15th INTERNATIONAL LEPROSY CONGRESS ABSTRACTS

CHEMOTHERAPY

CH01

ACTIVITY AGAINST LEPROSY BACILLUS OF A SINGLE DOSE COMBINATION OF OFLOXACIN PLUS MINOCYCLINE, WITH OR WITHOUT RIFAMPIN, IN MICE AND IN PATIENTS

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As steps for developing a fully supervisable, monthly administered multidrug regimen for leprosy, bactericidal effect against *M.leprae* of a single dose combination ofloxacin-minocycline (OM), and rifampin-ofloxacin-minocycline (ROM) was evaluated in mouse footpads and in patients. In mouse experiments, results of proportional bactericidal method demonstrated that the activity of a single dose OM was dosage-related; larger dosage, i.e., 300 mg O plus 50 mg M per kg body weight, displayed bactericidal effect, whereas smaller dosage, i.e., 150 mg O plus 25 mg M per kg, was not bactericidal. The activity of a single dose of larger dosage OM was significantly inferior to that of a single dose R, and the addition of either dosage of OM neither enhanced nor antagonized the activity of R. In terms of bactericidal effect, the consequence of excluding clarithromycin from drug combinations is only marginal. In clinical trial, 20 previously untreated lepromatous patients were randomly allocated to 2 groups with 10 each, and treated, respectively, with a single dose of 600 mg R plus 400 mg O and 100 mg M (ROM), or a single dose of 400 mg O plus 100 mg M (OM). Adverse events, mainly gastrointestinal complaints, were mild and transitory, did not accompany by significant findings on physical examination, indicating that both combinations were well tolerated. Seven days after the single dose, slight clinical improvement was observed in almost all patients in both groups; the mean values of bacterial index were virtually unchanged from pretreatment values; the mean value of morphological index was significantly reduced in patients treated with ROM but not in those with OM. Bactericidal effect was monitored by titrating, through mouse footpad inoculation, the proportion of viable *M.leprae* in skin biopsies taken before and 7 days after a single dose of treatment. A single dose of ROM displayed powerful bactericidal effect that the bacilli from 9 of 10 patients lost their infectivity for normal mice inoculated with 5000 organisms per footpad; a single dose OM also exhibited definite bactericidal activity in 7 of 10 patients, although it was significantly less bactericidal than that of ROM, as only in one patient whose organisms lost their infectivity for normal mice. Because of these promising results, a test of the efficacy of multiple doses of ROM in a larger clinical trial appears justified.

CH02

WHY MULTIDRUG THERAPY FOR MULTIBACILLARY LEPROSY CAN BE SHORTENED TO 12 MONTHS

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The 24-month MDT for MB leprosy is still too long and becomes an obstacle in implementing MDT. It would facilitate implementation if duration could be shortened without significantly compromising efficacy. Following information may be useful to define the appropriate duration. First of all, due to a series modifications, definition of MB has become much broader, resulting in classifying many cases that would otherwise be PB leprosy as MB, and, unlike in early 1980s when all newly detected MB cases were skin smear positive, the proportion of positive cases in 1996 was less than half. Because bacterial loads of majority of MB cases currently classified are significantly smaller than in the past, overall requirements of chemotherapy for MB may also be less. Secondly, relapse rate after MDT is very low, about 0.2% annually among MB cases, indicating that there is enough room for further shortening the duration to less than 24 months. Despite the possibility that relapse rate could be significantly higher among MB cases with high initial BI, such cases become relatively few in the fields, hence, total number of relapses caused by them in a control program will be small. Thirdly, major role of dapsone (DDS) - clofazimine (CLO) component in MDT regimen in to ensure elimination of spontaneously occurring rifampin (RMP)-resistant mutants, estimated to be no greater than 10^4 in an untreated lepromatous case. Recent findings indicate that 3-month treatment with the component alone killed ≥99.999% of viable *M.leprae*, suggesting that all RMP-resistant mutants are likely to be eliminated by 3-6 months of treatment with DDS-CLO component in MDT. Fourthly, in a THEMYC multicentre trial, not a single relapse has been detected among groups of 500 MB cases (initial BI ≥2) treated, respectively, with 24- or 12-month MDT, and followed-up for 3-5 years after stopping treatment, suggesting that 12-month MDT is as effective as 24-month. A clinical trial in Malawi also concluded that 18-month MDT may be sufficient for MB leprosy. Finally, clinical and bacteriological progress of defaulted MB cases also suggest that treatment with less than 12 months MDT exhibited promising therapeutic effects among majority of cases. Based on these information, the WHO Expert Committee on Leprosy concluded, at its latest meeting of 1997, that it is possible that the duration of the MDT regimen for MB leprosy could be further shortened to 12 months.

