCG gave good protection but low DTH.

FP 233

A POLICY FOR ENHANCING PROTECTIVE IMMUNITY IN CLOSE CONTACTS OF LEPROSY PATIENTS DEVELOPED IN THE ISLAMIC REPUBLIC OF IRAN.

Y.Dowlati[1], Sister F. Stefani[2], K. Ghazi-Saidi[3], C.A. Stanford & J.L.Stanford[4]. Iran Leprosy Organisation[1], Tehran, Baba Baghi Sanatorium[2], Tabriz, School of Public Health[3], Tehran University & School of Pathology[4], University College and Middlesex School of Medicine, London, U.K.

Healthy children (aged 1-20 years) of leprosy patients living with their parents in Baba Baghi Leprosy Sanatorium were examined for BCG scars and skin tested with reagents including Leprosin A. Children negative to this reagent, and without a BCG scar were immunised with BCG+10^7killed *M.vaccae*. Leprosin A negative children with a BCG scar were immunised with 10^8killed *M.vaccae* alone. 8-10 years later the children were retested with Leprosin A and 95% of both groups were found to have become positive in comparison with 65% positivity after BCG alone. A policy based on these results has been implemented at Baba Baghi and the results of the first years experience will be presented.

FP 234

PROTECTION OF MICE BY VACCINES FROM CELL WALLS OF M.LEPRAE

Robert Gelber, Shirley Hunter, Nahid Mohagheghpour, Jedd Monson, Lydia Murray, Patricia Siu, Mabel Tsang, & Patrick Brennan. Kuzell Institute, San Francisco, CA; Stanford U., Palo Alto, CA; & Colorado State U., Ft. Collins, Co. USA.

Shepard found that when mice are vaccinated intradermally in the right flank with $10^{5.8}$ or more but not less heat-killed M. leprae & challenged 30 days later in the right hind foot pad with 5000 M. leprae multiplying logarythmically in mice, growth of M. leprae is delayed at mouse harvests performed 7 & 10 months subsequently. Utilizing these techniques we vaccinated mice in the right flank intradermally with 0.01 ml containing γ-irradiated M. leprae (10^5,10^6,10^7,10^8, & 10^9) & 3 cell wall preparations derived from 10^5-10^9 M. leprae diluted with Freund's incomplete adjuvant: (A) crude cell walls, (B) cell walls treated with SDS so as to remove soluble protein, & (C) cell walls first treated with SDS & then via Smith degra-

dation so as to remove neutral carbohydrates. As a control Freund's incomplete adjuvant was utilized. Results represent counts of M. leprae from groups of 10 mice each; these were statistically analyzed by a two-sample rank test, P values being calculated by a two-tailed distribution. At 6 months significant protection ($P \leq 0.001$) was afforded generally by 10^7-10^9 M. leprae, but not by 10^5 or 10^6 M. leprae. The crude cell wall material (A) derived from 10^5-10^9 protected ($P < 0.03$). Cell wall preparation B derived from 10^8-10^9 M. leprae protected ($P < 0.01$), but lower concentrations did not. Cell wall preparation C, derived from 10^7-10^9 M. leprae, protected ($P < 0.05$) but not that derived from 10^5-10^6. Further results of 9-month harvests will be presented. In addition cellular immune responses to M. leprae were assessed in randomly selected mice within each vaccine group, & significant lymphocyte proliferation was found generally to parallel protection. These studies suggest that cell walls of M. leprae offer promise as future vaccines for leprosy.

FP 235

A COMPARISON OF THREE POTENTIAL VACCINES FOR LEPROSY CARRIED OUT IN 59 VILLAGES IN THE AHAR VALLEY OF EASTERN AZERBAIJAN, IRAN.

K.Ghazi-Saidi[1], C.A. & J.L.Stanford[2], & Y.Dowlati[3]. School of Public Health[1], Tehran University, School of Pathology[2], University College and Middlesex School of Medicine, London, and Iran Leprosy Organisation[3]. Tehran.

On the basis of Tuberculin positivity and whether or not they had scars of BCG vaccination, groups of children living in villages of the leprosy endemic Ahar Valley, were given 1 of 3 vaccines in 1978. These vaccines were BCG Glaxo alone, or in combination with 10^7killed *M.vaccae* or *M.leprae*. The children were followed up in 1986-8 by multiple skin testing with reagents including Tuberculin and Leprosin A. The villages were divided into 3 groups, 7 villages had new cases of leprosy since 1978, 4 had new cases of tuberculosis and 48 had no recorded cases of mycobacterial disease. In the "no disease" and tuberculosis villages there were no significant differences between the results for BCG alone or with *M.vaccae*, but in the leprosy villages the combination was associated with significantly more positivity to Leprosin A than was BCG alone. This suggests that BCG+*M.vaccae* may be the better vaccine for leprosy. Analysis of the effects of BCG+*M.leprae* is not yet completed.

FP 236

In vitro screening of anti leprosy drugs by mass spectrometric analysis of M. leprae

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Living cells, bacterial as well as mammalian, actively maintain lower intracellular concentrations of Na^+ ions and higher concentrations of K^+ ions than are found in the extracellular fluid. Dead or impaired cells are unable to maintain these concentration gradients. By applying laser microprobe mass analysis it is possible to measure the intracellular content of these ions in individual bacterial organisms. It could be shown for cultivable mycobacterial species that the intracellular Na^+, K^+-ratio of a cell measured this way is a sensitive indicator of its physiological state. Thus, the acquisition of these data from a limited number of single M. leprae organisms isolated from infected armadillo tissue, which were then exposed for typically 48h to different concentrations of a drug in an artifical medium, gives information on the efficacy of the drug. For an interpretation of the drug effects, however, the restricted metabolism of the bacteria in the medium has to be considered. The registration of cation ratios from a larger number of individual organisms (appr. 500) allows the calculation of their distribution and with that a detailed understanding of the drug response of a bacterial population. It will be shown that the administration of different drugs to M. leprae at comparable concentrations leads to significant differences in the distributions of the Na^+,K^+-ratios, indicating different mechanisms of action.

FP 237

ATTEMPTS TO SELECT RIFAMPICIN-RESISTANT MYCOBACTERIUM LEPRAE IN NUDE MICE

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One of the aims of the chemotherapy of leprosy must be to prevent the emergence of multi-resistant strains of M. leprae. Dapsone-resistant leprosy is widespread and there have been several reported cases of emergence of rifampicin-resistant M. leprae in human disease. A knowledge of the probable proportion of RMP-resistant bacilli in a patient's total M. leprae population is clearly desirable.
60 nude mice were inoculated with 2×10^8 M. leprae in both hind footpads and treated with RMP for 12-18 months. In a further group of nude mice the bacilli were allowed to grow to 10^{10} per footpad before RMP treatment was begun. After 1 year, growth had not been unequivocally detected. The bacilli were therefore subinoculated into RMP-treated nude and normal mice, and into untreated normal mice to detect persisters. Results will be published.

FP 238

Monitoring of in vivo response of M. leprae to anti-leprosy therapies

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The intracellular Na^+,K^+-ratio of a bacterial cell, which can be determined by mass spectrometric techniques, is a measure of its physiological state (viability). At present, however, it is not possible to define an absolute value for this ratio beyond which an organism is irreversibly damaged. Additional information on drug effects can be obtained from the analysis of mass spectra from the organic matrix of the bacteria [1]. From an evaluation of the in vivo drug effects on M. leprae the bacteria have to be isolated from patients' skin biopsies (50-100 mg) and prepared for single cell mass spectrometry. From each biopsy typically 500 bacterial organisms are analysed within a few hours. Taking skin biopsies from the same patients in defined time intervals (2-4 weeks) allows to monitor the time dependence of drug-induced impairments. It is reported on first results from a study on the in vivo effects of different drug re-giments (e.g. DDS monotherapy, multi drug therapy).

U.Seydel, B.Lindner,A.M.Dhople: Int .J. Lepr. 53 (1985), 365-372

FP 239

A PILOT STUDY OF THREE POTENTIAL VACCINES FOR LEPROSY IN BOMBAY SCHOOL CHILDREN.

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Children attending schools in the slums of Bombay were skin tested with Tuberculin, Leprosin A, Scrofulin and Vaccin. 296 children without BCG scars and who were Tuberculin negative (<5mm) were vaccinated with BCG

Glaxo alone, or combined with 10^7irradiation-killed *M.vaccae* or *M.leprae*. The children were followed up 1-3 years later with repeat skin testing. All 3 vaccines produced good Tuberculin conversion ($p<0.00001$) and the combination with *M.vaccae* produced significant conversion to Leprosin A positivity ($p<0.002$). The slums of Bombay are known to be highly endemic for leprosy and the Leprosin A positivity achieved is thought to be due to improved recognition of the organism in the environment rather than the direct consequence of vaccination. This study provides further evidence of the suitability of BCG+*M.vaccae* as a potential vaccine for leprosy, and of the importance of the recognition of common mycobacterial antigen in protective immunity from the disease.

FP 240

LOCAL IMMUNOMODULATION WITH DINITROCHLOROBENZENE IN PATIENTS WITH LEPROMATOUS LEPROSY: IMMUNOHISTOLOGICAL INVESTIGATIONS.

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2/5 patients with lepromatous leprosy (LL) were sensitized with 2% dinitrochlorobenzene (DNCB) epicutaneously. 48 hours and one week after elicitation of the DNCB reaction within a, LL lesional sites and b, unaffected skin in these two patients and in a normal control person, biopsies were obtained from an untreated LL lesion, from LL lesions+DNCB and from the nonlesional skin with DNCB contact dermatitis (CD) alone. Immunoperoxidase staining was performed on cryostat sections with monoclonal antibodies detecting phenotypic T cell- and monocyte/macrophage markers and class II antigens (HLA-DR and the invariant γ-chain of the class II molecule). Within 48 hours a lymphohistiocytic infiltrate typical of CD composed by CD3+/CD4+ cells exceeding CD3+/CD8+ cells was seen within LL+DNCB and DNCB CD lesions. Numerous CD1+/S100+ cells were interspersed. Most importantly, HLA-DR and γ-chain expression by keratinocytes (KC) indicative of class II antigen inducing activity of soluble mediators like interferon-gamma was observed on basal KC within LL+DNCB and DNCB CD skin after 48 hours. Our results thus support the specific nature of the defect of cell-mediated immunity in LL patients, leaving delayed type hypersensitivity reactions to other antigens than M.leprae intact. Class II antigen inducing mediator(s) can be generated within LL lesions in context with the recruitment of a nonspecific infiltrate.

CD3,4,8,1: clusters of differentiation

FP 241

RESULTS OF ONE YEAR OF PHASE II/PHASE III TRIALS WITH THE CANDIDATE ANTI LEPROSY VACCINE MYCOBACTERIUM W.

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Mycobacterium-w, a cultivable cross-reactive mycobacterium identified from a panel of 15 was proposed as a vaccine against leprosy (Talwar et al 14 Ref.Lep.India vol.50,1978). Phase I trials with this vaccine were reported previously (Int.J.Lepr.51:159, 1983). Phase II/Phase III immunotherapeutic trials started in December 1986 in two major hospitals of Delhi.

The vaccine trial is a double blind study in which half of the patients receive the vaccine given i.d. every 3 months multi drug therapy (MDT) and the other half receive placebo (micronized starch)+MDT. Bacteriologically positive, lepromin negative patients belonging to BB, BL and LL spectrum are taken for the study. At determined intervals, patients are assessed by clinical score, Bacteriological Index, histopathology of lesions and lepromin reactivity.

130 patients are presently enrolled in the trial. Results show a lepromin conversion of 96% in BB, 82% in BL and 60% in LL type of leprosy after three to four vaccine doses. The bacterial clearance observed on slit smears taken from 6 sites is more rapid in the vaccinated group as compared to the placebo. 13 LL patients with initial mean BI of 5.0 have shown a decrease to a mean of 2.3. 3 other LL patients have also been rendered bacteriologically negative in about one year of combined chemo and immunotherapy. Histopathologically, a significant number of patients have shown upgrading in the spectrum after vaccination. Patients receiving the vaccine have also shown marked clinical improvement.

FP 242

EXPERIENCE ON TRYING TO TRANSFORM A "COLONY HOSPITAL" INTO "COMMUNITARY INSTITUTE"

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Until 1983 "CURUPAITI HOSPITAL-COLONY" for Hansen Disease patients was a "TOTAL INSTITUITION". After this date was created The "COMMUNITARY INSTITUTE OF JACAREPAGUA" responsible for the residential area (houses, churches, benevolant societies) separated of the "STATE HOSPITAL DE CURUPAITI" in charge of the case of Hansen Disease patients and others skin disease of sanitary concern.

The goal of the "COMMUNITARY INSTITUTE" is the social reintegration of the patients. To fullfill this purpose, it was designed a dwelling plan to make the area an integral part of the municipality and not a "LEPROSY VILLA".

It was granted the suport of the population trough discussion with person and organized group of the community.

The main activities to note are: abolition of the "COLONY BY LAW" and its consequences summariaded by a) right of the patients to have in the same household their children and other relatives b) cancellation of all authoritary rules c) study of new criteria for admission in "ASYLUM": - only patients with irreversible disabilities and without social conditions for subsistence d) Phasing out of the "CHILDREN HOUSE" e) Admission of children in Public School without discrimination f) Activities of Health Education.

It will be evaluated the experience and the constraints observed, the main one is the no acceptance by the in-patients of the processed integration of the colony as a normal community of Rio de Janeiro city.

Considerations will be made about the behavior of the patients and the economical and political implications, consequence of 50 years of Curupaiti as a "CLOSED INSTITUTION".

FP 243

REORIENTACIÓN DEL INSTITUTO LEPROLÓGICO DE TRILLO PARA SU INTEGRACIÓN EN EL MARCO DE LA REFORMA SANITARIA EN ESPAÑA

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Espana es un país de baja endemia de lepra, donde todavía la base de la asistencia se centra en hospitales monográficos que son- más el reflejo de la marginación social de la enfermedad y de la propia resistencia del sistema al cambio que de la propia necesidad preventiva asistencial y rehabilitadora, caracterizándose la situación- por: Larga permanencia de la mayoría de los pacientes con bacilos copias nagativas, su elevada edad media, desarraigo familiar, insuficiencia económica de muchos de sus miembros, patología somática y - psiquiátrica relacionada con su avanzada edad, y efecto protector - afectivo-social de la institución con la considerable dependencia y fuerte resistencia al abandono de la misma. Ante esta situación el objetivo es la búsqueda de una alternativa en el marco del sistema general de salud, y de diferentes Comunidades Autónomas. Para ello se utiliza la metodología característica de la Investigación de servicios de Salud, planteando un análisis de: Políticas y Directices generales del País, y de las diferentes Comunidades Autónomes, Un análisis crítico de los indicadores de servicios relacionado con la situación epidemiológica de la Lepra, La relación del Instituto con los diferentes niveles asistenciales. Como conclusiones se ofrece un programa de adaptación en diferentes plazos.

FP 244

BEYOND CHARITY: DEVISING REHABILITATION PROJECTS FOR A COMPETITIVE ECONOMIC WORLD

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Economic self-sufficiency is a prime goal of rehabilitation projects in Third World countries. Unfortunately, those with extreme disabilities are often unable to produce high quality---i.e., marketable---items.

With careful attention to design, however, it is possible to produce handmade items of sufficient quality to compete in the open marketplace.

Support the Handicapped's Rehabilitation Effort (SHARE) is a project begun in India in 1986. Its aim is to increase employment among leprosy patients and other handicapped persons by providing assistance in the design, manufacture, and marketing of handmade items. Export sales to Europe and the United States in 1987 totaled about $20,000.

This paper describes the background and development of SHARE, outlines economic strategies for rehabilitation projects, and offers case histories of successful design-and-marketing campaigns.

FP 245

EXPERIENCE WITH A MULTI-ETHNIC SUPPORT GROUP IN THE TREATMENT OF HANSEN'S DISEASE.

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The social and psychological ramifications of Hansen's disease have been known to affect patients years after their medical symptoms have resolved. Fear of rejection, lowered self-esteem, and social isolation often pervade patients' lives subsequent to diagnosis. Individual counseling has been effective in reducing symptoms of depression & anxiety. Patients, however, continue to feel isolated & alone in adjusting to the diagnosis. Thus, we began a support group for patients in Northern California in 1987. The group meets on a monthly basis and is composed of both newly diagnosed and long-term patients of multi-ethnic backgrounds. The age range is from 25 to 62. There is a core group of 8 members and new patients join and leave intermittently. The group has proven effective in reducing isolation by the development of a support system among the members. The group has developed its own goal of reaching out to fellow patients by recruiting new members for the group and visiting hospitalized patients for emotional support. The early stages of the support group focused on patient information sharing of physical signs and symptoms, i.e., comparison of lesions, nerve pain, epistaxis, and emotional reactions following diagnosis. The group has discussed in great depth cultural misconceptions about Hansen's disease that still govern their belief systems. Intimacy and disclosure of the diagnosis are on-going topics of discussion. The group actively works at elevating individual feelings of self-worth. The major themes of the support group and barriers in starting one will be discussed in detail.

FP 246

STUDY ON SOCIO-ECONOMIC REHABILITATION

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With the widespread use of Multi-Drug Therapy in the treatment of leprosy, patients are rendered non-infective in a short period of time. Isolating patients in colonies is no longer practised. However, patients with deformities continue to have problems connected with both physical and social dehabilitation. Patients with deformities and facing social ostracism require support for economic independence. As far as possible they should continue to be in the main stream of the community. Rehabilitation is a means of patient acceptance by society. Socio-economic rehabilitation facilitates the process of social integration.

ONE HUNDRED leprosy cured persons rehabilitated between 1983 and 1986 were studied to highlight their socio - economic rehabilitation in the community. They were rehabilitated in industrial, agricultural and farm sectors and other occupations. Their progress in living with the community has been supervised and guided properly.

The study describes the problems encountered by them in socio-economic integration with community and also the results of rehabilitation offered. The economic and social well being of the rehabilitated persons is compared with their condition before rehabilitation. The need for rehabilitation service is emphasised.

FP 247

CHALLENGING THE STIGMA: FROM LEPROSY TO AIDS.

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Hawaii's experience with leprosy reveals the tragic long-term effects of a stigma that has been applied to undeserving members of our community. It illustrates the danger and cruelty of misguided public panic and the wisdom of refusing to automatically accept the stigma as part of the disease. It shows us that the best means with which to challenge the stigma are the individuals who are affected by it for their involvement enables us to "put a face on it" and deal with the disease in terms of individuals rather than statistics. Most important, Hawaii's experience teaches us that before making any medical decisions, we must consider the long-term social effects that will persist long after the disease itself is no longer a problem.

The advent of AIDS has witnessed repeated comparisons between the social reactions to leprosy and AIDS. Indeed, it has already been suggested that persons with AIDS be isolated at Kalaupapa. Consequently, how we approach the social aspects of leprosy has implications far beyond this particular disease. As we challenge the stigma of leprosy, we will also be challenging the stigma associated with AIDS and every other disease that society is afraid of or doesn't understand.

FP 248

PROBLEMS IN THE ANALYSIS OF SOCIO-ECONOMIC RISK FACTORS IN LEPROSY

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Leprosy is often thought to be associated with poverty. This relationship is explored here in an analysis of data from the Lepra Evaluation Project in Northern Malawi, using level of schooling as a surrogate measure of socio-economic status. Though the prevalence of leprosy was expected to be inversely related to level of schooling, the observed crude rates were 1.96 per 1000, 4.39 per 1000 and 3.74 per 1000 in groups with 0, 1-5, and greater than 5 years of schooling, respectively. After standardising these data by age, sex, urban or rural residence and BCG status, the rates were 3.93, 3.42, and 2.20 per 1000, respectively. The differences between the crude and adjusted rates reflect important differences in distributions, in particular of age, urban or rural residence and BCG status, between groups with different levels of schooling. Though these results are consistent with the hypothesis of schooling-defined socio-economic status as a risk factor for leprosy the mechanism remains unclear. The importance of standardising for known and potential risk factors in such analyses will be discussed.

FP 249

COPING STRATEGIES FOR MAKING THE TRANSITION FROM ISOLATION BACK INTO THE COMMUNITY.

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The decision to regain one's place in the community after many years of isolation requires a strong motivating force. This motivation can arise from personal relationships or simply out of a desire to "live again". Whatever the motivation, the transition is always easier if one has a supportive family. It is also helpful if one has already had the opportunity to interact with people from the "outside". Lions Club International was instrumental in exposing Kalaupapa patients to "outsiders" and vice versa through meetings and conventions. As Club members, we were accepted by outsiders while in the isolated setting, which made us less afraid of whether or not we would be accepted outside the Settlement.

Upon returning to the community, we each decided to tell people where we came from, even though this meant some people would not associate with us anymore. We felt that if we weren't accepted by one person, there would always be someone else. Now, years later, our involvement in community organizations such as the Lions Club, theater groups, the Council for the Blind, and The Hawaii Hansen's Disease Association, provides us with numerous opportunities to educate people about our lives during and after isolation.

FP 250

HANSEN'S DISEASE: THE STIGMA, THE FEAR, THE SOLUTION.

Bernard K. Punikai'a
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The Hansen's Disease patient is as important to his successful treatment as the physician. For physicians treating Hansen's Disease, the primary concern has always been to cure the patient, which is as it should be. However, since it has long been recognized that this disease has a traumatic impact on the individual and his family, the social impact of the disease needs equal if not more attention than the patient's medical treatment. With regard to social aspects, one physician commented: "It's all conjecture." From the patient's perspective, it is reality.

In Hawaii, we patients have overcome traditional barriers and taken a leadership role in promoting public education. We have worked with social scientists, community leaders and health professionals to create a public awareness of the modern day realities of the disease. In these efforts, the physician's role as advocate is vital. We have extended our efforts to develop humane alternatives to institutionalization, not only for Hansen's Disease patients but for others in our community who have special needs. Our participation in this Congress is a major step towards the development of an international partnership aimed at reaffirming the dignity of all persons with Hansen's Disease.

FP 251

A STUDY ON RISK FACTORS IN SOCIAL DISPLACEMENT OF LEPROSY PATIENTS.

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The study was aimed at to find out the factors responsible for social displacement of patients affected with leprosy.

The samples were selected from patients settled in care homes, where leprosy patients are settled due to their non-acceptance in the community. Fifty three patients were selected as the sample who were settled in the above homes for more than three years and have no contact with their respective families. Data was collected using a questionnaire on various socio-economic aspects at three stages, i.e. before diagnosis, before displacement and after displacement.

The following were the findings:-

1) 84.90% of the patients have grade-III deformity and are physically incapacitated.
2) 71.69% of the patients felt that their families did not want them because of social stigma.
3) 83% of the patients were aged above sixty and old age is the another cause for displacement.
4) 75% of the patients have no source of income.

The study shows that deformity, old age, socio-economic instability and social stigma are the risk factors in social displacement.

FP 252

CARE AFTER CURE IN LEPROSY

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Ever since the introduction of Multi Drug Therapy for Leprosy, many patients have been released from the leprosy control, after completion of MDT. However after the medical treatment is over, relapses are to be watched.

The residual problems of anaesthesia and motor paralysis are yet to be followed up with a view to prevent further disability. Provision of foot-wear and ulcer care are integral part of the "Care after Cure" Prosthetic services and eye care are also important.

A wholistic approach to the problem is suggested with physical, mental and socio-economic care of cured patients.

The existing pattern of rehabilitation carried out ranging from self-appointed colonies special schools to the sheltered workshops and after care institutions in India are reviewed. The needy cured persons are classified as children, women and aged patients.

Need for Vocational Training programmes and job oriented long range rehabilitation plans are envisaged. Co-operation of National, International, Governmental and Voluntary agencies are recommended.

FP 253

STUDIES ON SOCIAL MEDICINE OF LEPROSY IN CHINA

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Leprosy is a disease in which the socio-enviromental factors play an important role in its occurrence, development, rehabilitation, control and eradication. Only by eliminating the unfavourable factors we could achieve the goal of basic eradication of leprosy in China by the end of this century. For this reason, since 1984 we have carried out systematic studies of the social aspects of leprosy in a area with a population of about 1,500,000 in Jiangsu Province, where the endemicity of leprosy has come under control.

1. By means of the study of the epidemiologic features of leprosy and the analysis of their determinants, the epidemic trends of leprosy are forecasted. 2. An approach to the familial and areal aggregations of leprosy are taken. 3. analysis of the relationship between the socio-economic development and the epidemiology of leprosy are made, which shows that the development of the socio-economy is sure to speed up the eradication of leprosy. 4. An investigation of the mental conditions and the behavioural responses in communities towards leprosy and the patients showed that serious discrimination and prejudice are present in society, and measures to overcome these social phenomena are suggested. 5. An investigation of the changes in patients'psychology and behaviour is made and it is recognized that the patients' personalities and their due social status in society must be restored. 6. An analysis is made of the influences of leprosy on marriage, families, and children of the patients, and proposals for the better adjustment of the relations of marriage and family are offered. 7. An analysis of the loss of labour capability and social economic benefits from the somatic deformities and disabilities of leprosy are noted, pointing out the importance of prevention and correction of the disabilities and launching rehabilititive treatment. 8. An investigation of the nutritional conditions of leprosy inpatients comparing with tuberculosis inpatients notes that the comparative nutritive conditions of leprosy patients, especially the patients with deformities are very poor. 9. An evaluation of the social and economic benefits of the methods for case-finding and case-holding is made.

FP 254

POSTERIOR CHAMBER INTRAOCULAR LENSES IN THE REHABILITATION OF LEPROSY PATIENTS

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Blindness is a major disability in leprosy patients who are already handicapped by other deformities. Cataract, one of the leading causes of blindness is conventionally corrected by lens extraction and glasses. The hand, nose and ear deformities makes wearing of glasses difficult. Since in most of these patients contact lens wear is not possible intraocular lenses seems to offer the best visual rehabilitation.

We have implanted 34 lenses in 30 patients with a follow up of about 6 months to 2 years. Patients included both tuberculoid and lepromatous patients. Patient with evidence of past uveitis also had lens implanted. 4 patients with positive smear and advanced stages of cataract also had intraocular lens implantation.

Our results are very encouraging. Above 50% of patients had vision more than 6/12 and only less than 10% with vision less than 6/60. Patients with gross corneal opacities which would have made extracapsular lens extraction difficult were excluded from the study.

Except for moderate uveitis in the early postop period no other special complications were encountered.

Leprosy intraocular lens group has been compared to normal patients with intraocular lens, and hansens patients with intracapsular lens extraction.

Comparison between in the bag and sulcus fixed lenses have been made.

FP 255

THE PROTECTIVE EFFECTS OF METHYL CELLULOSE DROPS AND CONOID SHIELDS IN THE PRESENCE OF LAGOPHTHALMOS AND CORNEAL HYPESTHESIA IN OCULAR LEPROSY

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Lagophthalmos and corneal hypesthesia are one of the most frequently encountered lesions in leprosy. They can easily give rise to blindness. Many modalities (such as eye drops, muscle exercises, protective conoid shields, surgical treatment etc.) are used to protect the eyes from the hazardous results of these pathologies. 41 patients who are followed in the Ophthalmology Department of Istanbul Medical Faculty Leprosy Center are included in this study. All of them have different degrees of lagophthalmos and corneal hypesthesia. The first group has 15 patients, under mandatory, supervised methyl cellulose drops and shields. The second group also consists of 15 patients, under "self care" "when they feel they need it" drops and shield. The third and the last group is formed with 11 surgically treated (with tarsal strip) patients, those on only mandatory methyl cellulose. In this study, the protective effects of methyl cellulose drops and conoid shields on visual acuity and corneal epithelial breakdown will be discussed.

FP 256

Ocular Complications of Leprosy: Methods for Control.

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An international symposium on ocular leprosy was held in London from September 21-23 1987. Working groups prepared recommendations for service and research needs. Suggested tasks for primary health care workers and general paramedical workers include recognition of leprosy as a cause of blindness, knowledge of referral procedures, recognition of patients under therapy and knowledge of eye drop administration. The leprosy (paramedical) worker should be the frontline in ocular care due to the paucity of ophthalmologic facilities. This worker should be able to assess vision, lagophthalmos (involuntary blinking, gentle closure and forced closure), trichiasis, corneal abnormalities (dull or rough surface, opacity, sensation), and the red eye (iritis versus seasonal conjunctivitis). Training should include patient education, recognition and basic therapy. Medical officers and ophthalmic assistants, given training, should instruct and supervise these workers. Integration of ocular leprosy into existing programmes in endemic areas needs to be baed on data on ocular complications at the local level.

Research priorities include investigation of the following: a longitudinal study of ocular complications in the patient on M.D.T., field trial of suggested proformas for paramedical workers and medical officers, and histopathological and immunopathological examination of ocular tissues.

FP 257

THE RESULTS OF A MULTICENTRE SURVEY OF THE OCULAR COMPLICATIONS OF LEPROSY

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Since 1983 cross-sectional surveys of the ocular complications of leprosy have been carried out in 24 leprosy centres in 15 different countries throughout the world. An attempt has been made to standardise the methods of the eye examinations and the results show conisderable regional and ethnic variation in the prevalence of ocular complications.

There are a number of factors which influence ocular involvement and blindness and these will be discussed together with the findings of the study. From these it is possible to derive some idea of the extent of eye problems in leprosy on a global scale. The limitations of this type of survey will be assessed and compared with previously published studies.

FP 258

INTRAOCULAR PRESSURE CHANGES WITH POSTURE IN EXPERIMENTALLY INDUCED HANSEN'S DISEASE OF MANGABEY AND AFRICAN GREEN MONKEYS

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Robert Wolf DDM, University of Texas, San Antonio, Texas, USA
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In our long term evaluation of patients with Hansen's Disease, we noted significant reduction of intraocular pressure in a number of patients early in the course of their disease. Furthermore, significant postural changes occurred in the same patients.

In an effort to determine if these changes are meaningful, we evaluated the intraocular pressures of twenty four experimentally infected and seventeen control monkeys for similar changes in both a sitting and reclining position. We report, herewith, our findings and offer possible pathophysiologic explanations as to why the changes occur.

FP 259

OCULAR LEPROSY IN THE ARMADILLO AND MAN - A HISTOPATHOLOGICAL STUDY.

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The clinical manifestations of leprosy involving the eye are diverse but primarily in the anterior segment. Representative specimens from the human eye in disease are difficult to obtain hence histopathological documentations are few and the pathogenesis of ocular leprosy relatively unclear.

We present the pattern of involvement of ocular tissues in a retrospective study of twenty eyes and adnexa from armadillos and a pair of human eyes. The armadillo material was from experimentally infected armadillos with disseminated leprosy at the time of sacrifice. The human eyes were removed at autopsy from a patient with advanced lepromatous leprosy.

The armadillo and human eyes showed that in addition to anterior segment pathology, bacilli and inflammatory cells were present in the ciliary body, the choroid, the orbital fibro fatty tissue and in the retrobulbar adipose tissue around the optic nerve. In the human eye the ciliary nerves in the choroid also showed bacilli. These findings give histopathological support that the posterior segment of the eye can be involved in leprosy.

The details of the findings and their significance in the understanding of ocular leprosy will be discussed.

FP 260

EDGE-LIGHT PUPIL CYCLE TIME IN LEPROSY

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A thin slit lamp beam illuminating the pupil margin produces clearly visible pupil oscillations.These oscillations can be timed with a stopwatch, thus producing a measurement of the 'edge-light pupil cycle time'.The pupil cycle time is remarkably stable in various testing situations and is repeatable.When the optic nerve is normal, the pupil cycle time is dependent on the innervation and integrity of iris muscles.
The constriction-dilation cycles of pupils exposed to a stationary, discrete slit-lamp beam were significantly prolonged in 47 leprosy patients, compared to normal controls or subjects receiving dapsone,rifampicine and/or clofazimine.
In this study, usefulness of pupil cycle time as a diagnostic criteria for intraocular involvement will be discussed.

FP 261

INTRAOCULAR PRESSURE IN HANSEN'S DISEASE

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Because we observed that the intraocular pressure (IOP) of HD patients was often low on routine screening we retrospectively analysed 175 cases of HD patients and found low IOP in 15% of the sample. The condition was most frequently associated with avascular keratitis and iritis. In 56% of these cases no other ocular pathology was found.

Subsequently we conducted a pilot case control study of HD cases and family controls, comparing pressures in the upright and supine position. HD patients were more likely to have a low IOP (p .05) as well as asymmetric IOP between the two eyes (p .05) than controls. HD patients also had significant postural changes in IOP (.01). There was no correlation between presence of postural IOP changes and disease duration.

We believe that low IOP and variation in postural IOP in HD patients may be indicative of early insult and denervation of the autonomic nerve supply to the ciliary body. Prospective analysis of these patients will assist in determining if a low IOP is indicative of early M. leprae infiltration.

FP 262

INVESTIGATION OF 1692 CASES OF LEPROUS OPHTHALMIA IN GUANGDONG PROVINCE

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Eye affliction in 1692 active and cured leprosy patients were found in 17 leprosaria in Guangdong province in 1984 and 1986.We have completed 75 study projects on 10 aspects of ophthalmological examination that included obtaining histories of leprous eye disease,examination and correction of vision,looking carefully at the anterior segments with magnifying penlight and hand slit lamp, examing the funda oculi and lens after dilating the pupil,measuring intraocular tension, washing lacrimal passages, and doing conjunctival scraping in active leprosy patients.

Results:1538 patients (90.9%) were found to have leprous eye involvements. The leprous eye lesions were not sex-associated.The incidence of leprous eye involvement and visual acuity of less than 0.3 and blindness was higher in those with longer duration of leprosy.Cured patients has more active eye disease than active patients. Although the number of patients with leprosy eye lesions was more in multibacillary than in paucibacillary type, blindness and vision iapairment was much more in paucibacillary. The most common leprous eye involvement were in the anterior segments and one eye usually suffered more. 201 patients were blind in one eye (11.88%) and 95 patients were blind in both eyes. We also discuss Stellwag's and von Graefe's signs which were noted during the investigation.The causes of blindness and low visual acuity of less than 0.3 were enumerated and analysed.

Conclusion:Paralytic lagophthalmos and ectropion were found in 1/3 of the patients and their sequelae caused 1/2 of blindness. In addition to using medicine and functional exercises, we must study and determine the most efficient method of operation for lagophthalmos.

FP 263

THE EYE IN MULTI DRUG THERAPY

2 TO 4 YEARS FOLLOW-UP OF MULTI BACILLARY CASES

Dr.M.A.Rajan

A longitudinal study of ocular complications in 1457 cases of all types of leprosy was started in June 1983. Two hundred and thirty seven Multi Bacillary cases on Multi Drug Therapy were analysed and the findings presented in this paper. Twenty seven cases had ocular complications at the beginning of the study while 30 cases developed ocular complications during Multi Drug Therapy. Of these 30, 2 were reactors and the rest were non-reactors. The longer the duration of the disease the more are the complications. The uveal tract bore the brunt of the eye involvement. Steroid induced cataract was found in a few. The complications were mostly diagnosed by Slit Lamp examination. Under the Multi Drug Therapy the duration of scleritis and iridocyclitis has dramatically reduced as compared to monotherapy. Though the eyes are the last to be involved in leprosy they are the first to be involved in relapse. Reactions in the eye take a longer time to subside than in the skin and nerves. Routine eye examination is essential to prevent irreversible changes. Ophthalmic surgery can be performed even on bacteriologically positive patients under the cover of Multi Drug Therapy. Blindness perse does not occur among the adequately treated.

FP 264

Current Clinical Status of Uveitis in Leprosy under various Drug Regime.

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700 Leprosy patients with different ocular lesions have been studied between 1986 to 1988. 60% amongst them has got Uveitis in different degree. These patients are the sufferers of the disease ranging from 2 yrs to 48 yrs duration and were under various drug regime during their long course of the disease. The various pattern of the clinical manifestation of Uveitis and its sequele, which we come across nowadays, will be discussed.

FP 265

TARSAL STRIP PROCEDURE FOR SURGICAL CORRECTION OF LAGOPHTHALMOS.

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Lateral tarsorrhaphy is a simple procedure to correct lagophthalmos but produces cosmetic defect often disliked by patients and restriction of field of vision laterally. Temporalis muscle transfer operation is a relatively difficult surgical technique and offers best results in bilateral lagophthalmos with intact corneal sensation in young patients. Tarsal strip procedure is a relatively simple technique offering better results in all types of lagophthalmos without any cosmetic defects post-operatively.

The lateral orbital periosteum is exposed after a small horizontal incision on the skin. Tarsal plates on the lateral aspect for a distance of 3 to 4 mm. are separated from the anterior lamellae. Strips are fashioned out of these plates to be sutured on to the exposed orbital periosteum. The lower lid tarsal strip is sutured slightly at a higher level than the lateral canthus, giving an adequate elevation to the lower lid.

Twenty patients under went the tarsal strip procedure during the last three years. The results are compared with five to twenty years retrospective follow up on forty patients who under went temporalis muscle transfer.

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PO 300

PATTERN OF HAND INJURIES FOLLOWING PROLONGED USE OF AXILLARY CRUTCHES AND THE POSSIBLE SOLUTIONS

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Prolonged use of axillary crutches may cause transient blocking of the radial nerve, a condition commonly known as crutch palsy. In most leprosy clinics of the developing world, axillary crutches are prescribed as an aid to mobility and also to reduce weight bearing on problematic feet.

Between 1977 and 1987 at Karigiri we have come across only one patient who developed neuropraxia following the use of axillary crutches. Patients have however developed ulceration in their hands, particularly at the thenar and hypothenar eminences. Carpal bone disintegration has also been noticed in some cases. Because of this we have concentrated on investigating the following:

a) accurate localisation of pressure transmission while manipulating crutch handles.

b) identifying how these high pressure areas significantly affect the median nerve at the carpal tunnel level.

c) identifying the risk of possible carpal bone disintegration as a result of prolonged use of axillary crutches.

d) planning rehabilitative therapy techniques to manage these problems without modifying the basic design of axillary crutches.

To date, a detailed analysis has been carried out on 28 patients. Various modifications to axillary crutches were made. Of these, one modification was found effective in reducing the risk to the hand. The Summary of our findings will be presented.

PO 301

PROFUNDUS MINUS DEFORMITY (PMD) IN LEPROSY

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A typical "Profundus Minus Deformity" (PMD) in leprosy is a rare condition which has not been described in the past. Between 1984 and '87 we have observed only 7 cases at the Schieffelin Leprosy Research and Training Centre, Karigiri, India.

In the normal hand, rupture of profundus tendon produces a hyper extension of the terminal joint with loss of active flexion. In PMD a similar loss of active flexion at the terminal joint is seen; however, there is no hyper extension and most interestingly these patients have a normal, intact flexor profundus. Clinically we have seen this condition in patients where the flexor digitorum sublimus was removed for other reasons. These patients subsequently developed PMD with a normal range of active flexion at the proximal joint. We have termed this condition "the Profundus Minus Deformity".

The preliminary report suggests that this is a typical post-operative deformity. We attribute the following possible causes for this condition:

a) Adhesion of the profundus to the sublimus stump.

b) Post operative joint stiffness due to prolonged splinting.

c) Long flexor imbalance, thus producing a tenodesis effect.

This is a prospective study and the deformity will be analysed in bio-mechanical terms.

PO 302

CLAWFINGER CORRECTION
CONSIDERATIONS IN CHOICE OF TECHNIQUE

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Ulnar nerve damage is a common complication of leprosy neuropathy. Paralysis of intrinsic muscles innervated by the ulnar nerve may result in claw deformity of some or all fingers.
There are two major groups of surgical techniques to correct the claw deformity. They can be referred to as static or passive and dynamic or active procedures. In the 'static' group belong the arthrodeses, tenodeses and capsulodeses procedures. The authors believe that in leprosy there is no place for passive procedures, except for very badly contracted and deformed joints where arthrodeses might be considered.
Extrinsic finger flexors and extensors and wrist flexors and extensors have all been used to correct claw deformity. Should the choice of technique depend on the one procedure the surgeon has read about or the one the surgeon was taught? We believe that the choice of technique should depend on factors that are related to the three parties involved in reconstruction of the paralysed hand.

1. Patient. The condition of the patient's hand and the patient's ability to cope with reeducation.
2. Therapist. The therapist's level of training and experience.
3. Surgeon and surgical technique. An understanding of basic muscle mechanics, which includes muscle fibre length, tension fraction and mechanical advantage.

PO 303

Modern trends in correction of claw fingers in leprosy.

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Nerve damage in leprosy leads to deformities and finger clawing is one such problem. Due to better understanding of mechanics of finger clawing newer trends have emerged for correction of clawed fingers.The presently employed procedures put more emphasis on optimising the action of flexors on proximal phalanx. This is achieved either by increasing the efficiency of already existing flexor forces (flexor pulley advancement procedures) or by providing a new flexor force in the form of muscle tendon transfer to the volar surface of.proximal phalanx(pulley insertion procedures). The extensor forces are optimised either by a metacarpophalangeal joint capsulodesis or by extensor diversion procedure.

The paper discusses the indications of each procedure and describes the author's own experiences.

PO 304

A METHOD FOR CORRECTION OF CLAWHAND REQUIRING NO RE-EDUCATION.

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50 patients have undergone clawhand correction during the period 1983 - June 1987.
The method corrects clawing in extension as well as clawing under gripping and the metacarpal arch.
The surgical method is displayed.
Functional and cosmetic results are primarily good.
The method appears to be especially suitable for patients who have a tendency to inactivate tendon transfers from the extensor side (i.e. nursing women in an African village) and under circumstances where specially trained physiotherapists are not available.
The only postoperative training required is active flexion and extension of the fingers.

PO 305

CORRECTION OF INTRINSIC MINUS IN THE HAND BY LASSO PROCEDURE.

The dynamic correction of Intrinsic Minus is possible by 2 methods : first, direct substitution by transferring the tendon to Lumbrical's insertion at the Dorsal Expansion, and secondly, as suggested by Zancolli, and based on the Bouvier's maneuver, to provide an active stabilizer for the MP-joints. We have recently the second principle in preference.The reason for this are : more simple to perform, no interference in the mechanic of the Dorsal Expansion, not much physiotherapy needed post-operatively, no special splints and instruments are required.
The results of 43 cases when the Lasso operations (Zancolli) have been performed are presented.

Berbudi A.H., Tunar A., R.S. Kusta Unung Pandan, Indonesia

PO 306

Surgical correction of claw fingers in Leprosy by Anterior Capsulorraphy with Pulley Advancement. A new procedure.

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Clawing of the fingers is a common deformity seen in leprosy due to involvement of ulnar nerve. Many procedures both dynamic and static have been devised for the correction of deformity.

A new procedure has been devised to correct the clawing of the fingers. Anterior Capsulorraphy in which distal part of volar plate was excised and pulley advancement was combined with it. 26 hands with two fingers clawing, 2 hands with three fingers and 12 hands with four fingers clawing were corrected by this procedure. Correction of deformity was excellent in 38 of 41 hands. Functionally also there was improvement in pulp to pulp pinch, precision and power grip. The follow-up of the cases varied from 2½ years to 3 months. The indications and the results are presented in the paper.

PO 307

Reactivation of Flexor Carpi Ulnaris and Opponens of Little Finger for Correction of Reversal of Metacarpal Arch.

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This report presents a new surgical procedure to correct reversal of the metacarpal arch of claw hand in leprosy.
The procedure,using the flexor carpi radialis to restore antagonistic action against extension of the metacarpal V, can be easily performed along with a palmaris transfer for finger correction. It is also more simple than Ranney's procedure and Beine's combined opponens replacement of thumb and little finger, both decribed in 1973.
Its indication as an alternative procedure is discussed.
The patient feels that aside from the cosmetic aspect he also gains more control over his hand after flexor carpi ulnaris reactivation and he is better able to safely balance items kept on his palm in cupping position.

PO 308

SURGICAL RECONSTRUCTION IN INTRINSIC PALSY OF THE FINGERS. A STUDY OF HUNDRED CASES.

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The authors analyze the results obtained by surgical treatment in 100 cases of intrinsic palsy of the hand, involved with Hansen's disease.The distribution of the surgical procedures performed under regional anesthesia was as follows : Brand II: 41, Palande's lasso : 14, Zancolli : 15, Palande : 13, Littler13, Brand I : 2. Results were satisfactory in 74 p.cent, unchanged in 20 p.cent and poor in 6 p.cent of cases. The analysis of this series showed a significant difference in the results obtained in the little finger with better results when Palande's and the lasso procedures were used (for the hand in the lumbrical and open positions). Indications have thus been defined according to the degree of nerve damage and environmental factors. Physical therapy is essential for good integration of tendon transfers.

PO 309

RESTORATION OF MOTOR AND SENSITIVITY FUNCTIONS OF A LEPROTIC HAND WITH INTRINSIC PARALYSIS AND PARTIAL INSENSITIVITY USING TENDON TRANSFERS COMBINED WITH SENSITIVE NERVE TRANSFERS.

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All techniques used for correction of traumatic paralysis give the same result in Leprosy paralysis. But the leprotic hand also involves loss of sensation. Therefore, it is of great importance to reconstruct the motor function of the hand together with protective sensitivity.

Many classical surgery techniques used by Seddon, Brand, Moberg, Littler, Tubiana, Michon, Holevich, Anderson, McGregor, Ömer and others since 1950's, have been much improved with the introduction of micro-surgery to peripheric nerve surgery.

In this work, we are introducing 7 patients on whom micro-neural surgical technique was performed so as to provide sensitivtiy by sensitive nerve transfers from relatively less important parts to insensitive parts of fingers or hand together with intrinsic tendon transfer operations of motor reconstruction. From these 7 patients, 3 had Borderline Leprosy with only ulnar palsy, the other 4 had sustained traumatic ulnar or median nerve injuries. The first operation was performed on 10th of January 1985. The cases are discussed with regard to surgical technique and results.

PO 310

LONG TERM FOLLOW UP OF PALMARIS LONGUS 5 & 6 TAILED OPERATION FOR CORRECTION OF INTRINSIC PARALYSIS OF THE HAND

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Palmaris manytailed graft being the procedure mainly used by us for finger correction of intrinsic paralysis seemed to show us more encouraging results than other procedures. Hence we wishes to compare our results with those available from pertinent literature.

Well known procedures adopted to follow up the results after intrinsic replacement of active surgical procedures in leprosy were used.

41 cases operated upon in 1984-85 followed up for a minimum of 6 months to a maximum of 2 years showed 24 cases with good results, 9 with a relatively good result; 4 with fair result and 4 failures. The patients are mainly manual labourers. None complained of difficulty in carrying out their work.

We consider this procedure the one of choice in patients who have a PL Tendon width less than 2 mm.

PO 311

THE CLAW REVERSAL OPERATION

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Almost all the operations for the correction of 'claw' fingers in leprosy require difficult operative techniques involving precise in the judgement of tensions and their balance.

Almost none are capable of reconstruction the metacarpal arch so important in normal hand function. An operation is devised to correct both deformities, clawing and loss of metacarpal arch, simultaneously by rerouting The (FDS) Flexor Digitorum Sublimis from its insertion into the dorsal expansion case period of follow-up.

The procedure is simple, can be conducted under 'wrist-block' anaesthesia and dispensing with the tourniquet, on an out-patient basis. A sirgle POP shell is adequate to immobilize the corrected hand for 3 weeks. No special physiotherapy is required post-operatively, for reeducation.

PO 312

BLOOD FLOW VELOCITY IN THE CUTANEOUS LESIONS OF LEPROSY . A preliminary report .

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A laser-Doppler velocimetry technique have been used to measure the skin blood flow changes in the cutaneous lesions of 9 leprosy patients in Surabaya. All were male patients under treat - ment with the WHO-Multidrug regimens . They consists of 4 BT and 5 BL patients, con - firmed by histopathological study. One BT and one BL were in reversal reaction. The Blood - Flow Velocity (BFV) of Tuberculoid lesions not in reaction were slightly raised at the edge of lesions, but normal in the centre. In BT with reversal reaction, the BFV at the edge of lesi- ons were markedly accelerated (up to 20 times). In BL which were not in reaction, the BFV were raised 3-5 times greater over the centre of le- sions, while at the edge of lesions the BFV le- vel were not much greater than the adjacent normal skin. A similar BFV pattern was recorded from the 5th BL patient which were in reaction. Histometric study of biopsies taken immediately after the BFV measurement, showed a clear rela- tion between granuloma fraction and the BFV le- vel. This laser-Doppler velocimetric technique might prove to be useful, clinically accepted, non-invasive technique for monitoring the res- ponse of treatment in leprosy. Since it is very sensitive, it may detect very small changes in skin lesions during the course of the disease. It should also prove of value in monitoring the process development of ENL reaction in the ear- ly stage .

PO 313

A CLINICAL STUDY OF PRIMARY NEURITIC LEPROSY

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Primary Neuritic Leprosy is characterised by peripheral nerve involvement, without skin patches and negative skin smears for AFB. This condition has not been adequately documented and no long term followup studies are available.

Ninety two patients presenting with Primary Neuritic Leprosy seen at the Schieffelin Leprosy Research and Training Centre, Karigiri from 1977 to 1987 are included in the present study. The detailed records available were analysed for clinical manifest- ations and the distribution pattern of nerve involve- ment. Nerve biopsy confirmation was available in 72 of these patients. Follow up records ranging between 2 to 4 years, of patients seen at the beginning of the study are also available.

Six patients developed skin lesions while under observation and among them four were confirmed as leprous lesions by skin biopsy. The observations suggest that Primary Neuritic Leprosy is an early manifestation of the disease, restricted to peripheral nerves, and these patients are capable of developing skin manifestations during the slow evolution of the disease.

PO 314

The growth and phagocytic capacity for Myco- bacteria, of schwannomas and other brain tumours in vitro:light and electronmicroscopy.

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Fresh biopsy specimens of brain tumours collec- ted in the O.T., including all types of gliomas, especially low and high grade astrocytomas, acoustic schwannomas and other neoplasms, were grown in vitro by the explant method of tissue

culture. Growing cells of all tumours were strongly positive for acid phosphatase; and semithin araldite sections of the tissue culture preparations also showed presence of lipofuscin granules and vacuoles in the cytoplasm. Electron microscopic examination of these preparations confirmed the lipofuscin and also exhibited various stages of development of microtubules and filaments, i.e. the cytoskeleton of the growing cells. When the TC preparations were innoculated with mycobacteria, either M.scrofulaceum or the ICRC (Indian Cancer Research Centre) bacillus derived from original human M.leprae, the bacilli were found avidly endocytosed by the growing cells. They were also degraded to osmiophilic debris in a few days, as confirmed on fine structural examination. Light and Emscopic studies of TC preparations from schwannomas and other brain neoplasms, (i) confirm the capacity for ingestion and digestion of particles of the size of mycobacteria, by growing cells in vitro; (ii) show the operation of lysosomal machinery; and (iii) provide a model for cytoskeletal development and cell adhesion.

PO 315

BLOOD VESSELS OF THE PERIPHERAL NERVES IN LEPROSY.

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Various changes in the endothelial cells, basement membranes with breaking of blood-nerve barrier were reported by several workers (Boddingius, Dastur, Antia, Mehta). However specificity of these changes for leprosy infection was not established. In the present study sciatic nerves of swiss white mice were subjected to vascular mechanical injuries and M.leprae infection. Morphological changes were seen in all the nerve components. Schwann cells were vulnerable to loss of blood. Abnormal myelination was characteristic. The significant changes were the specific reactions of blood vessels to M.leprae infection were seen. In this presentation these observations will be discussed.

References : 1. Boddingius, J. Anat 111:516 1972.

2. Dastur et al. Int. J. Lep. 41 : 47, 1973.

3. Antia et al. Int. J. Lep. 43 : 106, 1975.

4. Mehta et al. Int. J. Lep. 430 : 250, 1975.

PO 316

M.LEPRAE ENTRY INTO SCHWANN CELLS AND ITS CONSEQUENCES: AN APPRAISAL USING NERVE TISSUE CULTURE.

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The nerve tissue culture model is a powerful tool to dissect early events in Schwann cell-M.leprae interaction as well as attempt modulation of bacterial entry. Modulation is possible by anti-leprosy drugs and by selective anti-mycobacterial antibodies towards surface components. Uptake of M.leprae by Schwann cells is dependent on bacterial viability and antigenic integrity. The former is crucial for early entry but plays a minimal role in late entry which requires only the presence of intact non-proteinic bacterial antigens perhaps mediating hydrophobic interactions with host cell membrane. Besides indicating 2 entry mechanisms, these observations have implications in both chemo and immunoprophylaxis of M.leprae infection. Ultrastructural observations favor a role for Schwann cell cytoskeleton during bacterial entry and subsequent activation of the host cell as studied in terms of expression of cell adhesion molecules, generation of reactive oxygen intermediates, MHC expression and ability to sensitize lymphoid cells.

Collectively, this information identifies very early events leading to both nerve damage and establishment of infection.

PO 317

CHARACTERISTICS OF ANTINEURAL ANTIBODIES IN LEPROSY PATIENTS

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In course of studies with a newly developed EIA, it was observed that nearly all leprosy patients carry high levels of IgG class of antibodies reactive with the peripheral nerve antigens. The antibodies were observed to bind to the inner lip of myelin membrane and node of Ranvier in an Indirect Immunofluorescence assay. On SDS-PAGE, the pooled sera from LL, BL, BB, BT, TT group predominantly reacted with a band migrating at 55 KD.

Epstein-Barr virus transformed cell lines were developed from one TT and two BT patients. In both categories clones were obtained secreting antibodies reactive with the nerve antigen(s) as seen by ELISA and immunoblots.

PO 318

Pathogenesis of the nerve lesion in leprosy

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Schwann cells of nerve afford the highest order of protection for the survival of M lepræ The death of M leprae in Schwann cells is followed by the binding of degraded bacterial products to myelin.This together with the externalization of bacilli and bacillary debris and the disintegration of the Schwann cells iniates micro-necrosis (depending on the group of the spectrum) and a non-specific inflammatory response. Immune recognition of externalized antigen results in granuloma formation. Such microreactions are the units of nerve damage. Recognition of bacterial material by regenerating Schwann cells and macrophages produces a self-perpetuating cycle of events. The restriction of neural architecture and the compactness of the granuloma impede the free movement of immunoreactive cells which adds to the delayed antigen recognition,the persistence of antigen,and the chronicity of the lesion. There are discrepancies in the Classification of nerve and of skin in some patients. These aspects of leprous neuropathy are demonstrated.

PO 319

ULTRASTRUCTURAL EVALUATION OF SURAL NERVE IN CONTACTS OF HANSEN'S DISEASE.

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It is well known that given adequate treatment in very early stages, Hansen's disease is curable. With this in view, several different studies have been undertaken to screen for early Hansens. One such study constituted was to evaluate the value of sural nerve biopsies in those subjects who have had contact with Hansens patients for a varying period of time; atleast for not less than a year. While the light microscopy features were non specific, at the

ultrastructural level, 4 of the 9 cases examined showed features of intraneural invasions by sparse number of mycobacteria. In two cases, proliferation of bacteria confined to a site within the nerve, could be identified. Other features seen, included minimal myelin breakdown and early collagen proliferation.

It is concluded that significant bacterial infection is probable in cases of long standing contact with Hansens patients and that ultrastructural examination of sural nerve of contacts might be an useful technique, contributory to early diagnosis.

PO 320

HEREDITARY SENSORY NEUROPATHY AMONG 20 CASES IN SOUTH INDIA - A PRELIMINARY REPORT.

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20 cases (including 4 pairs of siblings), with hereditary sensory neuropathy of varying types were seen at the Schieffelin Leprosy Research and Training Centre, Karigiri over a period of over 20 years. Some of the common presenting features include (1) possible inheritance; (2) selective involvement of peripheral sensory neurons, with a specific sparing of the motor neurons; (3) an involvement somewhat typical of system degeneration - that is, involvement of populations of neurons serving one function. The average age of onset was less than 8 years. The commonest mode of presentation was with plantar ulcers and/or absorption of digits of the extremities. 13 lower limbs had to be amputated before the age of 30 because of either chronic intractable ulceration, or neuropathic ankle and foot joints. All patients were screened in detail by clinical examination, skin smears, and in 6 cases by skin and/or cutaneous nerve biopsy, to rule out leprosy, which is endemic in South India. Other possible causes of sensory loss especially in the lower limbs were also excluded. A preliminary report of the clinical and certain other findings is presented. Detailed investigations including electrophysiological tests, biopsy studies, and other methods of studying nerve tissue are under way, and will be presented subsequently. (These patients are of interest because they are diagnostic challenges, and we believe that there may be many other patients with such a diagnosis who may be living for many years in leprosy hospitals and sanatoria because of wrongly diagnosed leprosy in such patients).

PO 321

RELATION BETWEEN NEURITIS OF A PERIPHERAL NERVE TRUNK AND THE PRESENCE OF SKIN PATCH/ PATCHES IN ITS AREA OF DISTRIBUTION.

Kesava Reddy P. and Somanath G.V.S.

Nerve and skin lesions are asymmetrical and localised in tuberculoid form of leprosy which is not usually associated with bacteremia. In this form of leprosy the spread of M. leprae is more likely to take place from Schwann cell to Schwann cell along the nerve trunk towards the site of predilection; in contrast to lepromatous form of leprosy where bacteremia plays an important role in dissemination of bacilli. Peripheral nerve trunks are damaged generally at specific sites. These sites of predilection along the course of a peripheral nerve trunk are well known.

The objective of this paper is to study the relation between the neuritis of a peripheral nerve trunk and the presence of skin patch/patches in its area of distribution. A total of 300 peripheral nerve trunks of 30 patients belonging to TT. BT classification were examined for signs of neuritis. It was observed that the prevalance of neuritis in peripheral nerve trunks with skin patch/patches in their area of distribution was higher than in the ones without skin patch/patches in their areas of distribution. This observation suggests that in tuberculoid leprosy. a peripheral nerve trunk with one or more skin patches in it's area of distribution is particularly at risk of developing neuritis.

PO 322

HISTOLOGICAL STUDY OF PERIPHERAL NERVE BIOPSIES FROM 30 PATIENTS WITH LEPROSY.

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A histological investigation of the sensory branch of a radial nerve from 30 patients with various forms of leprosy is reported. The patients were all examined at the Institut de Leprologie in Dakar (Senegal). The following techniques were employed : inclusion and classical staining procedures, teasing, electron microscopic examination.

The following points are discussed : the relationship between the clinical and anatomical findings, the histological lesions in relation to the classical forms of the disease, the highly focal nature of the lesions seen in some biopsies, the value of electron microscopy for detection of Hansen bacillus in the pauci-bacillary forms, and the pseudoneuronomatous proliferation of perineurial cells in some cases. In several cases, a second biopsy was taken one year later when the patient was receiving specific treatment. Severe lesions were still seen, and numerous hansen bacilli were in evidence. In 3 patients, although there were no signs of peripheral neuropathy on clinical examination, and the bacteriological tests were negative, examination of the nerve biopsy was able to confirm the diagnosis of leprosy, and thus instigate a treatment program.

PO 323

A PROGNOSTIC VALUE OF NERVE CONDUCTION VELOCITY ASSESSMENT IN THE PATIENTS WITH NEURITIS DUE TO LEPROSY.

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Leprosy neuritis accompanied by motor, sensory, vasomotor and trophic changes in tissues is the main cause of disabilities in leprosy patients. Disturbed integrity (light traumata, pricks, rubbings) of trophically changed tissues results in the development of trophic ulcers. Early prophylaxis of traumata could prevent from developing trophic ulcers. The assessment of nerve conduction velocity (NCV) in low extremities showed the possibility of developing trophic ulcers in area supplied with nerve damaged due to leprosy. 37 patients out of 80 studied showed a significant decrease in NCV in nn.tibialis and peroneus. 14 patients among those 37 had trophic ulcers in their feet (6 of them had the ulcers in both feet). Ten patients out of 23 with pronounced motor, sensory and trophic alterations (anaesthesia, amyotrophies, contractures, mutilations of toes and plantar deformities) but with no trophic ulcers by the moment of observation 2-5 years later showed them in one foot or in both. Thus, a significant decrease in NCV in n.peroneus and n.tibialis in leprosy patients with neuritis might be considered as a bad prognosis of developing trophic ulcers. The findings suggested the necessity of improved prophylaxis of trophic ulcers in patients with a sharp decrease in NCV in peripheral nerves.

PO 324

Autoimmune mechanism of peripheral nerve damage in leprosy.

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The cross reacting glycolipid antigen (GLA) is found in M.leprae and Schwann cells of human peripheral nerves.It is termostable (at 100°C-30'),resistant to urine action,

chymotripsin digestion, ammonium sulfate saturated solution soluble,with electrophoretic mobility of IgG. Leprosy patient's and experimentaly infected by M.leprae anymal's autoantibodies(IgG,IgM) against GLA produced myelinotoxic reaction of organotypic culture's nerve cells "in vitro".Transfer of mouse F_1(CBAxC57Bl) spleen lymphocytes sensitized to GLA to intact anymals cause peripheral nerve demyelination of the latter. Thus,experimental data demonstrate that nerve damage in leprosy is the result power autoimmune reaction caused by cross reacting antigen of M.leprae and human peripheral nerve's Schwann cells.