CH03

TWO NEW DRUG COMBINATIONS IN THE TREATMENT OF LEPROSY

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Our short-term clinical trials on clarithromycin monotherapy and fusidic acid monotherapy showed that the former to be rapidly bactericidal and the latter to have activity roughly equivalent to that of dapsone or clofazimine. Other data suggest that fusidic acid may have reaction-suppressive activity and we took the position that the future of this drug in leprosy was dependent upon the clinical demonstration of such activity. Two new multi-drug regimen were formulated consisting of (A) daily clarithromycin 500mg and minocycline 100mg plus monthly rifampicin 600mg and (B) daily clarithromycin 500mg and fusidic acid 750mg plus monthly rifampicin 600mg. Both regimens were taken for a total of six months. These regimens were evaluated against the current recommended 2-year WHO-MDT regimen (C) with regard to clinical and bacteriological improvement, leprae reaction, tolerance, adverse effects and patient acceptability and compliance. Fifty untreated multibacillary leprosy patients per regimen were recruited.

The clinical efficacy of regimens A and B as determined by rate of lesion resolution has been exceptional compared to C with a somewhat more rapid response observed with regimen A. The overall frequency of reaction among the three regimens is not significantly different. It appears however, that regimen B may be superior to regimen A and C with respect to moderate to severe reversal reaction. All the regimens were tolerated. The acceptability and compliance is better among patients on regimen A and B. Significant number of patient with pre-treatment bacillary index of 3+ and above reactivated with clinical and bacillary index deterioration several months after completion of treatment with regimen A and B. With this findings, it can be suggested that regimen A and B is effective and safe but treatment should be extended to a minimum of 12 months among multibacillary patients.

CH04

ROM SINGLE DOSE FOR PB LEPROSY WITH 1 TO 3 LESIONS.

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Chemotherapy (MDT) as a strategy is the only tool available to eliminate leprosy. However recent research on short course chemotherapy indicates possibilities of saving considerable manpower and resources. Single dose of rifampicin, ofloxacin and minocycline (ROM-1) is reported to be as effective as six months paucibacillary multidrug therapy for single skin lesion case of leprosy (WHO 1997). We present our observations on the use of single dose of ROM in 531 cases of 1-3 skin lesions in PB leprosy.

On confirmation of diagnosis, patients were given a single dose of rifampicin 600mg, ofloxacin 400mg and minocycline 100mg [half dose for children]. Patients under 5 years or over 65 years of age or those with pregnancy were excluded. Patients were assessed by scoring on the lines of WHO protocol initially and at 6 months and 1 year. Efficiency of treatment was evaluated on the rate of clinical regression and occurrence of reaction / relapses during follow up. The following table shows the occurrence of reactions over a period of 1 year.

Regimen	No. of Patients	Reactions
ROM - 1 :SINGLE LESION	438	4 [0.8 %]
ROM - 1 : 2 - 3 LESIONS	93	5 [5.3 %]

No toxic or adverse effects of the drugs were noted. The main problem was type I reactions which were easily manageable. Treatment compliance was excellent. Results demonstrate that a fully supervised regimen of single dose of ROM is efficacious, cost effective and well accepted by the patients.

CH05

ROM VS CROM IN MONOLESION HANSEN'S DISEASE

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Combination of Rifampicim, Ofloxacin & Minocycline is quite effective in Hansen's Monolesion cases. Adding Clarithromycin has additional advantage in terms of cure-rates & relapses.

476 cases, smear-negative, normal nerve monolesion (260 males 216 females), age-range 15-70 years (mean age 36.5 yrs) randomized in 2 groups.

Group A. 390 cases [Rifampicin (600 mg) + Ofloxacin (400 mg) + Minocycline (100 mg)] single dose empty stomach.

Group B. 86 cases [(group A regime drugs + Clarithromycin (500 mg OD)], single dose empty stomach.

Criteria for Cure : (1) Reduction in i) Size ii) Colour iii) Infiltration
(2) Disappearance
(3) Improvement in sensation

graded from 3 to 0 (score maximum 15, minimum 0). Follow-up-monthly for 6 months, 6 monthly for 2 years.

Drop-out	-21 (5.0%)	A-15	B-6
Completed Follow-up	-455	A-375	B - 80
Cure Rates		A-360 (96%)	B - 78 (97.5%)
Relapse		A - 15 (4.0%)	B- 2 (2.5%)

Side effects in both groups comparable. Single day CROM is better than single day ROM in Monolesion PB cases.

CH06

EVALUATION OF NEWER DRUGS IN LEPROSY

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Quinolones have synergism with rifampicin and a combination has better penetration and effective concentration rendering a leprosy patient mycobacterium free in shorter time. Oflaxacin / sparfoxacin in combination with Refampicin & Clarithromycin alone are being evaluated.

850 cases were divided in 3 groups : Group A (400) Rifampicin 600 mg OD (empty stomach) and ofloxacin 400 mg OD for 4 weeks Group B (400 cases) Rifampicin 600 mg OD (empty stomach) and Sparfloxacin 400 mg stat then 200 mg OD (for 4 weeks) and group C (50 cases) clarithromycin 500 mg O.D. for 8 weeks. Evaluation was done as per WHO guidelines.

Cure rate in 3 groups were 85%, 86% & 90 %. Side effects of nausea, vomiting, arthritis were equal in 3 series. Relapse rate in 3 group were almost equal(about 10%), Sparfloxacin being most economical of these 3 and cure rate being comparable, combination of Rifampicin & Sparfloxacin is best among the newer drugs.

CH07

SINGLE DOSE (ROM) IN MONOLESION PB LEPROSY CASES

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Monolesion is indicator of herd immunity. Effective MDT enhances monolesion cases. Rifampicin single dose kills about 99% M. Leprae, with Ofloxacin & Minocycline (ROM) synergism ensures 100% clearance.

750 fresh, smear negative, normal nerve, monolesion cases (male 390, female 360) Age (15-60 years) were randomized in 2 groups.

A : ROM (study group) 390 cases (Rifampicin 600 mg + Ofloxacin 400 mg + Minocycline 100 mg) empty stomach single dose.

B : WHO PB MDT (Adult) (Control) 360 cases - 6 pulses.

Criteria for cure :

1) Reduction in i) size ii) Colour iii) Infiltration
2) Disappearance
3) Improvement in sensation

were graded from 3 to 0 (Maximum score 15, minimum 0). Monthly follow-up for 6 months then 6 monthly for 2 years.

Drop-out 93 cases (12.4%) [ROM 48 (6.4%), MDT 45 (6.00%)]. Of 657 cases completing evaluation 639 cases [ROM 303 (97.10%), MDT 336 (97.40%)] showed clinical improvement. Replase & side effects in both the groups were comparable.

Single dose of 600 mg Rifampicin, 400 mg Ofloxacin & 100 mg Minocycline (ROM) is as effective as 6 monthsWHO PB MDT in the treatment of negative skin smear, normal nerve, monolesion leprosy cases.

CH08

EFFICACY OF 7, 14 AND 30 DAYS DAILY DOSES OF COMBINED RIFAMPICIN AND MINOCYCLINE IN SINGLE LESION PAUCIBACILLARY LEPROSY

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Aim -
To evaluate the efficacy of 7, 14 and 30 days daily treatment of rifampicin 600 mg plus minocycline 100 mg in single lesion paucibacillary leprosy.
Materials & Methods -
A total 52 patients were included in this study. All were bacteriologically negative and had histopathologically confirmed indeterminate, tuberculoid or borderline tuberculoid leprosy. They were randomly put into group A, B and C. Group A (17 patients) received 7 days, Group B (16 patients) received 14 days and Group C (19 patients) received 30 days treatment of rifampicin 600 mg daily plus minocycline 100 mg daily. All patients were followed monthly for 6 months and then 3 monthly for 24 months.
Results -
In Group A, 2 of the 17 patients showed treatment failure in the form of increase in the size of lesion whereas in Group B and C no treatment failure was observed within 2 years of follow-up.
Conclusion -
A minimum 14 days daily treatment of the above regimen is essential to treat a single lesion paucibacillary leprosy.