PO 325

THE ROLE OF PATIENTS/THECNICIANS ASSOCIATIONS FOR HANSEN'S DISEASE CONTROL

RUTH REIS DO AMARAL, MARIA LEIDE WAND'EL REI DE OLIVEIRA, GERSON F.M. PEREIRA, WAGNER NOGUEIRA AND/ MARLENE SANTOS BARROSO.
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Hansen's Disease in Brazil is a important Public Health Problem and,due to the weakness of the official action, some Instituitions jointing patients and technicians angaged in control activities are pressing the political level of the Health Sector to asign the deserved priority to the problem.

The MORHAN (ASSOCIATION FOR REINTEGRATION OF / HANSEN'S DISEASE PATIENTS) has participate effectively in all decision and policy making levels for the endemy control.

The importance of the problem was, at last, apraised and included as matter for discussion in the "VIII National Health Conference".

Following up the Ministry of Health and States of Health Secretaries have held 22 "Macro-Regional Meetings" when,patients and thecnicians have discussed the problem of discrimination and "Stigma" associated to Hansen's Disease, all matters related with the current Public Health Sistem.

After this meetings and hearing all working levels (Macro and Micro Regions of the Country) the Control Program was reformulated and aimed to maked effective the control activities. Many ma- / tters of tecnical and Administrative Norms was iscussed: patient care, treatment, social aspects and Health Education.

PO 326

SOCIAL ASPECTS OF LEPROSY: AN ANALYSIS OF ATTIRUDES AND BEHAVIOUR OF THE PATIENTS

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The psychological response of the leprosy patient in the long range depends upon the personal significance and this is mainly due to the influence of the environment,attitude towards the illness, cultural mores and societ-al norms. Thepresent study was an attempt to analyse the perceptual variation and behaviour noticed among 224 leprosy patients of different age groups in an area of Madurai city. Some of the findings of the study were: Leprosy owed its morbidity much less to the bacteria than to the sinister sociocultural systems; Age of the patient forms an index of his approach to stressful situations; the educated leprosy patients were apprehensive and introspective; A better economic status does not seem to afford better protection against the degree of maladjustment; Patients were found to show considerable degree of maladjustment in the marital sphere; Family members individually reject the patient and the stress on the individuals is evident from the degree of burden experienced by them; 75% ofthe patients rejected the idea that they could even lead a normal social life again. The ostracism is very much resented to by the patients. The shyness of the patients attributed for the failure of the patients to come for therapy. 40% of the patients held a a common belief that it is due to the wrath of God, who nas punished them for their past sins; Some of them have a common view that the disease is transmitted hereditarily. Social rejection of the patient is a common observation.

PO 327

PSYCHOLOGICAL STRESS AND DEVELOPMENT OF LEPROSY.

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The progress of leprosy control in large part of the world is slow since the social aspects of the problem are not yet equally and effectively tackled along with medical treatment A well planned extensive organised efforts towards total rehabilitation of physical, economical, social as well as psychological is absolutely necessary. Psychological stress produces the disease in many cases. And this psychological stress should be taken care of.
The 53 families rehabilitated in village Chatnalli and survey of 56,000 rural population & 25,000 urban slum population reveal that children born and who lost one or both the parents in young age below 5 years, are prone to develop leprosy. 27 children who developed leprosy both paucibacillary+multibacillary type from the age of 1year to 11years belong to the above category. The 30 women who are at rehabilitation centre reveal that the stress with unhappy married life and later stress due to developing disease in rejection by their husbands and in-laws are the root cause exacerbation of the disease. Most of them found rest and comfort in rehabilitation centre where physical, mental, spiritual and social need is taken care of. Many diseased women and men remarry and they live happily. The disease has removed cross cultural barriers Massive health education given in the district has helped to remove part of the stigma.

PO 328

The importance of activities for leprosy patients outside of hospital limits.

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Leprosy patients, who for various reasons of motor and visual incapacities and those with secundary diseases during the course of their treatment, require hospitalization. Rehabilitation cannot be divorced from medical treatment in these cases and their psychological state must be given first priorities. This paper describes the useful measures used in our hospital to incorporate these leprosy patients to society as well as their acceptance of the social environment. Also, this approach is aimed at acquiring a greater relationship between the patients themselves.

PO 329

THE PROBLEM OF ACCUMULATION OF LEPROSY PATIENTS AT THE DR.SUTOMO GENERAL HOSPITAL SURABAYA .

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A problem of accumulation of leprosy patients arised at the Leprosy Out-patient Clinic of Dr. Sutomo General Hospital Surabaya. During the period of 1980-1983, around 660 new leprosy cases were registered every year with approximately 75 patient visit/day. The total number of leprosy cases registered at the end of 1983 was 3264 patients. This huge number of patients was managed only by a small medical team and follow up in the field could not be performed. The drop - outs were high (620/yr) and the regularity of treatment were low (51.2%). Since 1984 some efforts have been done to reduce the number of patients by a closer cooperation between Sutomo

Hospital and the Municipality Health Services of Surabaya City, in the form of SURLECOP (Surabaya Urban Leprosy Control Project). Included in this program are: a)Referring down of leprosy cases to the HCs nearby the patients' domicily. b)RFC following the MDT program . c)Selective registration of new detected cases. d)Guiding and assisting the HCs' personnels to improve the leprosy services in the HCs. During the 1984-1987 period , 647 cases have been referred down, 796 discharged by RFC and 2035 by way of drop out or other caused. 1855 new patients were registered during the same period. The total number of patients was reduced to 1641 at the end of 1987 with approximately 39 patient visit/day. Although the number of cases has been reduced up to 50%, only a slight improvement (from 52.3 to 59.1%) of the regularity of treatment was observed. Factors that might take a role in this observation will be discussed.

PO 330

AN ANALYSIS OF EIGHT LEPROSY SELF-SETTLED COLONIES IN MADRAS - A METROPOLITAN CITY OF INDIA.

G.R.SRINIVASAN, DEREK LOBO, JAYARAJ DEVADAS

There are 8 Leprosy self-settled colonies in Madras City housing 512 patients.

A detailed analysis of the causes of DEHABILITATION of these patients, their clinical, bacteriological, vocational and economic status is done.

The following parameters are available-age/sex distribution, martial status, deformity rate, bacteriological status, educational status, economic status, Housing conditions etc.

The changing profile of the colonies is highlighted and a correlation drawn towards the role of effective leprosy control programmes in the PREVENTION of DEHABILITATION and formation of colonies.

PO 331

SITUATIONAL ANALYSIS OF LEPROSY PATIENT-CARE IN A NON-ENDEMIC AREA

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A retrospective analytical study of 820 leprosy patients attending an Urban Leprosy Centre situated in a cosmopolitan city in a non-endemic area over a period of three years is presented. Approximately thirty percent of patients were local inhabitants, 50% from adjoining non-endemic states and 20% were from distant endemic states. Thirty percent of the total patients belonged to non-bacilliferous group, viz, Indeterminate, Maculoaneasthetic, Neuritic and Tuberculoid types and the rest were bacilliferous. Unfortunately 50% patients never attended for follow-up after registration, 25.7% were regular and the remaining 24.3% were irregular in treatment. An attempt is made to highlight the difficulties in leprosy patient-care in cosmopolitan non-endemic areas in the context of emergence of resistant strains, monitoring of patients on MDT and integration of leprosy control through primary health care system.

PO 332

THE ROLE OF RAILWAYS IN THE CAUSE OF ANTI-LEPROSY ACTIVITIES

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Indian Railways (IR) is one of the biggest employers of the country that has a population of 800 millions (approximately). Western Railway (WR) is one of the nine Zonal Railways of IR. At Bombay Division of WR, we have been able to offer health care to 699 HD persons including employees (235) and family members (464) during the period 1982 to Dec.1987.

Current paper delineates on analytical study of these 699 cases emphasizing the emerged benefits in the Management of HD in this captive population. Recommendations are made from the experience of 34 Survey Camps, 16 Exhibitions at Railway platforms and residential colonies, 8 Check Up Booths at Railway platforms examining nearly 70,000 persons, 8 screening camps in Railway Workshops of 2000 workers each in the Metropolis of Bombay as to how Railways can contribute effectively in mass awareness about the disease(HD) in general and in providing privileges to the afflicted (patients) in particular.

PO 333

HOUSING AN IMPORTANT FACTOR IN THE SOCIAL REHABILITATION OF DISPOSSESSED LEPROSY PATIENTS

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One basic aim in the Rehabilitation of Leprosy patients is to make them self reliant and lead a life of Social approbation.

This study covered 30 leprosy patients who are dispossessed socially and economically and were provided with houses in three different location in Tamilnadu, India, with a cost of Rs.10,000/- per unit.

Moreover, 128 contacts of the patients and 75 neighbourhood persons were interviewed in this connection and following are the findings:

- 93.3% of the total beneficiaries believe that their social status have gone up and they are acceptable in the community after owning a dwelling of their own.
- 89.9% of the total contacts are of the opinion that the proprietorship of the house has given a sense of security for the whole family and their respect towards the patients have increased.
- 74.6% of the neighbours reported that they maintain normal relationship with the patients.

The ultimate solution of the social problem of leprosy patients in their rehabilitation process will come only if there is a remarkable up-liftment of their status in the community environment. Housing thus played an important factor in bringing back the self identity and social identity of the patients.

PO 334

Experiences in Rehabilitation of Leprosy-patients

Dr. I.S.Gilada, Secretary-General, Indian Health Organisation, Bombay, India.

The Indian Health Organisation, adopted in April 1985, one of the largest leprosy colonies in Asia & this presentation, presents our first hand experience in the rehabilitation of inmates of this very large leprosy colony.
The two main objectives, were to provide adequate & regular treatment with the latest Multi Drug Therapy Regimen & on stabilisation start a scheme to make the patients self reliant & self sufficient thro' vocational training.
We faced a variety of situations, generating a contrast between our plans and the attitude of donor agencies and the attitude & demands of the inmates.
THe donor agencies channelised the help thro donating clothes, food materials etc. , instead of utilising their funds for our suggestions of helping in purchase of drugs and helping our specific rehabilitation projects. They would utlise all funds in purchase of tools & machines

instead of spending half of the funds for raw materials, which would help in immediate viability of projects.
The attitudes & demands of the patients were also highly specific, so as they would prefer the spending for immediate gains rather than drug treatment & rehabilitation.
The presentation thus highlights the features that influence to a large extent, any rehabilitation work with leprosy patients in the developing countries.

PO 335

SOME PERCEPTIONS OF WORKERS IN LEPROSY

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That Leprosy is no longer a major problem in the world for medical researchers, is acceptable to most yet, paradoxically, in a country like India it is one of the major health problems. A commitment of heroic proportions a determined effort to resist prejudiced perception and a thurst towards social change, all constitute the goal of Leprosy eradication and the mainstreaming of sufferers. It is our belief that to work in this area of leprosy requires a special kind of personality with his/her unique set of perceptions, attitudes & will. To prepare for a detail study we sought for a viable benchmark. This study is a graphic preliminary; which we hope will guide us in future. At the 12th I.L.C. held at New Delhi in 1984 a questionaire was circulated to the delegates to know their attitude, practice & opinion on some vital aspects of Leprosy control /eradication. Majority had joined leprosy work by choice and almost all felt that Leprosy has been neglected & stigmatised by the medical profession itself. Majority have hope in the vaccine; though the results are not expected in near future. Most felt that eradicating Leprosy from the world by 2000 AD is difficult & few opined that it is impossible. There was a consensus that either Leprosy be an independent speciality or should be a part of Dermatology.

PO 336

TOWARDS A METHODOLOGICAL CRITICS TO THE STUDY OF HANSEN'S DISEASE

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FUNDAÇÃO LEGIÃO BRASILEIRA DE ASSISTÊNCIA - L.B.A.

This paper aims to discuss a new approach to the study of Hansen's disease in Brazil, in opposition to the approach / which favours quantification and individual treatment, in / spite the class society structure. This technical and scientific institutionalized procedure reinforces the ruling ideology, preserving the culturalist conception of the "stigma of leprosy", which is based upon the wrong supposition that culture is not a historical phenomenon.

We intend that the analysis of the peirtaining social aspects of Hansen's disease must take into consideration the following dimensions: The production relations in the under developed areas of the capitalist societies and also citi-/ zenship in class society.

We can justify this study though the existence of a theoretical foundation to support our proposal though methodological procedures based upon the aprehension of social reali / ty, conceived as a whole in its dynamic histoticity and / contradictory elements.

The results of the public health system in Brazil are not satisfactory, causing the participation of professionals related to social sciences as well as patients in the decision instance. Nevertheless, this "democratic" position does not take into account the whole question of Hansen's disease, because of the opposition between the decisions and the power structure. Those measures legitimate, this way, whatever they put in question.

PO 337

Rehabilitation of healthy children of leprosy patients, in a developing country.

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The Coordination Committee, a voluntary Organization of people from various walks of life from Delhi, has extended activities in 3 fields, viz., rehabilitation, health education and resource mobilization.

This paper aims to present the efforts the above Committee in the rehabilitation of healthy children of lepromatous parents, who lived in an atmosphere of dismay, despair and deprivation. Firstly, these children (both boys and girls) were institutionalised from the age of four and above, broughtup under the care of House Mothers at the government institutions, were given adequate housing and nutrition and were also imparted schooling and technical education. The nutritional status and mental maturity and physical growth were assessed by standard methods and these were found to be satisfactory. Some grown up children were helped to be employed in public and private sectors while a few were self employed. They were received into the young society of college students and National Service Scheme volunteers during their wedding receptions. The clinical followup of these children for 12 years revealed a small percentage developing childhood leprosy, even after seggregation from their infectious parents. Social stigma still appears to afflict these children since their origin when identified, they were fired from their vocation.

PO 338

OBSERVATIONS ON NON-ACID FAST ORGANISMS GROWN FROM LEPROMATOUS MATERIAL.

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Ten lepromatous biopsies, one nerve piece infected with *M.leprae* and a sample of purified suspension were inoculated into VS_1R and VS_2M media, having Dubos broth and RPMI (former) or MEM (latter) with 40% Foetal and Calf serum. The medium was adjusted to pH 5.5 and cultures incubated at 36°C. All the cultures and subcultures irrespective of the source showed similar characters. The cultures showed nonacid fast granules, and coccobacillary organisms. Auramine stained smears revealed fluorescing rods and granules. Aryl sulphatase, potasium telurite, urease and nitrate reduction were negative and catalase was midly positive. Iso-enzyme studies of LDH done on the various strains showed similar bands. The sonicated suspensions showed lot of acid fast coccobacillary forms, granules and rods in the deposit The same when inoculated on LJ medium again yielded mixture of acid fast and non-acid fast granules and rods. In late subcultures the morphology of non-acid fast forms was similar to acid fast forms.

PO 339

IN VITRO CULTIVATION OF ACID FAST CHEMOAUTOTROPHIC NOCARDIOFORM BACTERIA FROM MULTIBACILLARY HUMAN/ EXPERIMENTALLY INFECTED ANIMAL LEPROSY TISSUES.

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Nocardioform chemoautotrophic bacteria were cultivated and repeatedly passaged in vitro from all the 22 multibacillary cases of leprosy as against none from their non-leprosy(judged clinically & by skin smears) counterparts ; these grew well on mineral minimal medium when supplemented with only simple sources of C (e.g. liquid paraffin, tetradecane) and N (e.g. (NH_4) - salts, urea, asparagine or gelatin). Complex organic substrates e.g. glucose, sucrose, glycerol, tyrosin, casein, peptone(s), beef/yeast extracts, egg proteins, serum, blood and medium 199 failed to support their growth altogether like all conventional media. Similar, if not identical, chemoautotrophic nocardioform bacteria could be cultivated in vitro from the work-ups of 4 different mouse footpads into each of which had been continuously passaged, 4 different strains of human leprosy bacillus. The uninfected mouse footpads did not yield

such bacteria. A similar bacterium could also be cultivated in vitro from the spleen of an experimentally infected lepromatous, 9-banded armadillo. All these bacteria were mostly in bacillary form in the human and animal tissues, but both in the bacillary and sporulating mycelial forms with granules in vitro. These were DOPA oxidase and catalase positive, and acid-fast at $\leq$ 4% H_2SO_4 which was pyridine extractable. Best growth took place at microaerophilic O_2 tension and at 28°C. Their role in leprosy will be reported.

PO 340

IN VITRO CULTIVATION OF ACID-FAST CHEMOAUTOTROPHIC NOCARDIOFORM BACTERIA FROM 9 PAUCIBACILLARY CASES OF LEPROSY.

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and
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Acid fast nocardioform chemoautotrophic bacteria could be cultivated to purity from 9 selected, paucibacillary tuberculoid human leprosy cases in which AFB could be detected. These could grow and be continuously propagated on minimal mineral medium supplemented with only ammonium salts as sole source of N, and paraffins/hexadecane/tetradecane/diphenylamine/aniline/xylene/toluene/benzene as sole source of C; in addition, urea, asparagine or gelatin (as N & C sources) could also be used for their cultivation. No other complex media or substrates succeeded in growing these bacteria. Some of these could utilise xanthin/hypoxanthin/DNA. All these exhibited a dimorphic characteristic: a tissue bacillary phase and an in vitro cultural sporulating mycelial phase with granules. These were more aerobic than their counterparts from the multibacillary leprosy cases. Like others, these were DOPA oxidase and catalase positive, had an acid fastness which could be retained at $\leq$4% H_2SO_4 treatment but lost after pyridine extraction. Pathogenesis of these bacteria in leprosy is under study.

PO 341

FOSSIL FUEL METABOLISM OF ACID-FAST CHEMOAUTOTROPHIC NOCARDIOFORM BACTERIA ISOLATED FROM LEPROSY TISSUES.

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All the 27 pure cultures of acid-fast chemoautotrophic nocardioform bacteria isolated from different human(22) and experimentally infected animal leprosy tissues(4 mouse footpad and 1 armadillo spleen) were found to metabolise various fossil fuels/derivatives, in addition to those reported earlier (e.g. tetradecane, liquid paraffin). These were : benzene, naphthalene, toluene, xylene, aniline and diphenylamine from coal, and hexadecane from petroleum, as sole source(s) of C, when added to NH_4-salts as sole source of N in a mineral salt minimal medium. Xylene minimal and naphthalene minimal media proved the rapidmost enrichment culture media for these bacteria. These failed to grow altogether on any type of conventional medium e.g. nutrient, blood, Sabouraud's dextrose, tapwater dextrin agar and Lowenstein-Jensen medium, or utilise any substrates e.g. tyrosin, casein, glucose, sucrose, glycerol, peptone(s), beef and yeast extracts, egg proteins, serum, blood and medium 199. Enzymatically and biologically, these bacteria appeared to constitute a single dense cluster and be aetiologically closely related to leprosy in man and animals. From a practical point of view, xylene/naphthalene minimal medium proved to be useful for isolation of such bacteria from leprosy specimens as these could suppress most contaminating bacteria. Their role in leprosy is under study.

PO 342

INTERPRETACION DE LAS INCLUSIONES INTRADITOPLASMATICAS DEL MYCOBACTERIUM LEPRAE HUMANO AL MICROSCOPIO ELECTRONICO.

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Lembke y Ruska, fueron quienes primero demostraron las granulaciones intracitoplamáticas, como cuerpos de distinta densidad- electrónica al microscopia electrónico, distinguiendo entre gránulos y microgránulos. Imaeda y Convit, encontraron así mismo cuerpos de densidad moderada intracitoplasmáticos. Se ha sugerido que estos cuerpos son producto de la degeneración del bacilo leproso, aunque el hecho no está suficientemente probado. Ante esta polémica realizamos nuestro estudio comparando los resultados con los ya conocidos. Material y métodos: Utilizamos biopsias de piel, cuyos tejidos pertenecan a pacientes previamente diagnósticados de lepra lepromatosa. El tejido se prepara, de acuerdo a la técnica de Kellenberger para posteriormente ser observado a microscopía electrónica. Resultados: Se describe las inclusiones observadas en los bacilos leprosos, de pacientes lepromatosos, previamente diagnosticados. Este trabajo se inscribe dentro de los criterios actuales de estudio de las granulaciones bacilares.

PO 343

COMPARISON OF SUBSTRATE INCORPORATION INTO PHENOL-PHTHIOCEROL GLYCOLIPIDS OF M. LEPRAE AND M. BOVIS IN A CELL-FREE MEDIUM. E. B. Harris, N. Ramasesh and R. C. Hastings. Gillis W. Long Hansen's Disease Center, Carville, LA 70721, U.S.A.

Research in the past few years has revealed the importance of the complex phthiocerol-containing glycolipids in pathogenic mycobacteria. This includes the unique phenolic glycolipid of M. leprae, PGL-I. Our studies have shown that viable M. leprae readily incorporate radio-labeled palmitic acid [^{14}C] PA into PGL-I in both cell-free (modified Dubos) and tissue culture (mouse peritoneal macrophages) systems. We have successfully adapted this procedure for studying the antileprosy activity of various drugs. This paper describes further exploitation of [^{14}C] PGL-I formation in exploring substrate requirements and the metabolic maintenance of M. leprae in an in vitro environment.

The incorporation of radiolabeled tyrosine, bicarbonate or methionine as well as the lipid precursors, acetate and propionate was not detected in PGL-I of M. leprae in a modified Dubos, cell-free system. By comparison, the labeled substrates acetate and acetyl-CoA were incorporated into the phenolic glycolipid fraction of M. bovis growing in the same cell-free system. Deacylation of [^{14}C] PGL-I revealed that most of the radioactivity is associated with the fatty acid moiety. Further, the inhibition of [^{14}C] PA incorporation into PGL-I by the antibiotic, cerulenin, suggests that acyl carrier protein-dependent fatty acid elongation may be functioning in this system, with [^{14}C] PA as the primer fatty acid. The lack of acetate incorporation into PGL-I suggests the absence of de novo synthesis.

M. bovis growing in culture readily incorporated two primers of de novo fatty acid synthesis into its phenolic glycolipid fraction. These results suggest that substrate incorporation into PGL-I might be used to distinguish metabolic maintenance from actively growing M. leprae in a cell-free system.

PO 344

Xenodiagnosis of lepromatous leprosy

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Aedes aegypti mosquitoes were fed on lepromatous lesions of ten lepromatous

leprosy patients. The stomach content of each mosquito was immediately smeared on glass slide, dried, dehaemoglobinized, fixed and then acid fast stain was done. By this method acid fast bacilli were demonstrated all the patients. Altogether seventy three smears were stained and the bacilli were detected in 80%. The results indicate that xenodiagnosis can be used as one of the methods of diagnosis of lepromatous leprosy patients.

PO 345

Molecular Cloning of Mycobacterial DNA

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A shot gun approach was adopted for constructing genomic libraries of M.leprae, M.tuberculosis $H_{37}R_v$, BCG and M.vaccae, in a bacterial plasmid pBR 322, with E.coli as the host. One of the M.leprae recombinant clone, pMLD36 codes for an antigen immunoreactive with anti M.leprae sera and not with anti $H_{37}R_v$ sera. This clone has an insert of 5.1 kb and expresses a 35 KD protein. A few clones of BCG origin have been identified which react more with anti $H_{37}R_v$ sera and also with pooled sera collected from active pulmonary tuberculous patients as compared to sera collected from lepromatous leprosy patients. However some clones are cross reactive with both the seras. The immunoreactivity of the sonicates of the clones as determined by ELISA shows several fold more reactivity with patient sera as compared to normal human sera. Partial restriction map of two of these clones have been done, giving an insert size of 3 kb and 0.9 kb respectively. The size of the protein of one of the cloned gene product ranges between 12 KD - 19 KD. The precise molecular weight is being ascertained. The results will be discussed.

PO 346

PSYCHROPHILIC MYCOBACTERIA IN M. LEPRAE INFECTED TISSUES.

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Attempts to cultivate M. leprae resulted in frequent isolation of leprosy-derived cultivable mycobacteria (LDM). Investigations will be reported to develop a selective culture medium to grow M. leprae, but not the opportunistic LDM.

In a multifactorial medium (MFM), acid-fast psychrophilic mycobacteria were cultivated from M. leprae infected human and armadillo tissues. Media were enriched with growth factors for iron acquisition; mycobactin and exochelin from M. phlei as donor. Ammonium thioglycolate served as source of energy. β-cyclodextrin protected SH groups from decomposition. Growth developed at pH 5.8 at 15 to 22°C on the semi-solid MFM in 20 to 60 days, depending on the quality and quantity of the inoculum. Subcultures were obtained. Cultures are not fully identified. They do not grow on Dubos or Loewenstein media. M. phlei, M. avium-intracellulare and scrofulaceum do not grow on the MFM at 15 to 22°C.

Results also indicate that M. leprae is indeed a microbe-dependent microbe. Growth factors might be provided not only by LDM but also by nocardia, yeasts and diphtheroids often present in leprotic lesions. β-cyclodextrin might replace mycobactin-exochelin with high density M. leprae inoculum.

PO 347

IMMUNOCHEMICAL CHARACTERIZATION OF MYCOBACTERIAL ANTIGENS BY WESTERN BLOT USING PATIENTS' SERA.

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The most important question for the development of a serological test for leprosy and tuberculosis is which mycobacterial antigens are recognized by patients' sera.
The following sera were tested:
- Sera from both treated and untreated patients with leprosy ranging from tuberculoid to lepromatous.
- Sera from patients who received either short or long term treatment for their leprosy.
- Sera from healthy contacts of leprosy patients.
- Sera from contacts of leprosy patients who developed leprosy.
- Sera from treated and untreated tuberculosis patients.
- Sera from BCG vaccinated individuals.
- Sera from Mantoux positive individuals.
- Sera from Mantoux negative individuals.
- Sera from patients with reumatoid arthritis.
- Sera from patients with autoimmune diseases.
- Sera from patients with ulcerative colitis.
- Sera from patients with Crohn's disease.

We studied the reactivity of these sera with M.leprae and M.tuberculosis in Western blot. The specificity of the reactions were further analysed by absorption of the sera with M.avium and other common bacteria. The results of these studies will be presented.

PO 348

Acid-fast bacilli detected in umbilical codes and skins of human surgical operation.

Tatsuo Mori

Deputy director, National leprosarium Tama Zensho En, Toky, Japan.

Leprosy may be drived from tolerance disease which is induced by passage the pathogenic organism to embryo.
I detected many acid-fast bacilli from skins of surgical operation or umbilical codes of caesarian operation babys by microscopic observation and cultivation. Thirteen cases (27%) out of 49 skins of surgical operation were microscopic positive and 11 cases (22%) out of 49 were culture positive. Eight cases (17%) out of 48 human umbilical codes were microscopic positive and 6 (13%) out of 48 were culture positive.
In one case of umbilical code, 8×10^5 acid-fast bacilli were detected in 10 g umbilical code. The baby was born carring 2.8×10^8 acid-fast bacilli calculated from the body weights 3.5 kg. This bacilli were cultivated on egg medium as Mycobacterium simiae.
Name of the cultivable acid-fast bacilli were Mycobacterium scrofulaceum (6), Mycobacterium intracellulare (1) and Mycobacterium simiae (13). No cultivable acid-fast bacilli were 10 cases.
These acid-fast bacilli may introduce an immunological tolerance of a cell immunity against leprosy bacillus. Such immunological tolerance person may carry the acid-fast bacilli for his life. It may be a reason that Mycobacterium scrofulaceum can be isolated frequently from nodule of lepromatous leprosy patient.

PO 349

Studies on aspartate metabolism in mouse peritoneal macrophages and intracellular M. avium and M. leprae

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Aspartic acid uptake and metabolism were studied in cultured mouse macrophages under different conditions. Mouse peritoneal macrophages transported [u-^{14}C] aspartic acid by carrier-mediated diffusion which was inhibited by iodoacetic acid. Various factors including physical state of the macrophages, culture media constituents like serum, and phagocytosis influenced the uptake and metabolism of aspartate by macrophages and intracellular Mycobacterium avium. Cultured macrophages in suspension without serum being present in the culture media showed enhanced ability to transport and metabolise exogenously supplied aspartate. Cell free extracts from

macrophages stimulated uptake of amino acids by M. avium and M. leprae. The stimulatory factor was partially characterised and found to be a pH sensitive, heat stable low molecular weight substance(s). It is speculated that the stimulatory factor(s) could be a metabolic intermediate present in high concentration in macrophages which can be utilised as an energy source for the transport of various nutrients by the mycobacteria.

PO 350

FALSE HIV POSITIVITY IN LEPROSY

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In a previous survey on the prevalence of HIV antibodies in different African areas, we found 6% of false positive reactions in sera of 100 leprosy patients from Somalia. We have now extended the study to other leprosy patients from Italy (62 cases) and from Indonesia (75 cases). With confirmatory tests (W.B.) the reactivity to HIV appeared to be an artefact in 4% of the Indonesian leprosy patients, while in Italian patients all HIV tests (IFA, ELISA, W.B.) were constantly negative. No correlation has been recorded with the presence or the levels of PGL-I antibodies. It is interesting to note that the basic immunological alterations are similar in leprosy and AIDS:

- impaired deleyed hypersensitivity skin tests
- lymphophenia
- altered lymphocyte helper/suppressor ratio
- defects in natural killer activity
- defects in γ-interferone activation
- B-lymphocytes policlonal activation
- circulating immune complexes
- presence of autoantibodies
- large amount of non-protective antibodies.

The false reactivity to HIV could be due to the high levels of autoantibodies or circulating immune complexes present in leprosy patients, but appears to be more linked to the geographical origin of the subjects (tropical areas) than to the illness in itself. In Africa, as in other tropical countries, the high incidence of malaria, other parasitic diseases and leprosy must induce us to consider the possibility of false HIV reactivity in these populations. The correlation between leprosy and AIDS needs to be further investigated.

PO 351

Morphological and Bacteriological indeces of 1,224 skin smears from BL and LL patients using 3 staining methods.

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State Health Secretary of Amazonas-Manaus-Brazil.

As is well known, the bacteriological and morphological indeces of skin smears are the most important methods for the qualitative and quantitative evaluation of leprosy patients. There are already standard techniques of the preparation of smears, and the Ziehl Neelsen methods seems to be most utilized staining techniques. Besides this techniques others such as Nyka modification. Ziehl Gabbet are also used. In this work we decided to compare these three techniques.
Eighteen skin smears were were taken from 6 different sites from 34 patients, and slides, contain 3 skin smears each, were utilized for each technique. A total of 1,224 skin smears were otained. The 6 selected sites were: ear lobe, right, elbow nasal mucosa and proximal phalang of the third and fifth fingers the right hand. Reading of skin smears done by two independent teclinicians.
The Ziehl Neelsen method the most sensitive when compered With, Ziehl Gabbet and Nyka modification.

PO 352

MOUSE FOOTPAD PATHOGENICITY OF THE CHEMOAUTOTROPHIC NOCARDIOFORM ISOLATES FROM HUMAN AND MOUSE FOOTPAD LEPROSY TISSUES.

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And
Sujata G. Dastidar, Division of Microbiology, Jadavpur University, Calcutta 700 032, India.

Pathogenicity was studied of the acid-fast chemoautotrophic nocardioform isolates from infectious leprous tissues from 2 humans, 2 mouse footpad (MFP) and one armadillo isolates, in the mouse footpad, with respect to the granules produced by these bacteria in vitro, as well as that of the free bacilli derived from these granules. The granular pathogenesis was characterised by local inflammation and swelling by 4-6 weeks, which subsided; there was typical granuloma formation around these granules with gradual disintegration of the granules and infiltration of the mycelial mass into the muscels, connective tissue, epithelial cells and nerve bundles ; large number of macrophage globi were present from which plenty of mycelial tufts were seen to emanate. By 6-9 months these granules got completely disintegrated into large number of free bacillary bodies, small single-layered rings, small globi and some residual mycelium. The free bacillary forms from the MFP resembled the leprosy bacilli found in the original specimens, in morphology, in acid-fastness and its pyridine extractibility, metabolism and in exhibiting DOPA oxidase and catalase and in respect of multiplication in the MFP.

PO 353

AN ELECTRON MICROSCOPIC AND BIOCHEMICAL STUDY OF CHANGES IN MORPHOLOGY AND PERMEABILITY OF MYCOBACTERIUM LEPRAE

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Purified suspensions of M. leprae were prepared from aseptically-collected, fresh spleen of experimentally infected armadillos. The effect of exposing the bacteria to different conditions was studied. Ultrathin sections of the organisms were cut and examined in an electron microscope. Dapsone (DDS) is an inhibitor of the unique diphenoloxidase enzyme of M. leprae. The bacilli with intact cell envelopes were impermeable to DDS, as evidenced by its lack of effect on the bacterial enzyme. The cytoplasmic membrane and the peptidoglycan layer (cell wall) in untreated organisms and in those treated with trypsin remained intact. The cell wall of M. leprae treated with NaOH or exposed to -80°C became partially detached from the membrane; DDS inhibited diphenoloxidase of these bacteria. The organisms in all the above preparations multiplied in mouse foot pads, indicating that they did not lose their viability. At 50°C, the peptidoglycan layer was completely detached from the membrane and at 100°C, the structural organization of the bacteria was totally destroyed; the bacilli were no longer viable. There was no correlation between viability and permeability of M. leprae to dapsone. The electron micrographs also reveal the internal structure and cytoplasmic inclusions of M. leprae.

PO 354

EVALUATION PAR CHIMIOLUMINESCENCE DE LA PRODUCTION IN VITRO, DE RADICAUX OXYGENES LIBRES PAR LES CELLULES PHAGOCYTAIRES DE LEPREUX.

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La libération de radicaux oxygénés libres (ROL) par les cellules phagocytaires de lépreux est étudiée in vitro par chimioluminescence, sous l'influence de différents stimuli, soluble (PMA) ou particulaire (latex). Dans le groupe des lépromateux (LL/BL), la réponse basale (sans stimuli) est significativement plus élevée que chez les tuberculoïdes (TT/BT) et chez les sujets témoins normaux. L'addition de stimuli n'entraine que faible élévation des ROL chez les lépromateux, alors que les tuberculoïdes ont des valeurs proches de la population de référence. Ces résultats suggèrent une saturation de la capacité de réponse des cellules phagocytaires des lépromateux sous l'effet de la charge bacillaire au sein de la lignée monocyto-macrophagique. Cette étude réalisée chez les lépreux non traités, se poursuit actuellement pour évaluer les variations des ROL sous traitement et au cours des érythèmes noueux lépreux (ENL).

PO 355

CHARACTERIZATION ON T CELL EPITOPES ON AN IMMUNO DOMINANT MYCOBACTERIAL COMMON ANTIGEN THAT MIGHT PLAY A ROLE IN AUTO IMMUNE ARTHRITIS.

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3 Dept. of Immunology, Veterinary faculty, Utrecht, The Netherlands.
4 National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

A 65kD protein antigen cloned from Mycobacterium bovis BCG was found to be immunologically related to a similarly-sized protein present in all of a variety of taxonomically distantly related bacteria, including archaebacteria. The 65 kD antigen seems to play an immunodominant role as a high proportion of Mycobacterium-reactive T cells in leprosy patients, healthy PPD-positive individuals and in M.tuberculosis-vaccinated mice are reactive with the 65 kD mycobacterial protein. This protein might play a role in auto immune arthitis as an arthritogenic T cell clone, obtained from rats that developed adjuvant arthritis as an arthritogenic T cell clone, obtained from rats that developed adjuvant arthritis following injection with killed M.tuberculosis, did also react with 65 kD mycobacterial antigen. We here report the mapping of the T cell epitope on the 65 kD mycobacterial antigen recognized by the arthritogenic T cells and also the mapping of epitopes recognized by T cells from leprosy patients. A possible role of the common 65 kD antigen in the etiology of auto immune arthritis is discussed.

PO 356

RESTRICTION FRAGMENT LENGTH POLYMORPHISM ANALYSIS OF VARIOUS ISOLATES OF MYCOBACTERIA USING DNA PROBES OF PROTEIN ANTIGENS OF MYCOBACTERIUM LEPRAE.

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The classification of mycobacteria presents unique problems attributable in part to the fastidious growth characteristics of most of the members of this genus. In particular the inability to cultivate M. leprae in vitro severely limits comprehensive phenotypic analyses of individual isolates, leaving unanswered the question of relatedness of individual isolates. To study the relatedness of various isolates of mycobacteria we have employed the use of restriction fragment length polymorphism (RFLP) analysis of chromosomal DNA of several isolates of M. gordonae and M. leprae. The DNA probes used for hybridization experiments consisted of the 65-kDa and 28-kDa protein genes of M. leprae which were isolated from the lambda gt 11 M. leprae library, subcloned into the plasmid vector pKK223-3 and purified from plasmid DNA by restriction endonuclease digestion followed by gel electrophoresis and elution of appropriate DNA fragments from gels. The chromosomal DNA of several phenotypically distinct isolates of M. gordonae were digested with several restriction endonucleases. The DNA fragments were separated through 1% agarose gels, transferred to Immobilon® filters using a modification of the Southern transfer technique and hybridized under high stringency conditions with P-32-labeled M. leprae DNA probes. Analysis of the resultant autoradiographs showed that both the 65-kDa and 28-kDa gene probes of M. leprae gave distinctly different RFLP patterns for BstE II digests of six phenotypically distinct M. gordonae isolates. When the DNA from two geographically different isolates of M. leprae (Philippines and Louisiana) were digested with either BstE II, Pvu I or Pst I, and hybridized with the 65-kDa protein gene probe, identical RFLP patterns resulted. These results demonstrate the utility of RFLP analysis for differentiation of mycobacterial isolates.

PO 357

DNA PROBES FOR MYCOBACTERIUM DETECTION AND CLASIFICATION.

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A wide variety of DNA probes has been recently developed for diagnosis of bacterial, parasitic of viral diseases. These have proved to be very useful in clinical and epidemiological studies. In order to obtain mycobacterial probes we inserted pieces of M.BCG DNA into the pBR322 plasmid. Colonies were hybridized to M.BCG DNA labelled with ^{32}p. colonies that gave strong signals were selected and the hybrid plasmids specificity as probes, studied through dot and southern hybridization assays. It was observed that several independent probes gave very strong hybridization with **M. Tuberculosis** DNA and poor signals with **M. bovis, avium** and **grastrii.** No reaction was observed with **M. kansasii, flavescens, fortuitum, vaccae, leprae, smegmatis, phlei** and **marinum.** This indicates that M.BCG is more related to **M.Tuberculosis** than to **M. bovis.** Similar results were previously obtained through liquid hybridization assays (Baess, I, Acta, Pathol. Microbiol. Scan. Sect. B. 87:221, 1979). Therefore, M.BCG should be considered a variant of **M. Tuberculosis** and denomination **m. bovis BCG** is improper. Further studies on the clinical uses of the constructed probes are underway.

PO 358

Lateral Elevation Plasty in Lateral Footdrop

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The technique and indication of the LEP are described and discussed. Without loss of motor function a graft will elevate the dropped lateral margin and by doing so reduce trauma to the lateral footmargin.

PO 359

A Survey of Foot Radiographs of Leprosy Patients in the United States

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A survey of the foot radiographs of 2500 leprosy patients at the Gillis W. Long Hansen's Disease Center was performed. Records of foot type and pathology identified were established. The findings have been compiled into categories to obtain impressions of possible correlations between foot types and pathology.

PO 360

DIAGNOSIS AND MANAGEMENT OF NEUROPATHIC DISINTEGRATION OF THE FOOT

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Neuropathic disintegration of bone is a relatively common condition in leprosy. It was seen in 117 feet of 400 consecutively admitted patients reviewed in Hong Kong. It occurred in 10% of patients who resumed unrestricted, unprotected walking after immobilisation in plaster casts for 6 weeks or more.
Early lesions can be suspected by patients taught to look for painless heat and swelling.

History	- Non-specific, usually no trauma.
Signs	- Painless heat and swelling.
Early	- No deformity or disability.
Later	- Increasing deformity and hypermobility.
Predisposing factors	- Osteoporosis, immobilisation, sepsis, Acute neural deficit, steroids.
Radiography	- Early, very difficult to detect.
	- Later, progressively more obvious, increasing osteoporosis, disintegration and deformity.
Management	- Complete immobilisation for prolonged period, till no heat and swelling on resumption of supervised, graded walking. (Trial walking). If the foot is hypermobile it should be moulded into the optimum possible functional position, during plaster application.
Follow-up	- Patients can wear resilient soled footwear such as canvas shoes. They should not require special supportive or moulded footwear. Fully healed bone stands up well to stress of use. Follow-up of 20 years available. Feet with deformity due to disintegration, that is incompatible with ulcer free walking, can frequently be surgically reconstructed to give a useful foot. The diagnosis of neuropathic bone disintegration need not be a condemnation to deformity and amputation.

PO 361

LONG TERM FOLLOW-UP AFTER FOOT DROP CORRECTION

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Reconstructive surgery was introduced to Hong Kong Leprosarium in 1958. Between 1960 and 1974 a total of 245 tendon transfers were done for foot drop. In 1986 the authors reviewed all those who had had surgery in that period and still attended the out-patient clinics. Out of 114 patients seen, 6 had had an amputation, usually because of infection or ulceration.
Of the remaining 108 patients:

80 (74%) could dorsiflex above 90°
18 (17%) dorsiflexed between 90° and 100°
10 (9%) dorsiflexed less than 100°.

Some 51 (47%) had good gait) assessed as acceptable
48 (45%) fair gait) that is, not obviously
9 (8%) poor gait) abnormal in the street.

The main problem was residual inversion in 41 (37%). This obviously contributed to the presence of ulceration in 12 (11%) and of absorption of many toes. This review shows that:

1. Used tendon transfers achieve a stable range of motion in 3-6 months and maintain it for many years.
2. To achieve good results it is necessary to make the dorsiflexor short enough and to do this the Achilles tendon usually needs lengthening.
3. A tendency to inversion that cannot be passively corrected initially ought to be surgically corrected before the tendon transfer is performed.
4. Prolonged physiotherapy is necessary for education in using the transfer automatically in walking.
5. The patient needs to practise foot and skin care to minimise the chance of ulceration.

Tendon transfers are a very practical way of helping maintain functional ulcer free feet.

PO 362

Osteotomy of the tibia in the pes varus of Hansen's disease.

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The pes varus is one of the deformities encountered in leprosy patients who have not received rehabilitation treatment at the correct time. Generally this occurs when the disease is hidden and the patient only applies for medical attention when the deformity is very incapacitating for walking. The surgical treatment usually employed when the foot allows passive mobility consists of the tendon transfer in substitution of muscle paralisis. Triple arthrodesis is usually performed when the deformity is irreversible. It must be noted that varus deformity cause support on the outer edge of the foot and the following formation of ulcerative lesions with lesser or greater depth until osteomyelitis lesions occur. The peri-astragaline bone structures do not keep a normal anatomical relation and its consistency is altered. The triple arthrodesis, a relatively simple technique to carry out, becomes difficult and, also, its proximity to ulcerative lesions is, therefore, an infectious risk factor. Carrying out a bone excision in the external base, in the supramaleolar region can correct the deformity by changing the point of support and avoiding pressure on the outer border. This permits us to keep a distance from the septic focus.

PO 363

Chronic foot ulcers: conservative treatment versus amputation

A. Leviatan, Hansen Governmental hospital, Jerusalem, Israel

Three cases of amputation of feet and one case of conservative treatment are described. The advantages as well as disadvantages are discussed.

PO 364

Synovial Sinus Tract Detection and Treatment in the Feet of Leprosy Patients

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As people with insensitive feet walk on plantar foot ulcers, deeper structures of the foot become damaged by repetitive stress and inflammation. When a synovial membrane is damaged in this process, synovial fluid drains through the wound. The synovial fluid will interfere with complete healing of the wound. A treatment protocol, which has proven to be successful in the United States, is presented.

PO 365

REHABILITACION Y PROTESIS MAXILO-FACIAL EN UN CASO DE LEPRA LEPROMATOSA MUTILANTE.

- Montserrat Pérez,M.D,Tomás Escuín,M.D,Eulalia Fuster A.S. Rosser Suquet,A.T.S.
- Unidad de Lepra.Servicio Dermatología.Hospital de Sant Pau.Barcelona.España.

- Paciente de 41 años afecto de LL con gravísimas mutilaciones en cara y extremidades:pérdida de cejas,desaparición de nariz,pésimo estado de la boca y afectación e invasión de los globos oculares.
Para conseguir la reinserción social se estudia la posibilidad de una prótesis de nariz.Se propone la elaboración de dicha epítesis nasal en silicona blanda para evitar erosiones y decúbitos.
El problema mecánico de sustentación se solventa con gafas que se sustentan por medio de resortes en varillas auriculares.Ademas disimulan la gran mutilación ocular.
Se utilizan adhesivos de silicona para adaptar la epítesis nasal blanda durante los movimientos de la musculatura mímica facial.

PO 366

Plastic surgery of facial deformities in Hansen's disease.

Domingos Quintella De Paola, Curupaiti State Hospital, Rio de Janeiro, Brazil.

It is presented a critical analisys of techniques and effects of surgical correction in all facial deformities caused by leprosy. This abstract is based on 101 cases of spontaneous plea accomplished between the years of 1980 and 1986 in Curupaiti State Hospital, Rio de Janeiro, Brazil.

PO 367

Gynecomastia in Hansen's disease - Liposuction versus conventional surgical procedures.

Domingos Quintella De Paola, Curupaiti State Hospital, Rio de Janeiro, brazil.

The author presents a critical analysis of the results obtained in surgical correction of gynecomastia, in leprosy, by conventional procedures in comparison with the results obtained with liposuction. It is emphazised the absence of post-operatory complications in liposuctions, avoiding drainage or long compressive dressing. The presence of mammary glands is not contraindication for liposuction, being recomended its remotion after the suction of periglandular fat.

PO 368

Correlation of Funtional Results,Histology and Serology in Patients who underwent Nerve Decompression.

Wim.J.Theuvenet, W.Britton, P.Roche, N.Myazaki and Shyam P.Battaraj, S.P.Pradhan.

Anandaban Leprosy Hospital, The Leprosy Mission Int., Nepal.

Functional Results of Nerve Decompression because of longstanding loss of sensation are correlated with histology of biopsies and serology.

PO 369

TREATMENT OF FOREFOOT ULCERS BY DIFFERENT CASTING TECHNIQUES.

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The aetiology of plantar ulceration in Leprosy is well known. Increased pressure maintained over a long time will result in tissue breakdown. Since the cause of the plantar ulcer is mechanical,relief of the increased pressure results in healing. Such reduction of plantar pressure can be achieved by bedrest or by the use of crutches. These methods of treatment are often not acceptable to the patient.

A total contact cast extending from below knee to the toes has also been found to cause healing of plantar ulcers especially those situated in the forefoot. Since such a cast does not permit inspection of the ulcers of the forefoot while it is in position a trial of a cast extending from the tibial tuberosity level to the midfoot has been carried out.

The results are analysed and advantages and disadvantages are discussed.

PO 370

THE HEALING OF PLANTAR ULCERS.

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As many of today's leprosy patients are not being hospitalized or institutionalized, an alternative to the traditional plaster of Paris (POP), below knee total contact cast (TCC) has become necessary to convince patients to accept casting and to enable them to continue work or school while the ulcer heals. At our clinic we applied casts to 24 patients having plantar ulcers using POP and/or fiberglass fabric impregnated with polyurethane resin. We evaluated each for time needed to effect healing, health of the skin inside the cast, ease of application/removal, and patient satisfaction. We compared the time to effect healing using a TCC to the time healing occured when the patient refused casting (30 patients). These patients were debrided, given specially molded shoes and advised to decrease ambulation. The average time required to heal a plantar ulcer in those patients who were casted was 5.6 $\pm$ 2.6 weeks, while those refusing casts, if they healed, took an average of 9.1 $\pm$ 6.6 weeks ($P = 0.1$). All casted patients' ulcers healed. Only 23 of the 30 non-casted patients' ulcers healed. The traditional POP TCC is very effective in healing ulcers quickly and without complications when applied correctly. A minor modification, the addition of a fiberglass reinforcing strip, makes the cast lighter and stronger. However, the cast is still heavy and requires over 24 hours to dry before ambulation is permitted. This type of cast is also somewhat difficult to remove because it is not bivalved. Other modifications of this POP cast have similar drawbacks. A TCC of fiberglass was applied successfully to 7 patients. If applied skillfully, this is an excellent alternative as ambulation is possible immediately, it is lightweight, and removal is facilitated by bivalving.Casting to heal plantar ulcers decreases the time the ulcer is open and subject to infection. The lighter the cast, the more acceptable it is to the non-hospitalized patient.

PO 371

TREATMENT OF TROPHIC ULCERS IN LEPROSY - A PILOT STUDY COMPARING DILANTIN POWDER AND ZINC TAPE.

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Phenytoin and Zinc have been increasingly used in the healing of skin and soft tissue wounds and ulcers. A prospective study at our institution, comparing the efficacy of Dilantin powder and Zinc tapes against standard dressings for trophic ulcers in leprosy, was done on a pilot basis.

A total of 57 Leprosy patients with trophic ulcers were selected for this study. They were randomly allotted into one of the 3 groups:

Group I - Phenytoin powder alone.
Group II - Zinc Tapes containing 25 % Zinc oxide alone.
Group III - Saline dressings.

Most of the patients under the study received routine anti-leprosy drugs and a few received short courses of antibiotics for underlying secondary infection.

The advantages and disadvantages of Zinc and Phenytoin powder in comparison with standard saline dressings are described in detail with planimetry and clinical Photographs at pretrial, mid-trial and post-trial stages.

PO 372

WOUND HEALING IN TROPHIC ULCERS OF LEPROSY IN INDIA

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Fifty leprosy patients with chronic non-healing trophic ulcers of duration from 1 to 9 months were treated with topical diphenylhydantoin. Results were compared with another similar group with topical zinc dressings. Healing was recorded in terms of initiation of granulation tissue response, discharge, opportunistic bacterial infection and mean healing time. 69.7% of DPH patients showed complete epethelization as compared to 5.88% in zinc group in a hospitalised study of three months.

PO 373

Heel ulcers in leprosy treated with island flaps from the instep of the sole

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Ethiopia

In leprosy, ulcers involving the heel are less common than in the forefoot. When they occur it seems that they usually are due to external injuries. Small or superficial ulcers with intact pulp can usually be treated with simple rest or splitskin grafts. The large heel defects however, with loss of soft tissue and sometimes osteomyelitis of the calcaneus can be extremely difficult to cure. The conventional transpositionflaps can often not be made big enough for a successful long term coverage of the weigth bearing area of the heel. For a couple of years we have used fasciocutaneous island flaps from the instep of the foot elevated on the medial plantar vessels for large heel defects. Operative technique will be descriebed, and the results of about twenty operations carried out on anesthetic leprosy feet presented.

PO 374

MANAGEMENT OF STASIS LEG ULCERS IN HANSEN'S DISEASE.

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Ulcers in the distal third of the lower leg are not uncommon in patients with Hansen's disease. They are very similar to venous stasis ulcers but have some unique features. The pathophysiology is poorly understood and there is only very little to find in the literature. We would like to present our experience in managing this difficult problem and try to raise some hypothesis as to the pathophysiology of these ulcers. It is important to treat these lesions aggressively because they are one of the principle causes for amyloidosis when they become chronic. We also present several patients where these chronic ulcers have transformed into carcinomas. Detailed surgical management is presented. The surgical treatment can be successful in closing these longstanding ulcers. Although recurrences are common (since the basic pathology has not changed it is much easier and faster to treat the usually smaller occurrences). Probably the greatest advantage in skin grafting in closing the stasis ulcers is social. It eliminates the constant dressings needed and also the bad odor that usually accompanies these ulcers.

PO 375

TRATAMIENTO CON APOSITOS DE HIDROCOLOIDES SEMISINTETICOS EN ULCERAS HANSENIANAS

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José Terencio de las Aguas

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El número de enfermos tratados ha sido de 14,con un total de 19 úlceras tórpidas. La edad media de 63 años. La forma predominante LL. Baciloscopia actual negativa tanto en moco como en - piel.

Las úlceras eran de larga duración y rebeldes a tratamientos tópicos generales o reparadores.

La valoración de los resultados es buena o excelente en todos los casos, evolucionando por si sola a la curación o ayudándola con automicroinjertos.

La tolerancia ha sido buena.

PO 376

USE OF' EPIDERMAL SKIN GRAFT' IN MANAGEMENT OF UNCOMPLICATED FOOT ULCERS IN LEPROSY PATIENTS.

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Every effort should be made to prevent trophic ulcers in patients with loss of sensation in the feet. However, in the event of patient having trophic ulcer, it should be seen that the ulcer heals within the shortest time possible. Epidermal skin graft was used in patients with trophic ulcers in foot who were under treatment at Sivananda Rehabilitation Centre, Hyderabad. The procedure is simple, ordinary scalpet is used to take the epidermis from adjoining area and then covering it on the uncomplicated ulcer, followed by vasaline guaze dressing. 63 cases with uncomplicated ulcers were included in the study. Majority of ulcers healed with Ist graft itself. Most of the cases healed with second or third graft. 15 percent cases did not heal even after repeated graft procedures. (The response was comparitively less in active Lepromatous Leprosy patients). However, with each rejection of graft, better granulation was observed.

Among the healed ulcers three fourth of cases healed within 10 days and the remaining within 20 days.

The results of the study indicate that epidermal skin graft procedure for management of uncomplicated ulcers to be acceptable,effective and it significantly cuts down the hospitalization/healing time in majority of cases.

PO 377

Collagen Sheet and its usefulness in healing of Ulcers in Leprosy Patients.

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Collagen is a natural tissue present in the body. For healing of any part, Collagen is essential. Collagen has been made available in the form of sheets which is obtained from natural membranous tissue of healthy animals. It is purified, crosslinked and sterilised. Collagen Sheet as a dressing prevents air borne infection, minimises the discharge from the wound and helps in appearance of granulation tissue and epithelialization.

Plantar and Non-Plantar Ulcers are common in leprosy and pose a problem in healing. Therefore, Collagen Sheet application was done on 75 patients having plantar ulcers and other types of ulcers like Stasis Ulcers and Post-operative wounds. The results were excellent in 44(58.44%), good in 20(26.66%), fair in 5(6.66%), and poor in 6(8%). The healing time of the ulcer was shortened and healing takes place with minimal or no scar tissue. The indications, healing time, type of ulcers, cost effectiveness are discussed in this paper.

PO 378

THE EXTENT OF LEPROSY-RELATED DISABILITIES IN TURKEY

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Turkey has a national population of approximately 50 million and there are 3997 registered cases of leprosy.

In this study, realized between January 1986 and February 1988, 454 leprosy patients were evaluated according to their age, sex, province they live, classification of their disease and disability, using WHO grading.

71% were lepromatous cases and 76% were between 30 and 59 years old. There were 76% male and 24% female cases with ages ranging from 14 to 79.

36% had lagophthalmos, iritis or keratitis in one or both eyes and 8% had severe loss of vision or blindness.

29% and ulcer, mobile claw fingers or slight absorption, 18% had wrist drop, stiff joints or sever absorption.

41% had plantar ulcers, clawed toes, foot drop or slight absorption in one or both feet, 7% had contractures, severe absorption or amputations.

Only 24% of the total number of cases examined had no leprosy related disability.

PO 379

A STUDY OF THE HAND AND FOOT CONDITION OF PATIENTS ADMITTED TO İSTANBUL LEPROSY HOSPITAL DURING 1987

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In Turkey, many of the leprosy patients have secondary disabilities. Problems related to these disabilities is a frequent reason for hospital admission. In this study, reason for admission and treatment given was recorded and tabulated.

162 patients were admitted into İstanbul Leprosy Hospital in 1987. Although almost 50 of them were re-admitted for a second or even third time. 38% fell within the 50-59 age group, 54% of the admitted patients came from Eastern Anatolia.

Distribution of patients in the classification spectrum showed 62% Lepromatous and 33% Borderline Leprosy. 58% of the admitted patients were receiving multidrug therapy.

48% of the admitted patients had plantar ulcers and for 38% this was the primary reason for hospitalization. 77% of the patients had some ulnar or median nerve damage. 41% had bilateral ulnar and median palsy. Only 9% of the admitted patients had no hand or foot problems.

PO 380

THE RESULTS OF COMBINED TREATMENT OF LEPROSY PATIENTS WITH PLANTAR TROPHIC ULCERS.

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The results of treatment of 202 plantar trophic ulcers in 150 patients given specific antileprosy therapy are presented. The patients of test-group received a combined treatment including limited surgical intervention in soft and osseous tissues of feet, administration of the medicines ameliorating microcirculation (teonicol, complamin), irradiation with helium-neon lazer and ulcer phonophoresis, ointment applications proposed by us (kalanchoës-dimexide, doxycycline), orthopedic devices. Clinical and laboratory observations confirmed that the factors determining pathogenesis of neurotrophic plantar ulcers might be specific neuritis, skin and vessel damages, secondary infections. The results obtained showed healing of ulcers in 92,3% in test-group versus 69,5% in control group. Average terms of healing reduced 1,5 times. In test-group primary ulcers healed in 24,1 ± 2,1 days and relapsed ulcers improved in 35,1 ± 1,7 days versus 37,3 ± 6,2 and 56,6 ±4,0 days in control group, respectively ($p < 0,001$). Relapses of ulcers were twice less. Two years of observation showed 15,2% of relapses in experimental group as compared with 37,5% in control group. The data obtained indicate the effectiveness of proposed treatment of neurotrophic plantar ulcers in leprosy patients and permit to recommend it for wide use.

PO 381

PLANTAR ULCERATION IN LEPROSY A NEW OUT-PATIENT APPROACH

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Plantar ulceration is the single most cause of the dehabilitation of leprosy patients. The underlying causes of sensory and motor loss and vascular deficiency have been well established.

Various methods such as provision of padded footwear, plaster of paris immobilization, surgical, e.g., curettage, metatarsectomy and post tibial nerve release have been reported. The fact that recurrent ulceration continues to pose problems in rehabilitation signifies the inappropriateness and ineffectiveness of these procedures under the prevailing circumstances.

The author has demonstrated remarkable improvement in the rehabilitation of patients with plantar ulceration by releasing the sheath of the posterior tibial neurovascular compartment in a single outpatient procedure requiring no hospitalization.

The results have shown remarkable improvement over the previously mentioned techniques over a follow-up period of over 1 year in 46 cases.

PO 382

ENHANCEMENT OF TURNOVER OF BONE MARROW-DERIVED MACROPHAGES IN THE GRANULOMAS OF EXPERIMENTAL LEPROMATOUS LEPROSY.

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Previous studies from our laboratory have demonstrated that although macrophages (MAC) isolated from the lepromatous foot pad (FP) granulomas of M. leprae (ML)-infected nu/nu mice share most phenotypic and functional characteristics with peritoneal MAC, because of their heavy intracellular burden of ML these foot pad MAC are refractory to activation by recombinant murine interferon gamma (IFN-g). Regardless of IFN-g dose, ML burdened foot pad MAC cannot be activated to an enhanced microbicidal capacity (Toxoplasma gondii), enhanced oxidative burst (superoxide anion) or increased Ia expression. The defect is localized since peritoneal MAC from the same nu/nu mice are fully responsive to IFN-g. Extrapolation of these findings to the localized skin lesions of LL in man suggests that any killing, breakdown and clearance of bacilli resulting from immunotherapeutic or chemotherapeutic measures must be accomplished by MAC newly arrived at the site.

Autoradiography studies are being carried out to define the rate of ^{3}H-thymidine labelled bone marrow-derived MAC turnover in the ML-infected FP and other anatomical compartments (blood monocytes, peritoneal MAC) of untreated nu/nu mice. Our present studies are also concerned with enhanced migration of bone marrow derived MAC into the lepromatous FP lesions following immunotherapy (multiple treatments with IFN-g) or chemotherapy (dietary rifampin). Interestingly, in preliminary studies, although there was no clear evidence for breakdown and clearance of ML in treated mice, FP MAC from IFN-g or rifampin treated mice were partially responsive to activation by IFN-g in vitro.

These data suggest that the defective MAC response to IFN-g in experimental lepromatous granulomas may be reversible by inducing an increase in the rate of turnover of new MAC into the lesion.

PO 383

SUCCESSFUL AND DEFECTIVE MACROPHAGE EFFECTOR FUNCTION IN EXPERIMENTAL LEPROSY.

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We have recently shown that mouse peritoneal macrophages (MAC) activated in vitro by pretreatment with recombinant murine interferon gamma (rMuIFN-g) have a deleterious effect on the metabolism of M. leprae as measured by synthesis of phenolic glycolipid-I and bacterial ATP content. These data suggest that the broad spectrum of microbicidal capacity characteristic of the activated macrophage may extend as well to the leprosy bacillus.

In contrast to this example of MAC success in coping with M. leprae, we have defined 3 conditions where M. leprae, or its constituents, may markedly depress host resistance by inhibiting the ability of IFN-g to activate infected MAC. First, MAC isolated from lepromatous granulomas of the M. leprae-infected nu/nu mouse appear phenotypically and functionally normal but cannot be activated by IFN-g as measured by enhanced microbicidal capacity (for Toxoplasma gondii), oxidative burst (superoxide anion) and expression of Ia on the MAC membrane. This defect is localized to the M. leprae-burdened foot pad macrophages as peritoneal MAC from the same nu/nu mice respond fully to IFN-g.