CH09

STUDY OF SINGLE DOSE CHEMOTHERAPY IN PAUCIBACILLARY LEPROSY PATIENTS WITH TWO TO THREE LESIONS

2-3 Lesion Multicentric Trial Group, India

The comparative study on Single dose of Rifampicin, Ofloxacin and Minocycline (ROM), and the six-month WHO/MDT/PB regimen (Standard) in the treatment of single lesion paucibacillary (PB) leprosy, was extended to cover PB leprosy with 2 to 3 skin lesions. From five centres, 236 patients were allocated randomly to either of the two regimens. Information on clinical scores is recorded at admission and at 6, 12 and 18 months after admission. Follow-up at 6 and 12 months is completed and the 18-month follow-up will be completed shortly.

At admission, the mean clinical score was 19.86 and 19.78 ($P > 0.6$) for the ROM and Standard regimen groups, respectively. It was reduced to 7.15 and 7.06 ($P > 0.8$) at 6 months, and 5.10 and 4.90 ($P > 0.6$) at 12 months for ROM and Standard regimens, respectively. Clinical improvement was seen in most of the patients for both the regimens. Complete clinical cure (i.e., disappearance of all lesions) was observed in 13.0% and 13.9% ($P = 1.0$) at 6 months, and 31.8% and 33.7% ($P > 0.8$) at 12 months, with ROM and Standard regimens, respectively. Thus, in the study patients, over a period of 12 months, ROM administered as a single dose, compared well with the Standard regimen in the treatment of PB leprosy with 2 to 3 lesions. Final results upto 18 months, will be presented.

CH10

EVALUATION OF 4 DRUGS COMBINATION (CROM) FOR 28 DAYS IN MB LEPROSY CASES.

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Rifampicin is the most bactericidal among all anti-leprotic drugs. Among newer drugs, clarithromycin, ofloxacin and minocycline are most promising and all bactericidal. Synergism of these drugs in MB leprosy cases renders them free from living bacilli in just 28 days and generates a new hope as an alternative treatment of leprosy.

9 smear-positive MB cases from both sexes (6 males 3 females), age range 20-50 years, were given (Rifampicin 600 mg OD, empty stomach + Clarithromycin 500 mg BD + Ofloxacin 400 mg OD + Minocycline 100 mg OD) for 28 days.

Efficacy monitored clinically alongwith BI & MI changes. Side effects noted with follow-up monthly for 6 months then 6 monthly for 2 years.

All cases showed significant clinical improvement with zero MI after 4 weeks. BI reduced gradually during follow-up, No case showed relapse.

CROM regimen for 28 days in frank MB cases is very effective and promising to become a rapid alternative of MDT in selected population. High cost of therapy limiting its universal acceptance.

CH11

RECOMBINANT INTERFERON ALPHA 2b IN THE TREATMENT OF MULTIBACILLARY LEPROSY - PRELIMINARY OBSERVATIONS

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The deficiency of the macrophage regulation system in lepromatous leprosy has been well documented. Role of cytokines like interferon in macrophage stimulation has not been evaluated though this has been described. We report our observations on the clinical efficacy of alpha interferon in multibacillary leprosy.

Forty multibacillary patients (BL,LL) were randomised into two groups. First group received standard WHO-MB-MDT (MDT) while group II received WHO-MB-MDT (MDT + I) with Inj. Alpha 2b Interferon given subcutaneously for 6 weeks, initially. Clinical features, nerve status, histopathology, lepromin reactivity and photographs were documented initially and after 3 months.

Out of 30 patients (10 in group I & 20 in group II) who were evaluated for histology, the fall in mean histopathological score was significantly higher (p=0.029) in group II. In 37 patients evaluated for BI (18 in group I & 19 in group II), the mean fall in group II was also significant (p=0.001). Clinical regression also showed significant difference in Group II. No difference was observed in lepromin reactivity and nerve function impairment.

From these preliminary observations, it appears that a short course of alpha 2b interferon in addition to conventional multidrug therapy will enhance fall of BI and result in improvement of histology favourably. Long term follow-up patients in of both these study groups may reveal a definite picture on the alterations of the natural history of the disease based on the above parameters.