Secondly, defective MAC response to IFN-g can be induced in vitro by infection with live, but not killed M. leprae. This defective response is dose (30-50 bacteria/MAC) and time (3-5 days preincubation) dependent. Although the in vitro defective MAC response to IFN-g appears to be largely due to enhanced production of prostaglandin E_2 (PGE_2) and is reversible with indomethacin, defective MAC function from the nu/nu foot pad can not be reversed with indomethacin.

Thirdly, lipoarabinomannan (LAM), an abundant lipopolysaccharide found in the cell wall of Mycobacterium sp. and related genera, is a potent inhibitor of IFN-g-mediated activation of both mouse and human MAC. Mouse MAC treated with LAM derived from M. leprae or M. tuberculosis failed to respond to IFN-g with enhanced microbicidal capacity for T. gondii or tumoricidal activity. Likewise, treatment of human monocyte-derived macrophages (MdM) with LAM blocked the induction of enhanced microbicidal capacity by rMuIFN-g. PGE_2 production does not appear to be important. LAM treatments were not toxic and did not alter basal cell metabolism. Defective activation required pretreatment of MAC for 12-24 hours with the intact LAM molecule and was not evident using deacylated LAM. Studies with [^{125}-I] IFN-g showed that receptor function was normal in LAM-treated macrophages despite their unresponsiveness to IFN-g at doses 100x those which effectively activate normal MAC. Current experiments are aimed at defining the relevance of defective MAC response to IFN-g to the inability of the host to cope with M. leprae in lepromatous leprosy.

PO 384

KINETICS OF THE CELLULAR IMMUNE RESPONSE TO MYCOBACTERIAL ANTIGENS IN MICE IMMUNIZED WITH KILLED MYCOBACTERIA.

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Examination of in vitro lymphoproliferation of popliteal lymph node cells from Balb/c mice immunized with dead BCG, M. kansasii or M. leprae shows an initial peak at 4-7 days characterized by a high non-specific lymphoproliferation. The second peak becomes apparent by 21 days following immunization and is manifested as a strong antigen specific response. These findings are paralleled by in vitro IL-2 production. All antigens for immunization were emulsified with incomplete Freund adjuvant and injected into animals as subcutaneous injections in the foot pads. Phenotypic analysis of the lymph node cells shows that the early phase of the immune response is predominantly characterized by an absolute increase in both Thy1.2^{+}, L3T4^{+}, Lyt2^{-}, and Thy1.2^{+}, L3T4^{-}, Lyt2^{+} cells. The increase in the proportion of L3T4^{+} cells was, however, much higher than the increment in Lyt2^{+} cells with an L3T4^{+}:Lyt2^{+} ratio of >4. The percentage of either T-cell subset decreased during the first 14 days following immunization suggesting a higher increase in non-T cells over T cells during the early response to killed mycobacteria. The second phase of the immune response is associated with an increased proportion of L3T4^{+} cells over Lyt2^{+} cells. The proportion of L3T4^{+} cells, however, showed only a marginal increase over that seen in the early response, while there was a continued increase in the proportion of Lyt2^{+} cells giving an L3T4^{+}:Lyt2^{+} ratio of <2.

C3H/HeJ mice immunized with similar mycobacterial preparations develop a monophasic response peaking at day 21-28 following immunization. The in vitro lymphoproliferative responses of these mice appeared to be consistently lower than those of Balb/c mice when assessing the response to mycobacterial antigens. The responses to mitogens were, however, similar in both strains of mice. The lymph node cells from these animals were distributed more or less equally between the L3T4^{+} and the Lyt2^{+} phenotypes. These proportions were maintained for as long as 6-8 weeks after immunization.

The nature of the restrictions imposed by strain differences on the immune response to mycobacteria is still poorly understood. Our results suggest that analysis of the kinetics of the emergence of the cellular immune response may help in identifying strains that may be useful in vaccine development studies.

PO 385

THE EVOLUTION OF IGG AND IGM ANTIBODIES TO ANTIGENS OF MYCOBACTERIUM LEPRAE IN EXPERIMENTALLY INOCULATED ARMADILLOS.

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The nine-banded armadillo (Dasypus novemcinctus) is highly susceptible to infection with M. leprae and has become an important animal model in the study of leprosy. In an attempt to define the major immunogens of M. leprae and the isotypic antibody response to these molecules during infection, we analyzed the IgG and IgM antibody responses of experimentally infected armadillos to the supernatant fraction of sonicated M. leprae, lipoarabinomannan derived from M. tuberculosis, and phenolic glycolipid-1 using immunoblot and ELISA. Antibodies to the specific epitope (defined by monoclonal antibody IIIE9) on the 65-kDa protein of M. leprae were analyzed using a competitive antibody binding assay. Our results showed that protein antigens of M. leprae elicited a predominant IgG antibody response, whereas, carbohydrate antigens of M. leprae, including lipoarabinomannan, induced an IgM response. Phenolic glycolipid-1 elicited both IgG and IgM antibody responses. Some animals produced and maintained a strong IgG antibody response to phenolic glycolipid-1 which correlated with their ability to delay dissemination of the infection and with their ability to survive infection for longer periods of time. Antibodies to an M. leprae-specific epitope on the 65-kDa protein in crude cell wall extracts were detected during the later stage of infection in both "resistant" and "susceptible" animals. It is anticipated that antibody profiles to various M. leprae antigens may prove useful in monitoring the course and outcome of M. leprae-infected armadillos as well as establishing baseline information on the humoral immune response in armadillos during the course of untreated M. leprae infections.

PO 386

ANTIGEN PRESENTING CELLS IN GRANULOMAS INDUCED BY MYCOBACTERIUM LEPRAE IN GUINEA PIGS

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The injection of cobalt-irradiated Mycobacterium leprae intradermally into the ear of the guinea pig induces the formation in the draining lymph node of granulomas containing phagocytic macrophages. These cells are MHC Class II antigen positive and carry an antigen found on activated macrophages. Cells from the granulomatous lymph node proliferate in vitro in response to PPD. Macrophages separated from the granulomas using a monoclonal antibody to the macrophage antigen do not present PPD to sensitized T cells. The antigen presenting cells are present in the MHC Class II antigen positive population of the granulomatous lymph node cells and are enriched in the low density fraction on Percoll gradients. This fraction contains about 50% macrophages, 30% T cells and < 10% B cells. T cell and macrophage depletion had no effect on antigen presentation by this fraction. A monoclonal antibody to dendritic cells has been prepared and depletion of the low density fraction of Percoll gradients with this antibody completely abrogated antigen presentation. It appears that the main antigen presenting cell in the lymph nodes containing M. leprae induced granulomas is a low density dendritic cell which is strongly MHC Class II antigen positive.

PO 387

PATHOLOGY OF PERIPHERAL NERVE LESIONS IN INFECTED ARMADILLO WITH MYCO.LEPRAE

A LIGHT AND ELECTRON MICROSCOPIC STUDY

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The lesions of peripheral nerves in infected armadillo with Myco.leprae have been studied by light and electron microscope. We found some lesions in axons of nerve fibers which have not been reported in previous literature, including invasion of axons by Myco.leprae, various sizes of vesicle formation, rarefaction or condensation of neurofilaments, as well as the presence of myelin figures inside the axons. All these provide further understanding of the development and progression of nerve lesions in the armadillo and will be helpful in the study of the pathogenesis and development of lepromatous nerve lesions. Evidence for the spread of leprous lesions to the peripheral nerves is shown to be not only by the hematogenous route, but may also by the way of lymphatics involved in leprous lesions.

PO 388

LANGERHANS CELLS IN ARMADILLO SKIN
AN ELECTRON MICROSCOPIC OBSERVATION

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This study describes the distribution and the fine structure of Langerhans cells in the normal nine-banded armadillo epidermis. The emergence of the armadillo as a major animal model for leprosy, the identification of the langerhans cells as a component of the cell mediated immune system, and the description of changes in number and structure of langerhans cell in human leprosy make a study of langerhans cells in normal armadillo skin of fundamental importance. The present study shows that there are typical Langerhans cells in normal armadillo epidermis in all areas of skin sampled, i.e. abdomen, chin, ear and thigh, albeit in lower numbers than in human skin. The baseline findings are valuable for further studies on Langerhans cells and cell mediated immune function in armadillos with naturally acquired or experimentally infected leprosy.

PO 389

A MODEL OF BORDERLINE TUBERCULOID LEPROSY IN RATS.

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The possibility of obtaining a pathogenetic experimental leprosy was investigated. An attempt was made to infect rats with M.leprae with simultaneous 30-50% replacement of their blood with chemical blood substitutes containing perfluorocarbonic compounds. 13 rats were inoculated intravenously (i.v.) and 27 - intraperitoneally (i.p.). The inoculum was 10^6 - 4x 10^8 M.leprae per animal. In 12-18 months after inoculation the rats were microbiologically, morphologically and immunochemically studied. The bacteriological assessment of the internals showed the presence of M.leprae in 20 of 27 animals (70%) infected i.p. Lepromatoid granulomas were discovered in peritoneum of 7 rats of this group (28%). In peritoneal cavities of several animals the suppurated granulomas overloaded with acid-fast bacilli were found out. In all the other cases there were rare fragmented bacilli. Among i.v. infected rats in 12 (92%) single mycobacteria were present in the internal organs, in 9 rats (69%) granulomas were seen in lungs. Histological study of lesions showed epithelioid cell infiltrates with rare giant cells. Non-substituted control animals did not show any mycobacteria and granulomatous changes in their organs. The serological investigation of the infected rats demonstrated high titres of antibodies against granulomas and antigens of purified M.leprae. Mycobacteria isolated from lesions did not grow in the nutrient media. The data obtained suggest the development of the disease in rats similar to borderline tuberculoid leprosy in man.

PO 390

A COMPARATIVE CLINICAL STUDY OF PATIENTS UNDER MULTI DRUG THERAPY AND DDS MONOTHERAPY - 4 YEARS FOLLOW-UP.

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A prospective clinical study was started in the year 1980 to compare the efficacy of MDT over DDS monotherapy on multi bacillary patients. 79 patients were admitted for the study and were randomised into 3 groups namely A, B, C.

Group A received DDS 100 mg. daily

Group B received Cap.Ramp 600 mg. + DDS 100 mg. daily

Group C received Cap.Ramp 600 mg. + Tab. Isoprodian (DDS 50 mg. + INH 175 + Prothionamide 175 mg.)

Those patients found to be DDS resistant in mouse foot pad studies were treated separately. The duration of treatment was fixed as 3 years in all the groups and a follow-up period for 5 years. Now 61 patients are available for follow-up. The results of clinical, bacteriological, haemotological & histopathological assessments are discussed in this paper. No significant difference in therapeutic response between multi-drug and DDS monotherapy was noticed. A foot pad inoculation done one year after stopping treatment did not show growth in any of the regimens studied. No relapse encountered in any of the regimens in the 4 years of follow-up period after stopping treatment. 15 patients have completed 4½ years of follow-up period.

PO 391

APPLICABILITY OF ISOPRODIAN RMP (IN A 4 DRUG COMBINATION) UNDER "FIELD CONDITIONS" - A MULTI CENTRE STUDY IN INDIA:

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A total of 250 leprosy patients (MB and PB) were treated with Isoprodian RMP (a combination of four drugs) in nine leprosy centres in India.

Treatment phase: PB: 6 months, MB: 2 years.

Results will be presented with the main emphasis being on:

- compliance
- complications (side effects/reactions)
- skin smears
- other laboratory results.

Intensive follow up in the ongoing study is planned for a period of 5 years.

Special problems resulting from a multi centre study will be investigated.

PO 392

CLINICAL EXPERIENCE ON KOREAN LEPROSY PATIENTS WITH COMBINATION ISOPRODIAN AND RIFAMPICIN

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From September 1982 to August 1987, 97 cases of leprosy, new or previously treated cases were treated for a period of 6-60 months with 2 tablets of Isoprodian daily and 600mg of Rifampicin daily for the first 3 months,

followed by 600mg once-monthly. Marked to moderate clinically improvement was remarked in 68.3%(41 patients) after 6-24 months but 71.4%(56 patients) improved after 25-60 months. The conversion rate of bacteriologically positive to negative was 75.8% after 6-24 months but 79.2% after 25-60 montns, revealing that as the treatment lengthened, the conversion rate increased. No serious adverse effects and no relapses occurred.
Isoprodian seems suitable as an anti-leprosy drug for out-patient treatment of light skinned people.

PO 393

PROFILE OF MULTIDRUG THERAPY IN MULTIBACILLARY LEPROSY CASES IN AN URBAN CONTROL PROJECT IN INDIA.

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A prospective study has been undertaken to evaluate the effectiveness of four different regimens for MB leprosy cases in an urban leprosy control set up.
Of the 531 MB cases in the project area, 381 were included in the study which bagan in 1981 and is still in progress. The cases were randomly allocated to one of the following regimens:

I - 21 days of intensive daily Rifampicin, Clofazimine, Dapsone followed by daily CLOF, DDS + monthly RMP.
II - Daily CLOF, DDS + monthly RMP.
III - Daily Isoprodian + monthly RMP.
IV - Various older MDT regimens using RMP, CLOF, DDS.

All RMP doses were supervised. The 381 cases were investigated as follows:

1. Clinical profile, blood profile including Hb, LFT, TC, DC, Platelets, complete urine examination at initiation, every six months and at the time of Release From Therapy.
2. Skin smears at initiation, every 3 months and at RFT.
3. X-Ray Chest, VMT and stools for parsites at initiation and at RFT.

The paper analyses in detail the changes in the clinical, bacteriological and blood profiles, complications during treatment, relapses during surveillance, besides discussing the merits and demerits of the four regimens used.

PO 394

THE APPLICABILITY OF ETHIONAMIDE IN VARIOUS CLINIC FORMS OF LEPROSY, IN COMBINED CHEMOTHERAPY.

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MDT was introduced in Brasilia, in July 1983, to study operational aspects and its implementation.

113 patients were treated with the MDT regimen from July 1983 to September 1986. In 34 of these patients we substituted Clofazimine or Dapsone for Ethionamide, in the dose of 5 to 10mg per Kg bodyweight per day.

We checked our patients for blood counts, urine tests, and biochemical study, monthly for the first 6 months and then every two months.

We have 5 patients excluded. Two of them abandoned treatment for unknown reasons and 3 presented nausea and vomitting.

We have not found any alteration in 29 remaining patients treated.

PO 395

IMPLEMENTATION OF MULTIPLE DRUG THERAPY (MDT) IN THE NATIONAL PROGRAMME OF TANZANIA.

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In 1977 the National Tuberculosis and Leprosy Programme of Tanzania was launched, aiming at controlling the two diseases as an integrated programme, nation wide, using the same manpower and Health services, within the National Health structure. The programme is managed at 3 levels: 1)Min.of Health;3 medical officers,2)at regional level;20 MOs and 3)at district level;102 medical assistants. The case detection remained stable during the last 6 years at around 3000 patients per year,which is 15-16 per 100.000 of the population.The number of registered patients dropped from more than 50000 in 1979 to around 14.000 in 1987. In 1983 the Ministry started MDT,using the drug combination of Isoprodian and Rifampicin. Different MDT regimens were adopted,depending on classification and Skin Smear results.Rifampicin should be given under strict supervision. PB patients are treated for 6 months,whilst MB patients are treated for 24 months. In principle a step by step method was followed to implement MDT district after district.Registered patients were reassessed and medical personnel were invited for seminars.Cohort analyses show treatment results of 6034 PB and 1409 MB patients. Results are improving over the years. The avarage succes rates for PB and MB patients are 81% and 62% respectively. The proportion absconders for PB patients (8%) is half that for MB patients (16%). The reduction of the patient load provides the medical worker with more time to improve the service. It can be assumed that MDT attracts patients. Better treatment is the best propaganda in the villages, for bringing new patients to regular and early treatment

PO 396

MDT with Isoprodian-RMP (Experiences in 2000 patients as regards the practicability, compliance, duration and termination of treatment, alternative drugs and their evaluation; eradication by chemotherapy).

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The procedure used in the model trials in Malta and in Paraguay will be discussed in regard to its organizational and economic conditions and the therapeutic technique employed.

Already in the course of pilot clinical studies based on experimental laboratory results it became obvious that the patients were overtaxed if treated on the ambulatory basis with the drugs of the combination used (rifampicin + isoniazid + prothionamide + dapson) separately. It was necessary to administer fixed combinations. The advantages of such a fixed combination as regards practicability, acceptability, compliance and the resulting improvement of the overall therapeutic effect will be demonstrated.

The present status of experiences gained with new combinations including quinolones and sulfonamides and their evaluation will be shown, including the efforts to replace thalidomide by other immunosuppressive agents.

Eradication by chemotherapy (not as elimination of the bacteria from the organism of the patient but as the elimination of the endemic from the society) will be discussed as viewed from the experiences with the model trials performed in Malta and in Paraguay.

PO 397

FURTHER EXPERIENCE WITH ISOPRODIAN IN TANZANIA

H J CHUM, M R A van CLEEFF & M I GUNZARETH

Tanzania has adopted Isoprodian and rifampicin in its Multiple Drug Therapy (MDT) for Leprosy patients. The drug has been

tolerated in many regions, some serious side effects have been noted in a few patients. The paper discusses the follow up of over 200 patients (prospectively) from various regions and reports on the findings and probable implications of the drug regimen in the MDT.

PO 398

ESTADO ACTUAL DEL PROGRAMA DE LEPRA Y TUBERCULOSIS EN PARAGUAY

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Departemento de lepra-ministerio de salud publica y bienestar social asuncion-paraguay.

El programa de lucha anti-leprosa con ISOPRODIAN-RMP se está desarrollando desde octubre de 1979. La eficacia y tolerancia del Isoprodian-RMP ya han sido largamente demostradas, tanto en el Proyecto Malta como en el de Paraguay, informados al Congreso de Dehli (1984) y al IX Congreso Mundial en Enfermedades infecciosas y parasitarias (Munich, 1986). Actualemente se desarrolla en 31 centros de atención en Paraguay reemplazándose paulatinamente la monoterapia sulfónica. Hasta diciembre 1987 la situación era:
- Altas por curación (más de 3 anos de control post-tratamiento): 571 casos; bajo tratamiento: 1.144;
en control post-tratamiento: 1.090;
todavía con sulfonoterapia: 1.729
Tasa de abandono de tratamiento: 3,4%
El programa de lucha anti-tuberculosa comenzó en 1979. Con Isoprodian- RMP el tratamiento dura 3 a 5 meses. Además del Ministerio de Salud, partiipan otros organismos públicos y privados.
La tasa de morbilidad se ha modificado poco, con altibajos. lo cual se debería a la reciente cobertura total del país. La tasa de mortalidad muestra sostenido descenso: 13 x 100.000 en 1979 á 5 x 100.000 en 1987. En los 9 anos se detectaron 8.707 casos de los cuales curaron 4.607, abandonaron 265 (17,5%) y fallecieron 22 (1,5%). Tasa de recaidas:3%.

PO 399

Reactions in Leprosy : A Prospective Study

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The clinical manifestations of type I (lepra) and type II (ENL) reaction are now well appreciated. The correlation of clinical expression to bacterial index, lepromin response and histological features has already been attempted. In the present study of 35 reaction patients, comprising 18 type I (lepra) and 17 type II (ENL), the preceding parameters were studied in details. Their incidence amongst leprosy patients was 20 per cent. The males in the age group 20-30 years were frequently affected, the ratio of males to females being 6:1. The mean age at onset in type II (ENL) was younger as compared to type I (lepra) reaction. However, the duration of reaction was variable. They were frequently precipitated by antileprosy drugs. The clinical features were cardinal. The bacteriological features reflected wide variations, but were considered imperative. Early Fernandez and late Mitsuda reactions were useful adjuvants for monitoring their progress. The imperatives of changing microscopic pathology in determining the swing towards lepromatous or tuberculoid end of leprosy spectrum are emphasized.

PO 400

LATE REVERSAL REACTIONS AFTER TREATMENT OF MULTIBACILLARY LEPROSY.

Stefaan R. Pattyn, J. Bourland, G. Groenen, L. Jansens.
Leprosy Laboratory, Institute Tropical Medecine, Antwerpen, Belgium.

Among 864 multibacillary patients treated with combined regimens for periods from 52 to 26 and 13 weeks and containing rifampicin, a thioamide and dapsone or clofazimine, 22 cases (2.5%) of late reversal reactions were observed. They appeared between 35 and 63 months after the end of therapy, mean 50 months, median 52 months. The main clinical features are reappearance and/or swelling of old lesions, appearance of active looking new lesions, sometimes painful. Bacteriological examination shows no increase of BI, which is most frequently negative. Histopathological examination reveals epithelioid cell granulomas, BI=0 or more rarely influx of numerous lymphocytes.
It is important to differentiate these late reversal reactions from relapses, through bacteriological and histopathological examinations.

PO 401

REACTIONS DURING SHORT COURSE INTENSIVE TREATMENT OF MB LEPROSY.

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Reactional episodes among 376 MB patients treated with a regimen of 13 weeks duration and composed of RMP 600 mg 2/7, ETH 500 mg 7/7, DDS 02 CLO 50 mg 7/7 were analysed. Type 1 reactions (T1R) occurred among 43% of patients, ENL among 12%. Younger patients developed more ENL than older ones. For T1R the incubation time (from start of treatment) was shorter than for ENL. T1R and ENL occurred more frequently in patients with higher BI. Duration of reactional episodes varied widely : 1-24 weeks for T1R (mean 8.3 median 8w) 1-36 weeks for ENL (mean 7.1 median 5) Neuritis occurred in 34% of T1R, and in 11% of ENL. Half of T1R and 63% of ENL were considered slight (based on symptoms and duration of treatment). Full details will be presented.

PO 402

Reaction in Leprosy

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We analysed redrospectively the department records of 48 patiens with lepra reaction,Who admitted to Atatürk University Hospital between 1968-1987.The clinical diagnosis was confirmed by bacteriological and histological findings. Our series comprised of 38 males and 10 females with a mean age of 42.41. In 30 of our patients(62.5%)type 1 reaction(reversal or dowgrading)was observed.Type 2 reaction(Erythema Nodosum Leprosum)was recorded in 18 patients(37.5%).These patients could be placed in two groups with respect course:mild ENL(13patients)and severe ENL(5 patients). The relationships between reaction types and the symptomatology will be discussed.

PO 403

A STANDARDIZED SCHEME FOR STEROID TREATMENT IN REVERSAL REACTIONS

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This presentation is based on a clinical study covering more than 100 patients studied during 16 years in Zambia and Souh Africa.
For patients with Reversal Reactions, the author arrived at a standardized scheme of steroid treatment (below) given together with Clofazimine (300 mg weekly) as the anti-leprosy drug of choice.
In the presentation, photographs will be shown of patients before and after such treatment.

Scheme of steroid (prednisone) treatment:
1st day: 30 mg - 2nd day: 27.5 mg - 3rd day: 25 mg -

4th day: 22.5 mg - 5th day: 20 mg - 6th day: 17.5 mg
7th day: 15 mg. Next, 15 mg daily for four weeks. It should be emphasized that from then onwards, one should reduce prednisone with 2.5 mg every four weeks. The ensuing scheme ,thus, will be:
12.5 mg daily for 4 weeks - 10 mg daily for 4 weeks
7.5 mg daily for 4 weeks - 5 mg daily for 4 weeks -
2.5 daily for 4 weeks -
2.5 mg daily every other day for 4 weeks -
2.5 mg twice a week every 4 weeks -
2.5 mg once a week for 4 weeks. Then, discontinue prednisone treatment and continue with Clofazimine only.

This standardized treatment has already been succesfull in isolated aereas by experienced leprosy fieldworkers, thus preventing unneccesary additional nerve damage by a delay in transport of the patient to a leprosarium.

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PO 404

LATE ONSET OF A REVERSAL REACTION IN BORDERLINE LEPROSY

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Reversal or upgrading reaction usually happens during the 3 or 12 first months of antibacillary treatment. However, previous reports have noted that borderline lepromatous patients (BL) may develop reversal reactions over a much longer period but a delay longer than two years is unusual.

We report the case of a cambodian young male initially (1980) classified as borderline lepromatous with positive bacteriological and morphological index and a negative lepromin-test. After three years of a correct daily multi drug therapy by Rifampin (600 mg), Clofazimine (100 mg), and Ethioamide (250 mg) ; the patient was clinically healed and bacteriologically negativate. In 1983, he stopped treatment and medical visits. In 1986, he returned for an acute reappearance of cutaneous lesions. On clinical examination the lesions exhibited the same location and the same morphological aspect than in 1980 excepted for a superficial desquamation and well-defined tuberculoid margins. The bacteriological examination was negative and the lepromin 'test was positive. So, the diagnosis has been made of a reversal reaction occuring five years after the onset of treatment and 2 years after clinical and bacteriological healing. The patient received steroids and anti-bacillary therapy and rapidly improved.

This case typically raises the main diagnosis problem that may occur between reversal reaction and relapse.

PO 405

COMPARISON OF COLCHICINE AND ASPIRIN IN THE TREATMENT OF TYPE 2 LEPRA REACTION.

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34 episodes of of acute Type 2 reaction in patients with lepromatous leprosy was treated with colchicine (1.5 mg/day x 4) and the response was compared with a similar number of episodes treated with aspirin (1.8 g/ day x 4). Both drugs were found equally effective in mild degree reaction, where as colchicine gave marginally better result in moderate degree reaction. Neither of the drugs was found useful in severe degree reaction. A better efficacy of colchicine was observed in the management of joint and nerve pain associated with Type 2 reaction. Minor side effects like diarrhoea, nausea and vomit ing were noted in only one patient while under colchicine therapy.

PO 406

ASSOCIATION OF TUBERCULOSIS IN 10,000 LEPROSY PATIENTS

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Maharashtra Lokahita Seva Mandal is a voluntary organisation working for Leprosy and Tuberculosis control in a part of Bombay. It has over 10,000 cases of leprosy and 6,000 cases of tuberculosis registered. The paper discusses:

1) Incidence of Tuberculosis in leprosy patients.
2) Occurance of tuberculosis after patients have been put on steroid therapy for reactions and neuritis.
3) Tuberculosis as a cause of recurrent reactions in leprosy.
4) Anti-tuberculosis treatment altering the course of management in leprosy.
5) INH & its problem in cases of leprosy and tuberculosis control.

PO 407

Sudden Paralysis Associated with Multi-Drug Therapy - a Cautionary Tale.

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The use of Multi-Drug Therapy (MDT) was first implemented in 1984. Since then over 2,000 leprosy patients have been treated with MDT. During this time careful attention has been paid to new nerve damage and a series of 87 cases with new, sudden paralysis have been identified. 67.8% of these cases were associated with acute neuritis and 32.2% were silent. 16.5% of the 376 multi-bacillary cases treated developed paralysis compared to only 1.4% of pauci-bacillary cases.

A detailed analysis of the 87 cases has been carried out looking at the number of doses of MDT after which paralysis developed, the muscles affected as well as the recovery time and the order of recovery. All the cases were actively treated with a standard regimen of oral steroids, physiotherapy and leprosy chemotherapy. Paralysis was noted to occur from the first week of chemotherapy up to 2 years in smear negative multi-bacillary leprosy.

New paralysis, both silent and with acute neuritis, is an important complication associated with MDT. It is largely a problem of multi-bacillary leprosy and can occur at any time during treatment. It is essential that these cases are detected early and treated vigorously to prevent permanent nerve damage.

PO 408

PARALYSIS OF THORACIC ESOPHAGUS IN TYPE 1 LEPROSY REACTION REPORT OF ONE CASE

Zhou Daohai, Chen Jiakun and Feng Jianqiang, Zunyi Hospital,Shanghai,China

One male patient with borderline leprosy type 1 reversal reaction had involvement of rami esophagei nervi vagi. The upper part of the thoracic esophagus was paralysed. The patient had chief complaints of nausea and vomiting after taking food and drinking water. Esophageal barium meal examination showed that the barium stagnated in the upper thoracic esophagus. The upper part of esophagus was obviously enlarged. Peristalsis of the esophagus had disappeared.

The patient was treated with corticosteroid, the symptoms disappeared and the peristaltic function of the esophagus was recovered.

The esophageal paralysis due to leprosy reaction should be differentiated from Presby esophagitis, reflux esophagitis, scleroderma esophagus, achalasis of the esophagus and Barrett esophagus, etc.

By history, esophageal barium meal examination, clinical symptoms and signs, esophageal paralysis due to leprosy reaction can be easily distinguished from other diseases of the esophagus.

PO 409

Early leprosy lesions - Presentation and Progress

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For successful containment of leprosy early diagnosis is utmost essential. With increasing awareness of the population about early signs and symptoms of leprosy, the number of such cases presenting for diagnosis and treatment is bound to swell up in coming years.

Present study is based on analysis of records of such cases who presented themselves at JALMA with sensory symptoms. These cases were observed regularly. Later on some of these manifested two or more cardinal signs of leprosy. A percentage of such cases developed neuritic leprosy. A number of these neuritic cases further progressed to a clinical borderline disease.

Since many a times a serological diagnosis of leprosy is difficult, these positive neurological manifestations tell their own significance. This paper describes the evolution of leprosy lesions and discusses the place of neuritic leprosy in spectrum of the disease. A new model for evolution of leprosy lesions has been suggested.

PO 410

VALIDATION OF SINGLE MACULE IN PAUCIBACILLARY LEPROSY AS AN INDICATOR OF EARLY DIAGNOSIS AND OF PROGNOSIS

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The number of macules is usually registered at diagnosis, in the first clinical exam of leprosy patients. The question studied here is whether this practice is of any interest as an indication of the precocity of detection or the prognosis.

From 1955 to 1982, 47068 patients were registered in Polambakkam Leprosy Centre (South India). Of these cases, 31065 are included here, that is the paucibacillary patients for whom the number of macules is assessed and registered.

Except for the first two years where a lot of missing values regarding macule status were found, the trend of the proportion of single macule patients per year was similar to the trend observed for the proportion of patients without disability.

The relationship between age at detection and number of macules has also been analyzed.

To see whether the number of macules at detection could be used as a prognosis indicator, duration of treatment before inactivation and relapse rate are compared between patients with single and with several macules.

PO 411

AN ATTEMPT TO DEFINE INDETERMINATE LEPROSY.

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To define what is indeterminate leprosy we randomly selected 26 patients presenting with hypopigmented lesions from our leprosy clinic. They were further grouped into 3 sub groups. Gr.I had patients with well defined single patch with moderate to complete sensory loss. In Gr. II patients had single lesion but ill defined border and partial sensory loss, whereas Gr. III had patients with multiple illdefined lesions and doubtful sensory loss. All these patients were subjected to clinical charting, histological examination and lepromin test. Epidermal atrophy was common finding in all the groups. Presence of granuloma formation and nerve involvement was seen only in Gr.I , whereas in Gr.II and III only linear infiltrate in upper dermis and periappendicular region was seen. In none of our cases we could see changes suggesting dermatitic process. Our findings strongly suggest that patches which are well defined and present granuloma formation should be excluded from indeterminate group and should be labelled as maculoanesthetic or macular tuberculoid. To label a case as indeterminate, apart from clinical presentation there should epidermal atrophy and perineural and periadenexal lymphocytic infiltration.

PO 412

DEVELOPMENT OF A PORTABLE TESTER FOR TESTING THERMAL SENSATION FOR USE IN THE DIAGNOSIS OF LEPROSY

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European Organization for Nuclear Research (CERN) and Leprosy Unit, World Health Organization (WHO), Geneva

In the diagnosis of early leprosy testing for several modalities of sensation is more advantageous than testing for just one modality. As regards testing for thermal sensation, there is a definite need for an appropriate and simple device, particularly for use in the field. WHO, in collaboration with CERN, has been able to develop such a device.

A small portable robust instrument, similar in appearance to a pen light and which is ready for use within seconds, has been developed. The final version, which emerged after field-testing several versions, has a probe head diameter of 7 mm and operates on two type AA pen light batteries of 1.5 volts or two rechargeable batteries of 1.2 volts allowing several hours of continuous testing. The electronics, using a specially developed semi-conducter component, control the probe head temperature according to varying ambient temperatures. For instance, at an ambient temperature of 35°C the probe head is capable of reaching 45 to 50°C.

Field testing of the current and earlier versions of the thermal tester has shown that the addition of thermal sensory testing increases the ability to diagnose early leprosy. In a proportion of early lesions the only modality of sensation lost was thermal. The instrument has been found sturdy enough for use in the field.

PO 413

THE SIGNIFICANCE AND USEFULNESS OF VOLUNTARY MUSCLE TESTING IN LEPROSY CONTROL.

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Voluntary Muscle Testing (VMT) was performed routinely and graded according to the Medical Research Council (MRC) grading in the leprosy patients registered at the Dhoolpet Leprosy Research Centre. Among the 2122 patients reistered from 1982-87 recent nerve damage was detected in 335 cases. This involved a total of 611 nerves. The details will be discussed. In the case of Ulnar nerve, two muscles were tested and the VMT's added to get the 'Nerve Score' (Maximum 10). In the case of Median nerve where only one muscle was tested, the VMT was doubled to get the Nerve Score. This principle was also applied to other nerves tested. Majority of the cases (44%) had a nerve score ranging from 6-9 at the time of detection, which means that they would have been missed by otrer simple tests for field use such as those which advocate tests like positioning of hands in Dancing position (to detect Ulnar/Median/Radial Paralysis), lifting the foot (for Lat.Popleteal paralysis). These tests may fail to detect patients with muscle power of V.M.T.3 and 4.

Hence, the study indicates the urgent need to incorporate VMT as a routine test in all patients of Leprosy in order that we may detect early, treat adequately and follow-up recent nerve damage.

PO 414

POST-KALA-AZAR DERMAL LEISHMANIASIS (PKDL) SIMULATING LEPROSY - A CASE REPORT

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Leishamaniasis is reported from all continents except Australia. It is endemic in some parts of India and Africa. However, review of literature revealed very few case reports of PKDL simulating leprosy.

A 45 year female presented with skin lesions of ten years duration. She was partially treated for kala-azar 15 years ago in Patna, Bihar a state hyperendemic for this disease. After she migrated to Maharashtra State she was treated as a case of leprosy for three years before she reported to us.

She had bilateral asymmetrical well defined hypopigmented patches with normal sensation. Erythematous plaques and nodules were present on the face, hands elbows and ankles. Peripheral nerves were not thickened.

Skin smears for AFB were negative. Skin histology showed dense macrophage granuloma. LD bodies were demonstrated by Giemsa stain. Bone marrow aspirate cultured on NNN media showed growth of amastigote form of L.donovani. Patient improved with Intramuscular Sodium 20 mg/kg/day for 30 days.

The outstanding feature of this case was the very striking resemblance of lesions to BB/BL for which the patient received Rifampicin 600 mg daily for one year and DDS 100 mg for as long as three years from a dermatologist and response to antimonials was equally striking.

PO 415

The importance of differential diagnosis in leprosy.

José Luiz de Oliveira Cortes, Maria del Pilar Biot and Dominic Knorpel
Centro de Saude Washington Luis Lopes, São Gonçalo, Rio de Janeiro, Brasil.

The authors will present two cases of Granuloma Annulares, one case being disseminated and the other limited to the right forearm and hand, both of which were initially diagnosed as Tuberculoid Leprosy. In the disseminated case the clinical hypothesis of Tuberculoid Leprosy was corroborated by a histological diagnosis with the same conclusion. The two cases were sent to us to begin specific treatment.

In presenting these two cases, the authors hope to reaffirm the importance of the differential diagnosis in the day to day practise of Hansenology.

PO 416

Difficultes du diagnostic differenciel de la lepre sur la peau noire

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Les auteurs présentent sur les diapositives les difficultés rencontrées dans le diagnostic différenciel des manifestations cliniques des lésions cutanées de la lèpre et des autres dermatoses sur la peau noire au Zaïre

PO 417

QUELLE POLYCHIMIOTHERAPIE POUR LES FORMES INDETERMINEES ? A PROPOS D'UNE OBSERVATION SOULIGNANT L'INSUFFISANCE D'UN CLASSEMENT FONDE SUR LE SEUL EXAMEN BACTERIOLOGIQUE.

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Observation d'une patiente présentant des lésions cutanées de type Indéterminé, confirmées histologiquement, avec IB négatif et test de Mitsuda négatif. 7 mois après la fin du traitement OMS pour paucibacillaires, elle présente une récidive avec lésions cutanées de type Indéterminé confirmé histologiquement, avec IB négatif et Mitsuda douteux. Cependant, alors qu'elle présentait une névrite 2 mois après le début du traitement initial, cette patiente a subi une neurolyse à l'occasion de laquelle l'examen histologique d'un fragment d'épinèvre révèle une image de type lépromateux avec nombreux BAAR.

Plusieurs problèmes sont soulevés :
- La discordance (ou le décalage) pouvant exister entre les images histologiques des lésions cutanées et des lésions nerveuses.
- L'étiopathogénie des névrites isolées
- L'insuffisance du classement en paucibacillaire et multibacillaire fondé sur le seul examen bactériologique.
- L'avantage qu'il y aurait, au moins pour les formes I, à classer ces cas en fonction du test de Mitsuda facile à réaliser sur le terrain.

PO 418

STUDIES ON SKIN SMEAR EXAMINATION IN RELATION TO M.D.T. PROGRAMME.

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Skin smears examined end to end gave higher BI than routine. Some additional positives were detected. The bacilli were found to be distributed irregularly in the smear. The low BI smears required more thorough microscopic examination. The intra-observer variation was not significant. Many a time discrepancies were due to faulty techniques. Each step from smear preparation to reading must be standardized to make the cross-checking unambiguous and meaningful. A retrospective analysis showed that three smears instead of six is adequate for Programme. This may include one ear lobe and two active sites. The right and left ear lobes behave similarly. Taking smears from fore-head, chin, cheek and buttocks is not welcomed by the patients. The sites like thigh, arm and back were found to be equally good.

PO 419

Lucio's Leprosy

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Lucio's Leprosy is a variety of lepromatous leprosy, called "spoted" or "lazarine" by de la Pascua (1844), described with those names by Lucio and Alvarado (1852) and indentified by Latapí in 1936.

Clinical features: Skin generalized infiltration, suculent or atrophic, without nodules. Telangiectases on the face and chest, rosacea-like appearance of the face, milia cysts (advanced cases) and livedo of the limbs (early cases). Rinitis, saddle nose. Slow but total eyelashes, eyebrows and down hair alopecia. Panneuritis, impairment of sensation over whole body. Viceral lesions and a special kind of lepra reaction: "erythema necrotisans" with Lucio's phenomena, chills, high fever, insomnia...

Bacteriologically: Plenty bacilli not only in nasal mucosa but in any part of the skin. Histologically: Lepromatous infiltrates in small foci around vessels, nerves and appendages. Infiltrates are more dense in deep dermis and hypodermis. During lepra reaction: epidermal necrosis, intraepidermal bullae and ulceration. Vascularitis with thrombosis of small and medium caliber blood vessels, sorrounded by polynuclear foci with numerous bacilli. Immunologically: Lepromin reaction is always negative, but 4-6 hours after injection of 0.01 ml lepromin, the Lucio's phenomenon in its first

ıtages is reproduced. VDRL is positive in almost all cases.

Prognosis: It is the most serioud form of leprosy.

Treatment: Sulfones, rifampicin and clofazimine are more effective in these cases than in nodular ones.

PO 420

Classification of cases.

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The concept of leprosy is at present quite different from the former some years ago. To admit two "polar" types of the disease (Rabello Jr., 1938): Lepromatous and Tuberculoid, totally antagonistic, progressive and spontaneously incurable the first one, and progressive and naturally curable the second, no doubt, has contributed on it.

In spite of the advances that had been achieved in the last years, appropiate classification of cases continue to be an important aspect of leprology, since the disease understanding and the management of the patients depend on it. A brief historical review of the subject is done in this paper with special reference to the Havana and Madrid Classifications, this last one, accepted at the present as the international one.

Ridley and Jopling approach is taking into account, and it is emphasized that it does not nullify polarity conception as many assume, on the contrary, not only complements it, but also strengthen it. On the other hand is difficult to admit that all cases begin indeterminates as Ridley and Jopling affirm, because in that case infantile tuberculoid leprosy, and pure and primitive diffuse lepromatous leprosy would be out of the spectrum.

The author thinks that the two polar types: Lepromatous and Tuberculoid should remain, and also the indeterminate group, but she considers that too much importance has been given to the borderline cases. They are not as frequent as some people believe. They are always secondary to the indeterminate ones, and they are only an evolutive stage of the two polar types: Lepromatous and Tuberculoid.

PO 421

Sign of Differentiation between P.Alba and lesions of leprosy on the face in children.

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Study of 500 school children.

PO 422

COMBINED IMMUNO- AND CHEMOTHERAPY OF LEPROSY IN NUDE MICE

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In order to explore the effect of combined immuno- and chemotherapy, nude mice were infected by footpad inoculation and treated with rifampicin (RMP) and dapsone (DDS) in conjunction with once a week dose of 1000 U recombinant γ-interferon (γ-IFN). Period of treatment consisted of two months starting 30 days after infection until 90 days. Groups of animals were harvested each month starting on the 6th month until 15 months. Footpad counts were determined on the homogenates following staining by acid fast stain. DDS at both inhibitory (0.0001%) and ten times inhibitory (0.001%) levels failed to show synergy while used in conjunction with γ-IFN. RMP at subinhibitory dose failed to show any synergy but at 0.006% along with γ-IFN produced a highly significant growth delay in comparison with RMP alone at that level. These results will be discussed.

PO 423

REVISION DE NUESTRAS EXPERIENCIAS CON LA APLICACION DE OXIGENO HIPERBARO (OHB) EN LEPRA LEPROMATOSA (L.L.) -- ESTUDIO COMPARATIVO.

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Facultad de Medicina-Universidad de Buenos Aires

Los cambios observados luego del tratamiento con OHB senalan: a) Disminución del infiltrado; b) Reblandecimiento de lepromas; c) Aclaramiento de máculas y fenómenos involutivos de aspecto nodular pseudoxantomatoso ; d) Recuperación parcial de la sensibilidad y función sudorípara; e) Normalización de temperatura en extremidades; f) Tejido de granulación en las úlceras. Las modificaciones baciloscópicas en los diversos tipos evolutivos de L.L. evidenciaron alto porcentaje de negativización , francas alteraciones morfológicas y tintoriales. Los cambios histológicos ópticos y ultraestructurales fueron : a) Grandes estructuras vacuolares de aparente contenido lipídico, con restos de organelas citoplasmáticas z bacilares en deterioro; b) Proliferación fibrilar reticular y colágena; c) Reacción leucocitaria monoclear y polimorfonuclear. Pautas de coincidencia de los parámetros clínicos, baciloscópicos e histopatológicos.

PO 424

PLASMA RIFAMPICIN LEVELS IN MICE: A PRELIMINARY REPORT.

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Plasma rifampicin levels in CBA mice were determined by a microbiological assay (plate diffusion method) using a test strain of Staphylococcus aureus, sensitive only to rifampicin.

3 concentrations of rifampicin 0.01%, 0.003% & 0.001% were fed to 6 groups of 33 mice each either by gavage or by incorporation of drugs in diet. Rifampicin levels were assayed over a 24 hour period, and the values obtained were plotted to yield standard curves.

Drug levels were then assayed in mice inoculated with M. leprae obtained from biopsies of leprosy patients and fed 0.1%, 0.01%, 0.003% and 0.001% of rifampicin in diet.

Preliminary results suggest that when control mice show multiplication of M. leprae in foot-pads and when there is no multiplication in test mice at dietary concentrations of 0.003%, 0.01% and 0.1%, the plasma rifampicin concentrations are more than 0.06 ug/ml.

At the dietary concentration of 0.001% the plasma rifampicin concentration is between 0.02 ug/ml. and 0.04 ug/ml. However, at the 0.001% concentration, some isolates from patients show multiplication while others do not. The possibility that this inconsistent pattern of multiplication is due to strain variation of M. leprae is proposed.

PO 425

RESULTADOS DEL USODE OXICENO HIPERBARO (OHB) A LOS TREINTA DIAS DE SU APLICACION EN ENFERMOS CON LEPRA LEPROMATOSA Y CON TRATAMIENTO ESQUEMA O.M.S.

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Servicio Nacional de Lepra, Buenos Aires, Argentina

Con el objeto de reafirmar la acción del OHB en Lepra Lepromatosa, se realiya una experiencia "doble ciego" en 10 enfermos con tratamiento multidrogas (esquema OMS), evaluándose su histopatología y bacteriología a los treinta días, considerando que comunmente, los tratamientos antileprosos no provocan modificaciones detectables en dichos parámetros en tan breve período.

En uno de los grupos ("A", n=6) la anatomía patológica y la bacteriología mostraban resultados favorables , con excepción de un caso (escasa reducción del índice bacteriológico). Mientras que en el grupo "B" (n=4)no se observó cambio (excepto un paciente con reducción del índice bacteriológico).

La decodificación reveló que el grupo "A" había recibido OHB y el grupo "B", aire.

PO 426

PERIPHERAL NERVES IN EXPERIMENTAL IMMUNOTHERAPY

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New Delhi, India.

Though the clinical manifestations of leprosy become apparent on the skin, it remains a disease primarily of peripheral nerves and schwann cells. Ever since the leprosy and Mycobacterium leprae have been known, tremendous efforts are being made to study the peripheral nerves, yet the chain of events, precise pathogenesis of the nerve lesions and the nature of the neuropathy is not clearly understood. In the present paper an attempt is made to observe the effect of immunotherapy after a period of five months on the peripheral nerves in the mouse foot-pad model.

20 immunosuppressed mice (T/900r) with established leprosy infection and 10 thymectomized/irradiated mice without infection were transfused intravenously with syngeneic 10^6B and 2 X 10^6 T cells once a week for four weeks. No specific effect on the peripheral nerves could be observed. However, initially three months after the transfusion, the lymphocytes were found around the perineurium of the cutaneous and that in the sciatic nerve. Few degranulating mast cells were seen in the nerve. Details of the light and electron microscopic observations and the importance of the findings are discussed.

PO 427

THE DESIGN OF NOVEL ANTILEPROSY DRUGS AND TYROSINASE INHIBITORS AS NOVEL ANTILEPROSY DRUGS.

E.G. Beveridge[1], S.P. Hiremath[3], M. Hooper[1], R. Jagannathan[3], P.R. Mahadevan[3], M.G. Pruohit[2], S. Rajasekar[2], D. Varadkar[2] and S.K. Yeap-Morpeth[2].
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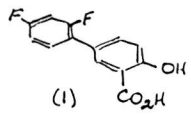
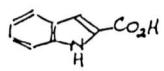
[2] Foundation for Medical Research, Worli, Bombay, India;
[3] Chemistry Department, University of Gulbarga, Gulbarga, India.

Previous studies[1] have identified diflunisal(1) and indole-2-carboxylic acid (2) as potential new anti-leprosy drugs. However initial tests in the mouse foot-pad were inconclusive. We have carried out further studies on these and related compounds including further in vitro and in vivo screening against M. leprae. The preliminary results are encouraging. Further in vivo data together with a more detailed structure-activity study will be presented.



(1)



(2)

1. M.Hooper, A. Bhagria, E.G. Beveridge, R. Jagannathan, P.R. Mahadevan and S.K. Yeap. O.C.S.I. Health Cooperation Papers, 1987 in press

P.R. Mahadevan, R. Jagannathan, A. Bhagria, S. Vejare and S. Agarwal, Lepr. Rev., 1986, 56 Suppl. 3, 1982.

E.G. Beveridge, J.S. Biradar, M. Hooper, J. Readitt and S.K. Yeap-Morpeth 4th SCI-RSC Medicinal Chemistry Symposium Sept 6-9th 1987, Cambridge, U.K.

PO 428

THE DEVELOPMENT OF DIAMINOPIMELIC ACID ANALOGUES AS BROAD SPECTRUM ANTIMYCOBACTERIAL AGENTS.

A. Haemers[1], D.C.M. Leysen[1], S.R. Pattyn[2], I. Van Assche[1], E.G. Beveridge[3], M. Hooper[3], and M.D. Yates[4].
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[2] Institute of Tropical Medicine and University of Antwerp, Antwerp;
[3] Tropical Diseases Chemotherapy Research Unit, Sunderland Polytechnic, Sunderland SR2 7EE, U.K.;
[4] Public Health Laboratory, Dulwich Hospital, East Dulwich Grove, London SE22 8QF U.K.

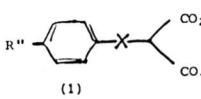
A series of novel diaminopimelic acid analogues have been designed as broad spectrum anti-mycobacterial agents. Some of the compounds are currently being screened in vitro against a wide range of mycobacteria in Antwerp and London. The design strategy, methods of synthesis and drug testing results will be reported. Active compounds identified in these tests will be prepared in sufficient quantities for testing against M. leprae in the mouse footpad.

PO 429

A STRUCTURE ACTIVITY STUDY OF SUCCINIC ACID DERIVATIVES AS NOVEL ANTI-TUBERCULAR AGENTS.

M. Hooper[1], S.N. Kulkarni[2], A.M. Salunke[2], M.D. Yates[3].
[1] Tropical Diseases Chemotherapy Research Unit, Sunderland Polytechnic, Sunderland SR2 7EE, U.K.;
[2] National Chemical Laboratories, Pune 400 018, India;
[3] Public Health Laboratory, Dulwich Hospital, East Dulwich Grove, London SE22 8QF, U.K.;

A series of substituted succinic acid derivatives (1) have been investigated for their anti-tubercular properties



(1)

R = OH, NH_2, NHR^1
R' = alkyl, aryl
R" = O-alkyl, Cl, NMe_2 NO_2, alkyl, Cl etc.
X = NH, S, SO_2

Initial results in the series (1) R = OH, R" as above, X = NH indicated that only the compounds in which R" = O-n-hexyl showed broad spectrum activity against a variety of fast and slow growing mycobacteria in an agar medium. The analysis of the activity of further series of compounds and the initial results will be reported.

PO 430

2,4-DIAMINO-5-BENZYLPYRIMIDINES AS INHIBITORS OF M.LEPRAE DIHYDROFOLATE REDUCTASE

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The inhibitory activity of commercially available DHFR-blockers like trimethoprim (TMP) which is highly active against gramnegative bacteria is dissappointingly low against grampositive strains.
In course of our studies to design inhibitors of mycobacterial DHFR using M.lufu-DHFR as a model for the M.leprae-DHFR we noticed that TMP - which is inactive in whole cell systems - is a potent inhibitor of the isolated DHFR enzyme. These results demonstrate two aspects:

1) The structures of DHFR could be quite similar
2) Different cell-walls might be responsible for the great difference in whole cell inhibition activity (MIC)

Knowing the 3-D-structure of E.coli-DHFR as a model and the results of Kuyper et al.(1) and including new techniques of computer graphics we tried to develop new inhibitors of mycobacterial DHFR. Several of these derivatives show a higher activity against the enzyme as compared with TMP and in addition could permeate the mycobacterial cell wall. The most active of these new compounds is the derivative K-130 (I_{50} = 0.034umol).

Reference (1):
L.Kuyper et al., J.Med.Chem. 25:1120(1982).

PO 431

A series of clofazimine analogues active against M. leprae in vitro and in vivo and active against a clofazimine-resistant M. smegmatis 607 in vitro.

J.F. O'Sullivan, M.L. Conalty and Joan Byrne, Health Research Board of Ireland Laboratories, Trinity College, Ireland.
N.E. Morrison, Johns Hopkins University, Baltimore, U.S.A.
(C.C. Shepard), R. Van Landingham, L.L. Walker and T.M. Shinnick, Centers for Disease Control, Atlanta, Georgia, U.S.A.

Clofazimine analogues active against a strain of Mycobacterium smegmatis 607 made resistant to the antileprosy agent have been synthesized. Activity (i.e., $\leq 2 \mu g/mL$ causing complete inhibition of growth) requires that there be a basic nitrogen in the "rimino" side chain and that the spacer distance between this nitrogen and the imino nitrogen be at least three carbon atoms.

The compounds have been shown to have growth inhibitory activity against human-derived M. leprae in murine macrophages in culture. In the mouse foodpad test a number of the agents showed activity against M. leprae, when fed to the animals at 0.01% in the diet.

PO 432

ANTIBACTERIAL ACTIVITY OF SEVERAL FLUOROQUINOLONES AND ANSAMYCINS ON MYCOBACTERIUM LEPRAE IN MICE.

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In the proportional bactericidal test (PBT) and based on amount of drug administered per body weight O-floxacin (OFL) administered 5 days a week (5/7) is more active than Pe-floxacin (PFL). Minimal effective doses (RED) are 50 and 100 mg/K respectively. PFL even at 300 mg/kb.w. is inactive when administered intermittently 3/7 or less frequently. OFL at 150 mg/K is active when administered 3/7 but not when administered with greater intermittency. The quinolone A 56619 is active when administered at 150 mg/K 5/7 but not 1/7. A 56620 is inactive even when given 5/7. The results on the "long acting" quinolone Fleroxacine will be presented as well as on some dihydrofolate reductase inhibitors.
The MED's of several ansamycins are as follows : (administered as a single dose on day 21) in mg/K : rifampicin 5, rifapentine : 0.62, rifabutine 0.62 SPA-S-565 10, FC 22250 0.62.

PO 433

CLINICAL TRIAL WITH DEOXYFRUCTOSEROTONIN [DFS] IN LEPROMATOUS LEPROSY.

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* CNRS, Paris, France. CRC, Harrow, U.K.
* Slade Hospital, Oxford, U.K.

DFS shows anti-leprosy activity in vitro and in mouse foot pad. It may have an immuno-potentiating and neuroprotective action. The first human trial was conducted as per the WHO THELEP protocol on 12 untreated lepromatous patients. While 8 patients showed significant improvement, marginal regression was observed in 2 and 2 failed to respond after 6 mths. of DFS monotherapy. In view of their remarkable overall improvement, 2 patients were continued on the drug for 1 year. No side effects of drug were observed in any patient with a dose of 10mg/kg wt. The trial conclusively indicates that DFS has definite anti leprosy activity as demonstrated by clinical, bacteriological, histological improvement and absence of growth in the mouse foot pad.

The paper discusses the findings of the trial and the possibility of incorporating DFS with immunosuppressive components of multidrug therapy like dapsone and rifampicin for faster bacterial clearance. It may also be used in the treatment of cases resistant to one or more drugs used presently in multidrug regimens.

PO 434

IN VITRO BIOSYNTHESIS OF PGL-I AS A RAPID TOOL FOR THE EVALUATION OF NEW DRUGS AGAINST LEPROSY.

Nalini Ramasesh, Eugene B. Harris, James L. Krahenbuhl and Robert C. Hastings. Gillis W. Long Hansen's Disease Center, Laboratory Research Branch, Carville, LA 70721, USA.

Mycobacterium leprae synthesize large quantities of a specific phthiocerol-containing phenolic glycolipid, (PGL-I), in vivo. Studies in our laboratory have established that viable M. leprae readily incorporate radiolabeled palmitic acid [^{14}C]PA into PGL-I when residing in cultured mouse peritoneal macrophages or in a cell-free, modified Dubos medium. This paper reports on the application of this observation for the in vitro screening of new drugs against M. leprae.

M. leprae maintained in the macrophage and cell-free systems were exposed to the drugs for 4 days, and then pulsed with [^{14}C]PA for 7 or 8 days. Using established procedures glycolipids were extracted and fractionated from the samples and the radioactivity associated with PGL-I was determined. The inhibitory effects on PGL-I synthesis of over 25 antimicrobials was established in both systems.

As determined by [^{14}C]PA incorporation into the PGL-I fraction there was decreased synthesis of the glycolipid in the presence of the antileprosy drugs dapsone, rifampin and clofazimine. Two analogs of clofazimine were also active. Among protein synthesis inhibitors, minocycline and erythromycin (including two analogs of the latter) showed activity. Interestingly, low concentrations of minocycline, ethionamide and tetracycline stimulated PGL-I synthesis in the cell-free system. Comparatively lower concentrations of most of the drugs were found effective in the macrophage system.

The compounds inhibiting PGL-I synthesis also have proven effective when compared to previous data reported in the mouse footpad system. This correlation lends support to the feasibility of using these in vitro systems which measure a specific marker metabolite of M. leprae for the rapid evaluation of new drugs against leprosy.

PO 435

TRAITEMENT IMMUNOMODULANT DE LA LEPRE LEPROMATEUSE PAR EXTRAITS DE RIBOSOMES MICROBIENS (RIBOMUNYL)

SAINT-ANDRE P., BAQUILLON G., DAVID M.

A l'Institut MARCHOUX de BAMAKO (MALI) 28 lépromateux volontaires nouvellement dépistés ont été traités pendant 18 mois par des fractions ribosomiales de germes bactériens (Klebsiella pneumoniae, Diplococcus pneumoniae, Streptococcus pyogenes groupeA, Hemophilus influenzae) associés à des protéoglycanes membranaires administrés par voie aérienne (aérosols) et parentérale (injections sous-cutanées hedbomadaires). Trimestriellement était pratiqué un contrôle: 1° Bactériologique (indice bactérien, index morphologique), 2° Anatomopathologique (examen histopathologique des biopsies cutanées), 3° Immunologique (intradermoréaction de Mitsuda, tests d'inhibition de la migration des leucocytes (T.I.M.L.) à la P.H.A. et à la lépromine). Les effets ont été rapides sur les rhinites (avant 3 mois) puis sur les signes cliniques cutanés et nerveux et les signes paracliniques : bactériologiques, histopathologiques.Sont survenus :
- 10 érythèmes noueux lépreux (ENL),incidence peu différentes de celle constatée chez d'autres lépromateux traités différemment,
- 5 réactions reverses, confirmant la récupération immunitaire.
Au total, l'efficacité de cette monothérapie se traduit par : - à 3 mois par la guérison des rhinites dans 100 % des cas
- à 6 mois chez 87 % des lépromateux par l'affaissement des lépromes et l'amélioration des examens bactériologiques cutanés
- à 12 mois par l'amélioration d'une part des névrites dans 80 % des cas d'autre part du TIML dans 45 % des cas.
Toutefois l'efficacité faiblit après 12 mois de traitement comme dans nos autres essais thérapeutiques d'immunomodulants.

PO 436

NEW INHIBITORS OF M.LEPRAE DIHYDROFOLATE REDUCTASE - IN VITRO AND IN VIVO RESULTS

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D-2061 Borstel, FRG, *Medical Research Institute. Institute of Technology, Flor. 32901, USA

New inhibitors of mycobacterial dihydrofolate reductase (DHFR) have been developed in our laboratories. They were tested in cell-free extracts of the cultivable mycobacterial strain M.lufu to test the interaction with the target enzyme. M.lufu shows similar sensitivities towards folate inhibitors as compared to M.leprae. The inhibition of whole cells was determined by MIC tests using various mycobacterial strains. The results show that benzylpyrimidines can be powerful inhibitors of mycobacterial DHFR but that in addition special structural requirements are necessary for cell-wall permeation which are not present in trimethoprim but in brodimoprim (BDP) and especially in K-130. These inhibitors show strong synergistic effects in combination with dapsone and other drugs. The in vitro results are in excellent agreement with those from mouse foot pad experiments. BDP stopped multiplication of M.leprae at a diet concentration of 0.1 % and in combination with dapsone (0.001 %) at 0.05 % BDP. After 4 months treatment with 0.03 % K-130 alone no viable M.leprae were detected. Relapse controls remain negative. Pharmacokinetic data of DDS and BDP alone and in combination in human are also presented.

PO 437

IN VITRO EFFECT OF THALIDOMIDE ON T-CELLS, T-SUPPRESSOR AND T-HELPER CELLS.

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As identified by fluorescein conjugated anti-Leu-3a monoclonal antibody (MAB), a significant reduction in Leu-3a-bearing helper/inducer (T_4) subset of T-cell population was noted in humans after 4 days of receiving 100 mg daily dose of thalidomide. The reduction was noted in both the percentage of T-helper/inducer population of T-cells, and their absolute numbers in vivo; no reduction was seen in either the percentage or in absolute numbers of T-cells as detected with Leu-1, anti-Pan T MAB. The possibility of steric hindrance of Leu-3a epitope of the helper/inducer (T_4) subset by thalidomide was investiagted in vitro.

One x 10^6 mononuclear cells in 500 ul of RPMI-1640 with 2% fetal calf serum (FCS) and 0.01% sodium azide was incubated with 10 ul of thalidomide dissolved in DMSO. The stock solution of thalidomide was prepared freshly and contained 1 mg of thalidomide in 10 ml DMSO. Mononuclear cells not treated with thalidomide received 10 ul DMSO. The cells were incubated at 37°C for 1 hr and washed two times using 2.0 ml of RPMI-1640 for each wash. The pelleted cells were resuspended and incubated with the manufacturer's recommended concentration of MAB. This was usually 1 ug/10^6 mononuclear cells. The final volume of the incubation media was 500 ul. The media was RPMI-1640 in 2% FCS and 0.01% sodium azide. After one hr incubation at room temperature, the cells were analyzed on a Coulter Fluorescent Activated cell counter EPICS 541. The percentage of fluorescent cells detected after reading 5 x 10^3 mononuclear cells did not differ significantly in the thalidomide treated group when compared to the group not receiving thalidomide. The intensity of fluorescence of the T-cells, T-suppressor and T-helper cells appeared to be similar; hence thalidomide in these in vitro conditions had no effect on their surface antigen profile.

PO 438

HETEROCYCLIC HYDRAZONES, INHIBITORS OF M.LEPRAE

K.-J.Schaper[1], A.M.Dhople[2], J.K.Seydel[1] and M.Kansy[1]

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Starting with 2-acylpyridinethiosemicarbazones a new class of highly active antimycobacterials (derivatives of 2-acylpyridine-2'-pyridyl-hydrazone, I) has been developed. These compounds are inhibitors of the bacterial ribonucleotide reductase and show strong synergistic potentiation of in vitro antimycobacterial activities when combined with other inhibitors of the DNA synthesis pathway. As drug development has been performed using leprosy model strains (M.lufu, M.smegm., M.marinum, M.tbc) the effect of several derivatives of (I) on M.leprae was tested in vitro by measuring their inhibitory activity on ATP production and ^{3}H-thymidine uptake of M.leprae.

The most promising compound of this step was synthesized in larger amounts and its inhibitory effect on the in vivo multiplication of M.leprae was tested in mice by mouse foot pad tests. At a concentration of 0.1 % in the food of mice I-26 significantly reduces the multiplication of M.leprae. Similar experiments were started with additional derivatives and with combinations of I-26 with compounds previously shown to be synergistic potentiators.

PO 439

A NEW GROUP OF CHEMICAL COMPOUNDS WITH ANTILEPROSY ACTIVITY.

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Leprosy Research Institute, Astrakhan, USSR.

Antileprosy activity of new chemical compounds belonging to the derivatives of polychlorocarbonic acid has been studied. Five compounds out of 17 showed a marked ability to suppress the multiplication of M.leprae in mice fed with the compounds studied. MEDs against M.leprae of the most effective derivatives of polychlorocarbonic acid equal 0,01% - 0,00005%. The kinetic method showed that after withdrawal of the compounds under study M.leprae multiplication in mice foot pads did not recommence, suggesting the bactericidal properties of the compounds. The dependence of the antibacterial effect and toxicity of the derivatives of polychlorocarbonic acid on their chemical structure was found out. Three compounds (laboratory codes 202, 203 and 205) proved to be the most suitable for therapy of leprosy patients. The possibility of using compound N 202 in a combination with dapsone was studied. The data obtained demonstrated satusfactory synergistic action of the compound and increased antibacterial effect of the combination. The prospects of developing a new antileprosy drug based on polychlorocarbonic acid are being discussed.

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

PO 440

ON DRUG REGULATION OF THE ACTIVITY OF OXIDATIVE-REDUCTION PROCESSES IN LEPROSY.

A.A.Rezaev
Leprosy Research Institute, Astrakhan, USSR.

The dynamics of metabolic changes under the influence of specific drugs might serve as a marker of the effectiveness of treatment of leprosy patients. In an experiment a more rapid resolution of lepromas was noted when the drugs activating aerobic processes had been administered. To improve the effectiveness of antileprosy therapy and to choose optimal drug combinations the effect of specific (solusulphone) and nonspecific (antihypoxants referred as PSH and TB-6) drugs on the activity of the enzymes involving in anaerobic and aerobic oxidative processes was studied. In homogenized lepromas from M.leprae-infected animals the activities of enzymes lactate dehydrogenase (LDH), glucoso-6-phosphate dehydrogenase (G-6-PDH), malate dehydrogenase (MDH) and succinate dehydrogenase (SDH), cytochrome oxidase (CO) and the levels of lactate and pyruvic acids were studied. The findings showed that solusulphone in a combination with PSH increased CO activity and decreased the level of G-6-PDH. Solusulphone administered together with TB-6 increased the activity of LDH. 3 months later the activity of the enzymes was decreased. The most pronounced therapeutical effect was noted when firstly aerobic processes were activated. The data obtained permit to recommend administration firstly the medicines intensifying aerobic metabolism and then the drugs activating anaerobic glycolysis.

PO 441

THE KILLING OF MYCOBACTERIUM LEPRAE IN MICE BY VARIOUS DIETARY CONCENTRATIONS OF THE FOUR PRINCIPAL ANTIMICROBIALS USED TO TREAT LEPROSY.

Robert Gelber, Lydia Murray, Mabel Tsang, and Patricia Siu
Kuzell Institute, San Francisco, California, U.S.A.

The killing of Mycobacterium leprae by various dietary concentrations of dapsone, rifampicin, clofazimine & ethionamide was assessed by the proportional bactericidal test. Dapsone 0.00001% & 0.0001% in mouse feed were not bactericidal, while dapsone 0.001% & 0.01% were both found 87% (± 22%) bactericidal. Concentrations of dapsone required for killing the strain of M. leprae were higher than had previously been found necessary for inhibition of bacterial multiplication (0.0001%). Rifampicin 0.01% & 0.005% in mouse food were found to be respectively 99.9% (± 0.1%) & 90% (± 6%) bactericidal. Rifampicin 0.003%, 0.001%, & 0.0003% did not result in significant killing. The strain studied was found to be killed by high dietary concentrations of rifampicin similar to that of previous studies but was far more resistant to killing by lower dietary concentrations of rifampicin than had been reported previously for other strains. The two highest concentrations of clofazimine studied, 0.01% & 0.003%, were respectively 99.6 ± 0.2% & 98 ± 1.0% bactericidal. Though less killing was afforded by 0.001% & 0.0001% clofazimine, even the latter concentration retained significant bactericidal activity (84 ± 10% bactericidal). The minimal bactericidal dietary concentration of ethionamide was found to be approximately 0.02% (68 ± 13% bactericidal). Higher concentrations of ethionamide, 0.05% & greater, were consistently more active, at least 95 ± 3% bactericidal. It is noteworthy in these studies that significant bactericidal activity of both clofazimine & ethionamide was retained at lower dietary concentrations than had been demonstrated previously. This is especially important as the undesired side effects of these agents are, at least in part, dose related. Because bactericidal therapy is key to effective short-course therapy of tuberculosis and likely leprosy, such studies are critical to our understanding of optimal chemotherapy of leprosy patients.

PO 442

The search for new antileprous compounds and their enhancement with immunostimulants in experimental leprosy with nude mice and nude rats

Sadae Tsutsumi and Masaichi Gidoh

A quinolone compound, Enoxacin, or an antimycobacterial compound, 2,2'-dithiobis(N-(4-butylphenyl-1-yl)benzamide) of Okachi, et al. failed to inhibit the growth of Hansen's bacilli (HB) inoculated in a dose of $3x10^6$ into both hind footpads (fps) of BALB/c (nu/nu) nude mice, even though dosed during a long period of 1 year at a content of 0.02% in diet. Whereas, all of the orally dosed compounds, antimalarial pyridyl thiosemicarbazone (Klayman), in vitro antimycobacterial 2-adamantyl benzimidazole (Kuźmierkiewicz), and an intramuscularly injected compound, 2-mercapto-3-hydrazinoquinoxaline (Tsutsumi) once every other day into both hind feet could delay the appearance of growth phase when dosed during the 9th-21st weeks after inoculation of $3x10^7$ HB/fp (dosage 10 mg/kg). The oral dose of an antitumor β-1,3-glucan, ATSO, or the intraperitoneal injection of an arthrogenous lipoidal amine, CP-46665 (CP, Pfizer Inc.) when combined with a low dosage of DDS in diet covering 1 year could somewhat enhance an inhibition due to DDS alone. In addition, a strain of mice, Jcl:AF (nu/nu) and (+/nu) from Japan Clea Co. established by the hybridization of male FNS/N (nu/nu) with female IAI (+/+) is being used for examining the enhancement due to the oral dose of ATSO, the intraperitoneal dose of muramyl dipeptide or CP once weekly (9th-32nd weeks) during and following DDS administration (9th-20th weeks). The results will be presented.
The counts of acid-fast bacilli found in fps of highly arthrogenous Australian DA rats after inoculation of 10^8 HB/fp were lower than those in F344 nude rats (inoculation 10^7 HB/fp). The development of an animal model which can induce ENL-like symptoms with the growth or acute destruction of HB is indispensable.

PO 443

SHORT TERM TRIAL ON THE ACTIVITY OF RIFAMPICIN AGAINST MYCOBACTERIUM LEPRAE.

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Institut Marchoux, Bamako, Mali.
Financial support of UNDP/WB/WHO Special Programme.

The objective was to measure the bactericidal activity of monthly doses of rifampicin (RMP) against Mycobacterium leprae in man. Twenty nine previously untreated lepromatous patients were randomized to receive 2 doses of either 600 mg (14 pts) or 1200 mg (15 pts) RMP at days 0 and 28. Bacilli from skin biopsies were inoculated into mouse foot pads on days 0, 7, 28 and 35 to determine the viability of the bacteria. The pretreatment biopsies were infective for more than 50% of the mice inoculated, in 11 pts receiving 600 mg and 10 patients receiving 1200 mg. All later biopsies were noninfective for mice except one at day 28 in a patient who took 600 mg of RMP.
It is concluded that monthly doses of 1200 and 600 mg RMP, the latter being part of the WHO treatment regimen, render M. leprae non infectious for mice within less than one week.

PO 444

PREVENTION ET TRAITEMENT DES MAUX PERFORANTS PLANTAIRES DANS LA STRATEGIE DE LUTTE CONTRE LES COMPLICATIONS DE LA LEPRE SUR LE TERRAIN

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Denis Daumerie, Pierre Bourrel

Unité Chirurgie, Institut Marchoux, Organisation de coordination et de coopération dans la lutte contre les Grandes Endémies. Bamako, Mali

Dans un premier temps, les problèmes médico-chirurgicaux et socio-économiques que posent les séquelles et complications de la Maladie de Hansen en Afrique de l'Ouest sont étudiés sur un plan clinique et statistique, puis les troubles trophiques habituellement rencontrés sont définis et classés, enfin suit l'étude des conditions de mise en place des moyens et méthodes proposés quant au traitement et à la prévention des maux perforants dans le cadre des soins de Santé Primaire.

PO 445

Wound Care and The Prevention of Injuries in The Hansen's Disease Patient.

Luanne Roberson, Michelle J. Freeman, and Donna E. Breger
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Disability in Hansen's disease has been greatly reduced by primary disease treatment and preventative education. Until the disease is stopped in the early stages before peripheral nerve involvement occurs, there is a great need for aggressive wound care and patient education to decrease the deformities and, therefore reduce the disabilities. The insensitivity and muscle imbalances caused when the nerve is permanently damaged can secondarily lead to deformities that identify the Hansen's disease patient and cause them to be socially stigmatized. The role of injuries and infections in this deforming process cannot be minimized. This paper discusses the treatment methods used in injury prevention and wound care at the Gillis W. Long Hansen's Disease Center. This includes agressive treatment of all wounds, fabrication of protective devices and patient education.

PO 446

Clinical Guidelines for the Establishment of a Management Program of Foot Problems in Hansen's Disease

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Wim Brandsma and All Africa Leprosy Research and Training Centre, Addis Ababa, Ethiopia

Often, in clinical situations, a patient's management of foot problems is supervised by different groups of health care providers simultaneously. To insure a coordinated treatment effort and to avoid conflicting therapies, general management guidelines should be established in each treatment center. For leprosy patients, these programs should also include an extensive and agressive system of injury prevention. Algorithms have been created to represent a scheme

of management of prevention and treatment of insensitive foot problems. These algorithms include risk categorization of uninjured patients, classification of soft tissue injury and management of neuropathic fractures.

PO 447

Footproblems in a mountaneous country like Nepal.

Wim J.Theuvenet, S.P.Ruchal, J.Daniels, P.K.Failbus.

Anandaban Leprosy Hospital, The Leprosy Mission Int, Nepal.

An analysis is presented of footproblems in leprosy patients in Nepal. New types of foot-wear are presented.

PO 448

MICROCOMPUTER BASED ANALYSIS OF FOOT PRESSURE IN ANAESTHETIC AND DEFORMED FEET OF LEPROSY PATIENTS

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This paper describes a microcomputer based analysis of foot pressures in anaesthetic and deformed feet of leprosy patients. In this method, light images of the foot print are obtained by breakdown of total internal reflection of light on a device called barograph. The intensities in the image are related to the pressures under the feet of a subject standing on the barograph. The image is digitized using a video digitizer and analysed for foot pressure pattern using software developed for the purpose. The pressure patterns are presented in the form of zonal grey scale, or three dimensional pattern along the length and breadth of each foot giving more details of minute pressure changes which could be useful for clinical and diagnostic use. The centre of foot pressure (CFP) for both the feet and regional CFP for each foot is displayed which could possibly be used for clinical and diagnostic use. The results show an even peak and average pressure distribution from lateral to medial part of the foot for normal subjects. The peak pressures observed in the case of normal subjects depend upon the subject's posture such as leaning towards a particular foot or a part of the foot, whereas the leprosy subjects develop high peak and average pressures on the foot with deformity or impaired motor function inspite of leaning towards normal foot. The microcomputer display of foot pressure patterns could possibly be used for identifying problem areas on the sole of the feet relating to impaired motor function.

PO 449

PROTECTIVE FOOTWEAR FOR PATIENTS IN THE FIELD

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The purpose of this presentation is to inform and inspire field personnel struggling to provide acceptable, protective footwear for large numbers of patients having sole sensory loss.

Many outpatients with insensitive but undeformed feet are at present without protective footwear. This is a tragedy as it puts them at unnecessary risk of foot injury. Their need is for protective footwear that is:
- locally available,
- standard sized, and
- in a style that is not distinguishable by the community as footwear for leprosy patients.

The following will be displayed:

1. Samples of protective footwear available for sale in different countries ... with buying details where available for export:
   1.1 Shop-bought footwear.
   1.2 Footwear made by town shoe-makers, provide with microcellular rubber.
   1.3 Footwear specially made at leprosy hospitals, or in factories ... but in standard sizes.
2. Samples of protective footwear from different countries that is not for sale, but that might be copied and/or modified for use in other situations.
3. Patterns and sewing instructions for standard-sized sandals ... with details as to where copies of the patterns can be obtained.
4. Samples of micro-cellular rubber from different sources, with prices and addresses of manufacturers.
5. Samples of useful articles and pamphlets relating to protective footwear.

PO 450

FIELD EXPERIENCE WITH PERSONALISED GRIP-AIDS FOR LEPROSY PATIENTS

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Community based rehabilitation programmes are developing in many countries of the world. In the future there will be potential for rehabilitation even in very rural areas by measures like the given Grip Aid Programme developed jointly between HEARU London and CIBA-GEIGY Ltd., Basle, designed for use by paramedics.

The challenge: Leprosy field workers have a full programme which necessitates concentration on curative work. Very individualised hand-grips or footwear are necessary in the management of patients with disabilities resulting from leprosy.

The results of the field studies underway in Ethiopia, India, England and Pakistan will be presented. The grip-aid material used in these studies is based on a two component epoxy putty and allows patients to mould their own made-to-measure grip-aids under medical and/or paramedical supervision. The principle aim of these studies is to determine the practicability of the use of grip-aids in patients with deformed hands. These grip-aids will be made available internationally by CIBA-GEIGY Ltd., Basle, in 1989.

PO 451

CARVABLE SILICONE PROTHESES FOR FIRST WEB IN THE HAND

Marcos Virmond & Frank Duerksen F.R.C.S.
Secretaria da Saúde do RS - Brazil / ALM

Muscular atrophy of the first web is a common finding following ulnar palsy in the hand and this deformity is stigmatizind specially among Hansen's diseased patients.

We present a technique for cosmetic restoration of the first web with an individual silicone implant carved out from a soft silicone bloc. The procedure includes an incision following the interdigital line of the first web and a pocket that is created by blunt dissection between the paralized adductor pollicis and the first dorsal interosseous. A piece of silicone is cutted out the main bloc and is carved in a fuse form shape The piece is introduced into the pocket wich is closed with fine nylon sutures. A plaster cast is apllied.

We discuss the procedure, results and its advantages compared to other techniques such as dermal grafts and testicular prostheses. We believe that this is an efficient method because it is cheap, ease to perform and have a low incidence of complications.

PO 452

USE OF PREFABRICATED SPLINTS FOR PREVENTION OF DEFORMITIES, AS PREOPERATIVE PHYSICAL AID AND AS POST RECONSTRUCTION THERAPY

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For the last two years we have been using prefabricated splints standardised by us. Application of prefabricated splints is easy and feasible even in the field work. Splintage help as temporary support during acute neuritis, during recovery while patient is on steriod therapy and following release of compression neuropathy by decompression of fibrous tunnels or alongwith epineurotomy. In established mobile deformity it strengthens the extensor expansion, provides assistance to lumbricales and prevents adductor contracture. In long standing cases it corrects the joint stiffness and strengthens the voluntary muscle power. Following reconstructive surgery splints are necessary till the transfered muscle tendon unit is able to perform properly and reeducation pattern is established. Different, standardised, prefabricated splints were provided to 150 patients. The method of making patterns of the minimum splints to be distributed by paramedical workers, indications and results of its applications will be demonstrated. This work was supported by research grant from LEPRA - England.

PO 453

LEPRE ET PROTHESE TIBIALE

François RIGAL Pierre VERSCHOORE

Quinze millions de lépreux sont répartis dans les régions déshéritées.

L'amputation chirurgicale tibiale reste fréquente et relève d'une prothétisation adaptée à cette pathologie et aux conditions socioéconomiques et climatiques des pays

Le Centre National d'Appareillage Orthopédique et l'Institut de Léprologie Appliquée de Dakar ont réalisé 35 prothèses tibiales en 1986 et 1987, répondant aux critères de qualité suivants :

- *Le prix de revient*
- *La résistance des matériaux*
- *La simplicité de la fabrication*
- *La légèreté, la simplicité d'entretien de l'appareillage.*
- *La facilité de mise en place de la prothèse par le patient*
- *Enfin l'esthétique de l'appareillage.*

Ainsi notre choix s'est porté sur l'utilisation de deux matériaux thermoplastiques à savoir : le Polypropylène et le PVC (carbonate de polyvinyl).

L'emboîture contact en polypropylène de type KBM est réalisée avec une plaque de 4 mm d'Epaisseur sur moulage plâtre rectifié.

L'axe tibial est un tube PVC renforcé. Cette prothèse tibiale peut être montée sur pilon ou sur un pied creux en polypropylène. Ce type de Prothèse tibiale, modulaire, bien tolérée répond aux besoins des lépreux.

Un film dont le résumé du commentaire est ci-joint, illustrera cette présentation.

PO 454

DELIVERY OF MDT THROUGH BLISTER CALENDER PACKS (BCP) IN LEPROSY ERADICATION PROGRAMME

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Delivery of MDT to leprosy patients through BCP is emerging with the objective of
(a) improving compliance of patients and programme
(b) facilitating drug delivery and supply
(c) self-monitoring of drug intake by patients
(d) increasing cost-effectiveness

Four DANIDA assisted districts under NLEP will administer MDT through BCP, manufactured by Pharmanova, Denmark, to an estimated 130,000 patients. Already 48,000 patients were given BCP till April, 1988.

Preliminary observation show that BCP is very popular with patients and staff who find them easy to handle in the field. The cost of completing treatment course for MB patient is US$ 87 and for PB patient is US$ 5. One reservation regarding use of BCPs in control programmes is the additional cost of about 15%. However, this should be considered in conjunction with the increased efficiency and cost-effectiveness of using BCP in leprosy control programme.

To evaluate use of BCPs in the field, a trial has been started using patients receiving loose capsules as a control group.

From this trial, a questionnaire study of leprosy patients and treatment providers is presented.

PO 455

CHEMOTHERAPEUTIC COMPLIANCE AMONG LEPROSY PATIENTS IN URBAN AREAS OF THAILAND*

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***School of Public Health, University of Hawaii
****School of Medicine, University of Hawaii, U.S.A.

Chemotherapy in leprosy control is greatly handicapped by non-compliance. This study examined this problem. Appointment keeping and urine levels of DDS were used as indicators of compliance and noncompliance. Possible determinants included epidemiological, behavioral and demographic variables. 532 MDT patients from three central urban sites were followed over five months. Data were collected from interviews, medical records, and urine D/C ratios. 130 patients served as controls for measurement bias.

Preliminary results using discriminant analysis suggested the importance of previous appointment keeping, perceived appointment interval, belief that the disease was cured, employment status, duration of treatment, perceived subjective norms, type of leprosy and deformity all effected compliance. The efficiencies of functions in classification of group memberships ranged from 52.96 % to 86.63 %. By using path regression coefficients, intention, perceived subjective norms and perceived self-efficacy were also found to be important variables. The results are discussed for their relevance to future efforts to increase compliance toward leprosy control in urban areas of Thailand.

*This investigation received financial support from UNDP/WORLD BANK/WHO Special Programme for Research and Training in Tropical Diseases(TDR)

PO 456

TECHNIQUES USED IN ASSESSING COMPLIANCE AND REGULARITY OF ATTENDANCE IN A BLISTER PACK TRIAL FOR MULTI DRUG TREATMENT OF MULTIBACILLARY LEPROSY IN THAILAND

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Recently blister packs (BPs) have been designed for the administration of Multi Drug Treatment (MDT) along the lines recommended by the World Health Organization for patients with either pauci- or multibacillary leprosy. We describe the methodology of a controlled trial initiated in late-1987 in Thailand to establish if BPs have significant advantages compared to the usual loose supply of drugs for the implementation of MDT in Multibacillary leprosy on:

- regularity of attendance for monthly supervised treatment (Rifampicin and Clofazimine)
- compliance to the ingestion of daily unsupervised drugs (Dapsone)
- logistics involved in the distribution of anti-leprosy drugs to patients
- attitudes, motivation and performance by patients and staff.

A total of 480 cases of multibacillary leprosy (adult patients only, cases currently under treatment and new cases) will be included in the study and followed up for a six months period during which compliance and attendance at the clinic (monthly visits, during which urine specimens for dapsone -creatinine examination are taken) as well at patients motivation and attitudes at home ('surprise' visits, structured interview) are assessed. In addition time and motion studies and a structured questionnaire are used to assess the motivation and effectiveness of the leprosy control staff. The usefulness of assessment techniques utilized in recording information to assess the value of blister packs for MDT in Multibacillary leprosy, is discussed.

PO 457

BLISTER PACKS FOR THE TREATMENT OF MULTIBACILLARY LEPROSY; PRELIMINARY RESULTS FROM A COMPARATIVE TRIAL IN THAILAND

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Mahidol-University, Bangkok Thailand, Colin McDougall, The Slade Hospital, Oxford, UK, K. Suljaga-Petchel, CIBA-GEIGY, Basel, Switzerland.
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Blister packs (BPs) have recently been designed for the administration of Multi Drug Treatment (MDT) along the lines recommended by the World Health Organization for the treatment of all forms of leprosy. In late 1987 a controlled trial was initiated in Thailand to establish if BP's have significant advantages over the usual presentation to the patient of 'loose' drugs, and to assess its influence for the implementation of MDT in leprosy in view of regularity of attendance for supervised treatment, compliance and patient motivation, logistics of drug supply to patients, and motivation of the leprosy control staff. A total number of 480 patients will be entered into the study, and divided into 4 groups of different schemes of drug supply ('loose' versus blister) and health services ('integrated' versus 'vertical'). Cases are followed for a six months period, during which compliance and motivation is measured through a variety of assessment techniques. To date (February 1988) one hundred and seventy-nine patients have been admitted to the project. Sixty eight are using blister packs, 57 in vertical and 11 in integrated areas, one hundred and eleven cases are in the loose drug regime, 44 in vertical and 68 in integrated areas.
We review the data on compliance and patient motivation in each of the four cells, in those patients for whom data is complete, and compare the early motivation of the leprosy control team in each cell.

PO 458

STRATEGIES FOR IMPROVED DRUG UTILIZATION IN THE IMPLEMENTATION OF MULTIPLE DRUG THERAPY FOR LEPROSY

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The alarming development of dapsone resistance in recent decades, followed by the World Health Organisation recommendations in 1982 for the treatment of all patients with multiple drug therapy, have focussed attention on the need to improve standards of medical care in both vertical and horizontal programmes, whilst at the same time assuring adequate finance for the purchase of the drugs concerned.

Improvement of health staff performance for this purpose calls for attention to a "package" of activities, including accurate diagnosis and classification, skilful and sympathetic handling of patients and their families and a broadly-based plan of health education for the community. Even where all this has been achieved, implementation will fail unless all the necessary drugs, in both adult and child doses, are available at the outset and during the entire duration of the programme, on an absolutely regular basis.

Blister calendar packs for the presentation of dapsone, clofazimine and rifampicine may be of value in this context. Following a publication by Winsley et al in the International Journal of Leprosy in 1983 (51, Number 4, pp 592-594), giving detailed designs, blister calendar packs have been used quite extensively, first in the Philippines and later in Thailand and India.

This paper will review the potential importance of this and other developments related to drug utilization in the overall context of the management and mobilization of both patients and staff in Leprosy Control Programmes.

PO 459

Compliance, compliers and non-compliers How to analyse ?

W.'t Mannetje and M. Becx-Bleumink

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A simple method is developed for the analysis of compliance data in case repeated observations of patients are available.

The method is applied to the analysis of data about dapsone intake, as measured with the urine spot test.

From about 500 patients, paucibacillary and multibacillary, treated as out-patients with the WHO-MDT regimen, urine was collected at month 4 and 6 after start of treatment.

From multibacillary patients also at month 12, 18 and 24.

We identified groups of typical compliers and non-compliers and analysed which other differences existed between these two groups.

PO 460

COMPLIANCE: A PATIENT'S POINT OF VIEW.

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Most Hansen's Disease patients have the ability to confirm or deny our health. Why do some people continue their medication while others don't? Is it because one feels there is simply no need of continuing? Perhaps one feels the need for a different dosage or a change of drugs. Ultimately, compliance requires a good doctor/patient relationship with good rapport and confidentiality. One hundred percent dominance by the doctor can be disastrous. Good communication between equals can avoid a breakdown that leads to non-compliance.

There is oftentimes a strong resistance to continued medication and a rigid routine over a long period of time which can conflict with one's desire to do right. To certain patients, compliance becomes defiance. Non-compliance becomes a way to feel some sense of control over one's life, even if it results in hurting oneself. Defiance can take the form of stubbornness, neglect and a failure to compromise which can lead to total disaster. Most patients feel that if you need the medicine, take it; if you don't, don't. To really understand compliance, one must understand full well what it means to stay on what seems like a plateau for years at a time.

PO 461

Analysis of longterm compliance with dapsone therapy in an outpatient Hansen's disease clinic.

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Previous reports have demonstrated non-compliance with dapsone in 30%-60% of patients. In our clinic, 64 patients followed on a regular basis were evaluated retrospectively for factors affecting dapsone compliance and bacteriologic improvement(66% male, 34% female, mean age 41+15.3 yrs). A majority of the patient population originated in South East Asia(47%), Mexico(30%), or India/Pakistan(15.5%). 61% were paucibacillary(PB) and 39% were multibacillary(MB). ENL and reversal reactions (RR) were noted in 22(34%) and 9(14%) patients respectively. 88% of patients with MB experienced ENL and 20% of patients with PB experienced RR. Mean duration of evaluation was 2.7+1.4 yrs. Overall, 38(59%) patients showed bacteriologic improvement, 19(30%) showed no change, 1(1.5%) worsened and 6(9%) could not be evaluated due to short follow-up. 48(77%) patients had optimal urinary dapsone: creatinine for at least 50% of points sampled (mean number of data points =13+10). Similar compliance rates were found in patients who improved 29(78%) as well as those who showed no change 12(67%), but the large number of patients with initial BI values of zero(16) in the no change group probably accounted for this finding. Similarities in compliance were also found when comparing patients who experienced ENL and RR [18(81%) and 6(75%) respectively]. Gender, nationality and the number and types of concomitant medications did not affect compliance. While none of the factors evaluated affected compliance, the overall compliance rate of 77% reflects the benefit of a continuous monitoring program for dapsone in outpatients.

PO 462

THE ATTITUDE OF NIGERIAN LEPROSY OUT-PATIENTS TOWARDS THE USE OF A DAPSONE DEPOT INJECTION

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Widespread patient non-compliance has lead to the concept of a sustained release formulation of dapsone that can be implemented in the MDT programme as recommended by the WHO in 1982. An injectable depot formulation of dapsone was used as a part of an MDT programme among 52 leprosy out-patients in two leprosy clinics in Jos, Plateau State, Nigeria. The injection was administered with intervals of 4 weeks. Blood samples were taken at regular time intervals during the first four months to follow the dapsone serum concentration. Also a questionnaire was obtained to evaluate the acceptability of the treatment.
The injection appeared to yield good sustained release results throughout the study period. The mean trough dapsone serum concentration was 0.4 mg/l, while none of the 816 samples contained more than 3.0 mg/l dapsone. Accumulation occurred after repeated administration.
In general the injection was well received by the patients. The overall attendance was 91 % and only 3 female patients did not complete the study for reasons not related to the treatment. In one male patient an abscess occurred, otherwise local side effects were restricted to a slight tenderness at the injection site in some of the patients, which never lasted longer than a week. Of 44 patients asked, 41 preferred the injection to daily oral treatment, because of the convenience of the regimen and an improved general well-being. Two patients preferred oral therapy.
Considering the dapsone serum concentration/time profiles and the favourable judgement of the patients, the dapsone depot injection provides a useful tool against non-compliance among leprosy patients.

PO 463

MONITORING DAPSONE LEVELS FOR PATIENT COMPLIANCE, A COMPARATIVE STUDY OF BLOOD AND URINE LEVELS.

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Regularity of drug intake and patient compliance has been an ongoing concern of leprosy control programs for many years and various methods have been used to measure and increase patient compliance. Urine spot tests for monitoring dapsone intake have now been widely used for a number of years. This study compares the results of urine spot tests for dapsone as proposed by H.C.J. Huikeshoven, with blood levels measured in the same patients by the modified Bratton Marshall colorimetric method, and by high performance liquid chromatography. Approximately 300 specimens were obtained from patients who were taking supervised and unsupervised medications, as well as from controls who were taking no medications. The results indicate that the urine spot test is as accurate a measure of patient compliance for clinical purposes as blood levels done by the colorimetric method, and correlates well with blood levels done by high performance liquid chromotography. It was also shown that blood levels for dapsone as a means of monitoring patient compliance are not useful in patients taking daily rifampin because rifampin alters the dapsone blood levels significantly. Urine spot tests, however, remain useful as an indicator of dapsone intake in such patients.

PO 464

INFLUENCE OF SELECTED DEMOGRAPHIC VARIABLES ON COMPLIANCE OF LEPROSY PATIENTS TO TREATMENT IN NIGERIA.

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Selected demographic variables, namely sex, age, marital status, religious affiliation and ethnic groups of 870 leprosy patients who believed that their disease is either very severe or moderately severe, were examined in relation to their compliance to treatment. Family income and educational level of these patients were not used in the study for obvious reasons. Structured interview was used to obtain information from the patients and this was analysed using the chi-square to test for significance at $P<0.05$. Results showed that sex and marital status of the patients influenced their compliance to treatment, while age, religion and the ethnic group into which the patients belong, did not have any influence on it. It was therefore recommended that the gender and marital status of leprosy patients should be considered and positively used in improving their compliance to treatment.

PO 465

USE OF ELISA TESTS FOR RIFAMPICIN AND DAPSONE IN MDT COMPLIANCE STUDIES IN DUTCH LEPROSY PATIENTS.

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An ELISA inhibition test for rifampicine has been developed using specific antibodies against rifampicine. These antibodies were produced by immunizing rabbits with a 3-formylrifamycin-BSA conjugate. The ELISA test has been compared with other methods for detection of rifampicin in urine. The ELISA test was much more sensitive and could still detect rifampicine in the urine 3-4 days after intake. Together with a tests for dapsone, these test were applied to investigate MDT compliance in Dutch leprosy patients, taking daily 600 mg rifampicin , 100 mg dapsone in case of tuberculoid leprosy patients supplemented with 100 mg clofazimine every two days in case of lepromatous patients. Compliance for both rifampicin and dapsone was found to be >75 %.

PO 466

ABSENTEE CHASING-
A CHALLENGE TO PARA MEDICAL WORKERS

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Even those MD patients who receive the drugs may not consume them regularly. Irregular treatement leads to several complications. The reasons for irregular treatment may be ignorance, indifferance, economic, Social, physical or psychological. Non complaiance is a complex interaction of many factors namely the patient, family, treatment setting, society, disease and the medication itself. Whatever the factor may be, it should be tackled carefully. Patient compliance can be improved by a continuous monitoring.

The present study was undertaken in an area of one lakh population with 672 cases under treatment . By random sampling, 10 percent of the cases were verified for regularity. Pill countings were done. The results were analysed. Interviews were conducted to find out the reasons for irregularity. The Para Medical Workers were entrusted, after due motivation, for absentee chasing. Results will be published.

PO 467

The importance of patient compliance in the control of leprosy.

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Since leprosy, like tuberculosis, is a disease in which child cases are generally non-infectious,

the most effective method of controlling its transmission is through improved case-finding and treatment rather than by vaccination. The multidrug treatment regimens recomended by the WHO Study Group are extremely well tolerated and highly effective if regularly delivered to the patient and then ingested. However if multibacillary patients fail to ingest the dapsone and clofazimine prescribed for daily self-administration, they run the risk of eventually relapsing with rifampicin-resistant leprosy. Recent studies of patient compliance with multidrug treatment will be described as well as novel approaches to improving drug self-administration.

PO 468

The incidence of hypersensitivity reactions to dapsone therapy.

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Dapsone has proved a safe and effective drug since its introduction in the 1940s. The toxic effects and adverse reactions to dapsone have been well documented.

In the early years hypersensitivity reactions to dapsone occured frequently but then rapidly declined, however in recent years these reactions have reappeared. This is confirmed by a review of the literature and a survey of leprosy treatment centres in 1985. Further surveys have now been conducted in 1986 and 1987 and the situation assessed. The hypersensitivity reaction continues to occur in a sporadic fashion. Possible underlying factors are discussed.

PO 469

Multidrugtherapy and Pregnancy: Preliminary report on toxicity.

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In 1983 a study on MDT as recommended by O.M.S. was initiated in the Curupaiti State Hospital. We have observed the side effects of the drugs most frequently used, with special concern to our female patients who became pregnant in the course of treatment. In this paper we show some of the data gathered since then, with special atention to the low frequency of side effects and of toxicity to the mother and her baby when using the O.M.S. scheme.

PO 470

A POSSIBLE ANAPHYLACTIC REACTION TO RIFAMPICIN

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A 60 year old male with untreated tuberculoid leprosy was advised for multi-drug therapy. One hour after the intake of 1st dose of Rifampicin (600 mg.) empty stomach, the patient developed breathlessness, urticarial lesions and features of peripheral circulatory failure. The patient was revived with O_2 inhalation and drugs like adrenaline, chlorpheneramine maleate and steroid. Although the clinical diagnosis of anaphylactic reaction was made, the possibility of anaphylactoid reaction could not be ruled out.

PO 471

Spontaneous and Multidrug Therapy Induced Sister Chromatid Exchanges in Patients with Tuberculoid and Lepromatous Leprosy

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Leprosy is a chronic infectious disease caused by Mycobacterium leprae. Estimates for the total number of leprosy patients in the world vary from 10 to 12 million. India, with an estimated four million leprosy patients, accounts for one third of the global incidence. One of the greatest advancement in the field of leprosy treatment is the introduction of multidrug therapy. Combination drug therapy reduces the incidence of drug resistance, shortens the treatment period and prevents the emergence of drug resistant strains. However, the effect of multi-drug therapy on human chromosomes has not yet been investigated. In the present paper we report the spontaneous and multidrug therapy induced sister chromatid exchanges (SCEs) in patients with tuberculoid and lepromatous leprosy. The spontaneous SCE frequency was investigated in 16 tuberculoid and 28 lepromatous leprosy patients. The frequency of SCE was found to be 7.52 $\pm$ 2.11 and 9.86 $\pm$ 2.93 in tuberculoid and lepromatous leprosy patients respectively. These frequencies were significantly higher than the SCE value of 6.38 $\pm$ 1.31 observed in 41 age and sex matched healthy controls ($p < 0.001$). The SCE frequency was also investigated in 13 tuberculoid and 19 lepromatous leprosy patients receiving multidrug therapy. Combination drug regimens elevated the SCE frequency to 9.16 $\pm$ 2.62 in tuberculoid leprosy and 11.25 $\pm$ 3.43 in lepromatous leprosy. These values again were significantly higher than the corresponding spontaneous SCE levels of tuberculoid and lepromatous leprosy patients ($p<0.01$ and 0.05 respectively). The significance of these findings are discussed in the light of differential immunological response vis-a-vis cancer susceptibility of tuberculoid and lepromatous leprosy patients.

PO 472

Hypersensitivity to Rifampicin in a patient undergoing multidrug therapy for lepromatous leprosy.

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The authors present the case of a patient with Lepromatous Leprosy undergoing multidrug therapy, who one day after the second supervised dose presented disseminated purpuric skin lesions and necessitated immediate admission to the State Hospital of Haematology where she underwent intensive Corticotherapy. The skin lesions were considered a result of the monthly dose of Rifampicin. Multidrug therapy has since been suspended and the patient is now on monotherapy using dapsone.

PO 473

DAPSONE POISONING.

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Cases and suicidal poisoning due to dapsone over a period of 12 years (1976 to 1987) were analysed with reference to clinical features and recovery. There were 22 cases (M:F = 14:8) age ranging from 10 to 35 years. The quantity of dapsone consumed varied from 1000 mgs. to 2800 mgs. Earliest features were vomiting and bluish discoloration. Clinical examination revealed cyanosis in all, restlessness in 7 and drowsiness in 5. One of them had choreoathetotic movements of the upper limbs. Among the 22, 3 were taking dapsone regularly for leprosy, and the rest were not suffering from leprosy but had an access to dapsone available at home. Methemoglobinemia was tested in 12 and was positive in 8 of them. Cyanosis started disapoearing from 3rd or 5th

day and it was related to the quantity of dapsone consumed, both for intensity and clearance. Three (3/22) individuals who expired consumed about 2200 to 2800 mgs. and brought about 18 hours after consuming the poison, and autopsy revealed petechial hemorrhages in the brain and cerebral edema. Their visceral organs were congested. From these observations, it is considered that whenever a patient is brought with cyanosis to emergency room without any organ disease, look or ask for dapsone over ingestion until proved otherwise especially in areas where dapsone is issued on monthly basis to patients, since early recognition and simple management helps for complete recovery. (Sponsored by TNSRC, Madras).

PO 474

EVOLUTION DU TAUX DE TRANSAMINASES TGO AU COURS DE L'ADMINISTRATION DE 4 PROTOCOLES ASSOCIANT RIFAMPICINE ET ETHIONAMIDE DANS LE TRAITEMENT DE LA LEPRE MULTIBACILLAIRE.

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Les auteurs ont étudié l'évolution du taux de transaminases TGO chez des malades multibacillaires traités pendant 2 ans par 4 régimes de polychimiothérapie. Le premier régime est calqué sur celui préconisé par l'OMS mais avec adjonction de 500 mg d'Ethionamide (ETH) à la prise mensuelle supervisée de Clofazimine et de Rifampicine (RMP) ; le second se différencie du premier par une phase initiale de 2 mois d'administration supervisée quotidienne de RMP-ETH ; pour les récidives, la dose de 100 mg/j de DDS est remplacée par 250 mg/j d'ETH dans les 2 régimes précédents. Constatations :

- L'introduction d'une phase initiale intensive d'administration de RMP-ETH n'accroit ni la fréquence globale, ni l'importance des élévations anormales de TGO.
- Les taux maximum de TGO sont obtenus lors des 2 premiers mois dans les régimes avec phase initiale intensive ; entre les 4° et 8° mois pour les autres régimes.
- La proportion de cas de TGO élevées ne varie pas lorsque la dose journalière de 100 mg/j de DDS est remplacée par 250 mg/j d'ETH.
- Cependant, dans quelques cas, des élévations importantes de TGO (> 240 URF) ont été observées, toujours durant des périodes où l'ETH était administrée quotidiennement.

PO 475

HAEMATOXIC SIDE EFFECTS OF DAPSONE.

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Methaemoglobinemia and haemolysis are side effects most often reported in connection with dapsone intake. In studies with volunteers, who were administered 50-300 mg dapsone maximum methaemoglobine levels were directly correlated with peak plasma levels of dapsone and intake dosis, showing an increase of 3-5 % with each additional 100 mg dosis. Maximum in methaemoglobin formation is found at a later time than the peak in DDS plasma levels. Using an in vitro methaemoglobine formation assay, it could be shown that N-hydroxy DDS, the metabolite of DDS responsible for the haematoxic effects, reaches its maximum plasma concentration, when also DDS levels are maximal. In vitro methaemoglobin formation upon incubation with N-hydroxy DDS is dependant on the G-6-PD activity of the erythrocytes of the donor. Intravascular haemolysis due to intake of dapsone could be demonstrated by decrease in haptoglobine and haemopexin plasma levels in volunteers who had been taken DDS or administered DDS depot injections. The decrease being dependant on maximal DDS plasma levels reached.

PO 476

INVESTIGATION OF SIDE EFFECTS OF A MAXIMAL MULTIPLE DRUG THERAPY REGIMEN USED IN DUTCH LEPROSY PATIENTS.

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Leprosy patients, who had already been under treatment, were given a maximal multiple drug regimen, consisting of daily 600 mg rifampicin and 100 mg dapson for six months in case of tuberculoid leprosy patients (N = 53) and daily 600 mg rifampicin, 100 mg dapsone and 100 mg clofazimine every two days for 12 months with lepromatous patients (N=66). Blood was collected at two monthly intervals for monitoring liver (SGOT,SGPT,LDH,γ- GT) and kidney function tests (AP and creatinine) . No appreciable elevation in these parameters was seen in both groups of patients, so that daily rifampicine in combination with dapsone and clofazimine seems to be a safe drug regimen. Only in one patient who was receiving prothionamide, hepatoxic side effects were observed. Methaemoglobin formation was observed in all patients. In a few patients values reaching 10-15% were sometimes found.In nearly all patients a sharp decrease in serum haptoglobin and hamopexin levels was seen, pointing to intravascular haemolysis. This was also seen in a volunteer taking rifampicin and DDS for one week. When no decrease is observed of haptoglobine serum levels it may be an indication for poor compliance.

PO 477

A COMPUTERIZED REHABILITATION WORKSTATION

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Despite continuing efforts, long delays exist in the distribution of new information on rehabilitation in Hansen's Disease. To help correct this problem, a Computerized Rehabilitation Workstation is being developed which will draw from an archival library containing more than 10,000 research, anatomical and clinical slides. Computer Aided Instruction (CAI) programs are being developed which allow trainees to take interactive, comprehensive courses on the rehabilitation of the Hansen's disease patient. In addition, to more effectively utilize this broad spectrum of material, a Knowledge Based System (KBS) is also being developed. This system consists of the knowledge, experiences and decision making capabilities of experts. Contrasted with CAI, the main focus of KBS is to assist the medical professional in the diagnosis, evaluation and treatment of real patients. The KBS and CAI programs together will form the Computerized Rehabilitation Workstation. When completed, the workstation will be an inexpensive, portable personal computer that can be easily transported to Hansen's disease facilities around the world.

PO 478

METHODOLOGIE NECESSAIRE A L'ETUDE DES NEVRITES HANSENIENNES

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I - Déclenchement : L'étude de 258 obs. de névrites d'évolution récente (702 localisations) a montré que le déclenchement est indépendant de l'échelle de R. et J. et qu'il est provoqué par les réactions ENL et RR; 2/3 contexte réactionnel indiscutable, 1/3 réactions subdermatologiques confirmées par la biologie et les biopsies tronculaires.
II - Modifications consécutives et associées
. Remaniements pathologiques, différents dans les deux

réactions : macroscopique, microscopique (invesion de cellules inflammatoires, concentration bacillaire, microvaculaire immunopathologique, remaniement de l'épinèvre du fascia extra-épineural et des périnèvres).
. Dérèglements pathophysiologiques
- de l'hémodynamique (gêne circulatoire, hyperfiltration liquidienne, hyperpression tronculaire de 2mm à 25mm, angiographie.
- effet de compression passive par les canaux ostéoligamenteux sur le nerf hypertrophié (mensurations, neurographie, hyperpression canalaire de 5mm à 40mm).
- dérèglement de la myéline
. Apport de l'expérimentation animale
- souris sans thymus. Rôle exclusif de l'hyperconcentration bacillaire. Différent de l'homme
- primates non humains. Téguments L, nerfs BT ou T réaction reverse.
Tous les résultats sont détaillés.

PO 479

Hallux Limitus: Relationship With Ulceration of The Great Toe.

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Torque range of motion (TROM) measurements of the great toe were made to determne the relationship between hallux limitus and plantar ulceration. Subjects included 20 patients with a history of plantar ulceration on the great toe (GTU), 20 patients with a history of ulceration on the plantar surface of the foot excluding the great toe (NGTU) and 20 normal controls. Peak MTPJ extension was significantly reduced in the GTU group compared to the NGTU and control groups ($p < 0.0001$). The slopes of the TROM and stiffness curves were significantly steeper ($p < 0.0001$) in the GTU group as compared to NGTU and control groups. These results support the hypothesis that stiffness of the great toe is an etiological factor in plantar ulceration of the great toe.

PO 480

Neurophysiological (EMG) Study in Leprosy

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EMG studies were performed in 71 patients either with leprosy (57) or their contact (14). Among the patients 55 (97%) had many different EMG abnormalities, more often in the dimorphic (D) form, and decreasing in the Virchow's (V) and Tuberculoid (T) forms, whereas the Indetermined (I) form was the less affected.The reduced motor conduction velocity of the ulna nerve across the elbow was the most striking abnormality (49% among the patients, 64% in the D form and 33% in the I form). Sensory amplitude reduction with or without conduction velocity abnormality wasfound in 46% in the median nerve and 40% in the ulnar nerve, among the patients (64% and 40% respectively in the D form). Motor amplitude was also reduced in 50% of the tibial nerve 41% of the median nerve, 41% of the peroneal nerve with no relation with the conduction velocities.Sural amplitude was reduced in 33% of patients and sural nerve conduction velocity was reduced in 44% of them. Accurate EMG examination may be a lot helpful to the diagnosis of leprosy, and it demonstrate that peripheral nerve abnormalities other than demielination are frequent suggesting the possibility of axonal neuropathy. There are also evidence of subclinical neuropathies in the I form. Many of the assimptomatic contacts had EMG abnormalities, particularly slow conduction velocity in the ulnar nerve across the elbow (39%), suggesting either a mild form of leprosy or the neurofisiological scar (primary complex of leprosy). The EMG abnormalities were assimetric in 100% of the patients, on the contrary ofthe known peripheral polineuropathies what may possibly differenciate leprosy from other neuropathies.

PO 481

A frequency domain analysis of myoelectric signals in Hansenology.

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Electrodiagnostic studies in HD though attempted two decades back could not make headway mostly due to the random nature of the myoelectric signal. The discovery of efficient mathematical tools coupled with cheap computer power has changed the scene. This work involves surface recorded ME signals from the abductor digiti minimi muscle of a group of HD patients all with partially damaged ulnar nerves. This is compared with data collected from healthy individuals. The analysis is performed in the frequency domain where signals convey more inside information. Of the three parameters studied the power spectrum shows that the healthy score over the diseased in terms of signal power upto a frequency of about 200 Hz. The autocovariance, a measure of signal randomness, shows a declination of stochastic pattern with progressive nerve damage. The median frequency, the third parameter varied widely for the diseased vis-a-vis the healthy, though there is overlap in their limits. The nature of this study being preliminary conclusions cannot be sweeping. Quantification of results with large amount of data can open new vistas for electrodiagnosis in HD.

PO 482

RECORDING DISABILITIES ON A NATIONAL INDIVIDUAL PATIENT FORM

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This paper stresses the importance of having a simple but useful disability section incorporated in the national Individual Patient Form used in the field. Supportive data is given, illustrating the use to which such forms are being put in Ethiopia and Zambia.

The paper outlines:
1. Uses to which a good disability record can be put:
   - in identifing action needed to minimise disability.
   - in monitoring changes in disability, and
   - in evalutating the effectiveness of action taken to minimise disability.
   - as an indicator useful in monitoring early case-finding.
2. A suggested disability record format ... with examples shown of this as already incorporated into various national Individual Patients Forms.
3. The usefulness of each section of the record. Comments are made as to which uses can and cannot be met through WHO disability grading.
4. How the information from the record can usefully be summarised for planning and evaluation purposes. Charts are shown to illustrate findings elicited using this disability record in Ethiopia and Zambia.
   - Baseline disability information obtained from many records in summarised
   - Changes in disability over a 6 month period in pauci-bacillary patients are summarised.
   - Changes in sensation and strength, before and after a Prednisolone course, are summarised.

PO 483

TUBERCULOID HANSENS ON HAIRY SCALP
(A CASE REPORT)

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A patient of tuberculoid Hansens with a lesion on the hairy,occipital area of scalp is reported

The patient had a well defined,circular, raised anaesthetic plaque with sparse hairs on the occiput,well within the hair line. The diagnosis was confirmed by histopathology. To the best of our knowledge,this is the first case report in the world literature,of involvement of hairy scalp by a tuberculoid lesion.

PO 484

Histoid leprosy: A prospective diagnostic study

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Histoid leprosy is a fascinating expression of multibacillary leprosy, the incidence of which was 3.6%. It was predominantly seen in males of the younger age group, who were on inadequate, and irregular dosage of diaminodiphenyl sulfone. Papules, cutaneous and/or subcutaneous nodules and plaques appearing over an apparently normal skin were its exquisite prospective clinical features. It was invariably supported by enormous, uniformly solid staining discrete bacilli from the skin in contrast to their virtual absence from the surrounding normal appearing skin. Encapsulated tumorous mass formed primarily by spindle shaped histocytes, displayed in intertwining, cris-cross or whorled fashion in haematomylin-eosin stained sections, were supplementary. The display of acid-fast bacilli was, however, similar to skin-slit smears.

PO 485

PENILE AND SCROTAL LESIONS IN LEPROSY

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Involvement of genitals in leprosy has not been well documented in the literature. Lesions on the external genitalia may be encountered in leprosy of all types in the entire Ridley-Jopling spectrum. It is however not known whether lesion of indeterminated leprosy, representing the earliest clinical manifestation of the disease can occur in these organs.

We present clinical photographs of leprosy lesions ranging from BT to LL types involving the penis and the scrotum in six patients.

We feel that no clinical assessment in leprosy is complete till thorough examination including external genitalia of patients is carried out.

PO 486

Unusual presentation of a Verrucous Lesion in a patient with Borderline-Tuberculoid Leprosy

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An unusual case observed in the Curupaiti State Hospital was a large Verrucous Lesion on the right superciliar region of a woman with BT Leprosy and one large erithematens plaque on the same hemiface. In this paper the clinical and histopathological findings are presented and discussed.

PO 487

Neural Leprosy - With Unusual Presentation

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Neural leprosy presenting as a single Radio Cutaneous palpable nerve not enlarged and not tender with a high bacterial count is a rare occurrence. Such a case has been seen at All Africa Leprosy & Rehabilitation Training Centre (ALERT) 030982. The nerve biopsy showed some dense lymphocytic infiltrations between the nerve fibers. Many schwann cells contain small globi of fragmented/granulated bacilli. Slit skin smears from six standard sites were negative. The patient was treated with dapsone monotherapy with satisfactory response. In the literature neural leprosy does not occur in Africa, but since we have seen 83 Neural leprosy cases which have been proven by nerve biopsy in the evaluation of new leprosy cases with unusual neural presentation. Without such information, these cases would have not been confirmed.

PO 488

TONGUE CHANGES IN LEPROSY

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An attempt was made to study the tongue changes among leprosy patients (Tuberculoid - 175, Lepromatous - 85 and lepra reaction 40 ; M:F = 236 : 64 ; age 10 to 50, Mean age 28.4 years) attending leprosy clinic of Government Rajaji Hospital, Madurai. In all these cases other associated systemic illnesses were ruled out. Similar number of healthy individuals (age and sex matched) living in the same environment or their family members were kept as control. Tongue was examined in the day light for size, shape, color, surface, papillae, ulceration and modules. The neurological evaluation of tongue was done for each case. Macroglossia was seen in 4, coating in 28 (central in 7, Margins in 12 and both in 9), prominence of papillae in 17 (Fungi Form in 7, Fili Form and Fungi Form in 12 and circumvallate in 6) and nodule is only one case (lepromatous type without reaction - in the middle of tongue). The coating of the tongue and prominence of papillae observed among leprosy cases were significant from control, but were independant of the type of disease or with reaction. There was no neurological involvement of the tongue in the leprosy subjects studied. However, if any nodule or ulcer is seen in the tongue, it has to be investigated accordingly to find out the appropriate cause. (Sponsored by ICMR, Student Fellowship).

PO 489

ESTIMATION OF HIGH DENSITY LIPOPROTEIN CHOLESTEROL (HDL-C) IN THE DIAGNOSIS OF LEPROMATOUS LEPROSY.

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A high incidence of increased plasma level of high density lipoprotein cholesterol (HDL-C) has been reported in cases of lepromatous leprosy from many parts of world.
HDL-C estimations were performed for the diagnosis of lepromatous leprosy in patients aged below 60 years, taking plasma HDL-C levels as 28-71 mg./dl.in men and 34-91 mg./dl. in women. as range of normal values.
The paper discusses the results of HDL-C estimations as applied to 96 (50 under treatment and 46 untreated) lepromatous leprosy patients and 84 randomly selected matched control patients suffering from other skin diseases attending skin out-patients department.
The study revealed that HDL-C levels in lepromatous leprosy group were raised and significantly different when compared with control group ($t = 22.96$ and $P < 0.001$)
The sensitivity of the test was very high,97.9% (94/96), but specificity was low, 80.95% (68/84),false positive and false negative results were 19.04% (16/84) and 2.08% (2/96) respectively.
It is opined that a negative test will be mainly useful in excluding diagnosis of lepromatous leprosy. The procedure is less painful and without facial scar.

PO 490

STUDY OF PREVALENCE AND INTENSITY OF SOIL-TRANSMITTED HELMINTHIASIS IN LEPROSY, SOUTH SULAWESI, INDONESIA

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In order to study the prevalence and the intensity of the soil-transmitted helminths in leprosy patients compared with their contacts, a total of 368 speciments of the individual coming from a leprosy camp, South Sulawesi, Indonesia, were examined and cultured. They consisted of 243 leprosy and 125 their contacts. The quantitative measurement for the intensity of the infection of each parasite was determined by modified Kato-Katz technique. Midified Harada-Mori method was used in the determination of species of hookworm and Strongyloides stercoralis. There were 98.1% of intestinal nematodes found positive, 98.8% in leprosy and 96.8% in contacts. Of the positive cases 97.1% Trichuris trichiura, 62.1% hookworm, 53.9% Ascaris lumbricoides, and 2.1% Strongyloides stercoralis in leprosy, compared with 97.5%, 44.6%, 68.8% and 0.8% in contacts, respectively. Of the hookworm larvae 77.1% Necator americanus, 7.1% Ancylostoma duodenale and 15.8% mixed infections in leprosy were found, compared with 85.7%, 4.8%, and 9.5% in contacts, respectively. Most of the leprosy patients (80.8%) got mixed infections, 44.6% double infections, 34.6% triple infections, 1.7% quadruple infections, and only 19.2% single infections, compared with 78.5%, 45.5%, 32.2%, 0.8%, and 21.5% in contacts, respectively. More than 75% of leprosy got light infections less than 20% intermediate and, less than 5% heavy infections. The prevalence rate of both sexes and between single and mixed infections either leprosy or their contacts of soil-transmitted helmithiasis were not significant different. The intensity of Ascaris lumbricoides and Trichuris trichiura infection in leprosy patients was less than the intensity of their contacts. This difference was significant. However, the difference in hookworm was not significant.

PO 491

CANCERS IN THE LEPROSY PATIENTS OF JAPAN.

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In Japan it had been said that cancers were very rare among the leprosy patients. Nowadays,however,we can see many cancers here and there in the leprosariums of Japan. The number of cancer patients is growing remarkably. In our Leprosarium,about 20 percent of the dead has been resulted from cancers. From 1950 to 1955,we can see nothing but a few gastric cancers. From about 1960,it began to increase.And from 1981,the number of the death from cancers has rapidly increased in size. At last,in 1982,it became 14-30th. It is not rare to see the survivors from cancers in our Leprosarium. On November 7 in 1985,the number was 35-1132nd of the whole patients of our Leprosarium. the details were: 9 gastric cancers,7 colon cancers,5 lung cancers,3 hepatomas,3 uterus cancers,2 cancers of the gall bladder,2 cancers of urinary bladder,2 breast cancers,1 cutaneus cancer,1 prostatic cancer. They were diagnosed by:Echography-7,Fluoroscopy-5,Chest X-ray exam.-5,Inspection or Palpation-3,Gastrofiberscopy-2,Cystoscopy-1,Uterine cancer exam.-1,Unknown-5.

PO 492

INFECTION PAR LE VIRUS DE L'HEPATITE B DANS LES FORMES POLAIRES DE LEPRE (ETUDE REALISEE AU SENEGAL)

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Les marqueurs sériques du virus de l'hépatite B (VHB) ont été recherchés dans deux populations d'hanséniens provenant de l'ILAD (Institut de Léprologie Appliquée de Dakar). La première étude réalisée de 1973 à 1977 était constituée de 329 patients présentant une forme lépromateuse et 224 une forme tuberculoïde ; la deuxième (1982 à 1986) concernait 434 sujets (236 formes lépromateuses et 198 formes tuberculoïdes).
Les prévalences des différents marqueurs du VHB obtenues dans ces populations ont été comparées entre elles et également à celles obtenues dans une population témoin composée de 6187 adultes sains.
Les détections des différents marqueurs du VHB (Ag HBs, anti-HBs, anti-HBc, Ag HBe, anti-HBe) ont été réalisées par différentes méthodes (contre immunoélectrophorèse, techniques radioimmunologiques et immunoenzymatiques).
La présence d'au moins un marqueur du VHB a été retrouvée respectivement chez 98,0 % et 96,5 % des deux populations.
L'Ag HBs détecté par RIA est présent chez 25,5 % des patients de l'étude n° I et 23,0 % dans l'étude n° II, alors que seulement 15,2 % des sujets contrôles sont porteurs. Ce marqueur de contamination a été étudié suivant l'âge, le sexe, l'ethnie et la forme de lèpre des sujets ainsi que le facteur hospitalisation.

PO 493

NUTRITIONAL STATUS IN LEPROSY PATIENTS.

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Leprosy patients especially lepromatous leprosy cases are likely to be ignored by their family members and unable to find a job for their living due to disfigurement, and hence their nutritional status are likely to be lower than that of their counterparts tuberculoid leprosy and healthy persons. To confirm this hypothesis, the height and weight of 300 leprosy patients (comprising of both sex and both types of leprosy) attending leprosy outpatient centres of Madurai urban leprosy control unit were measured by standard technique. Their own family members living within the same environment (age and sex matched) were kept as control. The height and weight of the leprosy patients (altogether) and the control were 159.1 ± 7.7 cms. and 48.8 ± 6.9 kgs ; and 162.1 ± 6.8 cms. and 49.1 ± 6.1 kgs respectively. Thus the nutritional status of leprosy patients did not vary significantly from the control in contrast to the belief.

PO 494

OLFACTION AND LEPROSY

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Involvement of nasal mucosa or tendency of nerve affection in leprosy is liable to impair the sense of smell. Anosmia, if present in leprosy, is responsible for an additional misery for the patient. The sense of smell was assessed in 50 leprosy patients. The method used and results are presented. Twenty-six patients (about 26%) showed some or more degree of anosmia and this was found to be related with severity of local (nasal) lesions and also with systemic manifestations. The importance of this clinical aid in leprosy patients and also etiopathogenesis of anosmia are discussed in light of available literature.

PO 495

Middle ear function in Hansen's (Tympanometric study)

Dr. N.K. Soni
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Involvement of nasal fossae in leprosy may impair the function of eustachian tube resulting in disturbed middle ear function. Thirty patients of lepromatous leprosy with variable stages were subjected for tympanometry to assess the middle ear sound conducting system. Negative middle ear pressure was found in 18 patients (10 patients with unilateral and 8 with bilateral affection). Various patterns of tympanograms were recorded, common being showing conductive deafness with intact ossicular chain. Thus function of middle ear was found to be affected in 60% of lepromatous leprosy patients.

PO 496

THE ORAL AND MAXILLOFACIAL CONDITION OF 1155 LEPROSY PATIENTS IN GUANGDONG PROVINCE

Tu Yifu and Qiu Weiping, China Leprosy Center, Guangzhou, China

Abstract: The oral and maxillofacial damage caused either directly or indirectly by leprosy were investigated and suggestions for a dental-occlusion functional rehabilitation program are suggested.

1155 cases were examined: multibacillary type 842, paucibacillary type 308 and 5 uncertain cases. Age range was 15 to 90 years. Most (86.3%) were over 40 years. The average age was 55.7.

994 cases (86.1%) had disfigured faces and 483 cases (41.8%) suffered impairment of sensation of various sized areas on the face. Both manifestations appeared in higher proportion in patients of longer leprosy duration and having had more leprosy rections.

Enlargement of the supraorbital nerve was encountered in 333 cases (28.8%), of which 110 cases (33.0%) had sensation impairment of the innervation areas.

Microamp electric pulp test was carried out for 770 cases. 233 cases (30.2%) showed retarded pulp reaction and 291 cases (37.8%) had no pulp reaction. Multibacillary types had a higher occurrence than paucibacillary ($p<0.01$). The disappearance of dental pulp reaction to the electric pulp test in leprosy patients has not been reported before.

The destruction of oral tissues was essentially on the palate and was always along the central line. The statistical significance of multibacillary vs. paucibacillary also is $p<0.01$.

No limitation of tongue and jaw movement, no taste impairment, and no dental ankylosis was observed.

Oral hygiene was generally poor. The caries prevalence rate was 84.5% and the mean caries teeth per person was 5.23. Periodontal disease was found in 887 cases (76.8%). The toothlosing rate was 69.5% and the mean tooth loss per person was 7.7 teeth.

The authors suppose that the poor dental condition of leprosy patients is due to segregation and neglect by the dental profession.

According to the data gained from this pilot examination, 50% of the patients need operative dental work, 72% need exodontia, 78% need periodontal treatment and 67% need prosthodontic restorations.

Should a dental-occlusal functional rehabilitation program for leprosy patients be established, there would be much work for the dental profession.

PO 497

COMPLICATIONS IN THE TREATMENT OF LAGOPHTHALMOS BY THE TEMPORALIS MUSCLE TRANSFER (GILLIES ANDERSEN); MANAGEMENT AND PREVENTION.

Frank Duerksen, Rosemary Baccharelli and Marcos Virmond. Hospital Lauro de Souza Lima, Bauru, S. Paulo, Brazil.

Analyzing the result of thirty-nine consecutive temporalis muscle transfers done for lagophthalmos we found a significant high number of complications related to surgical technique. There were seven instances of post-operative ectropion due to dislocation of the inferior tendon strip, two patients with rupture of the medial canthal ligament and one case where the inferior tendon ruptured. The operations were all performed by three different surgeons at the Lauro de Souza Lima Hospital in Bauru from 1978 to 1983. All three surgeons had good basic training in this technique. The treatment of these complications and its' possible cause and prevention are discussed in this paper.

PO 498

Participation of after care Leprosy sufferers in comprehensive Eye Health Care Service for Fellow Patients.

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Social Stigma against leprosy is still the main obstacle to fight against cataract blindness in leprosy patients in this part of the country. Though under Our National Programme for Control of Blindness, Eye Camps are being held in the Rural Corners of Our State, yet the leprosy patients can hardly get entry into these camps. So eye camps only for leprosy patients are organised in the different leprosorium by the active participation of the After Care leprosy sufferers' Organisation who not only arrange the food & lodging aspect of the patients but also look after the patients in the para medical opthalmic field during their pre-operative, operative & post operative phase. They are also organising different programmes related to community Eye Health awareness.

PO 499

EVALUATION OF PHENOL GLYCOLIPID ANTIGENS IN THE SEROLOGICAL DIAGNOSIS OF LEPROSY AND TUBERCULOSIS.

J. Torgal-Garcia§, H.L. David§§ and F. Papa§§
§ Fac. Ciencias Médicas, U. N. Lisboa, Portugal
§§ Institut Pasteur, Paris, France.

Mycobacterial infections constitute one of the major problems in infectious diseases: leprosy and tuberculosis are highly prevalent in developing countries, while infections caused by "atypical mycobacteria" appear increasingly in developed countries.

The need for methods for early diagnosis and for prognostic evaluation, is prominent in all mycobacterial infections.

The usefulness of phenol glycolipids from M. leprae, M. tuberculosis, M. kansasii, M. bovis and M. marinum were evaluated in a selected population including individuals with leprosy, tuberculosis, "atypical" mycobacterial infections, leprosy contacts and healthy individuals; the sera from about 500 individuals were examined using E.L.I.S.A..

The frequency of E.L.I.S.A. test results in respect to each population group was statistically analysed, and the possible usefulness of these phenol glycolipids antigens in clinical medecine and epidemiology will be presented.

PO 500

Study of anti-Myocbacterium leprae antibody levels in leprosy patients and their contacts.

Elba González-Abreu, Roberto Olivares, Nancy Mora, Milagros Pérez and Angel B. González

Instituto de Medicina Tropical "Pedro Kouri", Ciudad de la Habana, Cuba, and Centro Provincial de Higiene y Epidemiología, Guantánamo, Cuba.

Serum samples from 184 leprosy patients and 3219 contacts were studied by ELISA with the semisynthetic disaccharide-BSA antigen. The patients were grouped according to leprosy type and length of treatment. For the multibacillary patients, the results showed a gradual and steady decrease of the mean absorbance values which were inversely correlated to the length of treatment. However, a few skin smear negative patients still maintained high absorbance values even after 8 years of continued treatment thus indicating that the humoral response had not ceased yet. Consequently, the test can be useful for monitoring the efficacy of treatment in multibacillary leprosy. As for the contacts, the overall number above the established absorbance cut-off value was 9.6%. There was a significant inverse correlation between lepromin reactions and absorbance values. Among those ELISA positive and clinically examined contacts 6 new leprosy cases were detected, 3 of them with positive skin smears. It should be noted that a seventh contact was detected with a very high absorbance value in whom not a single skin lesion was found but whose lepromin reaction was 0 mm and the skin smear showed a BI 3+.

PO 501

PHENOLIC GLYCOLIPID I OF MYCOBACTERIUM LEPRAE CAUSES A DECREASE IN THE SUPEROXIDE ANION RELEASE BY MONOCYTES IN RESPONSE TO M. LEPRAE

Mona Vachula, Timothy J. Holzer, Burton R. Andersen. University of Illinois at Chicago and Westside VA Medical Center, Chicago, Illinois, USA.

Phenolic Glycolipid I (PGI) is unique to Mycobacterium leprae. It is a phenol-phthiocerol triglycoside with the characteristic trisaccharide 3,6-di-O-methyl-β-D-glucopyranosyl-(1→4)-2,3-di-O-methyl-α-L-rhamnopyranosyl-(1→2)-3-O-methyl-α-L-rhamnopyranose. PGI is similar in structure to mycoside A of Mycobacterium kansasii, however the trisaccharide portion of mycoside A is made up of 2,4-di-O-methylrhamnose, 2-O-methylfucose, and 2-O-methylrhamnose. PGI and anti-PGI antibodies have been detected in the sera of lepromatous leprosy patients. PGI and the non-glycosylated, non-phenylated dimycocerosyl phthiocerol (DIM) are found in large amounts in experimentally infected armadillos, even in tissues freed of M. leprae.

The role that M. leprae-specific lipids play in modulating phagocytic cell function is of interest. Thus, peripheral blood monocytes, purified by elutriation, were incubated in teflon vials with sonicates of either PGI, DIM, mycoside A or buffer alone for 2 hrs. The cells were washed and cultured in 96-well microtiter plates overnight. Monocyte superoxide anion (O_2^-) generation was then assayed by the ferricytochrome c reduction method. Mycobacterium bovis BCG, M. leprae, zymosan and phorbol myristate acetate were used as stimuli. Monocytes pretreated with PGI released markedly less O_2^- when stimulated with M. leprae than did monocytes pretreated with the DIM, mycoside A or buffer alone. There was no significant difference in the O_2^- release by monocytes in response to the other stimuli regardless of the lipid pretreatment. PGI causes a decrease in O_2^- release by monocytes in response to M. leprae by perhaps masking the organism once inside the cell or scavenging the O_2^- produced, thus contributing to the failure of phagocytic cells to kill M. leprae.

PO 502

Synthesis of the Trisaccharide-base Neoglycoconjugate of PGL for the Serodiagnosis of Leprosy

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Nara University, Nara, Japan and *National Institute for Leprosy Research, Higashimurayama, Japan

The trisaccharide segment of PGL I of M. leprae, O-(3,6-di-O-methyl-β-D-glucopyranosyl)-(1→4)-(2,3-di-O-methyl-α-L-rhamnopyranosyl)-(1→2)-3-O-methyl-α-L-rhamnopyranose was synthesized effectively in the form of p-(2-methoxycarbonylethyl)phenyl glycoside by the condensation of p-(2-methoxycarbonylethyl)phenyl 4-O-benzyl-3-O-methyl-α-L-rhamnopyranoside and 2,3-di-O-methyl-4-O-(2,4-di-O-acetyl-3,6-di-O-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranosyl chloride in the presence of silver triflate and 1,1,3,3-tetra-N-methylurea. This was coupled to BSA by acyl azide method to give trisaccharide-based neoglycoconjugate, NT-P-BSA.

The NT-P-BSA showed very high reactivity and specificity to leprosy sera. Several kinds of NT-P-BSA with various sugar contents were synthesized and tested for the activity to leprosy sera. No significant difference was found. Molecular size distribution was analyzed by gel filtration and ultracentrifugation, which showed the presence of dimeric form of NT-P-BSA. Both forms showed almost same activity. These results showed that the change of the quality of NT-P-BSA from lot to lot was very small, which is very favorable to the continuous supply of the NT-P-BSA.

PO 503

Prevalence of phenolic glycolipid I and its antibodies among leprosy patients and their contacts in resettlement villages.

Sang-Nae Cho, Jeon-Soo Shin, Joo-Deuk Kim, Do-Il Kim* Koo-Weon Cheong*, and Seong-Hwa Kim**. Dept. Microbiol., Yonsei Univ. Coll. Med., Seoul; *Korean Institute for Leprosy Research, Anyang; and **Catholic Skin Disease Clinic, Taegu, Republic of Korea.

Countries like Korea have numerous resettlement villages for leprosy patients and their families as a part of leprosy control programs. As an attempt to establish a seroepidemiological surveillance of the disease, this study was initiated to investigate the presence of PGL-I and anti-PGL-I antibodies in sera from leprosy patients and their contacts in resettlement villages. Among 169 LL or BL patients, 69 (40.8%) were seropositive and the mean absorbance (A_{490}) was 0.252, and only 4 (14.3%) of 28 TT or BT patients were seropositive. In contrast, 87.9% of LL or BL patients with less than 2 years of chemotherapy and the mean absorbance was 1.019 in an accompanying study. The majority of LL or BL patients in the villages thus seemed to be serologically inactive. Among 103 contacts of leprosy patients in the villages, 10 (9.7%) were seropositive and the seropositivity seemed much higher than 5.5% among normal control populations from high endemic provinces and than 1.5% from low endemic areas, thus suggesting that contacts in the villages have more chances to become seropositive. However, none of 83 seropositive sera from leprosy patients and their contacts had detectable PGL-I, although 7 (87.5%) of 8 relapsed patients were seropositive and 4 (50%) had detectable PGL-I in their sera. The results suggested that the PGL-I based serology might be useful for the surveillance of leprosy among residents in the resettlement villages. The relationship between the PGL-I based parameters, bacterial indices and clinical findings were also discussed.

PO 504

SEROLOGICAL REACTIVITY OF PHENOLIC GLYCOLIPID-I RELATED SYNTHETIC SUGAR ANTIGENS AND SERODIAGNOSIS OF LEPROSY.

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2) Department of Natural Science, Nara University.
3) National Leprosy Hospital, Ohshima Seishouen.

The success in synthesis of antigenic sugar parts of Mycobacterium leprae specific phenolic glycolipid-I provides us a powerful tool for serodiagnosis of leprosy and for immunochemical analysis of the glycolipid antigens. In the process of chemical synthesis of trisaccharide, we have synthesized various delivatives of the sugar or oligosaccharides with different α, β-configuration to analyse the molecular mechanisms in antigen recognition by antibodies.

The synthesized sugars were conjugated to carrier protein such as BSA via linker arm and the serological reactivity was tested by indirect ELISA or competitive

ELISA inhibition assay. The following observations were obtained:

1. In general, trisaccharides have higher avidity to the antibody than disaccharides when used the same molarity of sugar.
2. Some methyl groups on the sugar molecule are critical in the antigen-antibody reaction.
3. Some combinations of sugar and linker arm influence the specificity or sensitivity of the antigen.
4. Among the sugar-protein conjugates tested so far, trisaccharide with the natural molecular structure of phenolic glycolipid-I was the best antigen for practical use.

PO 505A

Serological activity to a 36 kD antigen of M.leprae among household contacts of lepromatous patients.

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+Leonard Wood Memorial Center for Leprosy Research, Cebu City, The Philippines.

An ELISA-inhibition test measuring antibody reactivity to a species-specific epitope on a 36 kD antigen of M.leprae has been evaluated for its use in the detection of preclinical leprosy. Prelimnary data are presented from a continuing prospective study in the Philippines on household contacts of newly diagnosed lepromatous patients, which have lived in association with the index case for at least three years prior to their diagnosis and treatment. Serum samples from 27 of 310 contacts (8.7%) were consistently positive when following the ELISA-inhibition reactivity in a prospective fashion. Of the 27 seropositive contacts, 4 have developed disease. These contacts showed antibody reactivity up to 12 months prior to clinical onset. Of the 283 seronegative contacts, 2 developed disease. These findings indicate a possible increased risk of developing disease in seropositive individuals. These results will be discussed in relation to the findings in patients and controls.

PO 505B

EARLY DETECTION OF LEPROSY WITH A SEMI-SYNTHETIC DISACCHARIDE ANTIGEN(ND-O-BSA)

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University of Hawaii, Honolulu, Hawaii, USA and Leonard Wood Memorial Center for Leprosy Research, Cebu, Philippines.

We describe our preliminary findings from study still in progress on: 1)the prevalence of antibody to the ND-O-BSA antigen, in contacts of multibacillary (MB) patients and 2)the development of disease in relation to seroconversion. The ND-O-BSA antigen presents a construct of terminal and penultimate sugars of the PG-I molecule of M. leprae. Contacts are household members of MB patients. Controls and contacts were free of leprosy by skin examination at time of admission to the study. The reactivity of the controls was 1.7% (7/401) compared to 8.5%(35/410) of the contacts. Six contacts developed leprosy during a 4 to 30 month period. Chi-square analysis on the data is significant ($p<0.01$) when comparing the proportion of test positives out of those who have developed disease (4/6) to the rate of test positives who did not develop disease at the time of blood draw (31/404). The 4 positives developed MB disease and the 2 who tested negative developed paucibacillary disease. The test, with the data accumulated thus far, is able to indicate those contacts who have a high risk of eventually developing MB disease. It should be noted that the numbers in the disease category naturally would be small in comparison to the population of contacts of tested.

PO 506

ANTIBODY ACTIVITY AGAINST NEOGLYCOPROTEIN AND 36 K ANTIGEN IN THE FOLLOW-UP OF LEPROSY PATIENTS IN THE NETHERLANDS

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Leprosy patients attending the outpatient departments of the Department of Dermatology of the Dijkzigt Hospital in Rotterdam and of the AMC in Amsterdam were bled regularly during and after treatment. From over 300 patients serum samples were available and analysed. Antibody activity was determined against a neoglycoprotein mimicing the 2 terminal sugars of phenolic-glycolid-I using an indirect Elisa and against a 36 K protein using an Elisa inhibition test.
Results will be analysed and discussed against the background of possible relapses.

PO 507

STUDY OF ANTI-PGL-I ANTIBODY LEVEL AS AN INDEX OF BACTERIAL LOAD IN LEPROSY PATIENTS.

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Phenolic glycolipid I (PGL-I) is an antigen unique to M.leprae. Leprosy patients develop predominantly IgM antibodies against PGL-I. The present study was aimed at evaluation of anti-PGL-I antibody (IgM) levels in relation to bacterial load in leprosy patients. Sera of 188 leprosy patients were analysed in enzyme immunoassay. The antibody titres in lepromatous sera were much higher than that in tuberculoid sera. The coefficient of correlation between antibody levels and the bacterial index (BI) was 0.510 ($p < 0.001$). The antibody titres in long term treated patients were significantly decreased. A similar study in BALB/c mice infected with live M.leprae in the foot pad revealed a broad correlation between anti-PGL-I antibody levels and the duration of infection. The mice giving a positive response had bacterial count of more than 7×10^5 per foot pad. The coefficient of correlation between antibody levels and the bacterial count was 0.566 ($p < 0.01$). Thus measurement of anti-PGL-I antibodies may be an useful parameter for monitoring the disease activity in leprosy patients during the course of chemotherpay.

PO 508

A SLIDE ELISA - TEST TO DETECT SUBCLINICAL INFECTION AMONG LEPROSY CONTACTS.

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A qualitative ELISA test using teflon coated slides has been standardized. There was a good correlation of grading in slide test and O.D values obtained in microplate method. Take 2+ or more as positive as O.D. value in microtitre plate method for these grades fell above 0.100 for the both IgM and IgG conjugates. The amount

of antigen required is only 5 µl in 1:1000 dilution (0.1 ug/5ul). Thus the slide ELISA appears to be economical and sensitive. Even-though qualitative it can be adopted to field and results expressed as titres. The test can be used for screening large number of sera. If necessary the positive results can be confirmed by quantitative assay using microtitre plate method in a central Laboratory.

PO 509

A RAPID AGGLUTINATION TEST FOR THE DETECTION OF LEPROSY AND TUBERCULOSIS

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Leprosy and tuberculosis are major mycobacterial infections afflicting the developing countries. We describe here a test which puts into evidence both, the infectious form of multibacillary leprosy and pulmonary tuberculosis. The test is an antibody detection assay. Polystyrene or carboxylated latex bead particles are coated with sonicate of a laboratory grown atypical non-pathogenic mycobacterium, M.w. A drop of test serum is added to a drop of sensitized beads, mixed throughly and gently rocked. Positive sera cause agglutination within two minutes. With this test, sera from, 110 leprosy, 82 active tuberculosis, and 70 apparently healthy control were screened. The results demonstrated that the test detects 79% of patients with infectious form of multibacillary leprosy and 85.6% of active pulmonary tuberculosis patients. False positivity was 2%. The reproducibility of the test in several hands was evaluated using coded samples. The test is rapid, simple, and easy to perform and can be a useful aid to clinical diagnosis.

PO 510

A Preliminary Study on Comparison of Serological Activity in Sera from Patients with Leprosy, Contacts of Leprosy Patients and Normal Controls

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Middle Road Hospital, Singapore

The presence of phenolic glycolipid (PGl) in M. leprae has been described in recent literature. Antibodies directed against the lipid were found in serum from leprosy patients. Using the phenolic glycolipid antigen, ELISA method has been developed for serodiagnostic test of leprosy infection. In this preliminary study for comparison of serological activity using ELISA method, a total of 209 sera were studied. They were collected from leprosy patients (37 cases), family contacts of leprosy patients (29 cases), health workers in direct contact with leprosy patients (21 cases) and normal controls (122 cases). 37 leprosy patients (40.54%) had positive antibody level as compared to 4.0% in normal controls. The difference was statistically significant ($x^2 = 22.9$, $p < 0.001$). Comparisons made against the family contacts (40.5% compared with 3.4%) and the health workers (40.54% compared with 4.8%), indicated significant results, ($p < 0.005$ and $p < 0.025$ respectively). 75% of patients with lepromatous (LL) leprosy had positive antibody compared with 31.25% tuberculoid (TT) leprosy patients. The difference was not statistically significant as the number of sera tested was small. LL leprosy patients also tended to have higher antibody levels than TT leprosy patients.

PO 511

SEROLOGICAL ANALYSIS OF LEPROSY PATIENTS UNDER MULTIPLE DRUG THERAPY(MDT) IN VIETNAM. A PRELIMINARY REPORT.

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Nguyen Duy Khang & Le Kinh Due(2);
P.R.Klatser(3) & J.T.Hendriks(4).

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(3)Royal Tropical Institute,Amsterdam,The Netherlands
(4)Dep't of Medical Microbiology,University of Amsterdam,The Netherlands.

In an ongoing survey to study the immune status in leprosy patients under multiple drug therapy (MDT)
we determined on regular 3-month intervals total immunoglobulin levels and specific antibodies to a synthetic antigen based on M.leprae derived phenolic glycolipid.
Local negative control values have been established for these parameters in healthy persons,patients contacts and tuberculosis patients.In leprosy patients, total-IgG declined from initial(before therapy) high values to normal during the course of therapy. Total-IgM increased during the first three months of MDT,but then gradually decreases in most patients. In lepromatous cases,IgM-DMG levels decreased during the first year under MDT,but went up again after 15 months in some patients.
The relation of these findings in the humoral immune response under MDT with accompaning changes in clinical parameters is currently being investigated.

PO 512

SEROLOGY OF LEPROSY: THREE DIFFERENT TECHNIQUES.

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An ELISA assay for **M. leprae** where two antigen was absorbed on a membrane filter has been developed in our laboratory. **M. leprae** was isolated from subcutaneous lepromas of untreated patients using the procedure described by Philip Draper in 1979. A suspension of 2×10^6 bacteria per ml in 0.01 M amonium acetate-carbonate pH 8.2 was used as antigen. Five ul of this suspension were spotted in different positions and the filter was blocked with 10% BSA and washes were performed with phosphate buffered saline pH 7.2, 0.1% Tween 20. Horse-radish peroxidase labelled antihuman rabbit IgG was used in the secondary reaction and hidrogen peroxide and 3.3' diaminobenzidine Tetra HCl in the color reaction. Immunofluorescense tests were performed on glass slides using the antigen suspension described for ELISA tests. ELISA-ABS on plates was performed as previously described by us (R.J.Franco y col., Temas de Leprología N° 74, 1987) and FLA-ABS using the technique described by Abe et al (Int.J.Lepr. 48:109-119, 1980). Serum of lepromatous patients and from healthy people from non-endemic areas were used as positive and negative controls. All serums were absorbed with **M. vaccae** and BCG. We have tested serum from several groups, household contacts, blood relatives, hospital workers, patients with pulmonary tuberculosis, healthy people with BCG and leprosy patients'sons which have been isolated from their parents. Results show that the sensitivity and sepcificity of the proposed assay is satisfactory for clinical investigation of serology of **M. leprae.**

PO 513

SERO-IMMUNO REACTIVITY OF MOLECULARLY ISOLATED PROTEIN ANTIGENS OF MYCOBACTERIUM LEPRAE

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Studies were conducted on over sixty sera from patients in BT, BB, BL and LL stages of leprosy infection employing armadillo-derived M.leprae cell sonicate and the different molecularly cloned proteins. Preliminary data using immunoblot technique indicate the presence of several sero reactive bands against the M.leprae cell sonicate, predominantly in bacillary active patients. These bands occurred in the range of 14 to 65 Kd.

The sera were also screened for the presence of antibodies reactive to M.leprae antigens present in plaques of the lambda gt 11 recombinant clones Y3184 (12Kd), Y3164 (28Kd), Y3180 (36Kd) and Y3178 (65Kd). Drops of recombinant phage were placed in lawns of E.coli Y1090, the phage were grown and the antigens transferred to nitrocellulose for immunoblotting. Early results showed the presence of 65Kd and 36Kd in a few of the sera studied. No reactivity was observed with the other proteins.

These studies are being continued for further confirmation, using sera from all stages of leprosy infection (TT to LL), both treated and untreated, lepromin positive and lepromin negative contacts and normal healthy individuals.

PO 514

SEROLOGICAL RESPONSES TO DEFINED MYCOBACTERIAL ANTIGENS IN BORDERLINE TUBERCULOID LEPROSY

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Patients with leprosy of the Borderline Tuberculoid form are a heterogenous group with a range in clinical appearance and immunological responses. This has been evident in Nepal during the implementation of Multi Drug Therapy, when it is often uncertain as to whether a BT patient should have the Multibacillary or Paucibacillary type of therapy. We have prospectively examined the serological responses of 100 untreated BT patients to carbohydrate and peptide antigens to determine if these are possible indicators of increased bacterial load. Antibody response to Phenolic glycolipid and lipoarabinomannan were measured by ELISA using synthetic D-BSA and LAM of M.tuberculosis as antigens. When compared to healthy Nepali control subjects, 20% of BT patients had IgM anti-PGL antibodies and 35% had IgG anti-LAM antibodies. By contrast 72% of sera from untreated BL patients and 94% of sera from untreated LL patients contained IgM anti-PGL antibodies and 90% of BL sera and 100% of LL sera contained IgG anti-LAM antibodies. Few BT sera contained antibodies to the M.leprae specific epitope on the 35 KD protein as measured by MAb inhibition assay. The clinical extent of disease and bacillary index of the seropositive and seronegative patients will be presented.

PO 515

Monoclonal Antibodies Against Different Fractions of Mycobacterium leprae

Tsehay Atlaw, Rolf Kiessling, Ayenew Nurilign, Armauer Hansen Research Institute, Addis Ababa, Ethiopia.

Murine monoclonal antibodies produced previously in the leprosy system have been generated after immunization with preparations derived from whole M. leprae. We have used a more refined approach whereby individual fractions of Western blots of SDS-PAGE preparations were used to immunize mice in order to generate monoclonal antibodies. Thirty one fractions, ranging in molocular weight from above 200 KD to 14 KD were emulsified in DMSO and in complete Freund's adjuvant and used to immunize Balb/C mice and a second immunization was given two weeks later. Mice were killed three days after the final(third) booster immunization and spleen cells from these mice were fused with the mouse myeloma fusion partner SP2/O. Thirteen mice have been killed and supernatants from more than 300 hybrids tested in the ELISA. A total of 48 hybrids were positive for antibody production and of the ones tested in the Western blot, one hybrid (15-3-C-11) showed reactivity with strong bands in the molecular weight range of the original fraction used for immunization. After cloning this hybrid, 373 clones were tested, 36 of which are strongly positive in the ELISA against M. leprae sonicate antigen and are being expanded for testing in the Western blot to see if the original bands used to immunize can be recognized.

This novel approach of producing monoclonals against individual antigenic components is important in that unique M. leprae antigenic components which are of importance can be used selectively to produce hybrodomas with better specificity and more potential towards immunodiagnosis and as probes in molecular studies of leprosy.

PO 516

"SEROLOGY BY IMMUNOENZIMICASSAY (ELISA) ON LEPROSY PATIENTS AND THEIR CONTACTS, SUBCLINICAL INFECTION AND HIGH RISK GROUP DETECTION".

Liliana María Olivares, Raúl Franco, Lilian Cecere, María Elena Fariña and Juan C. Gatti. "Leprosy Center"-High School of Medicine, Buenos Aires University - F.J. Muñiz Hospital and B. Sommer National Hospital. Buenos Aires, Argentina.

Summary. The authors propose: 1) To study the serology by immunoenzimicassay (ELISA) on Leprosy patients and their household/non household contacts. 2) To appraise the subclinical infection and high risk group incidence. Materials and Methods: There are two groups under analysis. The first one composed by: lepromatous and dimorphous patients (active and non active) and tuberculoid ones. The second group is composed by: leprosy contact healthy subjects, including the following subgroups: household/non household contacts of lepromatous, dimorphous and tuberculoid patients (untreated or with recent treatment, less than five years) and recent household/non household contacts of inactive leprosy patients or old ones (more than five years treatment). Within both groups sera are studied through the immunoenzimicassay procedure with previous absorption by Mycobacterium BCG and vaccae and there are also developed clinical, bacterioscopy, histopathological examinations and Fernandez-Mitsuda reaction. Results: Positive serologies are observed in all active leprosy patients (lepromatous and dimorphous ones). It is verified a high subclinical infection incidence among normal subjects householding with LL and BL leprosy patients (2/3 of household subjects). It is found the high risk group composed by those subjects with subclinical infection, negative Mitsuda reaction, householding with active leprosy patients. Conclusions: It is emphasized the importance of serology by immunoenzimicassay, as early detection methodology of subclinical infection and high risk groups. Groups to which should be oriented chemoprophilaxis procedures, with clinical and serologycal subsequent follow-up, in order to appraise their evolution.

PO 517

Multi-media Educational Campaign about Hansen's Disease

Oliveira, Maria L. W; Moreira, Maria B. R.; Pereira, Gerson F. M.; Alves, José J. P. National Division for Sanitary Dermatology - MS.

The stigma associated with Hansen's disease is widely disseminated throughout Brazil. The prejudice is felt not only in society at large but also among health professionals and it has become an obstacle in the path of effective leprosy control actions.

The official change of the name leprosy to Hansen's disease was intended to occur together with a far-reaching mass media campaingn. That was not the case, however. To the contrary, both society and the government circles were incline to underplay the problem.

The results observed after the first six months of th multimedia campaingn - TV, radio, newspapers, as well as films posters and leaflets - point to the desirability of keeping up this campaingn.

PO 518

A MODEST BUT USEFUL TOOL TO GUIDE THOSE WHO, ALTHOUGH NOT ENGAGED IN HEALTH ACTIVITY, WISH TO COOPERATE IN CASE FINDING.

Donini Palmiro and Veroma Sisters
Kalongo Leprosy Project, Lira,
Uganda.

A 6-Page booklet with 39 colour photos has been produced, to meet the requests of all those who, though not engaged in health activities, are willing to assist in the detection of leprosy cases. The cooperation of these people of good will is very valuable, not only because they permit to expand leprosy case finding, but because through friendly and informal relations they often have a better chance to persuade suspected leprosy sufferers to let themselves be examined and treated by doctors.
The text has been arranged according to the suggestions received from the target users themselves. Accordingly it deals with the cause of leprosy; it shows the effectiveness of present day treatment; it gives facts which may counteract wrong popular beliefs; it gives guidance in dealing with individuals who may be affected by skin diseases other than leprosy.

Copies of it, in English , are available writing to:
fr. dr. Benini - via S.POLO 337
25 010 S.POLO (Bs)
Italy

PO 519

INVOLVEMENT OF STUDENTS IN LEPROSY HEALTH EDUCATION PROGRAMME - AN EXPERIMENT.

S.S.Naik, S.G.Samant, P.M.Godbole.
Acworth Leprosy Hospital Society for Research, Rehabilitation and Education in Leprosy, Wadala, Bombay-400 031. India.

The students' participation at college and high school level can be obtained for leprosy Health Education Programme if proper motivation is done and involving non-leprosy agencies such as student community will help to overcome the stigma of leprosy in Society. The details about the experiment of last four years of "Involvement of college students volunteers" and "Mitra" ("Friends" action oriented programme for high school students) has been discribed. The participation of 25 active members in college students' group gives approximately 200 Health Education talks on leprosy per year which costs at 30% of routine health programme. In "Mitra" activity has 6000 students membership and participation of 116 high schools in Maharashtra State. The programme work out as cheaper and effective and acts as an auxillary force to augment routine services in leprosy. Both these experiments have potential of multiplication in different regions.

PO 520

INCREASING PUBLIC AWARENESS OF LEPROSY THROUGH TOURISM.

Richard Marks
Leprosy Patient; Owner, Damien Tours, P.O. Box 1, Kalaupapa, Hawaii, 96742.

Founded on the principles that people fear what they don't understand and cannot understand something unless they see it, Damien Tours has been in operation at the Kalaupapa Settlement for 22 years. Approximately 5,000 tourists a year travel to Kalaupapa and go on this guided tour. Many other visitors come as guests of patients.

The tour is patient owned and operated and is designed to show how far medical knowledge and treatment have come. It tells the story of Father Damien and Mother Marianne but at the same time shows that nowadays the major wreckage from the disease comes from misunderstanding rather than the disease itself. Recognizing that for too many years leprosy has been covered up, the tour operates on the premise that unless you bring the disease out in the open and talk about it, you won't do anyone any good.

Not only has visitation to Kalaupapa increased public awareness, it has had an effect on the patient community itself. Seeing that they are accepted by tourists simply as people with problems, the patients themselves have become more at ease with strangers and now travel freely throughout the United States and the world.

PO 521

AN URBAN RURAL CONTRAST STUDY ON COMIC STRIPS, A NOVEL MEDIUM FOR LEPROSY HEALTH EDUCATION.

C.S. Cheriyan, Health Education Materials Department, German Leprosy Relief Association, 4. Gajapathi Street, Shenoynagar, Madras - 30.

This study is the first of this kind conducted in order to assess the impact of comics as a medium for health education on the knowledge and attitude of peopleabout leprosy. A questionnaire was administered at random on 2000 literate people from 3 urban (1200) and 2 rural (800) areas in South India for this study.

On analysis of the data collected it was found that 98.4% in the urban and 91.2% in the rural areas said that they believed leprosy is curable. Interestingly enough 97.6% and 89.3% respectively in the urban and rural areas were able to reproduce the signs andsymptoms of leprosy. With regard to attitudes 80.8% in the urban and 78.2% in the rural areas had said that leprosy patients should not be driven out of homes, instead they should be cared.

It was also found that comic strips were welcomed by an overwhelming majority of the respondents in urban (93%) and in rural (78%) areas as a medium for health education in leprosy. It is obvious that they made a definite impact on enriching the knowledge of the respondents and in helping them change their attitudes and beliefs about leprosy. It was also found that the comics were very well received by all, especially the younger generation.

PO 522

EDUCATION SANITAIRE DANS LA LUTTE CONTRE LA LEPRE EN MARTINIQUE

M. CONSTANT-DESPORTES, S. VEILLARD, A. YEBAKIMA, J.M. GEMIEUX (Comité Raoul POLLEREAU, MARTINIQUE).

En Martinique, la lutte contre la Lèpre remonte à plus de 50 ans (depuis Etienne MONTESTRUC). L'organisation actuelle est basée sur :

- un dépistage actif et passif
- une information sanitaire très poussée
- une polychimiothérapie.

Les axes d'information de la population sont essentiellement des supports audiovisuels (diaporamas, films, dépliants, livrets, affiches) et des émissions radio-télévisées.

La Journée Mondiale de lutte contre la Lèpre est une occasion où la population est totalement associée (messe, gala d'artistes, exposés-débats...). Les thèmes de ces dernières années ont été :

1985 : la Lèpre dans le conte créole
1986 : la Lèpre dans la Bible
1987 : Hommage à Etienne MONTESTRUC
1988 : la Lèpre dans la Caraïbe.

Une enquête effectuée en 1985 a permis de situer le niveau des connaissances populaires sur la maladie. La majorité des personnes interrogées connaissent l'existence de la Lèpre, citent l'apparition d'une tâche comme symptôme initial, attribuent la maladie à un manque d'hygiène et ont une grande peur du lépreux. Tous ces résultats sont mis à profit pour une meilleure information de la population.

PO 523

The knowledge and the attitude of leprosy in junior high school teacher in Taiwan

Pao-Feng Tsai and Pesus Chou
Der Yuh Nursing Junior College
Taipei, Taiwan

The knowledge and the attitude of leprosy were studied among 7257 junior high school teachers in Taiwan during July 21 to August 20, 1986.

The knowledge of leprosy was categorized into five items: (1) etiology, (2) clinical sign, (3) cause of disability and deformity, (4) curability, and (5) transmission. Excluding the transmission item, the correct answer rates of the other four items of knowledge were above 50%. The etiology item was the highest (74.4%) and the clinical sign was the lowest (52.1%). About half of the teachers thought that leprosy is easily transmitted or had no idea about the transmission, hence their attitude toward leprosy was negative.

The attitude of leprosy was categorized into three items: (1) fear, (2) shame, and (3) refusal. Except for the refusal item, the attitude of the other two items were toward positive.

There was a positive relationship between the knowledge and the attitude. Age was inversely correlated with the total score of both the knowledge and the attitude. Educational level, the teacher's major course and teaching course were not significant factors for the snowledge and the attitude of leprosy. The attitude of "shame" was influenced by the mass media and the caring experience.

PO 524

A THREE TIER COMMUNICATION MODEL FOR COMMUNITY PARTICIPATION IN LEPROSY CONTROL

H.M. Saleem, T. Jayaraj Devadas and R.S. Mani
Indian Leprosy Foundation, Shenoynagar, Madras 600 030, India.

The model adopted by Indian Leprosy Foundation aims at: 01. Transmitting scientific information on leprosy to the general public 02. Utilising community institutions to achieve this purpose and 03. Providing opportunity for large scale participation of youth in leprosy awareness campaign.

Methodology: Educational institutions are selected as settings for implementing this three tier model of communication. Tier I: Full time Field Officers are recruited and given intensive orientation on leprosy and alloted a geographical area of operation Tier II: Field Officer with the permission of authorities addresses the entire students of each institution collectively and in batches on facts about leprosy with suitable aids and orient them for community communication and Tier III: Each student is given a maximum target of 60 persons from the neighbourhood to be contacted and conveyed facts about leprosy within a time schedule.

Tools: Students are given a fact sheet format to be returned to their schools after recording details of contacts. Certificats and mementos to students and institutions are given in appreciation of their participation.

This model ensures communication effective through peoples participation.

PO 525

THE KALAUPAPA SETTLEMENT AS PART OF THE UNITED STATES NATIONAL PARK SERVICE.

Henry G. Law
Park Superintendent, Kalaupapa National Historical Park, National Park Service, U.S. Department of the Interior, Kalaupapa, Hawaii, 96742.

The U.S. National Park Service is entrusted with the preservation of such natural wonders as The Grand Canyon, Yellowstone and Yosemite National Parks. However, it is also responsible for areas that are deemed to be of great historical value, such as Independence Hall, the Statue of Liberty, Ellis Island, Alcatraz Prison and the White House. Due to its extremely educational and inspirational history, Kalaupapa was declared a National Historical Park in 1980 and thus became a part of the National Park System. While ensuring that the history of Kalaupapa will not be forgotten, this action also ensures that the remaining patients may live out their lives in the place they have come to regard as home.

Although the Park is filled with significant natural and archeological resources, the primary resource is the patients and their history. It is their story that makes Kalaupapa National Historical Park unique. Dedicated to the education of present and future generations with regard to the realities of leprosy, the Park stands as a monument to the patients' ability to endure and overcome, both physically and spiritually, not only disease but man's inhumanity to man.

PO 526

VOCATIONAL REHABILITATION OF LEPROSY PATIENTS

A-STUDY IN HARYANA STATE

(Duggal S, Minocha H.S. and Sujata)

In this presentation, we have attempted to extend the analysis with reference to the vocational rehabilitation of the dehabilitated Leprosy Patients to find out the number and nature of placement in which they are absorbed. We have also attempted to analyse the record from the various employees in order to find out how many of these are able to obtain fitness certificates after treatment. Analysis of 600 inmates of the 6 different colonies of Haryana were studied for the present problem. The study revealed that while the job problems of Leprosy Patients belonging to non-lepromatous types have been solved satisfactorily, the infections patients continue to suffer from job problems. Further it was felt to relax the rules governing issue of fitness certificates and bring them more in tune with the endemicity of leprosy at least in industrial area.

* Dr. Mrs. Suman Duggal,
Honorary General Secretary,
Hind Kusht Nivaran Sangh, Haryana,
Chandigarh, India.

** Mr. Harbhajan Singh Minocha,
Organising Secretary,
Hind Kusht Nivaran Sangh, Haryana,
Chandigarh, India.

*** Dr. Miss Sujata Sharma, Ph.D,
Psychologist,
Hind Kusht Nivaran Sangh, Haryana,
Chandigarh, India.

PO 527

Strategies for training human resources with a view to the implementation of the proposal for restructuring the Leprosy Control Program in Brazil.

Oliveira, Maria L.W; Fontanive, Nilma S.; Patroclo, Maria A. A; Moreira, Maria, B.R. - National Division for Sanitary Dermatology/MS

The problems with human resources for the restructuring of the Leprosy Control Program in Brazil are not related to the scarcity of said resources, since we have an overabundance of university trained professionals (physicians, nurses, and social workers).

Nevertheless, the deeply rooted prejudice regarding leprosy and the lack of a govermental policy in this field accounts for the fact that staffs cannot be counted on to perform their duties. Also, salaries are low and, therefore, seldom comply with their working schedules.

In an endeavor to use the services of this personnel training methodologies have been adopted which deal exhaustively with the development of an awareness about the problem of leprosy control, as well as proper consideration of the above mentioned attitudes of the personnel in question.

In connection with above, the following topic will be discussed:

* "A methodology for problem management" and the application thereof in the training of nurses, physicians, social workers, and educators;
* The adaptation of this methodology to the training of secondary and elementary school level personnel; and
* Instructional material (videotape recordings, slides, tap recordings, and texts), to be used in medical schools.

PO 528

THE PATIENT AS LEARNER. By Jeanette Hyland MPH.

The Author spent nine years in Paramedical training, Control Program planning and administration. She observed that patients were often expected to absorb the same load of information and adopt the same new habits and attitudes irrespective of the varying manifestation of their disease and their differing circumstances.

In 1979 the Author formulated a GUIDE TO HEALTH EDUCATION NEEDS OF PATIENTS, identifying what the patients needed to learn after taking account of the type of disease, likelihood of complications arising, presence of deformity or disability etc..

This guide is submitted in its 'pre-multi-drug-regime' form for information, discussion and adaption should participants find it useful.

It is recognized that this guide deals only with formulation of the CONTENT of the educational message, but it tries to emphasize some of the tasks that must be undertaken by the PATIENT AS LEARNER.

In the Autnor's experience many health workers who deal routinely with patients often over-simplify the dull repetitive job'of giving health education'. As long as health workers regard 'a patient as a patient as a patient' their efforts at education will tend to be inadequate and inappropriate.

Perhaps their job would be brighter if they thought of each patient as a learner with specific but varying learn learning needs.

The usefulness and effectiveness of this guide is to be studied by the Author in 1989 as part of a Ph.D. thesis on Health Education in Leprosy Control in Nepal.

PO 529

HANSEN'S DISEASEPUBLIC ENLIGHTENMENT CAMPAIGN IN NIGERIA.

Uchenna M. Ekekezie.
Leprosy referral& Research Centre, Uzuakoli, Nigeria.

This paper is a review of the methods used and theconstraints facing a new Health Education campaign started in Nigeria. The aims of the campaigns are among other things, to educate the general public on the facts on leprosy in order to renove the age-old social stigma which is still very strong in this environment, to foster early case-finding, to publicise MDT and prepare Health workers and the public for the integration of Leprosy into the General Health Service.

This campaign is the very first time in Nigeria that a clear-cut publicity or prominence of any kind is given to Leprosy. The basic starting capital was provided by Rotary International.

Being a relatively new aspect of leprosy control activity, the project is beset with constraints of equipment and therefore scale.

The major goal of the presentation therefore is to bring this project to the notice of colleagues in the field of Leprosy, with the hope that as a team we shall together find solutions to the numerous problems that hinder the project. Itis also hoped that they may make suggestions on how to improve on the campaign..

Finally, sharing the experience may also stimulate leprosy workers in other areas especially those who have as yet not started any public education programmes.

PO 530

Chemoprophylaxis of leprosy in Southern Marquesas by a single supervised dose of 25 mg/kg rifampicin.

J.L. Cartel, R. Taylor, S. Chanteau, J. Roux, Ph. Celerier J.H. Grosset. Institut Malardé, BP 30, Papeete, Tahiti.

From 1967 to 1987, the average annual detection rate of leprosy all forms remained stable in Polynesia : 8.8 new cases per 100.000 inhabitants. An epidemiological study pointed out that, during this period, the detection rate was similar in all of the archipelagoes except in the Southern Marquesas archipelago where it was of 60 per 100.000. In order to reduce this high detection rate it was decided (i) to insure that all known cases detected in Southern Marquesas receive multidrug therapy (WHO regimen) and (ii) to give a single supervised dose of 25 mg/kg of rifampicin (RMP) to the entire population of Sth Marquesas and to the Southern Marquisians living outside of their home island. For a 99 %, 90 % or 80 % effectiveness of the chemoprophylaxis, the number of expected cases of leprosy could be significantly reduced 4, 5 and 6 years, respectively, after chemoprophylaxis. In addition, a seroepidemiological study based on the evaluation of the PGL1 antigen and antibody levels before and after chemoprophylaxis was decided for the entire Southern Marquisian population. In 1987, a demographic census of the South Marquisians living in their home island or outside in Polynesia was performed. The administration of the chemoprophylaxis and the blood sample collection were carried out from January to March 1988. The coverage of the trial, the expected impact of the chemoprophylaxis and the first results of the sero-epidemiological study are reported.

PO 531

Study on the association between some epidemiological characters and basic and associated (multiple) causes of death among groups of leprosy patients deceased in São Paulo State, Brazil.

Lombardi, C.; Souza, J.M.P.; Costa Jr., M.L.; Lima, F.D. & Buchalla, C.M.
Public Health School, University of São Paulo, Brazil.

Within a universe of 13,066 leprosy patients (n = 13,066) who died in São Paulo State, Brazil, the basic and associated (multiple) causes of death were codified by a nosologist, according to 9th I.C.D.. The following epidemiologic characteristics are compared: 1) age at diagnosis; 2) age at death; 3) duration of disease before diagnosis; and 4) total duration of disease, among the five sub-groups: 1) the total universe; 2) basic cause of death = leprosy; 3) basic cause of death = nephropathy; 4) basic cause of death = leprosy + nephropathy present as associated cause ; 5) basic cause of death = leprosy + nephropathy absent as associated cause.

PO 532

Secular trends of leprosy incidence (detection) in São Paulo State, Brazil, 1935-84.

Lombardi, C.; Costa Jr., M.L.; Souza, J.M.P.; Lima, F.D.
Public Health School, University of São Paulo, Brazil.

Secular trends of detection rates of leprosy in São Paulo State are described within a 50 year period. Specific rates by age, sex, leprosy clinical type and by some counties of the state are also presented. Implications between distributions profiles and control policies/therapeutic regimens are discussed in the light of an historical approach.

PO 533

Réflexions sur la lèpre en Algérie:à propos d'un cas autochtone dans la région de Tlemcen (ouest algérien)

Omar BOUDGHENE-STAMBOULI; Abdelkader MERAD-BOUDIA et Otmane BOUALI.

Services de Dermato-Vénéréologie et Maladies Infectieuse Centre Hospitalo-Universitaire de Tlemcen (ALGERIE)

Au Maghreb,en 1984,la situation de la lèpre était la suivante:Maroc=incidence annuelle de 200 cas,Algérie=21 cas vivants et TUNISIE=176 cas vivants.
En 1987,nous signalions le 3ème cas de la région de Tlemcen(60 km du Maroc) en un siècle.Après les 4 cas de OUGHANEM et coll.,il représentait le 5ème exemple de lèpre autochtone,sans contacts connus avec des hanseniens vivants.
En Algérie,l'apport exogène était de 167 sur les 228 cas répertoriés de 1888 à 1974.En 1984?il était de 3 sur 21.
Nous assistons donc à une extinction de la maladie de HANSEN avec cependant quelques cas sporadiques(résurgence de foyers résiduels).
Les voyages et l'accroissement des échanges vont-ils modifier cette tendance?

PO 534

LEPROSY ENDEMICITY IN YALISOMBO, A PREVIOUS LEPROSARIUM-VILLAGE IN ZAIRE.

Guy Groenen, Stefaan R. Pattyn, Peter Ghys, Jo Colston. Bureau National Lèpre, Kinshasa, Zaire. Leprosy lab. IMT Antwerp, Belgium.

Yalisombo (YAL) is a previous leprosarium 25 km downstream from Kis(angani). After 1960 DDS treatment was very irregular and frequently non existent. In 1984 a population survey was conducted with clinical, bacterial, histopathological exams, lepromin testing and PGL antibody tests on a sample of people. Among 1590 people there were 256 leprosy (L) patients (16.1%) 30 MB and 226 PB, prevalences 1.9% and 14.2%. 78% of families had at least one case. 59% of patients had L when settling in YAL, 41% developed L during their stay. Surveys during 85, 86, 87 revealed 2, 5, 4, new L cases among the persons examined in 1984, all PB. The results of the findings will be presented in detail.

PO 535

EPIDEMIOLOGICAL SURVEY OF THE "VILA IDEAL" SLUN - RIO DE JANEIRO - BRAZIL -

MOREIRA A, TADIANA AND ALMEIDA T., JACIRA.

Due to the high endemicity of Hansen's Disease in "Duque de Caxias Municipality", Rio de Janeiro State, Brazil, a Epidemiological Survey of the "Vila Ideal" slum was planed. The goal was / to know the prevalence of skin disease of sanitary concern and, also, to analise the socio-economical conditions of the population, especialy / those related with environement sanitation. 450 dwellings were visited and 86% of the population (1903) screened by dermoneurological examination performed by auxiliary personnel. Tables will / show the frequency of skin diseases that recei-/ ved treatment on domiciliary basis. 19 cases / were suspicious of Hansen's Disease. The social profile will be assessed trough the study of several parameters of the population:- economical, sanitation, personnal and home higyene.

PO 536

15-YEAR REVIEW OF LEPROSY CONTROL WORK IN MADRAS-A METROPOLITAN CITY IN INDIA

DEREK LOBO, MANI MATHEWS, JACOB MATHEW, T.S. PETRO AND R.NARAYANAN.

GREMALTES REFERRAL HOSPITAL AND LEPROSY CENTRE, SHENOYNAGAR - MADRAS, INDIA.

MADRAS is the third largest metropolitan city-India, with a population of 3.75 million, out of which a population of 1.75 million is covered for leprosy control work by our institution, thus making it one of the largest URBAN LEPROSY CONTROL programme under a single agency.

A 15-Year Review of Work is presented spanning 1972 to 1987. The following parameters are available-Annual new case detection rate, prevalence rate, deformity rate, ulcer rate, Lepromatous rate, Percentage of Monolesions, School children prevalence, Slum prevalence, Age / Sex ratio, Clinical Classification and Bacteriological Status.

The profile of leprosy over the 15-year period is discussed along with various problems related to URBAN LEPROSY CONTROL.

PO 537

THE RURAL LEPROSY CONTROL .

A.G.Soeparlan, I.Agusni, S.Martodihardjo , H.Sukanto, M.I.Ilias .
Dept.of Dermatology, Airlangga Medical Faculty, Dr.Sutomo General Hospital,Surabaya,INDONESIA.

In the management of leprosy are some important problems which have to be considered for a better result : 1)The absence of an accurate data. 2)The patient compliance, the long and tedious therapy. 3)The physical deformation. 4)The social-economic condition and the general attitude towards leprosy.
Point 2 could be solved with the MDT application, which can reduced the long duration of treatment to a considerable shorter time.
With this advantage of therapy, the Indonesian Leprosy Foundation in Surabaya try to overbridge the 3 above mentioned constraints by way of an integrated management, in which the Local Authorities, the Health Center Medical Team and the whole community are involved, so that the leprosy problem and management will become a common duty of the whole society.
Therefore a "Rural Leprosy Control Project" is established in Ngronggot and Tanjunganom, two subdistricts in the Province of East Java .
Method: Education and Upgrading in leprosy for the members of the already ecxisting Authorities Wifes Organization (Dharma Wanita) with their P.K.K. (The Family Welfare Education) project and Caders for Leprosy Control who are volunteers from the community .
A satisfactorily result is accomplished .

PO 538

MULTI-DRUG THERAPY AND THE OCCURENCE OF NEW CASES IN A LEPROSY COLONY

The Society for the Eradication of Leprosy
C/o. Mrs. Leela Moolgaokar,
Bombay House, 24, Homi Mody Street,
Bombay 400 023.

Dr. R. Ganapati Dr. C.R.Revankar Dr. V.V.Dongre

Mr. D. H. Gole Mr. M. R. Neet

The chain of transmission of leprosy will be broken, if the source of infection is curtailed off. The introduction of Multi-drug therapy, under supervision, in a compact, self settled, leprosy colony, not only eliminated the pool of infection but the emergence of new cases was also brought down to a near zero level.

The work of the Society in the said Colony with multi-drug therapy will be projected and the yearwise results of the successive six resurveys will be revealed. The epidemiological significance of the findings will be discussed.

PO 539

ANALYSIS OF THE HOUSEHOLD CONTACTS OF 129 MULTIBACILLARY CASES D RING THE FIRST CONTACT SURVEY IN ZARIA PROVINCE, KADUNA, NIGERIA.

DR. S.A.R. KRISHNAN, DR. T. SRINIVASAN, DR. LOUIS GUSSENHOVEN, DR. M.O. ADELEYE*

Ministry of Health, Leprosy Control Training & Research Centre, P.M.B. 1089, Zaria, Kaduna State, NIGERIA.

*Director, Ilorin University, Kwara State, NIGERIA.

The contact of 129 Multibacillary index cases have been screened clinically, supported by slit skin smear study. From the 129 index cases, the household cases of 3,186 were screened. The number of newly detected cases, age, sex, type, the deformity grades were discussed. This study was conducted as a parametre to measure the impact of Multidrug treatment for future comparative studies.

PO 540

EVOLUCION DE LA ENDEMIA LEPROSA EN REPUBLICA DOMINICANA 1966-1987.

Dr. Huberto Bogaert Díaz, Miriam Hilario y Barbara García. Instituto Dermatológico, Santo Domingo. República Dominicana.

Al inicio de las actividades de la dirección actuál (año 1966) se encontraban inscritos en registro activo - en la Secretaría de Salud Pública 282 enfermos. Al 31 - de diciembre de 1987 la cifra de enfermos inscritos alcanzó a 7,620 con un promedio de casos nuevos anuales de 346.4 siendo el máximo de 481 año 1975 y el mínimo de - 249 año 1987. La línea de tendencia, sobre 21 años manifiesta un carácter decendente que demuestra la eficacia de las medidas de control.

El porcentaje de formas Multibacilares da 34% siendo el de Lepra Lepromatosa del 20.5%. Las discapacidades en enfermos nuevos han disminuído de un 50 por ciento en 1966 a un 8 por ciento en 1987, presentando grado III dos casos solamente.

PO 541

Evaluation du Programme Contrôle Lèpre Sénégal depuis 1982.

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Selon les Directives Nationales depuis six anx chacun des neuf Services Lèpre Régionaux, couvrant 9495 malades ont évolué par trois phases d'activités.

- Prè Polychimiothérapie (PCT) : 1982-85 voit la réorganisation des Recueils de données, du fichier lèpre, le recyclage du personnel, toute directive résumée en un Fichier Technique. La gestion est centralisée et informatisée, les laboratoires et salles d'hospitalisations crées. Le Comité de Coordination (Ministère de la Santé, Institut de Lèprologie, DAHW) assure une liaison mensuelle avec chaque Secteur. Enfin sont lancés deux essais : PCT Sélective : (Nouveaux Cas-Rechutes sur Dakar et villes de Région) et Cordonnerie mobile.

- Phase PCT : En 1986 débute la PCT "indiscriminée" où sur Zones choisies tout malade sous Disulone est décidé "mis en PCT ou guéri". En 18 mois 20 % du Territoire est couvert avec, après évaluation positive faite (1987), l'espoir d'une couverture de l'ensemble des malades d'ici 1993.

- Phase Post-PCT : En 1986 est lancé le Programme Education Sanitaire des malades mutilés et 23 Centres ouverts, suivi en 1988 par le Programme "Chaussure pieds anesthésiques". La fin de l'installation du Programme est faite en 1988 par la Planification de l'Education Sanitaire Population (axes : écoles primaires, radiophonie et population cibles : hopitaux, PCT etc...)

PO 542

DECLINING INCIDENCE OF HANSEN'S DISEASE IN RIO GRANDE DO SUL STATE BRAZIL.

Jair Ferreira

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Rio Grande do Sul State, the Southern state of Brazil (Area: 282.184 km^2, population: 8859.000), has a prevalence rate of Hansen's disease running between 0,40 and 0,50/1000 pop during the last 20 years.
The control program (started in 1936), since 1968 is based in a horizontalized system of health care. Leprosy cases are treated in general health care centers, which belong to the Secretariat of Health of the State. The only relevant technical or administrative changes made in the program in this period were the improvement of supervision (since 1974) and the replacement of the sulphonic monotherapy by another standardized scheme which associates 100mg of sulphona with 600mg of Rifamipicine, daily, during the first three months of treatment of multibacillary cases, in 1977.
The detection rate of new cases, which maintain the same level, with small variations, in the period 1974-1981 decreased quickly in the last six year, falling from about 3,5 cases/100.000 in 1981 to about 2,0 cases/ 100.000 in the period 1985-1987. Other epidemiological indicator (decreasing proportion of paucibacillary cases and increasing age average among new cases and decreasing proportion of cases with positive skin smear among multibacillary patients in treatment) suggest that the decrease of the detection rate is not related to operational factors but to a real decrease in the incidence of the disease, probably due to introduction of a bactericide drug (Rifampicine) in the standardized treatment of multibacillary cases.

PO 543

A STUDY ON SUBCLINICAL LEPROSY INFECTION IN BUSIA DISTRICT-PRELIMINARY COMMUNICATION.

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J.K.Mwatha
M.Were.
) Kenya Medical Research Institute, Alupe Leprosy & Skin Diseases Research Centre.

The study is being undertaken to detect individuals with subclinical infection and those at risk of getting multibacillary leprosy. Factors influencing infection with Mycobacterium leprae are also being explored.

The study population is composed of various categories of contacts of leprosy patients and a control population. Infection by M.leprae has been determined by using M.leprae specific glycolipid in enzyme linked immunosorbent assay. Lepromin test has been done to detect ability of the study population to mount resistance to infection through cell mediated immunity.

27.5% (or 401 people) of the study population have subclinical leprosy infection. 22.9% (or 74 individuals) of the infected group are lepromin negative and are at risk of getting multibacillary leprosy. Both these groups form a target population for vaccination, chemoprophylaxis or close follow up for overt leprosy and early treatment. They can also be followed up to monitor changes in their immune status. Age, sex lepromin positivity and BCG status do not influence the prevalence of subclinical infection. The prevalence of subclinical infection does not vary significantly among contacts of paucibacillary and multibacillary patients so far.

The study continues.

PO 544

Programa de Control de lepra de la Republica Argentina

D.R. Achenbach M. Antola, J Ganopol, J.C. Granata, M. Liturri, R. Manzi, O. Terriles.

Se efectúa una descripción histórica del problema de la lepra en la Argentina y se mencionan los diversos sistemas aplicados para combatir la endemia, hasta llegar a la situación actual con

la paulatina integración de la enfermedad en la atención médica general con participación prioritaria en las acciones de atención primaria.
Se enfatiza sobre la necesidad de incluir el tema en los programas de educación para la salud en todos los niveles y promover su participación en diversos programas de investigación, estimulando áreas de interés, tales, como: inmunología, terapéutica, rehabilitación, bacteriología, epidemiología, etc.

PO 545

DOWNWARD TREND OF LEPROSY INCIDENCE IN POLAMBAKKAM, ASSESSED BY BIRTH COHORTS ANALYSIS

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The Polambakkam Leprosy Control Programme started in 1955. A birth-cohorts analysis has been performed on the 23.772 patients detected between 1962 and 1982, period during which case-detection rates approximated incidence rates. Cohorts studied were born between 1891 and 1980. Birth cohorts analysis mainly aims to assess how the risk of developing the disease is related with the past experience of life.

At all ages, incidences were higher for older cohorts. The results favor the hypothesis that infection has been decreasing over time, so that persons born later were exposed to lower rates of infection.
People born after 1941 and particularly the cohort born 1951-1955 have experienced a marked decline in the incidence of leprosy in ages 20 to 40.
This reflects the effects of control for preventing infection in people aged below 15 at the time the programme was launched. It also suggests that infections occur early in a large majority of cases, sometimes with a prolonged incubation period.
The limited downward trend in childhood is discussed.

Age seems to influence similarly the different cohorts. Incidence increases sharply in younger age-groups until the age of 14. For a given period of birth, older people have lower leprosy case rates than young people. The possible meanings of these observations are discussed.

Results are presented by type of leprosy and by sex.

PO 546

EPIDEMIOLOGIC DATA ON LEPROSY PATIENTS ATTENDING THE LEPROSY CLINIC OF THE DIJKZIGT HOSPITAL IN ROTTERDAM.

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Data available on 213 leprosy patients attending the leprosy clinic between 1945 and 1988 were analysed in retrospect concerning epidemiological data; classification, sex, origin of patient, age at onset, start of treatment, immigration into the Netherlands and duration of treatment.
Special attention was given to the occurance of complications during multi drug intervention treatment and possible relapses thereafter.
The findings will be discussed.

PO 547

INTEGRATED HEALTH CARE IN THE EPIDEMIOLOGY AND CONTROL OF LEPROSY.

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Epidemiology by determining the distribution and determinants of a disease grips at the root cause of disease. The old adage is all too true that 'Prevention is better than Cure'. Powerful drugs like Rifampicin or the promise of a vaccine will help to control leprosy, but there are other epidemiological factors which must be dealt with if a complete control and ultimate eradication is to be envisaged.

Immunity is one of the main factors in determining disease and where protein energy malnutrition exists, immunity is very low and concomittant infection also reduces immunity. In a country such as India, where there exists so much of malnutrition, parasitic infections, Tuberculosis, crowded and unhygenic living, immunity is bound to be low. Poverty and ignorance are contributory factors in the lowering of immunity.
For these reasons, we at Palamaner have modified the SET pattern of work at no extra operational costs, except for drugs and vaccines, so that our work is now directed to integrated health care with leprosy as our primary aim. In an area of 1817.29 sq.km. and a population of 3,04,123 we have 95 Mobile treatment points and a system of clinics that treat leprosy patients, non-leprosy general patients, T.B., eye, Mother and child care, Immunisations, Domicilliary rehabilitation and health education programmes.

PO 548

REACTULISATION DE L'EPIDEMIOLOGIE DE LA LEPRE EN TUNISIE

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En Tunisie, pays à faible endémicité lèpreuse, la lèpre est reléguée au second plan malgré que les sta--tistiques montrent que la forme lèpromateuse donc con--tagieuse de la maladie est de loin la plus rencontrée. Une étude épidémiologique faite après 2 ans d'activité de l'équipe mobile de lutte contre la lèpre sous l'égi--de du C.I.O.M.A.L., montre que 3 foyers à endémicité relativement importante existent : Mahdia : 55 cas ; Mednine : 40 cas ; Sfax : 39 cas. l'homme est 2 fois plus atteint que la femme, cette prédominance est sur--tout nette dans la forme lèpromateuse. L'âge présumé de contamination est situé après la puberté et avant l'âge de 20 ans, mais peut survenir à tout âge. Le pic de fréquence d'âge des malades dépistés est situé entre 55 et 70 ans, témoin d'une transmission faible à la po--pulation jeune. 65 % des patients sont sans profession par mutilations invalidantes dues à la maladie. 90 % vivent dans des zones rurales et appartiennent à des classes sociales pauvres. La contamination est le plus souvent familiale. 61 % des patients ont au moins un lépreux dans la famille. La forme lépromateuse polaire est la plus fréquente représentant plus de la moitié des cas (57 %). Ceci souligne la gravité de la lèpre en Tunisie. Les autres formes de lèpre sont beaucoup moins fréquentes et se répartissent en : lèpre interpolaire : 29,5 % ; lèpre tuberculoïde polaire : 3 % ; lèpre in--déterminée : 4,5 %. Les complications réactionnelles sont fréquentes : ENL : 26 % ; RR : 45 %. 55 % des ma--lades ont des lésions ostéo-articulaires plus ou moins avancées avec une impotence fonctionnelle totale par mutilation dans 27 % des cas. Les maux perforants plan--taires sont observés chez 15 % d'entre eux.

PO 549

THE PRESENT LEPROSY SITUATION IN KATSINA STATE IN NORTHERN NIGERIA

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As calculated from the available data (C.M.Ross 1951, WHO-LAT survey 1960, NSL survey 1977 and own findings 1983-87) the present leprosy situation is described. In total there are some 6,500 leprosy patients with signs of active/inactive infection of whom 1,200 (18%) have multibacillary and 5,300 (82%) have paucibacillary leprosy. A minimum of 5,500-6,000 have been registered at least once in their life and as such have received antileprosy drug treatment, sofar only DDS mentherapy. At present there are still 3,300 patients on the registers who are receiving either DDS monotherapy or MDT. With a rate of 9-15% in multibacillary and below 1% in paucibacillary patients, there are a maximum of 120 leprosy patients with DDS resistance. There are maximally 300 new leprosy patients a year which stands for an annual incidence rate of 0.0625‰. With a rate of over 60% disability grade 2 or more (involving hands in 50%, feet in 30% and eyes in 15%), there are at least 4,000 leprosy patients with gross disability of hands and/or feet and/or eyes.

It seems that with an intensified effort it is possible to have leprosy under control by the year 2000. However, the care for thousands of mutilated leprosy patients has to be continued at least till the year 2010.

PO 550

Evaluación del Plan de Lucha contra la enfermedad de Hansen en la Provincia de Las Palmas

Desde hace cuatro siglos la endemia de Lepra se ha mantenido sin grandes variaciones en estas Islas Canarias

En 1982 se realiza un estudio epidemiológico que -- abarcó indicadores sanitarios (Tipo de Lepra, Ingesta de medicación, controles realizados, pruebas analíticas, radiológicas etc.), indicadores sociales (Profesíon, Estudios, hábitos etc.), así como las variantes políticas y - económicas que podían ser causas del mantenimiento de esta endemia.

Desde 1982 hasta el final de 1987, se han ido introducciendo una serie de medidas correctoras sobre aquellos factores negativos que se detectaron en el estudio epide-- miológico anteriomente citado.

El presente trabajo intenta evaluar las acciones tanto sociales (ayudas para mejorar el medio ambiente, ayudas al transporte, Ayudas al Estudio, etc), sanitarias (control de convivientes, criterios terapéuticos, Educación Sanitaria, rehabilitación etc.) que se han venido realizando a lo largo de estos cinco años y que quedaban integradas dentro del Plan de Lucha contra la Enfermedad de Hansen en la Comunidad Autónoma de Canarias.

PO 551

THE TRENDS OF EPIDEMICS OF LEPROSY IN FUJIAN PROVINCE

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In Fujian Province,27506 cases of leprosy were found during the last thirty or more years. By the end of 1986,1723 active cases remained,with a prevalence of 0.06 per thousand, showing a decrease of 90.3% from the previous high. the case-finding rate decreased by 91% .The mean incidence decreased by 87.8% .the incidence of child cases decreased significantly from 2.13/100,000 to 0.09/100,000. The mean age of the patients at the time of confirming the diagnosis shifted to the older groups, denoting that the disease was well under control. In view of the shortening of the duration of the disease,the increasing of the percentage of the patients in early stage (from 28.3% to 52.8%), the decreasing of the cases with disability and deformity (from 31.2% to 18.4%), and the increasing of the percentage of the paucibacillary cases with a single skin lesion (from 9.4% to 16.5%)in this province, a significant accomplishment in leprosy control has been achieved, and the goal of basically eradicating the disease by 1995 should be reached.

PO 552

PREVENTION OF LEPROSY WITH DAPSONE AFTER 20 YEARS

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The use of dapsone as a measure of prevention of leprosy was studied in two neighbour communes(township) in Chenggu,Shanxi,of which the incidence of leprosy was high. All leprosy cases in the two communes were sent to local leprosaria before the study.Then 178 house-hold contacts were selected randomly in the Wenchuan commune as the chemo-prophylactic group and 147 house-hold contacts were selected in the Mengying commune as controls.All of the 178 contacts in the dapsone group were given dapsone for one year;no drug or placebo were given to the controls.The observation has been lasted for twenty years. One leprosy case occurred in the contacts with dapsone prophylaxis,six cases of leprosy developed among the controls.The difference in incidence per unit of person-year between the two groups was statistically significant($p<0.05$) The difference of the incidence rates showed that the protective effect of dapsone against leprosy was about 87.30%.The preventive effect during the first ten years was better than that of the latter ten years and the difference was statistically significant($p<0.05$). These results indicate that dapsone can be used as an effective prophylactic drug for the house-hold contacts.

PO 553

LE PROFIL EPIDEMIOLOGIQUE DU LEPREUX A ABIDJAN (COTE D'IVOIRE)

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A partir de 144 cas de LEPRE observés au C.H.U. de Treichville au Centre de DERMATOLOGIE, de janvier 1983 à décembre 1986, nous tentons de dégager un profil épidémiologique du lèpreux. Au terme de cette étude, il faut retenir que :

- la confrontation clinico permet d'éliminer de nombreux cas parfois facilement étiquetés cliniquement Lèpre. Elle permet également de classer la forme et de préjuger de l'état immunitaire.
- la prédominance des formes tuberculoïdes témoigne de l'ancienneté de l'infestation hansénienne en Côte d'Ivoire.
- la macule, longtemps indéterminée, garde une valeur diagnostique appréciable, surtout chez l'enfant.
- l'appréciation de la période d'incubation comporte actuellement de nombreuses inconnues, en raison de multiples facteurs : pour éviter d'être banni ou chassé de la communauté villageoise ou rejeté par les soi-disants bien portants, le malade lèpreux cache le maximum possible les lésions cutanées de lèpre - La maladie existe dans toutes les couches socio-professionnelles depuis le cadre, le haut fonctionnaire jusqu'aux chômeurs, en passant par les élèves, les paysans, les ouvriers - La distribution gratuite des médicaments anti-lèpre à des malades précocement diagnostiqués constitue un motif supplémentaire de motication et d'espérance de guérison - La réhabilitation et la réinsertion du lèpreux suppose un supplément d'âme, de générosité et de solidarité pour que ce dernier se considère comme un être comme tous les autres et accepté comme tel. Dès lors, une éradication de la lèpre serait possible par la conjonction d'un vaccin anti lèpre efficace, d'un changement des mentalités, d'une stratégie multidirectionnelle et à long terme anilèpreuse internationale rigoureuse.

Dr. Pierre-André Dermatologue-Lèprologue Abidjan (RCI)

PO 554

LA LUTTE CONTRE LA LEPRE DANS LE HAUT-UELE ZAIROIS : RETROSPECTIVE ET RESULTATS DU TRAVAIL DE FOPERDA DES ANNEES 1975 A 1987

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Institution : Fondation Père Damien, Isiro, Zaïre

Après un historique de l'action sanitaire menée depuis 1924 dans le Nord-Est du Zaïre -spécialement contre la lèpre-, les auteurs expliquent en détail le travail effectué depuis 1975.
Le centre de Pawa coordonne les activités anti-lèpre menées par 20 équipes mobiles en 1975, actuellement au nombre de 14, qui ont vu chuter le nombre de malades : 17 404 en 1975, 1 077 en 1987;
les nouveaux cas se sont réduits de 2 963 en 1975 à 220 en 1987.
Le taux d'endémicité est passé de 40 ‰ en 1919 à 13 ‰ en 1975 et à 2 ‰ en 1985.
la méthodologie de travail verticale pure a été modifiée : certaines zones de santé, celle de Pawa par exemple, bien organisées, ont pu intégrer les soins des lépreux aux soins de santé primaires, encadrées par un superviseur lèpre.

PO 555

EPIDEMIOLOGIC STUDY OF SUBCLINICAL INFECTION WITH MYCOBACTERIUM LEPRAE AMONG HOUSEHOLD CONTACTS OF LEPROSY PATIENTS IN CULIACAN, MEXICO

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A retrospective cohort study of subclinical infection with M. leprae among household contacts of lepromatous leprosy patients was conducted at the Public Health Center, Dermatology Clinic in Culiacan, Mexico. 175 index leprosy cases 15-65 years old and 645 household contacts of these cases aged 15-80 were followed up from January, 1981 to December, 1985. Data collected from this population were analyzed to assess the effectiveness of antibody testing to phenolic glycolipid antigen (PGL) of M. leprae and the Mitsuda Lepromin skin test (MITSUDA) in detecting subclinical infection among high risk contacts of the index cases. During 5 years of follow up, 34 new leprosy cases were diagnosed in these 645 contacts, for a cumulative incidence of 5.3%. The age-adjusted relative risk (RR) of leprosy among contacts with positive PGL antibody (PGL-Ab) was 13.59 (95% CI=6.71-27.49). Among contacts with negative/intermediate MITSUDA tests, the age-adjusted RR was 4.86 (95% CI=1.57-15.08). The increased risk associated with a positive PGL-Ab test or a negative/intermediate MITSUDA test was greater for males than for females, although this conclusion is based on small numbers. Blood relative contacts (first, second, and third degree relatives) of the index cases who had a positive PGL-Ab test

(RR=19.07) were at higher risk than spouses of the index cases (RR= 13.09). The risk among blood relative contacts with a negative/ intermediate MITSUDA test (RR=8.06) was higher than among spouses (RR=2.08). These results suggest possible genetic susceptibility to leprosy among the household contacts of index cases. Intervention against leprosy in this endemic area should be directed at blood relative household contacts of cases with positive PGL-Ab and negative/intermediate MITSUDA skin test results.

PO 556

FINDINGS IN THE LEPROSY CONTROL WORK OVER THREE DECADES IN A HYPER ENDEMIC AREA

Dr. E. Vomstein and Dr. Devarajan, Leprosy Relief Rural Centre, Chettipatty, Salem, India.

The project covers a population of 500,000 spread out in 96 villages in a typical rural area of the hyper endemic zones for leprosy.

Methodology: Survey Education and Treatment (SET) was the basic methodology followed in the programme.

26 peripheral clinics were located in the project. Each clinic is headed by a trained para medical worker.

At the project Head Quarters there is hospital well equipped with laboratory, physiotherapy and surgical facilities which takes care of the specilised medical needs of the patients.

Over 30 years the project recorded 23,259 cases. Existing cases under treatment as on November, 1987 are 2,471.

The average gross prevalence of the project area was recorded 46.6 cases per thousand population. Now the active prevalence is 5.5.

The individual village prevalence ranges from 9.8 to 207.2 per thousand population.

The prevalence among school going children has declined to 1.5 during 1987 as against 6.9 initially and found no Multi Bacillary cases.

There is conspicuous fall in the deformity rate from 13.7 to 2.3 per one hundred cases. 73% of the total recorded cases are early and self reported indicating leprosy consciousness in the community.

PO 557

EVOLUTION DE L'ENDEMIE LEPREUSE AU CAMEROUN (1967-1987)

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Depuis vingt ans, le nombre des malades officiellement pris en compte décroît de manière progressive et régulière passant de 57000 en 1967 à 19000 à ce jour.

Aujourd'hui on observe une prévalence globale de 2°/₀₀, dont 4,07 % chez les plus de 15 ans, un index lèpromateux de 0,4 °/₀₀ et une prévalence infantile très faible de l'ordre de 0,1 °/₀₀. La répartition des malades selon leur forme clinique est la suivante : lèpromateux : 21 %, Tuberculoïdes : 49,5 % et Indéterminés : 29,5 %.

En 1987,809 nouveaux cas ont été détectés pour l'ensemble du pays et 3414 malades rayés des comptes dont 1791 LDC.

Actuellement 15244 malades sont en traitement dont 4193, soit 27,5 %, en polychiothérapie (1933 multibacillaires pour 2260 pauci-bacillaires).

Le problème essentiel reste la recherche active des malades à détecter. Une enquête par sondage en grappe, réalisée sur 12000 adultes en zone rurale et sur l'ensemble du territoire, par le Ministère de la Santé Publique et l'OCEAC (Organisation de Coordination pour la lutte contre les Endémies en Afrique Centrale) a en effet montré que leur nombre était sous-estimé.

PO 558

SELENIUM CONTENTS IN HAIR OF NORMAL PERSONS AND LEPROSY PATIENTS LIVING IN QIN AND BA MOUNTAIN REGIONS OF SHANXI PROVINCE CHINA

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The Qin and Ba Mountain ranges are located in the southern part of Shanxi province. Although both regions are endemic for leprosy,but there is a difference in disease endemicity. Besides leprosy,the Ba Mountain region is also well known for its endemicity of Kushin-Beck disease and a kind of degenerative arthritis, diseases known as to be associated with difficiency of selenium.

Analysis of the selenium content in hair shows that there is a significant decrease in the following order: L leprosy) T leprosy) normal persons of Ba Mountain region) normal persons of Qin Mountain region. But there is no significant difference between L patients living in Qin and Ba Mountain regions.

The possible significance of these difference is discussed in the text.

PO 559

M.lepra soluble antigen covalently coupled to liposomes elicits both early and late delayed hypersensitivy skin reactions.

U.Sengupta,Sudhir Sinha, G.Ramu, R.K.Lavania and C.M.Gupta.

The soluble antigen of M.leprae was coupled to liposomes and used for skin testing in leprosy patients, hoping that this mode of antigen presentation would be identical to that of the integral lepromin. The covalently liposomised antigen elicited both early (24-48 h) and late (3-4 weeks) delayed type of hypersensitivity reactions, true to the nature of lepromin, unlike the soluble antigen alone which elicits only the early reaction. Immunohistological study using monoclonal antibodies against phenotypic markers of cells revealed that these reactions are similar to those of Fernandez and Mitsuda reactions induced by standard lepromin antigen. Hence, for the first time the study showed induction of a late reaction by a soluble antigen.

PO 560

Skin reactivity to the Rees soluble antigen of Mycobacterium leprae.

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The skin reactivity to the Rees soluble antigen of Mycobacterium leprae was studied in 192 household contacts of multibacillary leprosy patients. The control groups were composed of 10 lepromatous patients, 8 tuberculoid patients, 10 patients of pulmonar tuberculosis and 10 healthy individuals. In addition, tuberculin tests with PPD RT-23 were performed in all individuals. Among the contacts the mean reaction size was 5.0 mm, while it was 0 mm in the lepromatous, 18.6 mm in the tuberculoid, 2.7 mm in the tuberculosis patients and 1.7 mm in the healthy controls. A reaction size of 6 mm or higher was considered as positive. In 60 contacts (36.4%) the reaction to the SA was positive with a mean of 15.3 mm while the mean reaction size to PPD was 12.1 mm in the same individuals ($p < 0.01$).
Skin testing with SA might be useful for detecting delayed type hypersensitivity to M. leprae in epidemiological studies.

PO 561

SKIN TESTING WITH NEW TUBERCULINS IN VIETNAMESE LEPROSY PATIENTS AND THEIR CONTACTS.

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(1)National Institute of Hygiene and Epidemiology,Hanoi,Vietnam.
(2)Dep't Medical Microbiology,University of Amsterdam,The Netherlands.

A skin test survey using 15 new tuberculins (NT's; see accompaning abstract of Ly et al.) was carried out among 276 leprosy patients from a leprosarium in HoChiMinh-City(HCMC) in the south of Vietnam. Also included were 210 children of patients living in leprosaria (patient contacts).
Compared with normal Vietnamese schoolchildren, patient contacts were more frequently positive for NT derived from fast growing species (7.5% versus 20% resp.). In leprosy patients there was a lower percentage of positive responders to 11 out of the 15 NT(slow and fast growing species) studied. Lepromatous cases less frequently had positive responses to Leprosin-A than did tuberculoid patients(4.2% versus 11.6%), whereas the percentage of positive responders to Tuberculin was similar in both conditions. These results indicate that the reduction in the cell-mediated immune response which generates the delayed type hypersensitivity reaction in the skin is not only to specific M.leprae antigens but also to non-specific,cross-reactive mycobacterial antigens.

PO 562

SKIN TESTING OF VIETNAMESE SCHOOLCHILDREN WITH 15 NEW TUBERCULINS.

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Exposure to environmental mycobacteria is important in determining levels of immunity against tuberculosis and leprosy. A skin test survey was done among 1035 children (aged 7-19 years) from 3 cities in north(Hanoi) and south(HoChiMinh City(HCMC)and Nha Trang) Vietnam. Fifteen new tuberculins (NT),including leprosin-A, were applied;an induration of diameter >2mm was considered positive. Compared to other tropical countries,low levels of sensitisation were recorded .Further, remarkable regional differences were found: the percent positives(pooled data from 15 NT) among non-BCG-vaccinated children was significantly lower in Hanoi(13.1%) and HCMC (15.5%) when compared with Nha Trang(25.7%). The proportion of non-vaccinated children responding to Tuberculin ranged from 18.4% in Hanoi to 54.5% in Nha Trang.Leprosin-A induced a response in 14.9% of the children in Nha Trang,but in very few in Hanoi(4.3%) or HCMC(3.0%). In Hanoi most of the response was to fastgrowing species while in HCMC and Nha Trang ,it was mainly to slowgrowing species. These results may account in part for the observed differences in the prevalence of tuberculosis and leprosy between the north and the south of Vietnam.

PO 563

LEPROMIN RESPONSES IN RECIPIENTS OF A CANDIDATE ANTI-LEPROSY BACTERIN VACCINE (WHO-IMMLEP Mycobacterium leprae, KILLED PREPARATION) IN A HYPOENDEMIC, NON-BCG-USING AREA.

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The availability of large amounts of Mycobacterium leprae purified from infected armadillos by gentle methods has provided a basis for the formulation and testing of candidate anti-leprosy vaccines. One such early formulation (WHO-IMMLEP Mycobacterium leprae, Killed Preparation) was tested internationally in Phase I trials in non- and hypoendemic areas during 1983-4. Testing was done, both where BCG vaccination vs tuberculosis is routine, and, also, where it is not used. In the latter case, comprised by the U.S.A., a vaccine dose of 1.5 x 10^8 purified M. leprae was administered to 17 volunteers; all responded with vigorous local reactions to the intradermal inoculations, although no serologic responses to either integral M. leprae or its subfractions could be detected.

Inasmuch as a major measure of a vaccine is the duration of any effectiveness - whereas the incubation period for Hansen's disease is usually of the order of 3-5 years - original vaccinees were tested for response to standardized lepromin A, 3 years after inoculation, in comparison with an unvaccinated control group from the same population.

Although results of tests of cell-mediated immune response in vitro are still pending, no significant differences in degree or type of dermal reactivity to lepromin in vivo were found between vaccinees and normals in the U.S.A. This absence of a significantly greater lepromin response in the vaccinated group suggests that, whatever degree of immunologic enhancement may be provided initially by the single-phase bacterin at the dose employed, little, if any, effect on either Fernandez or Mitsuda reactions can be expected after three years. Conclusions regarding possible protective effectiveness must, therefore, continue to await the outcome of on-going vaccine field trials.

PO 564

IMMUNOLOGICAL STUDIES ON DERMAL LEPROSY GRANULOMAS.

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Immunohistological studies have demonstrated that the predominant lymphocytes infiltrating the leprosy granulomas were activated T cells expressing phenotypes characterstic of T cells. It has been possible to prepare a single cell suspension from the leprosy granulomas by collagenase treatment and further characterize the cells in vitro. Observations of these studies indicate a close similarty with the in situ characterstics. Using this system (a) certain biochemical characterstics of these cells have been investigated (b) Mechanism leading to lymphocyte deficit in LL granulomas have been studied. Our observations indicate that the cells from BT/TT granulomas exhibit a good rate of division and protein synthesis in comparison to cells from LL granuomas. Further, it appears that LL granulomas release factor(s) in vitro which are cytolytic to peripheral blood derived lymphocytes.

PO 565

DIAGNOSIS OF LEPROSY BASED ON PGL-I DETECTION.

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The detection of the phenolic glycolipid (PGL-I) of M. leprae, rather than its antibodies, offers great potential for the specific diagnosis of leprosy and definition of the pathobiological status of disease. We have been trying to improve on methodology already described (Cho et al., J. Infect. Dis. 153: 560-569, 1986). Use of silicanized glassware for all PGL-I solutions, an anti-PGL-I IgG3 high affinity monoclonal antibody (ML8B2) and nitrocellulose dot-ELISA will allow the detection of 60 pg of PGL-I, which, we estimate, is equivalent to 5 x 10^5 bacilli/g tissue, below the sensitivity of acid fast staining, and the numbers of bacilli expected in some forms of paucibacillary leprosy. Physico-chemical methods can achieve the same order of sensitivity. For instance, 100 pg of PGL-I can be detected based on gas chromatography/electron capture of the heptafluorobutyryl alditols of the three characteristic sugars. Selective ion monitoring of the alditol acetates of the three sugars is about 5x less sensitive but offers the advantage of surety in chemical identification and can be performed in the presence of substantial amounts of contaminating host material. Thus, the immunological techniques offer exceptional sensitivity and, with the use of monoclonal antibodies, acceptable specificity. Gas chromatography/mass spectrometry offers complete chemical assurance and lesser sensitivity, but, of course, the disadvantage of reliance on expensive equipment. Protocols to allow maximum recovery of PGL-I from fluids and tissues call

for ethanol extractions and the use of C-18 and silica gel 'Sep-Paks'. These increase the practical sensitivity of immunological-based detection by excluding host substances which limit the amount of PGL-I that can be applied to nitrocellulose.

PO 566

USE OF MONOCLONAL ANTIBODIES FOR THE DETECTION OF MYCOBACTERIUM LEPRAE SPECIFIC ANTIGENS DURING INFECTION.

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Mycobacterium leprae antigens were identified by an antigen capture assay (ELISA), sodium dodecyl sulfate polyacylamide gel electrophoresis (SDS-PAGE), chloroform-methanol extraction for phenolic glycolipid (PGL-1) and immunocytochemistry using specific monoclonal antibodies (MAbs) in skin biopsies from 10 patients with paucibacillary, 8 patients with multibacillary, 5 other diseases and healthy controls. Preliminary results suggest that the antigens can be extracted from infected skin lesions and detected by these various techniques. *M.leprae* associated protein, carbohydrate and PGL-1 antigens were generally found positive (i.e. 75 to 100%) in all 8 multibacillary cases analysed by various techniques, while less positivity (i.e. 20 to 50%) was observed in 10 patients with tuberculoid leprosy (B.I. negative or 1+).

These findings suggest that antigen detection tests could be an important for (a) evaluating active leprosy and (b) monitoring the effectiveness of chemotherapy.

PO 567

A REMARKABLE ASSOCIATION BETWEEN SKIN TEST POSITIVITY TO SOLUBLE ANTIGENS OF *MYCOBACTERIUM LEPRAE*, *M.VACCAE* AND *M.CHITAE* FOUND IN BCG VACCINATED KUWAITI SCHOOL CHILDREN.

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Skin test studies performed as part of an assessment of BCG vaccination in Kuwaiti school children uncovered a high degree of positivity to Leprosin A and an unexpected association in responsiveness between Leprosin A and Vaccin (made from *M.vaccae*). This was similar to that previously reported from Iran, but is not generally found in other places. Our finding was unexpected since leprosy is extremely uncommon in Kuwait, and climatic conditions are hostile to most environmental mycobacteria. When the study was extended to comparisons between Leprosin A and Chitin and Flavescin (made from *M.chitae* and *M.flavescens* respectively) the association was found between Leprosin A and Chitin, but not between Leprosin A and Flavescin. The mechanism of this association is currently under investigation and may be related to the fact that the 3 associated species all have potent suppressor determinants.

PO 568

Use of Soluble Skin Test Antigens in Leprosy.

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Approximately 3000 people from a leprosy hyperendemic area in Tamilnadu (India) were skin tested using Rees and Convit leprosy soluble antigens and tuberculin. About 200 suspects and patients of clinically diagnosed leprosy received in addition two lepromins, Mitsuda and Dharmendra. Rees and Convit antigen skin test induration measurements had poor reproducibility as compared to tuberculin PPD, when intra-observer, inter-observer and inter-batch variations were considered. One batch each of both Rees and Convit antigens gave comparable results in terms of skin test indurations. Frequency distributions of Rees antigen were similar and bimodal with antimode at 11 mm, in patients, contacts and general population. Correlations between Rees antigen indurations and Dharmendra and Mitsuda antigen early and late reactions were poor. Analyses of data according to different types of leprosy and in age and sex groups were done. In the leprosy endemic area, Rees and Convit antigens appear to elicit a response which is not sufficiently specific for epidemiological studies.

PO 569

EFFECT OF EXOGENOUS INTERLEUKIN 2 ON PROLIFERATIVE RESPONSE OF T CELLS FROM LEPROSY PATIENTS TO *MYCOBACTERIUM LEPRAE*.

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Patients with lepromatous leprosy (LL) but not tuberculoid leprosy (TT) have defective cell-mediated immunity specifically to *M. leprae*. It has been controversial whether the specific unresponsiveness of T cells to *M. leprae* can be reversed by exogenous interleukin 2 (IL-2). This study was thus initiated to determine the ability of exogenous IL-2 to reconstitute the proliferative responses of mononuclear cells (MNC) from leprosy patients to *M. leprae*. In general, MNC from lepromatous patients responded poorly to *M. leprae* compared to responses from TT patients, suggesting the specific unresponsiveness of LL patients to the bacillus. When MNC were cultured with *M. leprae* and/ or IL-2, the responses of MNC from 17 (81%) of 21 BL or LL patients were significantly greater than those to *M. leprae* alone and those to IL-2 alone, thus suggesting the recovery or enhancement of MNC responses of LL patients to *M. leprae* by exogenous IL-2. However, among 13 LL patients showing low responses to *M. leprae* the responses of MNC from 4 patients to *M. leprae* with IL-2 were not significantly different from those with IL-2 alone. The responses of MNC from TT or BT patients to *M. leprae* were not enhanced significantly by exogenous IL-2, indicating that the TT patients are fully capable of mounting cell-mediated immune responses to the bacillus. No relationship was found between bacteriological indices and MNC proliferative responses to *M. leprae* and IL-2. These results indicated that there might be two groups in LL patients; one is those unable to respond to *M. leprae* even in the presence of exogenous IL-2, and the other is those exhibiting proliferative responses to the bacillus in the presence of IL-2.

PO 570

RECOGNITION BY T CELLS OF INDIVIDUAL ANTIGENS FROM *M. LEPRAE* PRESENTED ON NITROCELLULOSE PARTICLES DERIVED FROM WESTERN BLOTS

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Antigens that are immunodominant for antibody responses in Balb/c mice may not be the most relevant to human T cell responses.

Therefore Western blots of SDS-PAGE separated antigen from *M. leprae* were converted into antigen-bearing particles as described previously (J. Immunol. Meth. 98,5). These antigens, and suitable controls have been used to screen proliferative responses of leprosy

patients (LL=29, BL=17, BT=24) and normal donors (contacts=24, non-contacts=11).

Contacts show an increased % of positive responders to 21 of the antigens, relative to non-contacts. These include several antigens in the 12-36 kDa range not usually causing proliferation of cells from any patient group.

The 36 kDa protein caused significant inhibition of the cells of 30% of the LL patients, but inhibited no BT's or contacts. 25% of the BT's but only one contact gave a significant proliferative response to it.

These and other observations suggest that the leprosy spectrum is not determined by the pattern of response to any one antigen, though the 36kDa (& the 18kDa protein to which only contacts respond) seem of particular interest.

PO 571

HLA CLASS II IR GENE CONTROL OF T CELL REACTIVITY TO THE 65KD PROTEIN OF MYCOBACTERIA

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In view of the fact that the cellular immune response is mainly responsible for protection against leprosy and tuberculosis, it is important for the development of a vaccine to know which antigens of M. leprae and M. tuberculosis are recognized by T cells. We will show data that the T cell response to a mycobacterial 65kD protein is under the control of HLA class II genes. With the help of T cell clones from leprosy patients and T cell lines from leprosy patients and healthy in vivo primed individuals, we mapped epitopes on the mycobacterial 65kD protein. For mapping we used recombinant deletion mutants of the M. bovis BCG 65kD protein and peptides synthesized according to the sequence of the M. leprae 65kD protein. To investigate whether HLA class II genes regulate epitope recognition by T cells at the population level, we tested 50 anti-mycobacterial T cell lines from in vivo primed individuals. For each T cell line the restriction element was defined and recognition of the 65kD protein was tested. Only 10 out of 84 APC-T cell line combinations reacted to the 65kD protein, of which 7 were restricted via DR3 and 3 via DR1. All 7 DR3 restricted lines recognized the same epitope (peptide 2-14) as the DR3 restricted T cell clones, but the DR1 restricted lines defined new epitopes on the 65kD protein. These results indicate that class II genes act as Ir genes for the T cell response to the mycobacterial 65kD protein, and suggest that in a future sub-unit vaccin different peptides should be combined to induce immunity in every individual of a population.

PO 572

HLA-DR PEPTIDES STIMULATE MYCOBACTERIAL 65KD PROTEIN REACTIVE HUMAN T CELL CLONES

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T cell clones from one tuberculoid leprosy patient recognized the recombinant M. leprae and/or M. bovis BCG 65kD protein. Six out of 12 DR3 restricted T cell clones reacted with both 65kD proteins and 2 out of 13 DR2 restricted T cell clones responded to the recombinant M. leprae 65kD protein. All DR3 restricted 65kD reactive T cell clones recognized a peptide 2-14 and both DR2 restricted 65kD reactive T cell clones recognized a peptide 418-427. To our surprise the DR2 restricted T cell clones also respond to peptides of the hypervariable regions of the DR2 molecule and the DR3 restricted T cell clones were all stimulated by peptides of the hypervariable regions of the DR3 molecule. None of the non-65kD protein reactive T cell clones from the same patient did respond to these HLA-DR peptides, suggesting that this response to peptides of hypervariable regions of DR molecules is specific for 65k protein recognizing T cells. The response to these HLA-DR peptides could be blocked by anti-HLA class II antibodies and anti-T cell receptor antibodies, it was antigen presenting cell dependent and HLA-DR restricted. All these data suggests that 65kD reactive T cells in tuberculoid leprosy patients may play a role in the immunopathology of the disease.

PO 573

HLA-DR MOLECULES PRESENT M.LEPRAE ANTIGENS TO MYCOBACTERIUM SPECIFIC SUPPRESSOR T CELL CLONES.

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In this study, we generated M. leprae activated human antigen specific Ts cell clones from a borderline LL patient. These clones recognize M. leprae antigens presented by autologous antigen presenting cells. In order to learn how those Ts cell clones recognize M. leprae we performed blocking experiments with monoclonal antibodies and mixing experiments using a panel of allogeneic HLA-typed APCs. The results indicate that
(i) the and chain of TCR is involved in antigen specific activation of these Ts cells. This was determined by blocking studies with Moab WT31;
(ii) inhibition studies with anti-HLA specific Moabs localised the restriction determinant for Ts cells on HLA-DR molecules.
(iii) compared with autologous Th clones, Ts clones are preferentially restricted by one haplotype. This was indicated by the presentation capacity of a large panel of fully class II typed allogenic APC. This suggest that allelic differences between DR molecules may control whether helper or suppressor cells are activated.

PO 574

MYCOBACTERIUM LEPRAE ACTIVATED HUMAN ANTIGEN SPECIFIC SUPPRESSOR T CELL CLONES FROM A LEPROMATOUS LEPROSY PATIENT.

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Eight Ts cell clones from a borderline lepromatous leprosy patient, which specifically suppress autologous Th cell clones reactive with M. leprae, are activated by M. leprae presented by autologous antigen presenting cells. Further study of the antigen specificity of these clones revealed that a highly purified 36 kD M.leprae protein but not a recombinant 65 kD M.leprae protein or unrelated antigens (such as tetanus toxoid) were recognized by these clones. They are also not activated by idiotype of autologous Th cells. These data suggest the presence of a suppressor epitope on the 36K M. leprae protein.

PO 575

HLA-DR3 MOLECULES ARE THE PRODUCTS OF AN HLA CLASS II IMMUNE REGULATOR GENE OF M. LEPRAE PREDISPOSING TO TUBERCULOID LEPROSY

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The type of leprosy that develops upon infection with Mycobacterium leprae correlates with T cell immune responsiveness against M. leprae as determined in DTH and LTT. The polar tuberculoid type (TT) of leprosy, characterized by high T cell reactivity is associated with HLA-DR3 in a population from Surinam, South America. In vitro we found that M. leprae induced T cell responsiveness in TT leprosy patients is preferentially restricted via HLA-DRnon3, whereas the M. leprae induced T cell response of healthy contacts and PPD induced T cell responses from either TT patients or healthy contacts were preferentially restricted via HLA-DR3, indicating that this HLA-DR3 restricted low-responsiveness in TT leprosy patients is M. leprae specific.
M. leprae reactive T cell lines from TT leprosy patients did neither recognize the 65 kD protein of M. leprae nor a 12 aminoacid peptide (2-14) of this protein, while M. leprae or PPD reactive T cell lines of healthy individuals recognized both the protein and the peptide.

We studied the HLA-DR3 restricted low-responsiveness in detail in one HLA-DR3 heterozygous TT leprosy patient. M. leprae reactive, CD4+, HLA-DR3 restricted T cell clones showed responsiveness to 65 kD protein and peptide 2-14, while HLA-DRnon3 restricted T cell clones were reactive to another peptide of 65 kD protein, indicating that peptide 2-14 may play a role in the HLA-DR3 restricted low-responsiveness in TT leprosy patients. Several mechanisms can be responsible for this phenomenon like the presence of peptide 2-14 specific suppressor T cells, for which we found preliminary evidence.

PO 576

ANTIGEN-SPECIFIC HUMAN SUPPRESSOR T CELL CLONES: PHENOTYPIC DEFINITION AND T CELL RECEPTORS.

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This study was undertaken to characterize phenotype and T cell receptor (TCR) of human suppressor T cell (Ts) clones as compared to the helper T cell (Th) clones from a borderline lepromatous leprosy patient.
There are three OKT phenotype types among eight Ts clones: $CD8^{++}$, $CD4^{++}$ and $CD4^{+}CD8^{+}$. A comparison of Ts and Th clone phenotypes from the same patient revealed that the CD28 (9.3) T cell surface antigen is present on Th clones but absent on all Ts clones irrespective of their OKT phenotypes. This indicates that the CD28(9.3) marker is important in distinguishing Ts and Th cells. All Ts and Th clones were strongly positive for HLA-DR, CD3, CD2 and CD25, suggesting that all clones were in an activated stage. All clones reacted with the WT31 monoclonal antibody (Mcab), thought to react with the TCR αβ /CD3 complex. Furthermore, seven Ts clones are positive for γ-chain but negative for δ chain mRNA of TCR. FACs analysis by using a Mcab directed against the γ chain of TCR (anti-TCR-γ 1) showed that Ts clones and Th clones do not express the γ chain on their surface. These data indicate that (1) OKT phenotype of Ts cells can be variable but they lack the CD28 (9.3) antigen; (2) Ts cell clones express a regular TCR αβ , and not TCR γδ, on their cell surface.

PO 577

FUNCTION OF T-LYMPHOCYTES DERIVED FROM LEPROSY LESIONS

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Development of a vaccine against leprosy hinges on the identification of antigens that stimulate protective but not suppressive cell-mediated immune (CMI) responses. The ability to extract T-lymphocytes from lesions provides an opportunity to study CMI responses at the site of disease activity. Limiting dilution analysis revealed that there was a 100-fold increase in M. leprae reactive T-cells derived from tuberculoid lesions compared with blood, suggesting that lesions are enriched with antigen reactive T-cells which are important to study. CD4+ cells extracted from tuberculoid lesions could be expanded in vitro with IL-2 alone and retain their specificity to M. leprae, demonstrating activation by M. leprae in situ. CD4 clones (n>100) derived from tuberculoid lesions proliferated and produced INF-gamma in response to M. leprae cell wall protein-peptidoglycan complex, but not to soluble or recombinant M. leprae antigens. In contrast CD4+ cells from lepromatous lesions were unresponsive to M. leprae. In fact, CD8+ lines and clones from lepromatous, but not tuberculoid, lesions suppressed mitogen and antigen-specific responses of CD4+ clones. The terminal disaccharide of phenolic glycolipid-I triggered 40% of T-suppressor clones tested. These results suggest that study of protein and carbohydrate antigens recognized by T-cells from lesions will be useful in understanding CMI responses in leprosy and lead to the development of an anti-leprosy vaccine.

PO 578

USE OF ARTIFICIAL ANTIGENS WITH M.LEPRAE-PGL-1 PROPERTIES FOR THE STUDIES IN LEPROSY.

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A new method of synthesis of 3,6-di-O-methyl-D-glucose (DMG), saccharide segment of phenolic glycolipid-1, characteristic for M.leprae, was developed. Based on a glycoside of this monosaccharide, a semi-synthetic antigen conjugated to BSA (DMG-BSA) and fully synthetic antigens on polyacrylamide (DMG-PAA) and on macropore glass (DMG-PG) were obtained.DMG-BSA and DMG-PG proved to be of high affinity and specificity in ELISA with sera from leprosy patients and M.leprae-infected animals. The comparative studies showed that DMG-PAA might be more perspective for serodiagnosis of leprosy. DMG-PG-conjugate was proved to be quite sensitive as a sorbent to obtain monospecific antibodies from sera of leprosy patients and M.leprae-infected animals. Artificial antigens appeared to be more active, sensitive and specific as compared with the native M.leprae antigens used in the serodiagnosis of leprosy. A diagnostic kit for ELISA involving the use of DMG-PAA as an antigen has been developed and is being tested in its applicability to the serodiagnosis of leprosy. Immunogenic and protective activity of a fully synthetic antigen with potential properties of an antileprosy vaccine has been studied. The preliminary results showed immunogenic properties and suggested a protective effect of a proposed vaccine. The further investigations are in progress.

PO 579

IMMUNOGENETIC ASPECTS OF LEPROSY.

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In order to specify the role of genetic factors in leprosy ABO blood groups, HLA-antigens, phenotype of acetylation and indices of cell-mediated and humoral immunity were studied in leprosy patients across the whole spectrum of the disease in comparison with healthy persons. It was stated that among leprosy patients AB blood group, antigens HLA-A10, B7, B12, B16 and B40 were more frequently noted as compared with healthy persons. Moreover, antigens B7 and B8 were found more often in the patients with multibacillary leprosy. The relapsed patients more frequently demonstrated B-blood group, antigens A10 and B7, being slow acetylators. Slow acetylators and those with AB blood group developed neurological disorders more often. The patients with AB blood group showed the highest levels of M.leprae-specific anti-IgG and the lowest responsiveness of lymphocytes to lepronin (M.leprae-sensitin). In the patients with both A10- and B7-antigens a significant decrease in lymphocyte response to PHA, PPD and lepronin was demonstrated. Moreover, they had a significantly decreased number of T-lymphocytes carrying Fc-receptors and increased number of null lymphocytes. A complex approach to the assessment of immune status of leprosy patients is discussed in the view of epidemiological, clinical and curative aspects.

PO 580

THE HYPOCALCEMIA OF PATIENTS WITH LEPROMATOUS LEPROSY

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The purpose of this work is to stablish the cause/s of hypocalcemia in patients with lepromatous leprosy (LL). Thirty four male patients (19 with possitive bacterial index (BI) and 15 with negative BI),with at least 5 years of treatment, were studied together with 36 healthy controls of comparable age and sex. Calcium and phosphate plasma levels of LL patients (9.1±0.1 mg % and 2.4±0.1 mg%

differed significantly from control levels (10.9±0.1 and 2.0±0.2 mg%) at $p < 0.01$. The differences were enhanced in possitive BI patients (8.7±0.2 and 2.3±0.4 mg%, $p < 0.01$) and were still significant in negative BI subjects (9.6± 0.2 and 2.6±0.2 mg%; $p < 0.01$).

Increased plasma albumin levels (LL:4.3±0.1 g %,Contr.: 3.4±0.1 g%, $p < 0.01$) were the cause of increased total plasma protein concentration (LL:7.2±0.2; Contr: 6.6±0.2 g%; $p < 0.05$). A significant correlation between the concentration of Ca and albumin ($r=0.50$, $p < 0.05$) was observed in the control group but not in LL patients ($r= -0.03$ $p > 0.05$).However, similar ionic calcium (Ca^{++}) concentrations were measured (LL:2.25±0.04, Contr: 2.10±0.03 mEq/L) No significant differences were observed in acid-base status, daily urinary excretion of free and peptide-bound hydroxyproline or in the activity of plasma alkaline phosphatase (total and bone isoenzyme levels).

These results suggests that LL patients synthetize an abnormal albumin molecule or a normal one with lower affinity toward Ca^{++} . This would explain the coexistence of normal Ca^{++} levels together with hypocalcemia and coincide with a normal parathyroid function.

PO 581

HISTOPATHOLOGICAL EXAMINATION OF ACTIVE AND INACTIVE LESIONS IN LEPROSY.

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Skin lesions of Borderline leprosy patients do not uniformly show clinical signs of activity, such as infiltration. Certain patches appear active while others appear quiescent. Adjacent areas of the same lesions may also show heterogeneous clinical features. These non-uniform clinical features are accentuated during reversal reactions.

This study describes the histopathological appearance of skin biopsies from clinically active and inactive lesions obtained from patients 'in reaction' and from those 'not in reaction'. 7 patients 'in reversal reaction' and 5 patients 'not in reaction', have been studied so far.

Clinical and histopathologic data from these and other patients will be presented and the significance of clinical 'activity' and 'inactivity' discussed.

PO 582

CHROMOSOME DAMAGE IN UNTREATED LEPROSY PATIENTS.

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The frequencies of Sister-Chromatid Exchanges (SCEs) and Chromosome Aberrations (CA) were analysed in blood lymphocyte cultures of untreated leprosy patients.

Twenty-eight untreated paucibacillary (TT/BT of Ridley & Jopling), 20 untreated multibacillary patients (BL/LL of Ridley & Jopling) and 20 normal controls were used for chromosome analysis.

Our study revealed a significant variation in the frequencies of SCEs and CA between the patient groups and controls. An increased frequencies of SCEs(10.4 per cell) and CA(7.3%) were observed in multibacillary group. The paucibacillary group and controls showed 7.8 and 6.9 SCEs per cell; CA were 4.7% and 1.9% respectively.

The observations suggest, that untreated leprosy results in chromosome damage; further a correlation may exist between the form of leprosy and the extent of chromosome damage.

PO 583

HYPOGONADAL OSTEOPOROSIS IN ELDERLY MALE LEPROMATOUS LEPROSY PATIENTS

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We measured the metacarpal index(MCI) of the leprosy patients,who are now under medical treatment in Okukomyoen for a long term,for the purpose of osteoporosis examination in 1987.
MATERIALS; tuberculoid male(TM):64, tuberculoid female(TF):58, borderline male(BM):1, lepromatous male(LM):238, lepromatous female(LF):137,(total:498 average age:66.2y.o.,age distribution:40-95 y.o.)
RESULTS; In LM,average MCI of every decade decreases almost linearly with age($p<0.05$). Average MCI of their 8th decade is about 30%(30.18%) less than that of their 5th,while in TM,the decreasing rate is less than 5%(3.76%). The average MCIs of LM are less than that of LF from their 5th decade to 8th. The average MCI of TF decreases every decade as that of LF does.
DISCUSSIONS; During last 10 years,autopsies had been performed on 58 LM patients in Okukomyoen,histopathological studies of whose testicles shows remarkable degeneration of Leydig cells in high percentage of materials(by Furuta).
The severe decrease of bone mineral contents in elderly LM patients is thought to be due to the male hypogonadism for the testicular dysfunction caused by lepromatous involvements primarily followed by severe degeneration.

PO 584

PURINE NUCLEOSIDE PHOSPHORYLASE ACTIVITIES IN SERA, ERYTHROCYTES AND LYMPHOCYTES OF LEPROSY PATIENTS

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Purine nucleoside phosphorylase (PNPase) is an enzyme, which catalyzes the conversion of purine nucleoside to the free purine bases.And it is known that PNPase deficiency is associated with a severe thymus-derived lymphocyte deficiency. Many studies have been carried out in recent years to clarify the nature of immune response in the various spectra of leprosy. The present study was designed to determine the PNPase level in sera, erythrocytes and lymphocytes from patients with tuberculoid leprosy (TL) and lepromatous leprosy (LL).

PNPase activity was measured according to the method of Kalcker. A unit of enzyme activity is defined as the amount which catalyzes the phospholysis of 1 mole of inosine in 1 hour. The protein content of enzyme solution was determined by phenol method of Lowry et al.

The PNPase activities in sera of TL patients [3.20 (±0.76 , SD) x 10^4 units/L] did not differ from those of normal subjects [3.90 (±1.03) x 10^4 units/L], but LL patients [1.87 (±0.62) x 10^4 units/L] showed significant lower activities than normal subjects. The erythrocytes PNPase activities of leprosy patients, especially of LL patients were significantly lower than those of normal subjects (Normal: 5.04±0.16 units/10^7 cells; TL: 3.80±1.96 units/10^7 cells; LL: 2.08±0.98 units/10^7 cells). The PNPase activities in lymphocytes of TL patients (1.55±0.63 units/10^3 cells) did not differ from those of normal subjects (1.74±0.35 units/10^3 cells), but LL patients (0.51±0.26 units/10^3 cells) showed significantly lower activities than those of normal subjects.

These results suggest that the enzyme may also participate in the cell-mediated immunity (CMI) and demonstrate that LL can easily manifest itself in persons who have severely compromised CMI.

PO 585

Degeneration of M.leprae: an immunohistochemical study of biopsies using anti-BCG antibody

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It is sometimes difficult to specify the biopsy specimens to be "leprous" when acid-fast bacilli are negative and there are only foamy macrophages and/or lymphocytes. Harboe (1979), Mshana (1982) and Ridley (1983) reported that anti-BCG antibody is useful in the study of degenerating M.leprae, thus we examined 32 cases of skin biopsy suggestive of leprosy with HE, Fite's staining and ABC-immunohistochemistry using anti-BCG antibody (Dako).

23/32 cases showed positive anti-BCG staining. Six staining patterns related to the degeneration of M.leprae were observed. It should be noted that 6 cases showed Fite's staining to be negative and anti-BCG to be positive. Our study revealed higher sensitivity of anti-BCG staining compared to previous reports.

Clinical:	Active	regressive		quiescent to healed		
Pattern:	1	2	3	4	5	6
Mø:	spindle -globi	globi -foamy	foamy++	foamy+	foamy+	-
Fite:	solid	gra.	±	-	-	-
anti-BCG:	solid -gra.	gra. >vac.	vac. >gra.	vac.	-	-
L (n=26)	5	2	5	6	1	7
B (n= 5)	1	1	2			1
T (n= 1)						1

gra.=granular vac.=vacuolated

This work is partly supported by Ohyama Health Foundation, Japan

PO 586

IMMUNOREGULATORY ROLE OF THYROID HORMONES IN LEPROSY AND TUBERCULOSIS.

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The levels of triiodothyronine (T_3), thyroxin (T_4), titres of antibodies against collagen (Abc) and elastin (Abe), lymphocyte transformation test (LTT) with PHA and mycobacterial antigens, suppressor activity of T-lymphocytes were studied in 46 patients with lepromatous leprosy and 35 patients with pulmonary tuberculosis. The levels of T_3 were significantly higher in patients with inactive leprosy process than in active leprosy patients and healthy persons. The levels of T_3 in tuberculosis patients were lower as compared with healthy persons. In active tuberculosis patients with excudative manifestations the above levels were higher than in the patients with cicatrical tissue reactions. A significant increase in levels of Abc and Abe was found out both in leprosy and tuberculosis. Suppressor activity of T lymphocytes tended to decrease in active tuberculosis and leprosy. In both mycobacterioses T_3 levels were directly correlated to Abc and Abe levels and inversly correlated to suppressor activity of T lymphocytes. The data obtained suggested a significant role of T_3 in destruction of connective tissue resulting in severe consequences both in active and quiescent leprosy (ENL, hepatic and renal damages). In tuberculosis, on the contrary, the role of such mechanism is possible only in active patients with excudative tissue reactions.

PO 587

FUNCTIONAL ROLE OF MAST CELLS (MCS) IN HISTOID LEPROMATOUS LEPROSY

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Mast cells have been studed in human and murine leprosy but their exact role is not known. The histoid lepromatous leprosy (HLL) is known by increased proliferative and functional activity of connective tissue cells. MCS, as one of the important cellular components of connective tissue, have been studied in HLL end their morphological changes have been correlated with the disease.

Skin biopsy from 10 HLL were taken. The biopsy included the nodule and surrounding healthy area. Each biopsy was processed for paraffin embodding. The sections were stained with a) H & E (b) Toludine blue and (c) fite faraco.

The activity of MCS in terms of Morphological changes, proliferation and degranulation was maximum in the nodular area, gradually reduced towards the pheriphery and almost normal in the surrounding healthy area. Mastocytosis, excessive degranulation and change in shape from round to thin, elangated and even irregular were the constant features in HLL. These changes reflected the increased functional activity of MCS in HLL which is the outcome of the host immune response.

PO 588

PATHOLOGIC CHANGES AND BACILLATION OF BLOOD VESSELS IN LL AND BL LEPROSY

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Blood vessel involvement and endothelial bacillation were observed histopathologically in 60 cases of LL and BL leprosy, including 3 groups: (1) 20 new patients, (2) 20 relapsing cases and (3) 20 cases after the treatment with combined chemotherapy for half to one and half years. The histopathologic changes and bacillation in group 1 were basically similar to that of group 2. Three cases of group 1 and 3 cases of group 2 were observed under EM also. The ultrastructural changes and bacillation of blood vessel were the same in both groups. But in group 3 the endothelial bacillation was much less than in group 1 and 2 histopathologically and the occurrence of vasculitis were less than in the other groups. However, a few bacilli were still found in errector pili muscles, small bundles of nerves, hair follicles, and muscle layers of small vessel in group 3. Therefore the remnant bacilli after the treatment with combined chemotherapy is still to be investigated.

PO 589

Statistical study on the agreement among histopathologic readings made by different pathologists of a series of 89 cases clinically diagnosed as "Indeterminate Leprosy" in São Paulo State, Brazil.

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89 cases of leprosy clinically diagnosed as "Indeterminate" and submitted to cutaneous lesion biopsy, were retrospectively selected from the Central Files of São Paulo State Pathology and Dermatology Department. Slides were provided for each case and the same material was handed to three different pathologists, for diagnosis and classification within one of the following groups:

A. no hystological evidence of leprosy
B. suggestive of leprosy
C. Definite evidence of Indeterminate leprosy
D. Definite evidence of Tuberculoid leprosy

Agreement ratio among the three pathologists diagnosis is discussed and analysed from the statistical viewpoint.

PO 590

Morphological alterations of Mycobacterium Leprae due to chemotherapy

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Using chemotherapy the number of microorganisms is reduced in multibacillary forms of leprosy.This fact can be characterized in the skin using staining methods like Ziehl-Neelsen or Fite.On the other hand,morphological alterations of M.leprae can also be established using scanning electron microscopy.
In multibacillary types of leprosy biopsies of the skin were taken before and during chemotherapy. Using light and transmission electron microscopy the specimens were also investigated using scanning electron microscopy.5u thick specimens were sputtered using gold particles.Using a tip-angle of 35° the sputtered specimens were investigated.
In the multibacillary type many Virchow-cells were found.Within the cytoplasm of these cells many typical bacilli were present.After a period of 8-10 weeks using parenteral chemotherapeutical regimens control biopsies of the same patients were taken. Many large inflammatory cells were found in the dermis. But most of these cellular elements showed either a few bacilli or bacilli fragments or remnants.The surface of the cellular membrane of the bacilli or the bacilli fragments was desintegrated.
Using the method of scanning electron microscopy specific alterations of the microorganisms can be demonstrated due to therapeutic influences.This method can prove therapeutic effects.

PO 591

EFFECTS OF LEPROMIN TEST ON THE TUBERCULOID LESION COMPARED WITH NORMAL SKIN

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In leprosy, youngest age incidence has been found to be 3 months - babies born to healthy parents and contacts. Eventhough intact leprosy bacilli are found in placenta and cord, congenital leprosy is not produced [1]. Pregnancy period, 265 days, are more than sufficient for the spread of the disease from the lepromatous mother to her foetus, if it is blood borne infection. Bacilli free Grenz zone and formation of graunlomas favouring the deeper dermis disproves spread of the disease through skin [2]. Leprosy bacilli found over the ENL lesions and ulcers are dead. Nasal mucosa acts as portal of entry and excit for viable bacilli [3].

Findings from the comparative study of lepromin test conducted on the lesion of 100 tuberculoid patients and their normal skin explains the exact mechanism of delayed hypersensitivity and spread of infection.

References :

1. Merlin L. Brubaker et al
Inter. J. Lep., 1985 ; 53 : 517
2. Jopling W.H. Hand Book of Leprosy
3rd edition page : 2
3. Cehl. S Job. K and Hastings RC
Am. J. Trop. Med. Hyg 1985 ; 34 : 1161.

PO 592

RENAL INVOLVEMENT IN MYCOBACTERIUM LEPRAE INFECTED MICE. HISTOPATHOLOGICAL, BACTERIOLOGICAL AND IMMUNOFLUORESCENCE STUDY.

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Swiss albino mice were inoculated in the footpads with Mycobacterium leprae obtained from untreated lepromatous patients. The kidneys obtained from the animals sacrificed during different periods were processed for histopathology, presence of AFB and immunofluorescence studies. Renal lesions, AFB and immune complex deposits were seen in the infected animals. Such findings have not been studied in great detail in experimental leprosy earlier.

PO 593

THE LONG TERM PROGNOSIS OF PROVEN RENAL AMYLOIDOSIS IN LEPROMATOUS LEPROSY

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Secondary amyloidosis still occurs in irregularly treated lepromatous leprosy or in inadequately controlled severe chronic erythema nodosum leprosum (ENL). The natural progression of amyloidosis leads to a nephrotic phase followed, usually within 2-4 years, by renal failure and death.

Five LL patients, diagnosed on renal biopsy in the pre-nephrotic phase, were treated energetically with thalidomide to suppress completely their ENL. Repeat renal biopsies showed no further deterioration histologically, and on a 5-15 year follow-up, no patient has developed nephrosis. In the light of this experience, the early diagnosis and management of amyloidosis in LL leprosy will be discussed.

PO 594

CHARACTERIZATION OF MONONUCLEAR CELLS WITH MONOCLONAL ANTIBODIES IN LEPROSY GRANULOMAS BEFORE AND AFTER IMMUNOTHERAPY

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We studied 22 patients with lepromatous leprosy divided in two groups: 1)twelve patients received immunotherapy according the protocol of Convitt et alli. consisting of a mixture of M. leprae and viable BCG,injected intradermally every 3 months during 2 years and 6 months;2)control group of 10 patients submitted to a placebo and followed the same protocol. All patients were evaluated clinically, and immunologically. Biopsy specimens were obtained before and after the immunotherapy or when the patient presented reactional states, like reversal reaction. The tissue was submitted to histopathological examination and the bacterial index was calculated; part of the tissue was frozen in liquid nitrogen, cutting in cryostat and the slides stained with immunoperoxidase technique(ABC method) using monoclonal antibodies against T cells antigens (CD5) T helper (CD4); T suppressor (CD8); interleukin - 2 receptor (CD25), B lymphocyte (CD22), HLA-DR(Ia) antigen and macrophages.
We compared the number and the microanatomic localization of mononuclear cells in leprosy granuloma before and after immunostimulation in order to detect "in situ" the effectiveness of the host cell-mediated immune response induced by immunotherapy.

This study was supported by a grant from Heiser Program for Research in Leprosy.

PO 595

Serum Immunoglobulins In Leprotic Arthropathy patients

By
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This study included two groups of patients. The first group consisted of 30 lepromatus patients, classified int:20 patients with arthropathy and 10 patients without arthropathy. The second group-the control group-consisted of 10 age matched patients suffering from arthritis.

It was found that the mean IgG and IgA levels were significantly higher in lepromatus patients with and without arthritis than the control group. An apparent decrease in the mean IgM level was observed in lepromatus patients.

It was observed that the mean IgG in leprotic arthropathy patients was significantly lower than the mean IgG in leprotic patients without arthritis. As regard the mean IgM and IgA levels they were significantly higher in leprotic arthropathy patients than those without arthritis.

PO 596

Interleukin 1, Interleukin 2 and Interferon Production in Leprosy Patients.

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Twenty three lepromatous leprosy (BL/LL) patients were studied for interleukin 1 (IL1) production when their monocytes were stimulated with LPS. More than 80% of BL/LL tested patients had significant low levels of IL1 when compared with normal subjects. Production of interleukin 2 (IL2) was studied in 47 BL/LL, 26 BT/TT and 30 normal subjects stimulated with PHA-P or Con A or PPD. The level of IL2 in BL/LL or BT/TT was not significantly different from normal subjects when stimulated with PHA-P or Con A. However, the level of IL2 in BL/LL and BT/TT was significantly lower than normal subjects when stimulated with PPD. Interferon (IFN) production in BL/LL, BT/TT and normal controls was not significantly different when stimulated with PHA-P or Con A. However, when PBML was stimulated with PPD, BL/LL and BT/TT showed significantly lower levels of IFN production than normals.

PO 597

OBSERVATIONS ON T-CELL SUBPOPULATIONS IN ENL REACTIONS.

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15 cases of LL with ENL were studied for phenotypics markers OKT_4, OKT_3, OKT_8 before during and after reaction. 15 LL cases, 15 TT cases and 20 endemic controls were also included in the study. It was found that OKT_4 cells were proportionally more during reaction.

The inversion of the OKT_4/OKT_8 ratio during ENL reaction has been observed by many investigators. The cause for the inversion is claimed to be due to the marked decrease in OKT_8 surface marker. In our studies we observed that the ratio, though affected it is not reversed and the disturbance observed was due to fluctuation in the T_4 phenotype marker and not due to T_8.

PO 598

The immunological profile of three generations of a family with numerous leprosy patients: A two part study. Part I

Ana Valdés-Portela, Manuel Hernandez Angulo, Odelaisy Suarez-Moreno, Elba González-Abreu, José E. Rodríguez and Alina Llop
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The occurrence of leprosy in a large family in a high endemic focus with a prevalence rate of 16.7/1000 inhabitants is studied. The immunological profile of this family, consisting of 11 sons and 4 daughters, 10 of which present the lepromatous form of leprosy and 1 the tuberculoid, as well as the second and third generations, is described in two parts. The second generation has two clinically defined cases of leprosy, one diagnosed as indeterminate in 1973 at the age of 3 and a 23 year old girl diagnosed as borderline lepromatous in 1976. Marriages to other leprosy patients is a common denominator in this family as well as consanguinity with marital relations to lepromatous close relatives. The first case, one of the daughters, was diagnosed in 1953 at the age of 14 and, thereafter, the brothers and sisters and the mother developed the disease in a stepwise fashion. Part one of this study refers to the DTH response to lepromin, antibody titers to M. leprae and macrophage capacity to destroy the leprosy bacillus in the "healthy" family members as compared to those of their leprosy relatives, to the results obtained in untreated and unrelated leprosy patients as well as age and sex matched healthy individuals with no known contacts with leprosy.

The immunological profile of three generations of a family with numerous leprosy patients: A two part study. Part II

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The occurrence of leprosy in a large family in a high endemic focus with a prevalence rate of 16,7/1000 inhabitants is studied. The immunological profile of this family, consisting of 11 sons and 4 daughters, 10 of which present the lepromatous form of leprosy and 1 the tuberculoid, as well as second and third generations, is described in two parts. Marriages to other leprosy patients as well as to lepromatous close relatives is observed in the family. The immunological profile of the "healthy" household contacts and family members in both parts is analyzed as a whole. The immunological tests carried out in Part II of this study deals with lymphocyte subpopulation surface markers, lymphocyte function and lymphokine release. The responses obtained are compared as described in the preceding paper. Those departing from the healthy control values and coinciding with the range of values obtained in leprosy patients is individually analyzed and the high risk individuals identified. The possible role of a genetic potential and/or environmental influence is discussed.

PO 599

Circulating immune complexes in lepromatous patients and the relationship with specific anti-Myocbacterium leprae antibodies and major immunoglobulins.

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A study is carried out on the humoral immune response in lepromatous leprosy patients, household contacts and healthy individuals with no known contact with leprosy. The patients were divided into 3 groups: group 1 were patients with less than 2 years of treatment, group 2 consisted of patients with more than 2 years of treatment and showing an unfavorable evolution and group 3 were patients

also treated for more than 2 years but with a satisfactory evolution. In this study immune complexes were determined by polyethylene glycol precipitation as well as anti-M. leprae antibody levels by the ELISA technique using the semisynthetic dissacharide-BSA antigen. IgG, IgM and IgA were quantified by radial immunodifusion. The values of IgG and IgA in group 2 were high in relation to the other groups as well as to the controls. IgM values in the patients were observed to decrease with time of treatment while the anti-M. leprae antibody values were inversely proportional to those of the immune complexes.

PO 600

Peripheral Helper: Suppressor Ratios and Natural Killer Cell Populations in Hansen's Disease.

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The purpose of this research was to study circulating T-cell subsets in individuals with Hansen's Disease. Correlations were sought based on disease type, reactional states, age and sex. Ethnic, sex and age-matched controls were recruited. Peripheral blood samples were collected in heparinized tubes, then lymphocytes were separated, and stained with monoclonal antibodies for dual flow cytometry. The following combinations of fluorescein (FITC) or phycoerythrin (PE) conjugated monoclonal antibodies were used: FITC Anti-leu 2 + PE Anti-leu 15 (suppressor-cytotoxic cells), FITC Anti-leu 3 + PE Anti-leu 8 (helper-inducer cells), FITC Anti-leu 7 + PE Anti-leu 11 (natural killer cells), and FITC Anti-leu 4 (pan T-cells). Major findings: There was no statistically significant difference in the total counts of pan T and natural killer cells in controls, paucibacillary and multibacillary (BI≥3) patients. Women with multibacillary disease had higher helper:suppressor ratios (mean 2.45; 13 samples) than men with multibacillary disease (mean 1.13; 17 samples). These ratios did not differ on a sex basis in controls nor in paucibacillary patients. In further study, women under 40 years of age with multibacillary disease had a higher mean value (2.49; 12 samples) than women over 40 years of age (mean 1.65, 21 samples).

This study shows that women with multibacillary Hansen's Disease differ significantly in their helper: suppressor ratios from women with no disease or paucibacillary disease. This difference is especially marked in the 20-40 year range.

PO 601

LONG TERM EVALUATION OF IMMUNE STATUS IN LEPROSY PATIENTS UNDERGOING MULTIPLE DRUG THERAPY (MDT) IN VIETNAM.

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(2)Dermatology Institute,Hanoi,Vietnam.
(3)Dep't of Medical Microbiology,University of Amsterdam,The Netherlands.

Since 1985 ,a group of newly-diagnosed, untreated leprosy patients in Hanoi are being monitored for immunological,clinical,and bacteriological parameters at 3-month intervals during multiple drug treatment(MDT). Immune status evaluation includes both humoral(Ig levels,see abstract Hang et al.; anti-complementary activity(ACA)) and cell-mediated (lymphocyte transformation(LTT) assays,see abstract Trao et al.;circulating lymphocytes; skin testing) variables.
ENL developed during MDT in over 50% of lepromatous cases,in some cases associated with an increase in ACA;reversal reaction occurred rarely. Bacterial indices decreased in lepromatous patients,but were still positive after 24 months in most LL/LLs cases, sometimes accompanied by a persistent anergy of the cell-mediated immune response (CMI). Lepromatous patients in the first year of MDT often had a restoration of CMI (increase in % circulating T cells,positivity to mycobacterial antigens in skin tests and LTT). In the second year of treatment, this trend in improvement of immune status was less consistent.

PO 602

Changes in cellular immune responses to leprosy antigens during multiple drug therapy

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Cellular immune response measured by in vitro lymphocyte proliferation in the presence or absence of added lymphokines was studied in new leprosy patients before and during up to 2 years of MDT. Responses to a crude sonicate of M. leprae and other mycobacteria and to synthetic peptide and dimethylglucose antigens did increase during treatment in nearly all cases but were reduced during reactions. Added lymphokines were usually needed to amplify the response. After longer treatment, most patients' cells responded without added lymphokines, but also produced factors suppressing responses of cells from healthy persons. Cellular immune responses were closely correlated with the clinical improvement or lack of it in all types of patients including those at the lepromatous end of the spectrum.

PO 603

DETERMINATION OF DIFFERENT POPULATIONS OF BLOOD LYMPHOCYTES IN BRAZILIAN PATIENTS WITH HANSENIASIS.

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B and T lymphocytes were determined in the blood of 35 Brazilian patients with hanseniasis (19 VH, 9 BH, 4 TH and 3 IH) and in a control group (30 individuals).The results were the following:
1 - B lymphocytes: there were no differences between the hanseniasis patients and the control group.
2 - T lymphocytes: there was an evident depletion in the VH patients compared to the control group and TH patients.
3 - The average of T lymphocytes in BH and IH was lower than that seen in the control group and in TH patients. In spite of that their variations approach them to the HT and the control groups.

Conclusion: There is an evident depletion of T lymphocites in VH and BH Brazilian patients, showing an impairment of the late hipersensitivity in those forms of hanseniais.

PO 604

CIRCULATING IMMUNE-COMPLEXES AND AUTO-ANTIBODIES IN LEPROSY PATIENTS

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Leprosy reactions are inflammatory processes in the course of the treatment as a result of not fairly

explained yet immunological changes in the response to mycobacterial antigens.The first type,"reserval" leprosy reactions,which may occur in all forms but polar-lepromatous leprosy,has been shown as an increased cellular immunity response,whereas the second,erythema nodosum leprosum(ENL) that occurs in lepromatous leprosy(LL) only,seems to relate to formation of immune complexes(IC)

We have investigated in dynamic circulating immune complexes(CIC),immunoglobulin levels,total compliment and fractions,rheumatoid factor and a variety of antobodies such as anti-nuclear(ANAB),anti-muscular(AMAB) anti-cardial(ACAB) anti-vascular(avab) etc.from the sera of 16 leprosy patients(four with and 12 without ENL).

In polar LL an overproduction of gamma-globulin (mainly IgG),raised CIC,higher titres of rheumatoid factor and antibodies(anab,AVAB,ACAB chiefly) was found.There was no evidence that leprosy reactions aggravated by full doses of rifampicin and DDS,so the multidrug regimen was maintained throughout the reactional period and the leprosy reactions were treated successfully with anti-reaction drugs,namely steroids and thalidomide in ENL-cases(clofazimine or antomonials) and single steroid therapy in the cases of " reversal" leprosy reactions only.

PO 605

MALADIE DE HANSEN ET SEROPOSITIVITE VIH

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Bien qu'ayant de nombreuses régions d'endémie communes l'association maladie de Hansen et infection par le VIH n'a été décrite que très récemment dans un cas. Nous en rapportons deux nouvelles observations.

La première observation concerne un patient martiniquais de 28 ans, bisexuel, suivi depuis 1976 pour une lèpre lépromateuse et traité efficacement jusqu'en mai 1985. Les contrôles bactériologiques répétés sont négatifs entre 1978 et 1986. En février 1987, à l'occasion d'une polyarthrite réactionnelle à clamydiae, sont découverts simultanément une infection VIH 1 stade III (CDC Atlanta) et une rechute bactériologique de la maladie de Hansen : indice de Ridley 1 + sur le F.B.O.

La deuxième observation est celle d'un patient guyanais de 27 ans, hétérosexuel, traité pour une lèpre BL depuis 1978 par une polychimiothérapie comprenant de la DAPSONE retard, jusqu'en 1982, où il arrête de lui-même son traitement. En septembre 1987, il est hospitalisé à Cayenne puis dans notre service pour une altération de l'état général et une multinévrite sensitivo-motrice. La sérologie VIH 1 est positive avec une infection stade IV C2 (CDC Atlanta). L'ensemble du bilan infectieux et neurologique est en faveur d'une névrite de réversion, sans qu'il soit toutefois possible d'éliminer un rôle direct du VIH, dont on connait le neurotropisme.

Ces deux observations permettent de discuter les problèmes diagnostique et thérapeutique que soulève l'association lèpre et infection par le VIH. Elles soulignent la complexité, prévisible, des rapports entre ces deux maladies infectieuses impliquant l'immunité cellulaire.

PO 606

Some Immunological Aspects In Patients With M. Leprae and M. Tuberculosis Infections In Egypt

By

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Cell mediatdd immunity parameters were studied in (1) 35 patients with leprosy, 20 with tuberculoid leprosy (TL) and 15 with lepromatus leprosy (LL) (2) 20 patients with skin tuberculosis and (3) 50 age-matched normal individuals. The study included (a) determination of peripheral blood T-lymphocyte subpopulation and (b) estimation of migration inhibition factor i.e. lymphocyte response to PHA.

Cell mediated immunity was impaired in patients with LL and lupus vulgaris and was intact in TL and scrofuloderma.

The frequency of HLA antigens in leprosy and tuberculous patients were also studied and the results revealed association between these diseases and certain HLA antigens.

PO 607

CELL AGGREGATION PHENOMENON OF CULTIVATED BLOOD MACROPHAGES ISOLATED FROM LEPROSY PATIENTS.

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In the cultivation of human blood macrophages from leprosy patients, we found that the macrophages from some leprosy patients were isolated as an aggregate form on a coverslip. On the other hand, the macrophages from almost all of the leprosy patients were isolated separately. The cell aggregate phenomenon was observed in the progressive stadium of leprosy, such as in a new patient, in many patients of Erythema Nodosa Leprosum (ENL) and many leprosy neuralgic patients. But, the macrophages from the quiescent stadium of leprosy were in a separated form. Materials and methods used were as follows. About 15 ml heparinized blood was isolated from every leprosy patient, and about 6ml plasma was separated. The plasma with penicillin was put in 6 plastic Leighton tubes with a coverslip, and was cultivated in a CO_2 incubator at 37°C. Three days later, a coverslip was taken out from the Leighton tube, and was fixed with methanol and stained with the Giemsa solution. The number of macrophage isolated was $I-2XI0^5$ per coverslip. The mechanism of this cell aggregate is such that we think the macrophages will react with any antibodies and antigens in the plasma of leprosy patients.

PO 608

Effects of thymopentin on the immune system of lepromatous leprosy patients

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23 patients with lerpomatous leprosy were evaluated for their immune status (T cells frequency and interferon gamma production).

In 6 patients with deficits of both immune parameters,thymopentin was administred.
At the end of the treatment, a full recovery of immune dysfunction was observerd.
The efficacy of thymopentin in LL patients is discussed.

PO 609

M. LEPRAE EPITOPE DETECTION IN ARMADILLO AND HUMAN TISSUES.

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With a panel of monoclonal antibodies directed against M. leprae specific and nonspecific epitopes, using an immunoperoxidase system, the presence of antigen was shown in infected human and armadillo tissues.
It was shown that different monoclonal antibodies showed different patterns of reactivity. Some monoclonals detected the M. leprae cytosceleton and showed bacilli,

others exhibited a more diffuse staining pattern, staining the cytoplasm of the host cells. It may be speculated that these antibodies detected epitopes on soluble antigens.
In armadillo tissue one of the antibodies detected cross reacting epitopes on the basal membrane of epidermis and vascular wall.
This finding is very interesting when we consider the ethiopathology of adjuvant disease in rats and of rheumatoid arthritis in man and may give food for thought.

PO 610

MODULATION OF IMMUNE DEFICIENT CELLS OF LEPROSY PATIENTS BY PROTEIN COMPONENTS OF MYCOBACTERIUM LEPRAE, LEADING TO INACTIVATION OF PHAGOCYTOSED BACTERIA I. DELIPIDIFIED CELL WALL

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In leprosy patients, Mycobacterium leprae are tolerated inside the macrophages. This presentation reports our observations to demonstrate the following. The viability of M.leprae inside macrophages was demonstrated by in vitro tests and mouse foot pad growth. Immunomodulation of the test component was carried out in immunized mice and in vitro test systems using cultured peripheral blood cells especially macrophages from leprosy patients and normal healthy individuals. In normal healthy individuals, encounter with M.leprae lead to production of superoxide and inactivation of the bacteria. This is totally lacking in the macrophages from lepromatous leprosy patients. A component of M.leprae, the delipidified cell wall (DCW) has been demonstrated to be a successful immunizing agent by the following criteria. a) It has been shown to activate the peritoneal macrophages of immunized mice so as to kill M.leprae through reactive oxygen intermediates. b) The macrophages of any leprosy patients are also activated on exposure to DCW-stimulated leucocytes culture fluids of the same patient, leading to production of superoxide on encounter with M. leprae and inactivation of the bacteria. Thus the immune deficient cells, that are at first unable to meet the challenge of M.leprae, are made to do so as normal healthy individuals, by the component of M.leprae, the delipidified cell wall.

PO 611

MODULATION OF IMMUNE DEFICIENT CELLS OF LEPROSY PATIENTS BY PROTEIN COMPONENTS OF MYCOBACTERIUM LEPRAE, LEADING TO INACTIVATION OF PHAGOCYTOSED BACTERIA II. DCW PROTEINS AS M.LEPRAE DNA/RECOMBINANT PRODUCTS EXPRESSED AS FUSION PROTEINS

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The delipidified cell wall (DCW) of M.leprae is an insoluble complex of proteins. Antibodies in the rabbit were obtained using this complex and the λGT11 M.leprae gene library was screened for clones expressing proteins of DCW. Six clones in which lysed proteins interacted with antibodies of DCW were obtained. The fusion protein referred to as Clone 3 on immunisation of mice, induced an ability to show FPE on challenge with M.leprae, but showed no activation of peritoneal macrophages to kill M.leprae, in an in vitro system. Clone 3 also showed positive LTT with cells from leprosy patients, but no substantial ability to induce killing of M.leprae by the cells. However, fusion protein 5, induced macrophage activation in immunised mice, to kill M.leprae but no FPE to challenge of live M.leprae. Clone 5 lysate stimulated-supernatant of cells from patients could activate same patient macrophages to induce superoxide and kill M.leprae. Fusion protein 5 induced LTT in leprosy patients. Thus it has been demonstrated that there are modulators existing as components of M.leprae that could activate immunodeficient cells of leprosy patients to inactivate M. leprae, and these may be potential vaccines for leprosy.

PO 612

INTERLEUKIN 2 STUDY IN SKIN AND BLOOD OF LEPROSY PATIENTS

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Using an avidin-biotin immunoperoxidase technique and monoclonal antibodies (MoAb), we have investigated the presence of interleukin 2 (IL2) and its receptor in the cutaneous granulomas of 26 leprosy patients = 11 tuberculoid patients, 7 unreactional baccilary lepromatous patients and 8 erythema nodosum leprosum (ENL) patients. Concomitantly we have studied the number of IL2 receptor positive circulating T cells and in vitro M.leprae response in presence or absence of IL2.
The labelling patterns observed with the MoAb used made us able to distinguish IL2 producer cells, and IL2 responder cells divided in two subsets : IL2 receptor positive cells and IL2 binding cells.
The results were as follows : 1 - Tuberculoid granulomas contain the highest number of IL2 producer cells and IL2 responder cells when compared to unreactional or ENL lepromatous patients. The IL2 responder cells belong to the IL2 receptor + cell subset and to the IL2 binding cell subset. 2 - Unreactional lepromatous granulomas exhibit a lack both IL2 producer and IL2 responder cells. The rare IL2 responder cells observed belong exclusively to the IL2 receptor + cell subset. None IL2 binding cell has been observed. 3 - ENL granulomas exhibit a significantly increased number of IL2 producer and IL2 responder cells in comparison to unreactional lepromatous granulomas.These cells, however, still remain fewer than in tuberculoid granulomas. The IL2 responder cells belong to the IL2 receptor + cell subset and to the IL2 binding cell subset. 4 - As expected, an absence of in vitro response to M.leprae has been observed in all the lepromatous patients (unreactional and ENL patients). After IL2 addition, 2 of 5 unreactional lepromatous and 1 of 4 ENL patients exhibit a significative response to M.leprae. These patients do not present any particularity on their IL2 and IL2 receptor granuloma content when compared to the non responder patients of their group.

PO 613

MONONUCLEAR PHAGOCYTE SYSTEM IN LEPROSY.

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Obligate parasitism of M.leprae in a macrophage cell is one of the main factors in pathogenesis of leprosy infection. Macrophages from human and animal (mice and armadillos) lepromas and cultivated monocyte-derived macrophages were studied using the methods of cytochemistry and transmission and scanning electron microscopy. Macrophages from untreated leprosy patients showed a high activity of glucose-6-phosphate dehydrogenase and markedly reduced levels of β-glucuronidase and lipase. The different levels and localization of peroxidase were noted in leprosy macrophages suggesting an important role of peroxidase system in intracellular phagocytosis of M.leprae. The effective anti-M.leprae therapy decreased dehydrogenase and esterase activities in tissue macrophages. Monocyte-derived macrophages underwent in vitro a more rapid giant cell transformation and showed a decrease followed by an increase in the levels of β-glucuronidase. Ultrastructure of macrophages cultivated from blood monocytes was changed when dapsone was administered while rifampicin had no such effect. The regularly obtained cultures of leprosy granulation tissue consist of M.leprae-laden macrophages as well as lymphocytes and fibroblasts. The addition of rifampicin or dapsone to culture media significantly diminished mycobacterial load of macrophages. The results of the investigations permitted to develop the tests for early assessment of effectivity of specific therapy and rapid screen of the drugs with potential antileprosy activity.

PO 614

Leprosy and Nutrition

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This study was undertaken since it was earlier suggested that undernutrition in leprosy might be due to food deprivation or poverty or due to the disease process itself. Also concomitant infectious diseases in them might also modulate their nutritional status.

In order to study the above problem, body measurements as well as assessment of daily dietary intakes were undertaken in these patients along with the evaluation of biochemical and endocrinal parameters. Also incidence of coexisting bacterial, viral and helminthic infections with special reference to pulmonary tuberculosis malaria and sexually transmitted diseases were evaluated. Our lepromatous patients often suffer from pulmonary tuberculosis, resulting in a negative nitrogen balance decline of body weight and decrease in various serum micronutrient levels, which proved ultimately to be fatal.

PO 615

Preliminary Efforts at the Reconstruction of the Epidemiology of Medieval Leprosy: Naestved Revisited

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Excavations at several medieval leprosaria have shown that the skeletons of those buried there have diagnostic changes of leprosy. This study centered on re-evaluation of the 123 complete skeletons excavated at Naestved, Denmark by Moller-Christensen (dated 1250-1550 A.D.). The intent was to determine the age of onset of disease, since this factor and the sex ratio of patients characterize the incidence of the disease. Resorption of the anterior alveolar process of the maxilla was chosen for study because the extent of destruction has been linked in Malaysian patients to duration of untreated disease and because this form of lepromatous osteitis protects from normal periodontal bone loss. First, the Malaysian data was subjected to statistical analysis and it was found that bone loss fit a straight line regression model with a slope of 2.4%/yr. and correlation coefficient of 0.83. Skulls from Naestved were measured directly for percent bone loss and a formula employing estimated age at death was used to estimate age of onset. Over 70% of cases indicated a childhood onset. Coupled with an equal sex ratio, these findings characterize late medieval Denmark as an area of extremely high incidence. This method may have a broader application both in estimating incidence for areas where such remains have been found and in using such insight as a perspective for understanding medieval leprosy in a broader context.

PO 616

ON SOME UNKNOWN SOURCES FOR THE HISTORY OF LEPROSY

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Some books of the Bible contain not only separate texts but also entire chapters on the epidemiology, prophylaxis, diagnosis, treatment, the clinical picture and the symptoms of leprosy.Therefore the Ancient World, especially Egypt and Babylon, exhibit through the Bible a remarkable degree of knowledge on many aspects of leprosy. The present-day doctor will find explanations on many of the problems of interestbto him.

The Bible describes with remarkable precision details from the clinical picture of the disease - forms, symptoms, diagnosis, treatment, prevention,etc. Let us recall in this respect that Werner Keller addresses to negative criticism the wise advice - 'And Still the Bible Was Right'.

The present paper is, within the bounds of our opportunities and within the framework of the literature available, a modest contribution to the study of the problem of leprosy seen in the context of the history of medicine.

PO 617

THE CREATION AND OPERATION OF A COMPUTERISED NATIONAL REGISTER OF LEPROSY PATIENTS.

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The Poster will present suggestions which might be followed for parties interested in using computerised records for leprosy control. It will illustrate the kind of reports which can be produced as well as details of data collection. Stationery used in the collection, coding and capture of data will also be displayed. The work will be based on the National Register of leprosy patients in Malawi.

PO 618

ANALYSIS OF TRENDS OF DETECTION AND SPECIFIC INCIDENCE RATES OVER A 32-YEAR PERIOD IN POLAMBAKKAM, SOUTH INDIA.

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Some 50,000 leprosy patients have been detected in the Polambakkam area between 1955 and 1986. An average annual decline of incidence rate of 4.5 % has been observed.

Mean age at registration was in average 5 to 7 years lower for paucibacillary than multibacillary patients, and was slightly decreasing for the former, while no change was observed for multibacillary patients. Distribution of incidence by age, sex and type showed that leprosy was more frequent in males than females for both multi- and paucibacillary types. Sex ratio was stable with age for paucibacillary cases, but was increasing for multibacillary leprosy, to reach a maximum in the age-group 35-39. A bimodality was observed for paucibacillary leprosy, the second peak of which tended to disappear along the years. Observations suggest that the first peak mainly concerns household contacts of leprosy patients, while the non-contacts are mainly responsible for the second peak.

The observations also suggest a slower decline of incidence among household contacts than in non-contacts.

PO 619

ADAPTATION OF THE OMSLEP SYSTEM TO ILEP REQUIREMENTS

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The Omslep Recording and Reporting System for Leprosy Patients is in use in 43 countries or projects, whether in its original form or adapted to local requirements. It is simple enough to allow health service workers at all levels, even the most peripheral, to collect the necessary data for operational or epidemiological evaluation in a decision making context.

It has been modified to meet the needs of monitoring multidrug therapy as well as monotherapy, and to be compatible with the reporting procedures of ILEP member-associations under the new name of IL-OMSLEP, in order to alleviate the administrative tasks at the projects level.

The three categories of leprosy patients (treated, under surveillance, under care) are fully integrated into the system and the micro computer software. This software requires no special knowledge of information technology. It can be used to record data on an individual and

personalized form; to update these data, to compile periodic returns from these data (ILEP B-questionnaire as well as OMSLEP Statistical Forms) to calculate ILEP or WHO indicators for evaluating control campaigns and to calculate other statistics, at the user's request for more detailed studies. The Epidemiology Unit of the Catholic University of Louvain, Brussels, can assist any projects to implement an information system for leprosy control programmes and to computerize it .

The OMSLEP booklet is available in 4 languages (English, French, Spanish, Portuguese).

PO 620

POSSIBLE ROLE OF PHLEBOTOMINE SANDFLIES IN THE TRANSMISSION OF LEPROSY.

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Mode of introduction of M. leprae into the human body being not clear, vector hypothesis gained much importance. Several arthropods existing in the leprosy endemic areas are found to harbour acid fast bacilli. Phlebotomine sandflies are one of the most commonly available arthropods found in the leprosy endemic areas, which have not been screened so far for mycobacterial infection.

Sandflies representing two genera and eight species were collected from the houses of few localities of Agra. Acid fast bacilli were seen in 47% of the sandflies collected from the houses of leprosy localities. Laboratory reared sandflies fed on the blood of leprosy patients showed that acid fast bacilli persist only upto eight days in sandflies. Morphologically granular and fragmented bacilli were more, compared to intact bacilli. Light and electronmicroscopy of sandflies did not reveal any cellular changes. Results of mouse foot pad harvest did not indicate multiplication of bacilli in the gut of sandflies. When refed on mouse foot pad very few bacilli were carried **mechan**ically by the contaminated proboscis. From the study it is evident that sandflies may not be having any role in the transmission of leprosy.

PO 621

DOES LEPROSY CLING TO HOUSEHOLDS : A RETROSPECTIVE STUDY OF HOUSEHOLD CONTACTS

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The purpose of this study is to test the hypothesis 'Leprosy clings to households'. The Data relates to 1184 Primary cases (PC) and their 6284 household contacts (HC), of the Sevagram Leprosy Control Unit run by the Gandhi Memorial Leprosy Foundation a non-Governmental agency, working for the cause of leprosy control. The Sevagram unit is situated in Wardha, a district in the State of Maharashtra, India. The Data for this study, on variables like period of contact, age, sex, type of PCs, closeness of relationship, and start of contact with PC before, at the time of and after detection, was culled from the case records maintained in the unit.

Analysis of the Data shows, that the attack rates per 1000 person years at Risk (PYR) ranges from 9.9 in the case of HC of L+BL+BB type of PC and 3.9 in other types of PC to 1.98 in the unexposed persons; the attack ratio being 5:2:1. Similarly the attack rate was higher in males than in females, more in HCs of L+BL+BB type of PC than in the other types of PC and relatively high in the case of higher grades in BI. The case rate per family having PC during the period of study was found to be 0.45 and that of unexposed family 0.35

The study reveals that the attack rate neither depend on the period of contact with the PC nor on their treatment. Significant difference in attack rates exist in close and distant contacts in case of females, but there is no difference in males.

PO 622

AN EXPLORATORY STUDY OF MULTIPLE-CASE LEPROSY FAMILIES : A GENEALOGICAL ANALYSIS

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Genealogies of twentyseven multiple-case leprosy families of two randomnly selected villages of Vizianagaram district, a high endemic area, of Andhra Pradesh (India) were studied in 1987. Pedigrees extending to 4-7 generations covered 1460 family members, among whom were 168 patients - 122 males and 46 females.

The study was intended to compare the offsprings of consanguineous and non-consanguious marriages in relation to occurrence of disease (i) in different generations (ii) disease of the parents (iii) among different sex (iv) by birth order and (v) acceptance/rejection of the patients.

In majority of genealogical trees, occurrence of disease was found intermittantly. Continuity was observed only in 12% of the trees. Both in consanguineous and non-consanguineous types of marriages occurrence showed similar pattern when both parents were patients and higher in non-consanguineous type where either the parent was a patient or both were healthy. Sex ratio among patients among non-consanguious type of marriage was 3:1 whereas it was 2:1 in the case of consanguineous type. No significant relationship was found in the birth order in either types of marriages. Culturally accepted mores of consanguinity has prevailed favourably both in cases of choice of spouses (irrespective of of disease) and in acceptance of patients.

PO 623

Age at onset of Leprosy among household contacts of primary cases.

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Most reported studies on age distribution of Leprosy are based on age at the time of detection of disease and not an age at onset of the disease. Even few studies on age distribution based on age at onset, have certain limitations as information is based on statements of patients with varying degree of dependability. However, in our present study we have based our finding on actual examination of contacts, every six months and there by getting accurate information of age at oneset.

8131 Household Contacts of 1970 primary cases of leprosy of all classification detected by different methods by Sivananda Rehabilitation Home, Hyderabad, in its control unit during the period 1979 to 1983 were included in the study. The cases were subjected to examination every six months during the period 1979-1985. Fresh cases detected during the survey were 299. These cases will be analysed as regards to age of onset in general and in relation to type of classification and sex of primary cases. Further the study will analyse the occurrence of leprosy in different age groups by calculating age specific incidence rates of each group and make comparisons.

PO 624

PREVALENCE OF LEPROSY AMONG HOSPITALISED PATIENTS FOR MEDICAL EMERGENCIES.

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Cases of adult acute medical emergencies admitted into the medical wards during 1982-1987 were screened for associated leprosy. Of the 1057 cerebrovascular accidents - 'CVA' (hemorrhage, infraction and embolisation), 1307 cardiovascular diseases (Coronary Heart Disease.

'CHD' congestive heart failure - 'CHF' and hypertensive heart disease - 'HHD'), 2518 gastrointestinal emergencies (Acute diarrhoeal disease - 'ADD' - with dehydration and/shock, Acute viral hepatitis - 'AVH' with hepatic failure, Portal Hypertension - 'PHT' with upper GI bleeding and / Hepatic encephalopathy), 550 Respiratory emergencies (hemoptysis, COPD, ARDS), 50 endocrine emergencies and 6800 cases of suicidal poisoning, leprosy was detected in 3 who had CVA ; one each with CHD & CHF, and 3 with HHD ; 17 with ADD, one with AVH with hepatic failure ; 3 with pulmonary tuberculosis and hemoptysis ; one with diabetic ketoacidosing ; and 27 with suicidal poisoning. No leprosy lesions were detected in patients with PHT, COPD and ARDS. Thus present study clearly denote that the medical men should look for associated leprosy in every case when brought for checkup or with emergency medical problems. in areas where leprosy is endemic. However, it is difficult to say at this juncture whether leprosy patients are less likely prone for these Acute medical emergencies unless population based studies are made.

PO 625

IMPLICATIONS OF NEW TECHNOLOGY FOR DATA PROCESSING IN EPIDEMIOLOGICAL STUDIES OF LEPROSY.

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Recent developments in data processing technology have important implications for field studies of leprosy. Projects lasting many years must be able to adapt and incorporate new information and technical advances with minimum upheaval.

In spite of increases in the storage capacity of microcomputers, some large studies may find the need to utilise mainframe computers. Even if this is so, it may still be possible to take advantage of some of the benefits microcomputers offer.

These points will be illustrated by experience of the Lepra Evaluation Project and leprosy vaccine trial in Northern Malawi. Among the logistic problems were considerations of machine maintenance and electricity supply in a remote location in Africa. Nevertheless, using a small generator solely to supply the microcomputers, having a system with modular components and having a spare hard disk, it has been possible to run the system largely without interruptions. It gave us all the advantages of being able to alter entry programs as required, and to incorporate quality control and validation at source shortly after data collection, by means of various check letters, double entry and cross checks. Examples of these procedures will be discussed to illustrate their value to other research groups considering the use of micros.

PO 626

A GEOMEDICAL STUDY ON THE SPATIAL DISTRIBUTION OF LEPROSY IN INDIA

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Leprosy is a chronic granulomatous infection of humans which in its various clinical forms attacks superficial tissues. India with her many millions of people has atleast a third of the World's leprosy patients. The major objectives of the present study are i) to analyse the spatial distributionof leprosy cases ii) to observe the spatio-temporal variation in the distribution and its trend iii) to identify the leprosy-endemic zones and to probe into the details iv) to find out the association with selected socioeconomic and environmental factors v) to evolve a conceptual frame - work towards planning for an efficient health care delivery system. The study revealed that large parts of the country are leprosy endemic zones and at least half the Indian population is exposed to the risk of infection and that too particularly 30% of the new cases are Children. It is estimated that there are more than 15 million leprosy patients in the world and nearly 4 million of them are in India. It is also inferred that 55% of the cases are found to be below the age group of 20 years. 80% of the cases of India belong to the non-infectious type of leprosy. The five states namely Tamilnadu, Andhra Pradesh, Orissa, West Bengal and Maharashtra alsone account more than 60% of the cases. Calcutta has the largest concentration for any city. In 76 districts of the country, the incidence of leprosy is 10 per thousand.

PO 627

STUDY ON OPERATIONAL EFFICIENCY OF MULTI DRUG THERAPY WITH A VIEW TO IDENTIFY THE FACTORS AFFECTING THE IMPLEMENTATION

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Multi drug therapy (MDT) has been implemented in the North Arcot District from 1983 onwards. The Community Health Department of Christian Medical College, Vellore is covering nearly 2,00,000 population in North Arcot District under the national leprosy eradication programme.

At start in 1984 January in the Leprosy eradication programme of this department was having a total of 4029 patients with a mean of 447 cases per sub centre (MB cases of 80 and PB cases 367). At the end of 4 years the case load is 955 with a mean of 106 cases per sub centre (PB cases 51 and MB cases 55). It was observed during the implementation of MDT in the 9 sub centres under this programme that they performed at different levels of efficiency. The following efficiency indicators were studied according to the sub centres which included the rate of intake of patients for MDT, attendance rate, rate of bacillary index (BI) converstion rate, rate of reporting of new cases, rate of release from treatment etc. The factors effecting the efficiency of implementation studied are the prevalance of leprosy at start, proportion of MB/PB cases, Mean BI, positivity rate, geographical distribution of villages, no. of previous years of leprosy work in the sub-centre etc.

From the above mentioned efficiency indicators and the factors and the factors affecting the outcome a series of operational models are developed. The data is analysed with the aim of quantifying the effect of explanatory variables on performance. Multivariate analysis is carried out and most appropriate model is presented. On the basis of these models a set of feasible operational targets for a subcentre are developed for a given set of variables affecting the programme implementation.

PO 628

IMMUNOLOGICAL RESPONSIVENESS TO *M. leprae* ANALYZED IN HEALTHY HOUSEHOLD CONTACTS FROM LEPROSY PATIENTS AND SUBJECTS NOT EXPOSED TO LEPROSY.

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It is generally accepted that lepromatous patients display a selective immunological unresponsiveness to *M. leprae* antigen (ML) demonstrated *in vitro* by the specific inability of their PBMC in proliferating and/or release IFN-gamma. This lymphokine has been considered the most directly related to the effective activation of macrophages and actually involved in the immunological resistance against mycobacterial infections. The aim of our study was to analyze the cellular immune response to ML in 113 household contacts of lepromatous patients supposed to constitute a ML-infected but healthy population. Forty-eight controls not exposed to leprosy were also included. PBMC isolated by Ficoll-Hypaque density centrifugation were cultured with ML for 5 days, when the supernantant of the cultures was removed and the levels of IFN-gamma determined with a RIA kit obtained from IMRX Corp. (Centocor, Malvern, PA). Sixty-five contacts showing levels>100 U/ml (57.5 %) were considered high responders (HR) to the antigen and 48 persons (42.5 %) were low responders (LR). Among the controls, 16.7 %

and 83.3 % were found to be HR and LR respectively. Four contacts had anesthetic areas clinically detected and histologically, all of them showed an inespecific chronic inflammatory infiltrate, AFB negative. Two of these persons were HR to ML and one of them healed spontaneously after one year of follow-up. The percentage of HR contacts was three times higher than that found in the control group and suggest the existence of active subclinical infection among them. As for the LR contacts, it is probable that other immunological mechanisms may be responsible for their unresponsiveness since it is very difficult to admit that they had never been exposed to the bacillus.

PO 629

THE USE OF ANTI M.LEPRAE ANTIBODY DETECTION FOR THE SERO-EPIDEMIOLOGICAL STUDY OF CONTACTS OF LEPROSY PATIENTS.

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IgM antibodies to the PGL1 of M.leprae were measured by an Elisa assay, using a semi-synthetic antigen, the natural disaccharide-octyl-bovine serum albumin (NDO-BSA). Sera were obtained from leprosy patients, healthy subjects and more than 1000 intradomiciliary contacts in 3 french overseas territories : New-Caledonia, Tahiti and Guadeloupe. Control sera from healthy subjects living in France were also tested. Similar results were obtained in Tahiti and New-Caledonia. Healthy controls from these areas displayed significantly higher background levels of anti NDO-BSA antibodies than controls from non-endemic areas. With a seropositivity level defined as the mean of healthy controls from endemic area +2 SD, the seropositivity rates in Tahiti were 100% among multibacillary patients, 21% among paucibacillary patients and 19.5% among contacts. In New-Caledonia, 97% of multibacillary patients, 23% of paucibacillary patients and 12.5% of contacts were found seropositive. In Guadeloupe, autochtonous healthy controls displayed low anti NDO-BSA antibody background, similar to that of controls from non-endemic areas. Moreover, such a background was still reduced in this study by the introduction of an anti human IgG antibody in the assay. Seropositivity rates then reached 43% among paucibacillary patients and 32% among contacts. These data indicate that a large proportion of contacts developed infraclinical M.leprae infections, and also suggest that procedures lowering the background antibody level in control populations should be developed to improve the efficiency of detection of paucibacillary leprosy.

PO 630

Leprosy Disability in a Control Programme - Trends Over 10 Years.

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A leprosy control programme has been implemented in a defined rural population for the past 10 years. During this period 3 population surveys have been conducted and the characteristics and prevalence of disabilities due to leprosy assessed at the end of each survey in 1979, 1983 and 1987.

There has been no decrease in the cases detected during successive surveys but the ratio of pauci-bacilliary cases to multi-bacillary cases has rapidly risen from 3.9 to 17.1. There was little change in the prevalence of active leprosy between the end of the 1st and 2nd surveys however the prevalence has fallen by two-thirds in the 3rd survey following the introduction of multidrug therapy in 1984. The prevalence rate of disability due to leprosy fell by ⅓ between the 1st and 2nd surveys. There has only been a small fall in prevalence between the 2nd and 3rd surveys but the degree of disability measured using the WHO Disability Index has fallen. The characteristics of the changes in disability rates by age, sex and type are described. The importance of disability assessment as an outcome measure in leprosy control is discussed.

PO 631

Transmitted leprosy from transfusion of lepromatous patient's blood and its incubation period of leprosy

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The patient named wang with lepromatous leprosy whose disease of leprosy could not discovered by a surgeon of a hospital was a blood doner in 1975-1980 to donate his blood to the 60 donees who needed the blood for surgical operations and anemia. Eight out of 60 donees were infected by blood transfusion to develop the leprosy during the observation of 6 years by us. The eight cases of leprosy were diagnosed by clinical, pathological and bacteriological methods, 2 patients had TT type of leprosy, 4 had BT type, 1 had BL type, 1 had LL type. Those patients' incubation period of leprosy were 1-19 months.

Transmitted leprosy from blood transfusion of lepromatous leprosy patient were fully proved. It tells us how long is the time of its incubation period and the blood doner must be examined by the doctor of skin department every year in epidemic area of leprosy and the leprosy indirect transmission of biting insects Should be studed deeply again.

PO 632

MULTIDRUG THERAPY OF LEPROSY IN HONG KONG
A REVIEW OF 425 PATIENTS TREATED BETWEEN 1977 AND 1987.

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A form of multidrug therapy with dapsone, clofazimine and rifampicin was first used for the treatment of leprosy in Hong Kong in 1977. All case records of leprosy patients have been studied and 425 patients identified who have taken multidrug therapy between 1977 and 1987. The indications for use, regimen used, clinical and bacteriological results, patient acceptability, compliance with treatment and side effects have been reviewed. The treatment was found effective and acceptable with no serious side effects and so far no patients have relapsed after multidrug therapy. An analysis of results with background information set against falling annual registrations of new cases is included.

PO 633

EFFICACY OF FIXED DURATION MDT ON PAUCIBACILLARY LEPROSY - CLINICAL AND HISTOLOGICAL FINDINGS

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During the 14 month period from May 1984 to July 1985, patients attending the leprosy clinic of the Christian Medical College Hospital, Vellore, India, with single leprosy patch were screened. Children below 5 years, patients with face patches or patches less than 2.5 cm and those who could not come for regular followup were excluded. Patients were randomly assigned to two regimes of therapy: Conventional dapsone monotherapy, or MDT for 6 months as per WHO recommendation for paucibacillary disease. Clinical, histological and immunological status were determined prior to initiation of therapy. Clinical and histological parameters were reassessed at 3 months, 6 months, 1 year, 2 years and 2 1/2 years.

This paper presents the findings of the study, showing the evolution of the disease through the treatment period with particular

emphasis on the status of the disease 2 1/2 years after starting treatment. Of the 17 patients who completed the study in the MDT group, 4 (23%) showed no treatment response and continued to have histological evidence of active disease. These findings did not differ significantly from those treated with dapsone alone. The implication of these findings are discussed.

PO 634

The implementation of MDT in Kenya 1983-1987

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The extent of the leprosy problem in Kenya is discussed. Total estimated prevalence: 25.000. Of 6558 leprosy cases on register in 1986 90% live in 10 districts with a total population of 6.683.445. Prevalence 0.88/1000; incidence 8.5/100.000. Among new cases: 5% children, 9% disability grade 2+3, 22% MB.

NLTP initiated modified WHO MDT for MB cases in 1983. Regimen: 1RCD/23CD/D until BI negative. MB cases put on this regimen from 1983-1987: 100. NLTP decided to implement WHO MDT in 1985. The NLTP manual gives all guidelines. Different is the maximum duration of treatment of 39 4-weekly doses of R, thereafter RFT regardless BI.

In 1985 and 1986 1072 patients were put on MDT. (643 PB and 429 MB). Results of 392 PB cases: 89% RFT, 7% TnC. From 203 MB cases put on MDT in 1986 and 1987 2% were declared O.o.C. so far.

The NLTP development plan 1987-1990 envisages the district-wise implementation of MDT in 4 regions with a high leprosy prevalence. The target is to have put all new and eligible old cases in 14 districts with 95% of all cases on MDT before 1-1-1990.

PO 635

The Effect of Seven Years MDT in Leprosy Control Unit at Miraj,India

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The MDT regime was implemented in the Leprosy Control Unit,Miraj,in 1982. The regime recommended by W.H.O. are being followed for multi bacillary and pauci bacillary cases. The programme is monitored by tablet counts and urine examination. Patients are assessed clinically and bacteriologically.

The following results are observed: 98% one-patch cases showed improvement in 9 months, 95% of more than one patch cases showed improvement in 9-12 months, 75% of multi bacillary cases with high B.I. showed improvement in 30-36 months. The remaining multi bacillary cases showed improvement within 20-24 months. Two pauci bacillary refractory cases and one multi bacillary case have not shown any improvement so far.

The overall activity of the Leprosy Control Unit, such as Case Holding and Case Finding has improved. The rate of deformity and lepromatous cases has declined and the detection of one-patch and voluntary reporting has improved.

PO 636

CLINICOPATHOLOGICAL CHANGES IN LEPROSY PATIENTS ON MULTIDRUG THERAPY DURING 1983-86.

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Hundred cases were given multidrug therapy according to a modified WHO regimen, without daily clofazimine. Changes in bacterial indices were followed annually. Changes in skin lesions, activity, nerve involvement, ophthalmological condition, degree of deformity (WHO scale) were followed over a 4 year period and results will be given. Changes in bacterial index were compared with published results for the unmodified WHO regimen. For each initial range of bacterial index, the reduction was the same as for the full WHO regimen. Number and type of reactions and the number of relapses were also monitored. Surgical methods used will be reviewed. By clinical assessment supplemented with laboratory investigations, no complications due to the drugs were reported.

PO 637

A step towards leprosy eradication through multi-drug therapy.

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Multidrug therapy, certainly, is a breakthrough for leprosy eradication. The study was carried out in the project area of Baroda district antileprosy association, a voluntary organisation, which has 31 villages consisting of 108270 population.The treatment schedule was according to WHO(1982). (1) 14 days intensive treatment followed with pulse therapy, (2) pulse therapy to all new cases. MB and PB patients were given 36 maximum doses and 6-12 doses respectively. The study shows analysis of 578 patients (218+360 PB) upto 31.12.87. 47 cases, out of regularly treated 203 MB cases, were positive and 46(97.87%) cases showed decline of B.I. Nine persister cases though showed decline in B.I.,remained positive after 36 doses. One case (2.12%) showed static B.I. 349 PB cases were removed from treatment (RFT) after 6-12 doses of M.D.T. But the remnants of hypopigmented patches and anaesthesia on the body continued the feeling of psychological trauma over patients. One MB case developed acute neuritis resulting into foot drop during M.D.T. Another MB case had exfoliative dermatitis. Only one PB case relapsed and 26 (15MB + 11PB) cases could not complete the M.D.T. due to anaemia, old age, ignorance and refuse. Incidence rate of leprosy in the area dropped from 0.99 to 0.49 and existing P.R. came down from 3.41 to 0.96.

PO 638

EXPERINECE OF MULTIDRUG-THERAPY IN PAUCIBASILLARY LEPROSY AT THE DR.SUTOMO GENERAL HOSPITAL SURABAYA .

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226 Paucibacillary (TT&BT) leprosy patients consisting of 145 male and 81 female, age ranging between 6-73 years old were put on MDT during the period of March 1985 to March 1987. 208 cases among them were fresh untrated patients and 18 cases has been treated with Dapsone monotherapy less than one year. The clinical diagnosis are based according the Ridley & Jopling Classification with the following criteria: Histopathological picture shows TT or BT type, the Lepromin test is positive and the absence of AFB in all smears. The evidence of clinical symptoms, side effect of the drugs and bacteriological examination were monitored during the MDT schedule and RFT period. At the end of February 1988, 202 patients has completed the MDT within the period of 6 to 9 months. 24 patients were discharged due to irregular of attandanced, 9 patients transferred to the HC, 2 patients were pregnant, 2 patients with jaundice and 11 patients discontinued their treatment before the end, but showed up again after 9 months. During the RFT observation period 2 patients developed a reversal reaction 6 and 8 months after completing the MDT. The reexamination of histopathology and smears all showed a negative AFB.
Conclusion: The diagnosis for typing of leprosy confirmed by the examination of histopathology, lepromin test, direct smears and the routine examination may prevent the eror of typing and also the misinterpretation of relapse cases in MDT of paucibasillary leprosy .

PO 639

FIXED DURATION COMBINED THERAPY IN MULTIBACILLARY LEPROSY.

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The objectives of this trial are:-

1) To define the precise relationship between BI and relapse in MB leprosy.
2) To measure relapse rates after treatment with MDT for 24 months.
3) To establish that if relapse occurs it will be with drug sensitive organisms.

Since 1984, about 175 newly detected, previously untreated, smear positive multibacillary leprosy patients have been put on two WHO recommended regimens for 24 months (doses). Treatment is then discontinued irrespective of the clinical or bacteriological status. The patients are subsequently followed up every month at the village clinics by our Medical Officers. Treatment has since been terminated in about 100 patients, and 50 patients have completed more than one year of surveillance with detailed clinical and bacteriological examinations. The majority of patients are showing sustained clinical and bacteriological improvement during the follow-up period.

This paper will present data on the incidence of lepra-reactions, the change in the clinical status and the BI after fixed duration therapy. Operational factors will also be discussed.

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

PO 640

M.D.T. CHEMOTHERAPY TRIALS IN LEPROSY. A FOLLOW-UP AND COMPARATIVE STUDY OF THE RIFAMPICIN 1500 Mg MONTHLY PULSE REGIMEN AND THE STANDARD W.H.O PULSE IN MULTI-BACILLARY CASES.

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A trial study of Rifampicin 1500 mg at pulsed monthly intervals along with Clofazimine 50 mg daily and Dapsone 100 mg.daily was started in 1981 in a typical rural population at Emmaus-Swiss Leprosy Project, Palamaner on 123 positive patients and presented at the XII International Leprosy Congress in 1984; and is now being compared with 123 positive patients who were subsequently started on the standard W.H.O, MB regimen.

In each group positive patients were selected from two geographical areas who (I)inspite of 3-5 years D.D.S monotherapy showed (a) an increase in B.I and clinical deterioration, (b) static B.I and (II) fresh cases of B.I. over 2+.

The study trial shows (1) the initial short-term effects in both groups (2) the comparative drop in B.I levels over a period of 36 months, (3) comparison of ENL and neuritic episodes, (4) the effect on 5 cases of pregnancy and (5) comparative relapse rates.

PO 641

ESSAI CONTROLE DE TRAITEMENT DE LA LEPRE PAR PLUSIEURS SCHEMAS DE POLYCHIMIOTHERAPIE : BILAN COMPARE APRES 5 ANS D'APPLICATION .

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Depuis 1982 , un essai contrôlé a été lancé à Dakar pour tester l'applicabilité sur le terrain de plusieurs protocoles de polychimiothérapie de la lèpre . Pour les paucibacillaires, le protocole OMS a été adopté. Pour les nouveaux cas multibacillaires, un premier schéma est similaire à celui préconisé par l'OMS ; un second s'en différencie par l'incorporation d'une phase initiale de 2 mois de traitement intensif. Enfin, dans les cas de récidives probablement résistantes à la DDS, la DDS quotidienne est remplacée par l'Ethionamide.
Près de 600 malades sont entrés dans l'essai. Les auteurs présentent pour chacun de ces schémas thérapeutiques un bilan concernant l'assiduité, la tolérance clinique, la fréquence des réactions et des névrites, et l'évolution à court terme de l'index bactériologique. Les auteurs soulignent les difficultés du suivi des malades dans cette grande métropole Africaine et déplorent la proportion importante de malades perdus de vue après l'arrêt de la PCT.

PO 642

Comparison of Effectiveness On Dapsone Therapy And MDT Of Multibacillary Leprosy Through Monitoring of The BI, Thirty Years' Observation In Taiwan.

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The study was designed to review the efficacy and effectiveness of three chemotherapy remedies namely 1) dapsone monotherapy (DMT), 2) multidrug therapy (MDT), 3) DMT followed by MDT, on the treatment of outpatients who have multibacillary (MB) leprosy. These cases were drown over a period of thirty one years, who visited the skin clinic of the Mackay Memorial Hospital in Taipei, from 1956 to 1987, and included 731 patients of which 263 (36%) were MB patients.

The statistical observation revealed that: 1) as their clinical symptoms improved their initial BI fall down quantatively every year as the number of years was up. 2) the data also showed initial high daily dose of DMT was substantially superior to the lower and slowly increased to daily dose of 100mg, the same high dose as earlier recommended in the DMT. 3) in regard to MDT group, it showed a remarkable reduction in the mean BI after one year treatment in our cases and also was far superior to the DMT group in the past as well as the group which was shifted to MDT from DMT due to the MDT implementation since 1982.

We regard regular attendance of the MB cases at the outpatient clinic with monitoring of the BI by regular bacteriological examination of slit skin smear is sufficient for the practice in general hospital skin clinic.

PO 643

MDT IN THE HEALTH CENTERS OF SURABAYA

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MDT (WHO regimen) was started in Surabaya in 1982 only for new MB cases and/or with smear po_6. Starting at the end of 1984, all cases who can be expected to come regulary, were given MDT.
Completion of treatment for MB cases were decided by CDC-Surabaya Municipality Health Office, while PB cases by Health Center Doctors. For completion of Surveillance and possible relapses, the examination were done by CDC-MHO.
A "package" supply of drugs for each patients were given to overcome the problems of regular drugs supply
The use of presentation list of MDT patients in each H.C. is very useful for monitoring, recording and reporting. Omslep 2nd edition cannot be used forMDT evaluation, while the 3rd edition can cover almost all items.
Between 1982-1987 779 PB and 491 MB cases were given MDT, 631 PB and 83 MB cases have completed treatment and 161 PB cases were declared completion of surveillnace.
During surveillance phase, 12 PB cases "relapsed" due to wrong classification at the start of MDT, one PB case had late reversal reaction and new anaesthetic patches appeared in 3 PB cases where biopsy from one of the case showed a picture of BT. while the other two were still under investigation.

PO 644

POLYCHIMIOTHERAPIE ANTILEPREUSE
AU TOGO: Résultats après deux ans

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Pour étudier la faisabilité des nouveaux schémas de polychimiothérapie (PCT) recommandés par l'OMS en 1981 avant de les généraliser, un plan d'activité est formulé et une zone d'introduction fut ouverte le 3 Mars 1986 dans la préfecture du Golfe.

Aussi, 183 malades, 80 multibacillaires (MB), et 103 paucibacillaires (PB) ont été traités dans neuf dispensaires par deux infirmiers mobiles. Pendant six mois, 99 % des PB ont accepté le traitement avec une excellente assiduité et une parfaite tolérance. A la fin des vingt quatre prises, seuls trois MB, décédés à la suite d'autres maladies, ont ramené de 80 à 77 le nombre des MB.

Ainsi, le Ministère de la Santé se prépare à étendre, dès 1989, en "peau de léopard", la PCT dans d'autres régions du pays. Toutefois, il faudra d'abord éloigner certaines contraintes techniques, logistiques et de faisabilité.

PO 645

FOLLOW UP STUDY OF 210 LEPROSY CASES
TREATED BY M.D.T. IN EGYPT

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210 Lep. cases (153 from Dumiat & 75 from a clinic in Cairo) were treated by M.D.T. as advised by WHO in 1982. Cases were classified as follows: TT 8, Border line 151, LL 51.

70 cases (33 multibacillary & 37 paucybacil.) completed the course of treatment for 2 years & were followed up for varible periods (16 cases 3-5 years). Out of the 70, 58 became clinically & bact. free of the dis., 10 suffered from reactions & 2 LL cases were still smear posetive.

Out of the 210 cases 26 suffered from reactions; 16 from ENL & 10 from reversal type. In 8 ENL cases the condition relapsed 2 to five times.

A peculiar type of reaction was observed in 2 LL cases, a crop of small red tender nodules 2 to 4 or more appear few days (2-3) after the monthly dose of Rifampicin. This was repeated 7 times in one case & 5 times in the other.

Most episodes of reactions were responsive to treatment, however, a 13 years old boy suffering from LL, died during a severe attack of ENL.

Detailed tables & colored slides will be shown, comparing the results in the 2 groups of cases studied.

PO 646

RECIDIVES MULTIBACILLAIRES DE LEPRE OBSERVEES APRES DIFFERENTS PROTOCOLES DE CHIMIOTHERAPIE COMPORTANT L'ADMINISTRATION DE RIFAMPICINE.

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Entre 1974 et 1980 ont successivement été utilisés à Dakar plusieurs schémas thérapeutiques différant par le rythme et la durée d'administration de la Rifampicine (RMP) ainsi que par les antibacillaires qui lui étaient associés. Tous devraient être suivis d'un traitement-relais illimité par DDS seule.

Les auteurs rapportent 27 cas de recidives multibacillaires confirmées cliniquement, bactériologiquement et histologiquement, survenus après de tels traitements.

Le temps moyen séparant le début de l'Administration de RMP de la constatation d'une récidive a été de:

91 mois pour 13 cas ayant reçu les associations RMP-ETH-DDS ou RMP-DDS, durant 3 à 12 mois (écarts : 72-112 mois)

78 mois pour 14 cas ayant reçu une dose unique de 1500 mg de RMP (écarts : 45-138 mois)

La durée d'inactivité clinique ne parait liée ni à la nature de l'association antibacillaire, ni à la durée d'administration de la RMP. Dans tous ces cas par contre, soit le traitement relais par DDS n'a pas été suivi, soit existait une résistance probable à la DDS.

Dans quelques cas la sensibilité à la RMP a pu être testée chez la souris : souches sensibles dans 8 cas de recidive après prise unique de RMP ; résistante dans 1 cas de traitement plus prolongé.

Les auteurs avancent quelques considérations d'ordre thérapeutique.

PO 647A

CHANGES IN EPIDEMIOLOGICAL AND OPERATIONAL INDICATORS BEFORE AND AFTER MDT

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The National Leprosy Control Programme in Sierra Leone has completed 15 years of its existence on January 1988. MDT as recommended by WHO using the Clofazimine combination for MB cases was introduced in 1983.

Regular evaluation of the programme is being carried out every 5 years using essential operational and epidemiological indicators as recommended by WHO.

These indicators in 1988, 5 years after the introduction of MDT, are compared with those at the end of 10 years (in 1983 before the introduction of MDT).

The changes are dramatic with certain indicators like a) proportion of children among cases under treatment b) attendance rates c) cases released from control, both PB and MB cases d) prevalence rate e) case detection rate or annual incidence rate.

On the other hand, some of the indicators like a) inactivity of the disease b) bacteriological

examination of the MB cases do not seem to have the same significance they had before the introduction of MDT.

These and other changes in the indicators will be presented in the form of posters of tables and graphs.

PO 647B

FIVE YEARS OF MULTIPLE DRUG THERAPY IN SIERRA LEONE - AN ANALYSIS

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As on January 1988 a total number of 4'828 cases have been put on MDT, of which 1'427 are multibacillary and 3'401 are paucibacillary cases.

The standard regimen recommended by WHO is being followed for both paucibacillary and multibacillary cases.

The following factors are analysed:

- for paucibacillary cases
  1. percentage of cases which completed the full course of treatment
  2. time taken for lesions to become inactive
  3. follow up ranging from 6 months to 42 months
  4. relapses and type I reaction.
- for multibacillary cases
  1. clinical improvement
  2. bacteriological improvement
  3. reactions - ENL and type I
  4. attendance
  5. side effects of the drugs used.

PO 648

COMPARISON OF DAILY RIFAMPICIN-LAMPRENE-DAPSONE VERSUS MONTHLY ONCE RIFAMPICIN WITH REGARD WITH B.I. AND RELAPSE RATES.

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Among the new patients registered during 1982 and 1983 at Sivananda Rehabilitation Home. Hyderabad. 350 patients were put on multidrug therapy. These patients were divided into two groups: and different regimens were given to them. Group A had 190 patients who received 450 mg Rifampicin daily with Lamprence 100mg on alternate days and 100 mg Dapsone daily. The monthly dose of Lamprene and Rifampicin were supervised in the second group and all drugs were administered under supervision in the first group.

These two groups were analysed after four years from start of treatment, and the results of Bacterial clearance and relapse rates among them will be presented; as also the occurence of type II reactions and side effects of the drugs will be discussed.

PO 649

STUDY OF RELAPSE AMONG 7445 CLINICALLY CURED LEPROSY PATIENTS IN WEIFANG PREFECTURE OF SHANDONG PROVINCE OF CHINA

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In order to study leprosy relapse and factors affecting it, and thereby to draw up pertinent measures to control this setback,in 1986,all surviving cured patients were followed up by clinical and bacterial examination.All files and records of all such cured patients were reviewed and analysed according to a uniform standard questionare. The total relapse rate was 4.3%(3.78 per 1000 person-years). The relapse rate of multibacillary leprosy patients was 5.67% (5.86 per 1000 person-years)and that of paucibacillary patients was 3.44% (2.76 per 1000 person-years).The relapse rate in males was significantly higher than that in females.The average lapse of time before relapse in this group was 5.31 years and the lapsed time in multibacillary and paucibacillary patients were similar, i. e. 50% of the relapses occurring within 5 years in multibacillary and within 4 years in paucibacillary patients.The regularity of maintenance therapy had some impact and the relapse rate decreased as the duration of the maintenance therapy was lengthened.However,prolonging the maintenance therapy only played a part in postponing relapse and did not decrease the relapse rate in multibacillary patients. No such influence on paucibacillary patients was observed.As the leprosy control program has developed,the decline in the relapse rate of leprosy has paralleled the decline in prevalence and incidence in Weifang. The factors possibly affecting these results are discussed.

PO 650

OBSERVATION OF MULTI-DRUG THERAPY FOR MULTIBACILLARY LEPROSY OVER TWO YEARS IN XICHANG FIELD, SICHUAN, CHINA

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In 1984-1987, in Xichang city, 111 multibacillary cases of leprosy were treated with the multi-drug regimen recommended in 1981 by the World Health Organization. Sevety-two cases were treated for 24 months (LL 39 cases, BL 30 cases, BB 3 cases).The results show clinical improvement and decrease of average bacterial index(BI).No deterioration of their disease was found in any case, among which,65 cases had been treated with rifampin and DDS and 7 cases were untreated. The average BI before the start of MDT was 1.50 and after 24 months of MDT the average BI was 0.62,so the decrease in the average BI was 0.88 Leprosy reaction and neuritis decreased with prolonged course of treatment. The pigmentation with clofaziminе in the skin lesions and ichthyosis-like skin lesions were primary side effects and a few patients had mild gastro-intestinal discomfort. THe treatment of two cases was discontinued because of damage to liver and kidney. We regard MDT as having little side effects and gives satisfactery results in treatment for multibacillary leprosy. It is suitable for field treatment.

PO 651

IMPLEMENTATION OF MULTIDRUG THERAPY IN GUIZHOU PROVINCE,CHINA

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The Guizhou Province has signed in 1985 with WHO a five-year collaborative leprosy control programme with MDT. Guizhou has a comparatively high prevalence of leprosy (1985, 0.24/1000) and the patients live widely seperated. We have successfully implemented MDT (WHO 1982) in 2,037 active cases of which 89 percent are multibacillary. The programme may be divided into the following phases:

A. Preparatory Phase:
   1) Health education to the public and the different categories of health personnel.
   2) Training of field workers in the three-tiered primary health system in standardized methodology and asignment of responsibilities.
   3) Active case-finding, confirmation of diagnosis and completion of case histories.

B. Implementation Phase:
   1) To ensure drug delivery and supervision (96.7%).
   2) To check on regularity (97.4%).
   3) To give immediate care to patients with indications of leprosy and drug reactions,admission to the subdistrict general hospitals, if necessary.
   4) Prevention of disabilities at monthly visits.

After 10-14 months of MDT,there were 446 patients(26.8%)with marked improvement, 1,081 (63.2%) with moderate improvement, 163 (9.5%) stationary and 20 (1.2%) deterioration. The reduction of BI was in average 0.58 at the end of 10 months and 0.8 at the end of 14 months of MDT.The main side-effect was gastrointestinal disturbances.(1.7%).

THe above experiences indicate that:
1) MDT has a high therapeutic effect.
2) MDT may be successfully implemented in a highly montainous and difficult terrain.
3) The three-tiered primary health system is a guarrantee to the success of the leprosy control programme with MDT.
4) The control programme should be well planned and properly implemented to avoid the occurrence of multidrug resistance.

PO 652

LEPROSY AND SIDDHA MEDICINE.

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Siddha Medicine (SM.) is a well recognised form of Traditional Medicine, and practised in TAMIL speaking areas at present. Description of leprosy in SM as well as in ancient TAMIL literature make one to feel that leprosy might have been prevalent in this part even before descriptions made in Ayurveda (5th century BC). The term "KUSHTAM" (popular in the community even today) in SM denotes leprosy. SM describes it as a highly contagious disease. The clinical

forms of leprosy, course, complications and therapeutic modalities were dealt in SM, and hence Siddha medical practitioners (SMP) continue to prescribe SM without any proven scientific value. Moreover some other skin diseases which simulate leprosy were also included. The deep enrooted wrong conception for leprosy and the therapeutic modalities of Siddha, continue to be a deterrant for its eradication. As sizables number of leprosy cases are found in TAMILNADU, it is suggested that the current concepts of leprosy, may be taught to SMP and incorporate them in the healthcare delivery like local dais for antenatal care and delivery. This procedure will help to identify the early cases, provide an opportunity for uniformity of therapy, and win the confidence of local people for eradication of leprosy. (Sponsored by TNSRC, Madras).

PO 653

THE CLOFAZIMINE THERAPY OF SULFONE RESISTANT LEPROSY: LONG-TERM FOLLOW-UP

Robert R. Jacobson

While monotherapy of leprosy can now no longer be recommended, between 1965 and 1978, 81 patients at Carville were placed on treatment with clofazimine monotherapy for proven or suspected infections with sulfone resistant Mycobacterium leprae. Although many of these left Carville, died of non-clofazimine related causes, or were changed to other therapy because of side effects (usually pigmentation), 50 continued treatment at Carville until their disease became inactive. All remained on clofazimine thereafter and follow-up has revealed no relapses. Clofazimine resistance could, of course, still develop in some of these cases and life time therapy is impractical in most control programs. However, these results are of interest because they suggest that clofazimine monotherapy was at least as effective as dapsone monotherapy, and resistance to clofazimine may be less common.

PO 654

ANTI LEPROSY THERAPY-RESISTANCE OF HANSEN´S BACILLI MONOTHERAPY BY D.D.S.-TRIPLE CHEMPOTHERAPY

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Several publications (mainly in USA) underline the phenomenon of sulfone resistance in M. leprae. Advocating treatment of H.D. by mother Sulfone (D.D.S.) since April 1949 we have not stopped from drawing attention om potential danger of sulfone resistance but we think that importance of resistance of H.b. to D.D.S., is now exaggerated. We must look to avoid it by the best use of Mother-Sulfone. It is caused by: utilisation of sulfone substitutes (of an unstable metabolism) and D.D.S. insufficient, irregular or prematurely interrupted treatments (leading to sulfonaemia deficiency). It is vital to prescribe the D.D.S. "maximum-tolerated-effective-dosage"= 200mgs. per diem, as a standard adult treatment (used with satisfaction for many years). Alas! Little by little the adult daily dose has been reduced to 50 mgs, even 10 mgs(!), then it was fixed at 100 mgs, but this dosage itself, is able to cause sulfonaemia deficiency leading to resistance (Browne). Isn´t it the common sense attitude to return to the dosage of 200 mgs? Advantages of D.D.S: good tolerance, parallelism toxicity-activity (easily controlled), regular metabolism, bacteriostatic action (perhaps bactericidal in strongest concentrations), easy administration "per os" and I.M. (same dose) and low net cost, vitally for countries with high prevalence, poor and under-developed. Since 1951, we have not ceased to underline the advantage of associating D.D.S. with other effective anti-leprosy drugs. It is obvious that triple associations will statistically eliminate the risk of appearance of resistant mutations in Hansen´s bacilli. Some products can be associated now, with D.D.S: RIFAMPICINE, CLOFAZIMINE, PROTHIAMIDE. But cases of resistance of these drugs are already published. The triple drug therapy is unfortunately quite expensive, inapplicable in most countries with high prevalence. Implemantation of this therapy also raises problems in order to avoid a potentially catastrophic emergence of multiple drug resistance in M. leprae.

PO 655

ESTUDIO DE TRATAMIENTO COMBINADO DE CORTA DURACION CONTRA LA LEPRA EN MEXICO

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Antecedentes:El estudio se inició en marzo de 1985, teniendo como antecedente que en el país se ha usado prácticamente sólo monoterapia suffónica. Se trata de un ensayo clínico comparado dos esquemas con politerapia, con tres drogas, aceptados por la OMS, por espacio de dos anos, uno de ellos con fase inicial intensiva de suministro diario, supervisado durante tres meses; con seguimiento de los pacientes de ambos esquemas por espacio de cinco anos al término del tratamiento. Objetivo:Evaluar la efacicia terapéutica y aparición de efectos secundarios comparando ambos esquemas. Esquemas usados: OMS MINIMO (A). Una dosis diaria de DDS 100 mg. y CLO 50 mg. complementada con una dosis mensual de RMP 600 mg.y CLO 300 mg. durante dos anos. OMS CON FASE INICIAL INTENSIVA (B). Fase inicial: una dosis diaria de RMP 600 mg., DDS 100 mg. y CLO 50 mg. supervisadas durante tres meses. Fase de continuación: Una dosis diaria de DDS 100
mg. y CLO 50 mg. complementada con dosis mensuales de RMP 600 mg. y CLO 300 mg. hasta completar dos anos. La asignación de los esquemas fué aleatoria; para evaluación se medirá eficacia terapeútica (evolución clínica, resultados bacteriológico e histopatológico), reacciones secundarias y recidivas post tratamiento. La unidad de investigación son enfermos multibacilares, vírgenes al tratamiento, con baciloscopía positiva y sin patología agregada. Procedimientos:
Los enfermos fueron pesquisados y diagnosticados dentro de las actividades habituales del programa de control de lepra; el tratamiento lo supervisa el personal de las unidades regulares de salud y la revisión clínica el leprólogo. Los exámenes clínicos y de laboratorio se realizaron a los 3, 6 y 12 meses.

El estudio se lleva en cabo en 4 estados con la mayor tasa de prevalencia del país.Resultados: Los resultados son preliminares al cumplirse doce meses de tratamiento. In-gresaron 61 pacientes, 34 con esquema A y 27 con esquema B. Salieron 15 enfermos que corresponde al 25% de los que ingresaron; de ellos salió el 24% de esquema A y 26% de esquema B. Eficacia terapeùtica: Como era esperarse, con ambos esquemas la proporción de enfermos con mejoría, conforme aumenta el tiempo de tratamiento, pero al hacer la comparación, en-contramos franca superioridad del esquema B, particularmente durante los primeros tres meses de tratamiento, en proporción de 4 a 1; la relación a favor del esquema B se hace menos ostensible a los 6 y 12 meses, pero permanece 2 a 1, de acuerdo al reporte mensual del personal tratante.Reacciones secundarias: El efecto indeseable encontrado con más frecuencia, fué la hiperpigmentación presentándo se en el 18% de los enfermos, mayor entre los que tomaron el esquema A (73%) que entre los del B (27%).Solamente una pacienta presento hepatitis tomando el esquema B. Conclusiones: Por ser resultados preliminares no se realizaron pruebas de significancia estadística, sólo se compararon los esquemas a base de relaciones y proporciones. Los resultados orientan a pensar que es más efectivo el esquema terapéutico con fase inicial intensiva de fifampicina y clofazimina para lograr evolución de lesiones y negativización baciloscópica, particularmente en los inicios. Los efectos secundarios encontrados también favorecen en la comparacion al esquema B. Estos
hechos en principio están en desacuerdo con la hipótesis planteada de que el suministro diario o intermitente mensual de RMP surte efectos similares, tanto benéficos como adversos. Esperaremos al término del estudio para utilizar también los otros indicadores (estudio-histopatológico y presencia de recidicvas), además se practicarán pruebas de significancia estadística más estrictas.

PO 656

Combination therapy vs. monotherapy in BL and LL patients: a prospective randomized multi-center study.

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307 patients with BL and LL were randomized to three different treatment regimens: a. DDS, b. DDS + rifampicin, c. DDS + rifampicin + INH + prothionamide in five treatment centers: Freetown/Sierra Leone, Chetput, Madras, Bombay/India, and Karachi/Pakistan in order to evaluate the efficacy in direct comparison in a 3 years' treatment period with 5 years' follow-up. Over the years patients dropped out for various reasons: 216 could be finally evaluated. At 3 years treatment was stopped. Treatment parameters: clinical evaluation, histopathological classification, B.I. in skin smears, B. I. in histology and staining of bacteria in histology, all of them did not show any significant difference between the three treatment regimens. Patients with established DDS resistance in MFP were assigned to combination therapy and evaluated separately. Again, no significant difference. Hitherto only single cases with relapse have been observed without difference in all treatment groups. It is concluded that DDS is very efficient, rifampicin or the combination with rifampicin, INH and prothionamide do not add substantially to the treatment success. Frequency of reactions was equal in all groups. The combination of DDS, rifampicin, INH, and prothionamide was under no circumstances superior to the rifampicin and DDS or DDS alone so far. Therefore, it is to be assumed that at least a substance like INH which is not active against m. leprae is unnecessary in treatment combinations and should not be used in view of its potential liver toxicity. However, the final conclusion can only be made after the termination of the 5 years' treatment-free period.

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PO 657

STUDIES ON DAPSONE TOXICITY

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Reports based on retrospective studies have indicated a possible Dapsone toxicity, resulting in deformities in leprosy patients. A prospective study is being carried out to verify the occurence of any such toxicity. TT and BT cases having thickening of one of the major nerve trunks with normal size of the nerve on the contra-lateral side were selected. They were randomly allocated to two groups, one group (28 cases) receiving only Dapsone and the other group (26 cases) receiving Rifampicin. The cases were followed upto 2 years, carefully monitoring the extent of anaestnesia, muscle wasting, motor functions, nerve conduction velocity and electromyographic changes. It was found that:
(i) None of the cases in the test or control groups developed deformities - (ii) There was no difference in the motor nerve conduction velocity (MNCV) between the affected and unaffected nerves initially or after 3-36 months of Dapsone therapy. The MNCV was within normal limits in both groups.
(iii) EMG studies on 10 lateral popliteal nerves showed a sensory deficit in 2 nerves. After 3,6 and 12 months of treatment, the sensory deficit showed no change.

The findings of the study indicate that with the parameters applied, there is no evidence of deterioration of nerve function with Dapsone therapy.

PO 658

Assessment Criteria and Multidrug Therapy.

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One hundred and thirty two untreated leprosy patients(77 LL + 55 BL) were randomised into 3 different regimens. They were treated with DDS, DDS + RMP and RMP + Isoprodian continuously for 3 years. Pre and post treatment biopsies were inoculated into the mouse foot pad. The effect of different chemotherapeutic regimens on bacterial viability, BI reduction, clinical improvement, the relationship between the smear BI and biopsy BI, the quantum of bacteria inoculated and the quantum harvested were investigated. A significant difference was observed between the pre and post treatment BI level. The BI reduction between the regimens was not significant. The percentage of bacteriologically negative patients after 3 year period in these regimens were not different from each other. Eighty three patients(63%) remained still BI positive at the end of the study. About 96% of the strains from bacteriologically positive patients after 3 years treatment did not multi ply in the mouse foot pad indicating a uniform kill after this period. No relapses have been so far encountered. No correlation was obtained between the smear BI and biopsy BI (per mg), between the quantum of bacteria inoculated and the quantum of bacteria harvested. Significance of the results, the present criteria to assess the superiority of the regimens are discussed.

PO 659

THE COMPARATIVE EFFECTIVENESS OF VARIOUS REGIMENS OF INTERMITTENT THERAPY IN LEPROSY.

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The results of the treatment of 44 patients with active lepromatous leprosy are presented. Three regimens of intermitten therapy were studied: I (17 cases) - dimociphone (200mg) + rifampicin (300 mg) and clofazimine (100 mg) alternately; II (15 cases) - DDS (200 mg), rifampicin (450-600 mg) and prothionamide (500mg) alternately; III - DDS + prothionamide (in the above doses) and rifampicin in a high dose of 900-1200 mg alternately (12 cases). The drug tolerance was satisfactory without deterioration of functional state of liver, kidneys and indices of peripheral blood. Clinical, histological and bacteriological investigations confirmed the effectiveness of all three regimens of intermittent therapy. The combination of dimociphone, rifampicin and clofazimine was the most effective one: 16 out of 17 patients showed marked improvement (morphological and bacteriological indices fell on the average by 52% and 76,4%, respectively ($p \leqslant 0,05$). Clinical regress was noted in 11 of 15 cases treated by regimen II: MI decreased by 37% and BI - by 86,5% ($p \leqslant 0,05$). The administration of single high doses of rifampicin did not increase the effectiveness of intermittent therapy, nor was it superior over regimens I and II. Side effects in patients given high doses of rifampicin were more often, so regimen III is only possible under supervised conditions and when the patients tolerate such doses well. The data obtained permit to recommend large-scale usage of intermittent therapy for leprosy patients.

PO 660

THE EFFECT OF CLOFAZIMINE ON THE PHARMACOKINETICS OF RIFAMPICIN AND DAPSONE IN LEPROSY.

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The standard therapy for multi-bacillary leprosy is atleast two years of daily Clofazimine (Clf) and Dapsone (DDS), augmented by Rifampicin (Rif) daily for 14 days and once a month thereafter. The purpose of this study was to examine the possible effect of Clf on the metabolism of Rif and DDS.

In the first phase of this study 15 untreated leprosy patients were given Rif and DDS for 7 days and then Rif, DDS and Clf for 7 days. Concentrations of Rif and DDS were estimated in timed plasma

specimens and in 24h urine specimens on days 7 and 14. No significant differences in the pharmacokinetics of Rif and DDS were observed between two occasions of sampling.

In the second phase of the study, after giving 100 mg DDS orally once to 15 healthy volunteers, 3h blood and urine specimens were collected. Basal and 3h blood and urine samples were also collected on the day of study from 150 LL patients on DDS 100 mg daily or DDS daily plus Clf 100 mg AD for 3 months to 5 years. All samples were analysed for DDS content. While there was a difference between plasma levels of DDS on single and multiple doses, there was no difference between two groups of patients on either DDS or DDS plus Clf for varying periods, thereby ruling out any significant effect of Clf on metabolic disposition of DDS.

PO 661

A STUDY OF RELAPSE IN LEPROSY IN MDT PROJECT IN BARODA DISTRICT

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The value of different treatment regimens in leprosy is measured using criteria : Clinical cure and the time necessary to attain it, bacteriological cure as ascertained by culture negativity and relapse rate. Pauaucibacillary cases of leprosy belonging to nono-lepromatous group consisting of tuberculoid, polyneuritic, indeterminate and maculoanaesthetic, Multibacillary cases belonging to Borderline lepromatous and lepromatous types were released from control from 1984 onwards. A total number of 13,752 cases consisting of 9522 paucibacillary and 4230 multibacillary cases, were so released in multidrug therapy project in Baroda by Government of India with active assistance of the State Government, the W.H.O. and the Swedish International Development Authority. Up till January 1988, 15 paucibacillary and 2 multibacillary cases relapsed after MDT within 3 years. Factors associated with the occurance of relapse will be discussed.

PO 662

MULTIDRUG REGIMEN IN LEPROSY ERADICATION PROGRAM, REPORT OF ACTIVITIES IN BARODA DISTRICT, (GUJARAT) INDIA.

N.K. CHOPRA, J.S. AGRAWAL & P.G. PANDYA.

Though much information is available on MDT organising, it poses a challenge to the field staff due to limited field trials conducted and varied field conditions.

The MDT project was begun on 11th June 1984 in Baroda by the Government of India with active assistance of State Government, the WHO and the SIDA. The drug combination for MB cases was rifampicin 600 mg, clofazimine 100 mg and dapsone 100 mg, daily for 14 days intensive supervised therapy, followed by once a month (Pulse) supervised dose of rifampicin 600 mg, clofazimine 300mg and dapsone 100 mg for 2 years and clofazimine 50 mg daily with dapsone 100 mg daily unsupervised for 2 years; for PB cases dapsone 100 mg daily for 6 months alongwith rifampicin 600 mg supervised (Pulse) once a month for 6 months.

Total number of active cases at commencement of MDT were 10706, out of these 10348(96.37%) cases brought under MDT till December 1987. Amongst 10348 old cases 9112 (88.05%) are cured with MDT (3110 MB + 6002 PB). 180 old MB cases BO + inspite of completed 24 Pulse. The rest 1056 (10.23%) stopped the treatment for various reasons. 790 (74.81%) cases have left the villages to earn their livelihood 30 (2.86%) cases dropped out due to complications, 150 (14.34%) cases were being treated by skin specilist. 86 (7.19%) refused to continue the treatment inspite of best efforts of field staff. New cases detected since June 1984 are 7628, out of which 7549 (96.28%) brought under treatment. New cases cured till December '87 are 4640 (1120 MB + 3520 PB). 17 cases relapsed after MDT (15 PB + 2 MB). 280 (1.56%) cases got complications, 250 developed reactions, 3 cases Jaundice, 15 cases Gastritis and rest 12 got anaemia. The study showed that MDT can be implemented in tribal, rural and urban population with high rate of compliance.

PO 663

Experience with multidrug treatment of leprosy patients in Israel

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The experience and follow up multi-drug therapy in Israel of leprosy patients in Israel from 1982 to 1987 is described.

PO 664

Clinical and histopathological assessment of patients who continue to be bacteriologically positive even after 36 doses of multidrug therapy - the WHO recommended regimen.

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80 partially treated, clinically active, smear positive BL/LL patients commenced treatment between June 1984 and June 1985. 37 of them, whose initial mean BI was 3.75, continue to be bacillated inspite of having had 36 doses of continuous and regular effective chemotherapy. 9 of these patients, selected at random, are subjected to clinical and dermatopathological evaluation, with in the existing constraints of a controlled programme. The results of this field-based study are presented and discussed.

PO 665

MDT. SUPERVISADO PARA ENFERMOS DE HANSEN

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Desde 1985 se desarrolla en Venezuela un Programa MDT Supervisado para todas las formas de Lepra, basado en recomendaciones de la OMS.

El esquema utilizado es el siguiente: Dapsona 100 mgrs/día autoadministrado con supervisión periódica de la toma y determinación de Sulfonuria; Clofazimina 600 mgr. cada 15 días y Rifampicina 600 mgrs. cada 30 días ambas supervisadas (administración en boca). La duración del tratamiento depende de la forma clínica, evaluaciones clínico-bacteriológicas semestrales.

En dos años de desarrollo en las áreas hasta ahora incluídas en el Programa, de un total de 5.236 casos activos existentes, han sido registrados y examinados 4.448,de los cuales 4.109 se encuentran bajo esta terapia (cobertura 78.5% en relación al total de activos y 92,3% en relación al total registrado). La regularidad en el cumplimiento es mayor al 86%. Porcentaje de abandono y/o renuencia 2%; bajo porcentaje de efectos secundarios (7,9%). Promedio porcentual de inactivación bacteriológica semestral: 3,9% e inactivación anual del estado clínico 10,4%. Altas de 356 casos que se mantienen bajo vigilancia post-terapéutica; sin presentar recidivas en 18 meses.

Las limitaciones operacionales presentadas en la implementación, fueron superadas con la participación creciente del personal local, permitiendo adoptar metodologías de trabajo acordes a las características y recursos de cada región.

PO 666

Clinical and Bacteriological Evaluation of patients after suspension of treatment with MDT-schemes.

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In 1983 a study on MDT as recommended by O.M.S. was initiated in the Curupaiti State Hospital. Up to this date, we have one hundred and fourteen patients who competed treatment. Out of sixteen patients, all paucibacillary, were released from control. Ninety-eight, seventy-four MB and twenty-two PB are undersurveillance after suspension of treatment. We have two defaulters (one MB and one PB). The clinical and bacteriological findings in a two years follow up are presented and discussed.

PO 667

USE OF MODIFIED RIDLEY'S BACTERIOLOGICAL INDEX SCALE FOR BACTERIOLOGICAL ASSESSMENT OF MULTIBACILLARY CASES UNDER MULTIDRUG THERAPY.

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Ridley's bacteriological index scale is used universally to judge bacteriological assessment of multibacillary leprosy cases. The scale is based on log. 10 and thus rise in bacteriological index 1 to 2 is not the addition of one unit but it is multiplication with 10. To get the proper judgement of bacteriological quantum in human source, the modification is suggested to Ridley's scale by applying formula such as Average Bacteriological Index of the group of a patients I No. of patients in the group and scoring point based on Ridley's logarithmic Bacteriological Index Scale. This scale has applied to the leprosy case in the model field unit and multibacillary cases under the treatment of multidrug therapy. This new system based on arithmetic scale revealed that (a) 92 to 99% bacteriological load is harboured in leprosy cases having Bacteriological Index more than 3 and (b) The introduction of multidrug therapy initiated the reduction in total bacteriological quantum is very fast such as 100% to 5% at 12 months and 2.5% at 24 months. So to achieve leprosy control within specific period the leprosy cases having Bacteriological Index more than 3 have to be treated on priority basis.

PO 668

MULTIBACILLARY LEPROSY CAN BE TREATED BY A FIXED DURATION THERAPY. THERAPY CAN BE STOPPED WHEN BI IS STILL POSITIVE.

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Since 1980 we have been applying in MB leprosy fixed duration combined treatment regimens of 52, 26, and 13 weeks, composed of rifampicin (RMP), ethionamide (ETH), dapsone (DDS), clofazimine (CLO).
Regimens, patient years of follow up and confidence intervals for relapses are as follows : 26+26w (26 RED or REC 6/7+26 ED or D or EC or C 7/7) 954 pt yrs of FU. 0 relapses, confidence interval (CI) = 0-0.37. 8+44w (8 RED 6/7 + 44 R 1/7 ED 7/7) 714 pt yrs. 0 relapses, CI : 0.052. 26w (2 RED or REC 6/7+24 R 1/7 ED or EC) 52 pt yrs. CI=6.85. 13w (R 2/7 ED or EC 6/7) 497 pt yrs. 1 relapse (at 35 mo. post treatment) CI : 0.01-1.11. Bacilli from the one relapse case are inoculated in mouse foot pads for drug sensitivity testing.

PO 669

RESPONSE OF THELEP TRIAL PATIENTS TO COMBINED DRUG REGIMENS

Subcommittee on Clinical Trials, Scientific Working Group on the Chemotherapy of Leprosy (THELEP), UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases
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Five combined drug-regimens were studied in a trial carried out among 215 previously untreated patients with lepromatous leprosy in Bamako, Mali, and in Chingleput, South India. The regimens--daily rifampicin (RMP), dapsone (DDS) and clofazimine (CLOF) or protionamide (PTH); a single initial large dose of RMP together with daily DDS; and daily CLOF or PTH for the first 3 mon, together with daily DDS and RMP, either in a single initial large dose or 900 mg once weekly--were administered for 2 yr. During this time, biopsy specimens were obtained, and the recovered *M. leprae* were inoculated into TR mice for detection of persisters. In addition, periodically, the BI and LIB was measured, patients were examined clinically and observed for side effects, and a number of laboratory tests were carried out.

Despite the widely varying "strength" of the experimental regimens, no differences were demonstrated among the regimens, with respect to the frequency with which persisting *M. leprae* were detected, clinical response, and adverse reactions, with two exceptions. The patients treated in Chingleput with Regimen A_1--daily RMP, DDS and CLOF for 2 yr--demonstrated more pigmentation than did those treated with Regimen D_1, which included CLOF administered only for 3 mon. 2) Those patients treated in Bamako with Regimen A_2--daily RMP, DDS and PTH for 2 yr--may have suffered more hepatitis and jaundic than di the patients treated by the other regimens.

PO 670

RECOGNITION OF MYCOBACTERIAL ANTIGENS BY SERA FROM LEPROSY PATIENTS.

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A knowledge of the antigenic composition of *Mycobacterium leprae*, and the role that these antigens play in the immune response during infection, are prerequisites for understanding the pathogenesis of leprosy.

In order to identify antigens in 3 armadillo-derived *M.leprae* sonicates and a soluble extract (SE) of *M.tuberculosis*, these preparations have been subjected to SDS-PAGE and Western blotting using sera from lepromatous patients and healthy controls. Eleven distinct antigens were recognized in the *M.leprae* sonicates by IgG class antibodies in leprosy sera. Proteins of 33, 25, 18, 15 and 12 KD were the most commonly observed and the 33 and 15 KD proteins were recognized with high intensity. The same sera recognized among others, antigens of similar molecular weight in the *M.tuberculosis* SE, although with less intensity and at a lower frequency.

The serum samples from healthy donors did not recognize the 33, 25, 18 or 12 KD antigens in the *M.leprae* sonicates. However, they did recognize a 33 KD antigen in the *M.tuberculosis* SE.

Using *M.leprae*-specific murine monoclonal antibodies it was demonstrated that the 33, 25 and 15 KD antigens are different from those well characterized protein components previously described (65, 36, 28, 18 and 12 KD) and already cloned.

A selection of serum samples from these lepromatous patients are being used as antibody probes in order to screen the recombinant DNA library of *M.leprae* expressed in *E.coli*.

PO 671

STIMULATION OF UNSELECTED T CELL POPULATIONS WITH PURIFIED RECOMBINANT PROTEINS OF MYCOBACTERIAL ORIGIN:

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The identification of antigens with potential value for the prevention and diagnosis of the mycobacterial diseases leprosy and tuberculosis needs to be done on the T cell level. Recently, recombinant proteins of mycobacterial origin have been expressed as fusion proteins with ß-galactosidase in the λgt 11 system by R.A. Young et al (Nature 316:450, PNAS 82:2583).

Some of these r- proteins have been shown to stimulate selected long term cultured T cell lines. In contrast, freshly isolated T cells cannot be used for the characterization of the T cell antigenicity of these proteins because their responses are obscured by various E.coli components. We have therefore developed a universal purification method consisting of an anti-ß-galactosidase affinity column and an anion exchanger which allows screening of mycobacterial r-fusion proteins with unselected T cells. Purified r-proteins were then used for stimulation of freshly isolated peripheral blood cells from normal donors. The r-proteins tested thus for (12 kDa, 19 kDa, 65 kDa and 71 kDa proteins of M.tuberculosis) were all capable of stimulating T cell responses while the ß-galactosidase control failed to do so. Thus screening of purified r-proteins with unselected T cell populations has become possible.

PO 672

IMMUNOLOGICAL SIGNIFICANCE OF MYCOBACTERIUM LEPRAE CELL WALLS.

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Both in vivo and in vitro studies suggest that resistance to M. leprae infection is mediated by T cells rather than antibodies. Thus to design new vaccines and skin test reagents there is need to identify antigens relevant for induction of T cell responses that are likely to be important in protection against leprosy.
It has long been known that the cell walls of mycobacteria can evoke DTH responses and have strong adjuvant activity. We have explored the possibility that the cell walls of M. leprae may contain important antigens for cell-mediated immunity (CMI) to leprosy. Highly purified cell walls of M. leprae stimulate proliferation of T cells from tuberculoid, but not lepromatous leprosy patients and elicit DTH skin reactions in guinea-pigs, tuberculoid patients and contacts sensitized to M. leprae. Analysis of the precursor frequency of antigen-reactive human peripheral T cells revealed that there are as many T cells reactive to antigens associated with purified cell walls as to intact M. leprae. Upon removal of mycolates and arabinogalactan, the protein-peptidoglycan complex retained all of the immunological activity, whereas, the reactivity was destroyed by protease treatment. Thus, one or more cell wall associated proteins appear to be a major contributor to CMI responses to M. leprae.

PO 673

Identification of a Major Immunostimulating Protein From M. leprae.

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Most patients with lepromatous leprosy (LL) have high titered antibody responses but fail to display specific cell-mediated responsiveness to M. leprae antigens. This immunologic defect is specific because cell mediated immune responses to antigens other than M. leprae are normal in these patients. Purified M. leprae antigens are essential for dissecting the cellular immune response to this bacterium. With the goal of obtaining such determinants, we initiated an effort to isolate native proteins from M. leprae. Using a relatively gentle acetone based extraction procedure, we have isolated a potent immunostimulatory protein from the pellet fraction of sonicated M. leprae, designated MLP, with a MW of 35 KD. This protein is recognized by mouse mAb, (MLO3-A_1), by a polyclonal rabbit antiserum generated to MLP, and by sera obtained from LL patients. In contrast, neither rabbit anti-M. bovis sera nor sera from healthy controls recognized MLP. MLP stimulated T cell proliferative responses in all M. leprae reactive patients with leprosy as well as healthy individuals vaccinated with BCG. T cells from patients unresponsive to wholeM. leprae failed to respond to MLP. MLP also stimulated proliferative responses in M. leprae reactive CD4+ T cell clones. These findings suggest that MLP represents a major immunostimulatory component of M. leprae. In addition to serving as a useful probe for studies of the T cell anergy which characterizes some patients with lepromatous disease, this protein may ultimately be useful as a component of a vaccine designed to provide protection against M. leprae infection.

PO 674

DETAILED ANALYSIS OF A DR2-RESTRICTED T CELL EPITOPE ON THE 65KD PROTEIN

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The study of M. leprae specific T cell epitopes is relevant for the development of M. leprae specific skintest reagents, because an antigen-specific skinreaction is induced by T cells.
We will report about the recognition of a peptide of the M. leprae 65 kD protein by two nearly M. leprae specific T cell clones (R2F10 and R2B6) from one tuberculoid leprosy patient. Both T cell clones were restricted via the DR2 molecule and recognized the recombinant M. leprae 65kD protein but not the recombinant M. bovis BCG 65kD protein. The minimal peptide determinant stretched from aminoacid 418 till 427. Multiple peptide synthesis was used to study the role of the different aminoacids within the peptide in binding to the HLA class II molecule (agretope) and the T cell receptor (epitope). For T cell clone R2B6 the glutamin at position 2 was critical for binding to the T cell receptor but not for T cell clone R2F10. Analysis of T cell reactivity to single substitution peptides showed that most peptides with substitutions in the middle 7-8 amino-acids of the 10-mer could neither stimulate the T cell clones nor compete for binding to the DR2 molecule of the "native" peptide. So, at least the middle 7 amino acids of this peptide cannot be replaced with another amino acid, probably because this leads to a change in the conformation of the peptide in such a way that both agretope and epitope are destroyed. These data show that there is a M. leprae specific T cell epitope on the 65kDa protein, and that for T cells reactive to the same peptide different aminoacids within a peptide determinant can be essential for recognition.

PO 675

DETECTION OF M.LEPRAE SPECIFIC ANTIGEN IN ANTIGEN PRESENTING CELLS IN LEPROSY SKIN LESIONS.

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By means of histochemical techniques M.leprae organisms have been described to be present in all types of antigen presenting cells(APCs) investigated in the dermal infiltrates in multibacillary leprosy.
The aim of this study was to find out if M.leprae specific determinant could be demonstrated in the different APCs in untreated paucibacillary as well as multibacillary leprosy. Biotinylated monoclonal antibody(Moab) F47-10 directed against a specific epitope on the 65kD M.leprae protein was used in a double staining technique.Moab F47-21 directed against a specific epitope on M.leprae phenolic glycolipid,which detected M.leprae antigen in a two stage peroxidase technique,could not successfully be biotinylated. Cells of the mononuclear phagocyte system(MPS) were detected by the following Moabs:OKM1(monocytes and granulocytes),RFD2(all monocytes-macrophages),RFD7 (mature tissue macrophages),RFD9(epitheloid cells); dendritic cells(DC) were detected by RFD1(interdigitating cells),OKT6 (Langerhans cells),M241(indeterminate cells).
No M.leprae specific antigen could be demonstrated in APCs in three biopsies from paucibacillary leprosy patients; on the other hand in two biopsies from multibacillary leprosy patients M.leprae specific antigen was found in the different APCs of the MPS as well as in RFD1 positive cells but not in OKT6 and M241 positive cells.In the cell types in which the antigen was found it was always present in part of these cells.Double staining with a Moab against HLA-DR gave the impression that HLA-DR expression did not differ on M.leprae antigen negative and positive cells.

It appears that this M.leprae specific antigen is present in all MPS cell types.The possible participation of DCs in antigen processing in leprosy needs further investigation.

PO 676

Involvement of stress proteins in the immune response to leprosy.

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Several of the protein antigens from M.leprae and M.tuberculosis which were originally identified using monoclonal antibodies have been further subjected to detailed sequence analysis and immunological characterisation. An unexpected relationship between some of these antigens and proteins which are involved in cellular responses to environmental stress stimuli have been observed. The structure and function of stress proteins will be discussed in the light of their potential involvement in intracellular survival and in induction of autoimmune pathology.

PO 677

Purification of M.leprae antigens by preparative SDS-PAGE.

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Purified antigens of M.leprae will enable us to identify immunologically functional epitopes. Purification of antigens from complex mixtures like sonicates by chromatographic techniques can be time consuming. We have exploited the resolving power of SDS-polyacrylamide gel electrophoresis and adjusted the technique for the purification of mycobacterial antigens. This technique is relatively simple and can be adjusted for optimal preservation of antigenic determinants. We have isolated several M.leprae antigens in this way, which showed a high degree of purity. Results will be shown of the exploitation of these antigens in functional immunological tests.

PO 678

Immunological characterization of the 36 kD antigen of M.leprae.

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The 36 kD antigen of M.leprae has shown prevoviously to play a role in the humoral and cellular immune responses of leprosy patients. We have purified this antigen from M.leprae sonicate by preparative SDS-PAGE and have used it for immunochemicical characterization. The purified antigen appeared as a single band in SDS-polyacrylamide gel electrophoresis and isoelectrofocussing and eluted as a single peak in ion-exchange chromatography. The antigen contained both a species-specific and cross-reactive epitopes. Different treatments of the antigen suggest that it is largely protein in nature. Results will be discussed of the exploitation of the purified antigen in serological assays and other functional immunological assays.

PO 679

T-CELL EPITOPES ON THE 36K AND 65K MYCOBACTERIUM LEPRAE ANTIGENS DEFINED BY HUMAN T-CELL CLONES.

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We studied the reactivity of M.leprae reactive T-cell clones from two tuberculoid leprosy patients towards a battery of different mycobacterial strains and purified mycobacterial antigens. Twenty percent of the clones appeared to be M.leprae specific. Twenty percent were cross-reactive with at least one of the three mycobacterial strains M.lepraemurium, M.vaccae and M.scrofulaceum. Thirteen percent were reactive with most but not all strains and the remaining 18 were reactive with all seventeen mycobacterial strains. All T-cell clones were tested with the 36K and 65K antigen isolated from M.leprae and with the M.leprae and M.bovis BCG 65K proteins produced in E.coli by recombinant DNA. At least three different epitopes could be defined on the 36K antigen of which one M.leprae specific. Two distinct epitopes were discerned on the 65K antigen of which one M.leprae specific and one cross-reactive. The M.leprae specific epitopes on the 36K and 65K antigen may help in the development of a specific serodiagnostic test and skin test.

Ref. Schooten WCA van, Ottenhoff THM, Klatser PR et al. T-cell epitopes on the 36K and 65K Mycobacterium leprae antigens defined by human T-cell clones. Eur J Immunol 1988,in press.

PO 680

IMMUNE RECOGNITION OF THE 18KD PROTEIN FROM MYCOBACTERIUM LEPRAE

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Several genes from M.leprae have now been cloned, based on the recognition of their encoded proteins by mouse monoclonal antibodies, but the role of these proteins in immunity to leprosy is not known. We have been working with the 18kD antigen (Young et al. 1985, Booth et al. 1988), using the techniques of lymphocyte proliferation, precursor frequency analysis, T cell cloning and ELISA tests to look for recognition of this antigen by patients and contacts from Karachi, and by UK donors. UK donors did not recognize the 18kD antigen, but leprosy sera contained antibodies to the protein. Non-specific immunosuppresion meant that the r18kD antigen had to be purified before use in cellular assays. In addition a variable but often strong response to β-galactosidase caused problems in cellular assays; this has been overcome by recloning the 18kD gene to remove most of the β-galactosidase. This antigen is now being used in the same assays to confirm that the 18kD antigen is specific to M.leprae and does not cross-react with M.tuberculosis or M.bovis BCG.

Young, R.A. et al. (1985) Nature 316:450.
Booth, R.J. et al. (1988) J.Immunol. In Press.

PO 681

IMMUNE CONTRASUPPRESSOR T CELL ACTIVITY IN HUMAN LEPROSY.

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Immune contrasuppressor T cells (Tcs) antagonize the activity of suppressor cells. Since some leprosy patients appear to posses an abnormal suppressor T cell activity, we decided to study the peripheral blood mononuclear cells (PBMNC) from 20 leprosy patients (10 lepromatous and 10 tuberculoid) and six healthy contacts regarding the percent

of CD8+, vicia villosa-adherent T lymphocytes (the putative Tcs cell subset) and expression of Ia and Tac antigens on these cells. In addition, we isolated Tcs cells and we studied their role on the in vitro proliferative response (^{3}H-TdR incorporation assay) of PBMNC to M. leprae (ML). The role of gamma interferon (rIF) and interleukin 2 (rIL-2) on the Tcs cell activity was also assessed.

We found that LL patients have a similar number of Tcs cells compared to TT patients or controls. However, the expression of Ia antigens was lower in LL compared to TT patients or controls (p 0.05). In 5 LL patients, the addition of an excess of mitomycin C-treated Tcs cells to autologous PBMNC + ML cultures, increased significantly the proliferative response to ML. The pre-incubation of CD8+, vicia villosa-adherent cells with rIF + IL-2 and ML resulted in an enhancement of the putative CS activity of these cells. In TT patients or controls, the addition of Tcs cells, pre-incubated or not with lymphokines, did not produce any noticeable effect on the ^{3}H-TdR incorporation of PBMNC + ML cultures.

Our data suggest that the in vitro immune response to M leprae can be modified in some LL patients by manipulating their Tcs cells. The role of CS cell activity on the in vivo immune response to ML remains to be determined.

PO 682

E-RECEPTOR (CD2) AND LEPROSY

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Our earlier studies have demonstrated that the sheep erythrocyte receptor (CD2) is modulated in bacilliferous lepromatous leprosy patients (LL) and this is strongly associated with T cell unresponsiveness to mitogens and antigens. This finding is confirmed and further extended to understand the mechanism of CD2 modulation by a series of experiments. The proliferative response of peripheral blood mononuclear cells (PBMC) from bacilliferous LL patients to mitogenic anti-CD3 and pairs of anti-CD2 monoclonals was significantly reduced; however PBMC from bacillary index negative LL and tuberculoid patients and controls showed normal level of response. Interestingly, the CD2 modulation and the associated suppression of proliferative response was brought about in T cells of tuberculoid patients and healthy controls by prior incubation of their PBMC with M. leprae (Dharmendra lepromin) in vitro for 12 h at 37°C. IL-1 secretion was found to be at normal level in the above cultures and the addition of IL-2 resulted in the recovery of proliferative response. M. leprae treated PBMC culture supernatant, but not M. leprae by itself modulated CD2 in enriched T cell population, thus indicating the importance of macrophage in this process. BCG- but not M. leprae-induced suppression of PHA and PPD response could be recovered completely by indomethacin. Activated T cells were found to be refractory to M. leprae-mediated CD2 modulation as well as suppression of proliferative response. On the basis of these results, the mechanism of immunologic unresponsiveness in leprosy will be discussed in the light of recent understanding on the importance of CD2 in T cell biology.

PO 683

MECHANISM OF IMMUNOSUPPRESSION IN TISSUES OF LEPROMATOUS LEPROSY PATIENTS.

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The absence of appropriately sensitized immune cells in lesions of lepromatous patients remains an enigma despite several theories. The present series of experiments carried out in lymph nodes and nerves of lepromatous patients highlight pathways of immunosuppression that may selectively operate in each tissue.

Lymphocytes from lymph nodes of lepromatous patients have the capacity to react to M.leprae without the addition of exogenous activating agents. This suggests either sequestration of circulating antigen specific lymphocytes by antigen trapped within lymphoid tissue or differential antigen processing by antigen presenting cells of the lymph node. Experiments in evidence of the above will be presented.

If sensitized lymphoid cells are present, then their absence in tissue lesions is puzzling. Because of its clinical significance, the nerve was chosen for further studies. Data utilizing the nerve tissue culture model indicate that M.leprae infected Schwann cells may secrete a factor[s] that is toxic or inhibitory in terms of lymphocyte function and also perhaps in chemotaxis. Such factors may also operate physiologically in normal conditions to maintain the nerve as an immunologically privileged site.

PO 684

A ROLE FOR HLA-DQ MOLECULES IN THE M. LEPRAE SPECIFIC SUPPRESSION OBSERVED IN LEPROMATOUS LEPROSY?

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HLA-DQw1 was found to be associated with LL in several populations (Van Eden and de Vries, Lepr. Rev. 55: 89, 1984; De Vries et al., (1984) Histocompatibility Test. 1984, p. 362; Serjeantson, S.W. Immunol. Rev. 70: 89, (1983). Is has been suggested by Sasasuki and co-workers, that this and similar assocations might be due to DQw1 being the product of an Immune suppression gene (Nature 327: 426, 1987). In order to test this hypothesis we added the anti-DQ monoclonal antibody SPV-L3. to PBMNC of fifteen LL patients, which were all non-responsive to M. leprae. In one out of these 15 cases the response to M. leprae was restored.
The results indicate that in a small minority of LL patients the HLA-DQw1 molecule may be involved in inducing M. leprae specific suppression. It seems unlikely however that this observation can explain the association between DQw1 and LL leprosy.

PO 685

METABOLIC STATUS OF PERIPHERAL BLOOD MONOCYTES TO GENERATE OXYGEN FREE RADICALS IN HUMAN LEPROSY.

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Phagocytic cells are known to generate oxygen free radicals on exposure to soluble and particulate stimuli. These oxygen radicals also possess bactericidal capacity and hence act as infantry of our immune system. Therefore,in the present study, the metabolic status of monocytes of human leprosy patients (including both bacteriologically positive and negative LL-BL and TT-BT patients respectively)have been investigated to know the reasons for the failure of the immune response to kill Mycobacterium leprae. The chemiluminescence and cytochrome - C reduction study revealed significantly decreased ($P<0.001$) oxygen free radical generation in patients of TT-BT and LL-BL group as compared to controls, further, no significant ($P>0.005$) change in the NADH and NADPH oxidase activity of macrophages was observed between leprosy patients and controls; whereas significant decrease ($P<0.001$) in glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase observed in leprosy patients than controls. This study suggests that there is suppression of oxygen free radical generating capacity in human leprosy and is probably due to block in HMP shunt to generate reducing equivalents i.e. NADPH required for the production of these toxic radicals.

PO 686

Characterisation of suppressive monocyte factors from Leprosy patients.

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Earlier studies from our laboratory have documented that factors derived from lepromatous monocytes (MoFs) abrogated antigen specific lymphoproliferation and the production of T cell growth factors (IL2). The present study indicates that such factors contain arachidonic acid metabolites such as PGE_2 (evaluated by Radioimmunoassay) thromboxane and leukotrienes (identified on HPLC). Whereas non-suppressive MoFs from 5 tuberculoid patients had PGE_2 levels ranging from 0.8 to 2.2 ng/ml, the suppressive factors from 13 lepromatous patients showed levels of 1.8 to 5.8 ng/ml. In addition, suppressive factors showed antigenic hierarchy at the effector levels of in vitro immune responses. Lymphoproliferation to M. leprae was abrogated maximally followed in order of importance by M. vaccae. M. smegmatis, $H_{37}Ra$ mitogen induced proliferation was not affected by the addition of suppressive MoFs.

PO 687

Expression of Mycobacterium leprae antigens and Modulation of Class II MHC Antigens in Human monocytes.

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Display of antigenic determinants in association with class II MHC molecule on the surface of monocytes has been considered to be critical in the generation of T cell mediated response. M. leprae is an intracellular pathogen naturally residing in human monocytes. Therefore, we monitored the expression of M.leprae derived antigens in cultivated monocytes using indirect immunofluorescence/ immunoperoxidase/FACSCAN techniques. Thirteen LL-BL, seven TT-BT and three healthy contacts were included in the study. A panel of murine monoclonal antibodies (Mabs) specific for phenolic glycolipid (PGL), protein and polysaccharide antigens (kindly supplied by Drs. Young and Ivanyi) were used. Monocytes maintained on coverslips with or without M. leprae(killed/live) were fixed and used for staining with various Mabs. The following observations were made: 1) Display of PGL and protein antigens were observed within 24 hrs following phagocytosis of M.leprae. 2) The staining pattern varied with different Mabs. ML04,ML10 and ML30 showed both cytoplasmic and membrane staining,while ML03 and ML34 showed,exclusively membrane staining. 3)5-17% of the uninfected LL monocytes were positive for the expression of M.leprae antigens. 4) The expression of M. leprae antigens on monocytes was found to be similar following infection in all groups of patients. 5)However, preliminary experiments showed down regulation of class II MHC antigen in LL monocytes,while its expression was unaltered in TT's and normals. Results indicate that LL monocytes are capable of processing and expression of protein,lipid and polysaccharide antigens of M. leprae, but simultaneous expression of class II molecule appears to be impaired.

PO 688

ESTUDIO DE LA CITOTOXIDAD DE MARCOFAGOS EN PACIENTAS CON LEPRA LEPROMATOSA EN PRESENCIA DE IL-2

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La susceptibilidad a la infección por el M. Leprae, es el resultado de un defecto de la immunidad mediada por células. En este estudio nuestro equipo de trabajo ha estudiado un grupo de enfermos de lepra lepromatosa procedentes del Instituto Leprológico de Trillo, de los cuales se obtuvieron células mononucleares de sangre periférica, previamente heparinizada se aislaron los macrófagos por adherencia al plástico, tras lo cual mediante técnicas inmunológicas habituales se testó la capacidad citotóxica de los macrófagos lepromatosos y de macrófagos del mismo número de sujetos control, en presencia de IL-2, la cual tiene como funciones fundamentales las iniciar la proliferación de células T activadas, inducir la síntesis de otras linfocinas y activar linfocitos citotóxicos, pero que aquí mostró también un efeto paracrino sobre los macrófagos.
Nuestros resultados muestran que hay:
1.- Un aumento de la citotoxicidad de los macrófagos lepromatosos y de los macrófagos control.
2.- El aumento de la citotoxicidad de los macrófagos control fué mayor que el de los macrófagos lepromatosos.
Concluimos en que, aunque recientes estudios experimentales- de diversos autores sugieren que los macrófagos en lepra lepromatosa- son competentes, hay una marcada diferencia en la capacidad citotóxica de estos macrófagos y macrófagos control. Consideramos que esta información puede tener relevancia para enteder tanto los mecanismos microbicidas como la inmunopatología de este proceso infeccioso.

READ BY TITLE ONLY

T001-T017

T001

Extraordinary presentation of leprosy, three case reports.

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This report deals with two cases of caseous leprous neuritis and one case of leprous synovitis.First,a 60 year-old male came with diffuse extensive thickening of Rt ulnar nerve The latter had gross and microscopic features, indistinguishable from those of caseous T.B. granuloma,with marked replacement of nerve tissue.Second,a 17 year-old male presented by Rt facial palsy,sensory loss of chin and thickened great auricular nerve.The nerve showed segmental thickening (2 cm by 8 mm),with multiple caseous areas.Nerve biopsy revealed abundant caseation and typical tubercles. The pathogenesis of this extensive caseation is discussed.It is noteworthy that tuberculoid leprosy neuritis with caseation must be differentiated from leprous neuritis with secondary infection and formation of pus .The third case was a 26 year-old male who had a swollen Rt middle finger in typical claw hand,associated with a thickened ulnar nerve.At operation,the synovial membrane of the proximal interphalangeal joint was nodular,with a turbidly yellowish synovial fluid and eroded articular cartilage. Synovial biopsy revealed leprous granulomata, made of a mixture of epithelioid cell tubercles and collections of lepra cells (dimorphous lesion).

T002

Type I (downgrading) reaction occurring in histoid leprosy

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Abstract: A 20-year-old female reported with asymptomatic, multiple painless nodules over the back and face,which continued to evolve over the past 8 months. Examination of the skin surface revealed multiple,translucent to opaque, skin coloured, non-tender, firm papules, nodules and plaques erupting out of an apparently normal skin. They were mobile and were distributed over the face, back and lower abdomen. Twenty days following the multidrug therapy, she had moderate fever, and irregular erythematous, painful, raised patches on the trunk,face, buttocks and thighs. The lesions were although well-circumscribed, yet serrated. The surface of the lesions was erythematous dry, tender and hot. Numerous small plaques were also seen in their vicinity. However, thickening and/or tenderness of the nerves feeding the plaques was conspicuously absent.

T003

STRUCTURES THROWING FURTHER INSIGHT INTO LIFE CYCLE OF M.LEPRAE.

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Certain interesting structures have been noticed in smears from preserved lepromatous biopsy suspensions. These include filaments with branching, conidial structures and membrane-like structures showing acid bacilli. The filaments showed round empty or pink stained areas in Ziehl Nelsens stained smears. On comparing suspensions in Hanks BSS incubated at 37°C, 30°C, 10°C and -20°C; the proliferation of filaments appeared to be favoured by cooler temperatures. Such tubes showed a mat of long thin branching and growing filaments. These filaments also showed pink dots within them in acid fast staining. Proliferation of filaments was associated with appearance of acid fast bacilli in bunches within the membranous structures. The acid fast bacilli were also seen in relation to filaments. The morphology of acid fast bacilli was same as that of M.leprae. The above findings and other relevant observations made at this Institute will be presented.

T004

The Possibilities of a Complex Life Cycle of Mycobacterium leprae

R. Albert, India

T005

A STUDY ON THE ACTION OF AN OIL BASED HERBAL PREPARATION ON WASTING OF MUSCLES.

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Wasting of muscles is a common phenomenon in this hyperendemic zone, thus aggravating deformity and disability. An oil based herbal preparation was used as massage as part of the physiotherapy on 125 patients. Specific instructions were given along with demonstration regarding its use which was to be done regularly once daily.

Definite improvement was observed within one month. Appreciable strength was regained within three months. The girth of the muscles were increased along with power by six months depending upon the degree and chronicity of the illness. 100% improvement was observed in 12% cases and no improvement was observed in 8% cases only. Details were studied and data analysed.

T006

Treatment of Leg Ulcers with Omnidom® Permeable Polyurethane Membrane

A. Leviatan, Israel

T007

The use of a new type of cellulose graft in the treatment of leprosy ulcers.

Domingos Quintella De Paola, Curupaiti State Hospital, Rio de Janeiro, Brazil.

The author presents a critical analysis on the utilization of "BIOFILL"(a new type of cellulose graft) in lower extremities ulcers of leprosy patients, in comparison with the results got with the application of daily dressings of zinc oxid.

It is presented,also, the period of wound healing of each kind of treatment and the criteria of stablishment for the eventual need of skin graft. This judgement was made after 90 days of the proposed treatment.

A comparison was performed between both operational costs. The use of "BIOFILL" shows that the patient does not need daily care or hospitalization, and is able to mantain his usual activities under ambulatorial control.

T008

Cellulose graft - a new biological dressing for improvement of the bed receptor for skin grafting.

Domingos Quintella De Paola and Mario G. P. Pires de Souza, Curupaiti State Hospital, Rio de Janeiro, Brazil.

It is presented a case of giant and infected basal cell carcinoma from esternal region submitted to surgical resection and receiving " BIOFILL " (a new type of cellulose graft) before skin grafting.

It is proposed the use of " BIOFILL " after infected tumor removal and other conditions (leg sores, etc) when local conditions are not adequate to desirable reconstruction.

T009

INOCULATION LEPROSY FOLLOWING TATTOOING
(TWO CASE REPORTS)

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Two female patients in whom tuberculoid Hansens developed at the site of tattooing are reported. Tattooing is very common in several parts of India and is usually done by using dirty, unsterile needles. It may be an important mode of spread of leprosy in places,where leprosy is endemic and tattooing is common.

T010

ON THE HISTORY OF THE LEPROSY CLINIC AT THE HOSPITAL OF ALBERT SCHWEITZER AT LAMBARENE FROM 1924 TILL 1986

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Our study of the literature available in different languages has found no articles, monographs, or other publications dealing directly with Dr. Schweitzer's activity against leprosy and also with his leprosy clinic. On account of that of special value is the information provided by G. Göting, who was a personal friend of Dr.Schweitzer, and by Miss Ali Silver, his tireless co-worker over the 1947-67 period.

The present paper fills this gap and is the first contribution to the history of the grandiose health service work of that unique humanitarian and is a new and positive addition to his biography. Through the presentation of statistics and other facts and conclusions the paper shows beyond doubt: 1/ the collossal dimentions of a peerless example of self-sacrifice for one's fellow-humanbeings and 2/ the boundless love and loyalty of the hospital staff - the European doctors and the Negro auxilliary staff. In that respect special gratitude is due to Dr. Takahasi, Dr. Trench, and others.

T011

LEPROSY AND IODINE.
ARCHITECTURE OF AN IDEA

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Continuation of Abstract N° IX/412(T) submitted to the XII International Leprosy Congress, New Delhi-1984:

In acordance with the "Leprosy-Iodine Hypothesis", the following possibilities are suggested:

Treatment of leprosy patients in regions renowned by their iodine-deficient environment and with drinking water containing less than 1 microgram of iodine per liter, such as areas bordering the Great Lakes of North America; some Cantons of Switzerland; some parts of the Alps; the Pyrenees; the Carpathians through Poland, Czechoslovakia, Rumania and Russia; Mendoza in Argentina; parts of the Himalayas; parts of Tibet and Guangxi (reported by Dr. Wang Cheng-yi); Finland and Sweden, etc.

Dietary factors: diet rich in certain foodstuffs that interfere with iodine metabolism such as: cabbage, cauliflower, brussels sprouts, yellow turnip, mustard, soya bean, rutabaga, groundnut, mandioca (cassava), millet, hard water rich in calcium carbonate and magnesium, unsaturated vegetable oils, milk of soya instead of cow's milk and iodine-free kitchen salt.

Elimination factors: no sea food at all nor algae, nor fresh-water fish.

Supplementary drug regimens may be considered.

This experimental therapy is an earnest request to Governments, Health Institutions and Medical Doctors of the world on behalf of leprosy victims.

T012

THE ECOLOGY OF LEPROSY IN THE THIRD WORLD COUNTRIES

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Leprosy is in general only one of the many public health problems which effect tropical third World developing countries. It is estimated that out of the fifteen million people afflicted with leprosy in Third World countries, nearly a quarter are Children. About 23 per thousand children are reported to be suffering from some stage of leprosy at any given time. The present study aims at analyse the following: i) to observe and to analyse the general situation in the ecological structure and spatial distribution of leprosy in the Third world countries ii) to map out the sptial distribution and to identify the major areas of concentration iii) to group the countries on the basis of prevalence rates and to observe the trend of its variation over space and time iv) to identify the risk prone areas and to probe into the factors v) to conceptualise the facts for drawing out a suitable planning methodology. It is observed from the study that some areas of the Andean Cordillera (Colombia, Venezuela) with cool and medium climate have relatively high prevalence rates. The leprosy endemicity is higher in African and Asian foci than Americas. Some limited foci (Paraguay, Colombia, Brazil) have prevalence rates upto 24 per thousand. In the case of Africa the lepsey is mainly concentrated in the Western, central and Eastern ports and is characterised by a low proportion of disabilities. The South-East Asia region contributes the largest

T013

Full thickness nasal tissue loss in leprosy.

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The loss of full thickness of nasal wall is not an uncommon problem. The putrid nasal discharges in multibacillary cases provide a favourable breeding ground to the flies. When larvae hatch out intense inflamation of surrounding tissues occur. The larvae eat off the local tissues before passing to the pupal stage. Sometimes the destruction of tissues is so extensive that ugly deformities result due to full thickness loss of the skin.

Twelve patients are being reported here with such deformities. The methods of reconstruction and the problems encountered are discussed in detail with a word on the prevention of such deformities.

T014

OESOPHAGEAL CARCINOMA IN LEPROMATOUS LEPROSY

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A 47 - year - old Indian male suffering from lepromatous leprosy taking treatment for about 20 years, has attended the leprosy clinic for the complaint of difficulty in swallowing of 6 months duration. Barium swallow studies showed entry of barium into the trachea suggestive of an obstruction in the oesophagus and tracheo-bronchial fistula. Endoscopic study showed a proliferative growth in the oesophagus obstructing the lumen. Histopathological features of the growth were in favour of squmous cell carcinoma. Radiotherapy was given after performing a feeding gastrostomy. The decreased CMI may be responsible for an increased incidence of malignancy in lepromatous leprosy. Though squamous cell carcinoma arising from chronic ulcers of leg and foot has been reported frequently in literature, the incidence of cancer oesophagus is very rare and hence this case was recorded and reported.

T015

CONCEPTS OF LEPROSY IN SOUTH INDIA
Its implications for health education and treatment.

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Underlying what are usually assumed to be the 'traditional concepts' of leprosy in South India (e.g. leprosy is the curse of God), other notions about the disease also play a role. These notions should be interpreted within the cultural framework of South Indian Hindu society. On the basis of data collected from unconventional sources such as Sanskrit and Tamil mythology, popular Tamil writing and film, as well as from informants, 4 hypothetic concepts of leprosy will be discussed. It will be argued that the association of leprosy with cultural taboes, esp. that of sexuality, accounts to a great deal for the continuing stigma. A practical implication, following from the association of leprosy with these taboes is, that the effectiveness of the health education could be improved when a more indirect approach is used. Preliminary results of an experiment in which traditional Tamil streettheatre was used to convey information about leprosy, suggest that traditional media can serve as excellent vehicles for transferring health education messages in an indirect way, that is understandable and acceptable for and appealing to a large rural public.

LEPROSY AND HUMAN DIGNITY

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The AHM Leprosy Relief Organization Munich e.V.has two aims:
1. to collect donations for those suffering from leprosy;
2. to free leprosy from its social stigma.

AHM has created a leprosy emblem which stands for the 3 distinct strategies of its leprosy campaign :
- to promote interest among healthy people in leprosy;
- to enable leprosy sufferers to receive confidential help and medical treatment;
- to support helpers who have devoted their lives to leprosy work.

For over 10 years AHM has concerned itself the following:
- Leprosy Health Education programmes aimed at activating young people in campaigns to prevent leprosy victims becoming outcastes in society.
- AHM's work is based on sociological research in the following areas:
  I) the phenomenon of leprosy in medieval Europe;
  II) present day projects of reintegration for leprosy victims.
- Developing strategies in cooperation with GMLF to combat leprosy in India.

Physical relief and a humane existence for those afflicted with leprosy will only be achieved as a result of the joint efforts of donor organizations and organizations directly involved in field work.
AHM has members in countries throughout the world. In cooperation with WAY and WHO, AHM continues to work for the human dignity of those suffering from leprosy.

T017

COMPREHENSIVE HEALTH PROGRAMME FOR EFFECTIVE CONTROL AND ERADICATION OF LEPROSY

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Leprosy control (LC) and eradication projects are catching up fast all over the globe to achieve the proposed goal of HFA by 2000 A.D. Yet the plans are not yielding expected results. Often there are reports of increase of new cases or no diminishing of their numbers in many pockets. It may be attributed to the consideration that the LC programmes get in 'absolute isolation'. It is, therefore, planned to have the control programme interwoven and co-ordinated with other health projects. A comprehensive programme including the community co-operative participation has been planned. It is recently being introduced in a small pocket in Maharashtra State of India. The programme is presented for discussion.