CH12

TREATMENT OF MB LEPROSY USING CONVENTIONAL AND NEWER DRUGS

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Multibacillary (MB) leprosy cases require a minimum of 2 years or more of conventional WHO MDT for the cure of disease. This study has been carried out to see if the addition of newer antimicrobial drugs could help in further reducing the duration of treatment. One hundred previously untreated smear positive (50 BB, 35 BL and 15 LL) patients were included in this study. A detailed history was taken, skin lesions and nerve thickening charted and smear examined and recorded. These patients were treated with a regimen comprising of rifampicin 600mg, minocycline 100mg and ofloxacin 400mg given as a monthly supervised dose combined with clofazimine 50mg and dapsone 100mg (unsupervised) daily. Treatment was stopped at one year and patients were followed-up on a placebo. Skin biopsies at the start and at the end of one year of treatment in each case were taken and viability was assessed by mouse foot pad, ATP and molecular methods. The patients tolerated the drugs well and there was no treatment failure. There was no increase in the incidence of reactions in the

patients. Clinically the lesions regressed and there was complete loss of viability at the end of one year. Follow-up is continuing to monitor the progress of patients.

CH13

SHORT COURSE CHEMOTHERAPY TO HASTEN THE PROCESS OF LEPROSY ELIMINATION

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Reduction in registered prevalence rate(PR) in leprosy is directly related to the duration of treatment and the treatment completion rate. Currently practised MDT regimens have shown promising results in reducing the PR in all the endemic areas. Based on rifampicin (R), ofloxacin (O) and minocycline (M) combination, trials with monthly intermittent doses of ROM(24 and 12 for MB leprosy and 3 and 6 for PB leprosy) and RO-28 days for MB and PB leprosy are underway in different countries. ROM single dose for PB single lesion leprosy has been already recommended by WHO and Government of India.

Bombay Leprosy Project, covering a population of 1.8 million(50% slum population) started investigations in 1984 with the aim of rationalising the duration of treatment. MDT-12 months to MB leprosy patients was initiated in 1991. Subsequently short course chemotherapy(SCC) regimens based on newer drugs were introduced for both MB and PB leprosy and treatment completion rate was increased.

An analysis was made to calculate the PR with WHO-MDT and the figures compared with the PR following SCC regimens, strictly applying trial duration as recommended by WHO. In 1982 when MDT was introduced the PR was 18 per 10 000 population. After practising SCC, the PR declined rapidly to 0.01 per 10 000 population by the end of December 1997, thus achieving the prescribed levels of elimination of leprosy. Had we persisted with the standard WHO-MDT regimen for the prescribed duration in respect of all the patients, the PR would have been 1.4 per 10 000 population in December 1997.

This analysis shows that SCC could hasten the process of leprosy elimination.

CH14

CONTROLLED CLINICAL TRIAL COMPARING THE EFFECT OF WHO-MDT WITH INTERMITTENT DRUG REGIMEN IN THE TREATMENT OF LEPROMATOUS (BL-LL) LEPROSY

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The objective of this study is to compare the effect of intermittent treatment using Rifampicin 600 mg., Minocycline 100 mg. and Ofloxacin 400 mg. given once a month for 24 months with the standard WHO-MDT on bacterial clearance in treating lepromatous leprosy.

A total of 20 patients diagnosed with lepromatous leprosy were sequentially admitted and given either of the two regimens, namely:

Regimen A - Rifampicin 600 mg., Minocycline 100 mg., Ofloxacin 400 mg., given once a month for 24 months.
Regimen B - WHO-MDT: Rifampicin 600 mg., B663 300 mg., DDS 100 mg. given monthly supervised, then B663 50 mg., DDS 100 mg. daily for 24 months.

Patients were evaluated as to clinical response, changes in bacillary load, occurrence of drug-related side-effects and the occurrence of reactions while on treatment.

Sequential average B.I. taken from skin smears at specified intervals in both therapy groups showed constant reduction in bacillary load.

The clinical and bacteriologic response to treatment at the end of 24 months will be discussed.

This study received financial support from the Leonard Wood Memorial Center for Leprosy Research.

CH15

POST SURVEILLANCE FOLLOW UP OF MULTI BACILLARY PATIENTS TREATED WITH M D T.

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Advent of M D T has made it possible to shorten the duration of anti leprosy treatment. Though now it is the era of Fixed Duration Therapy, Initially the drugs were given till bacterial negativity and were followed up for a further period of 5 years. In a study conducted by us in 138 Multi Bacillary patients, 6 had relapsed after 6 years or more of follow up after remaining negative for varying periods. Hence, we conducted a study in collaboration with Tamil Nadu Health Services in Poonamalle Leprosy Control Unit to do one time assessment of all the patients put on MDT during 1986-87 and had completed 5 years of surveillance after being released from treatment. Of the 156 patients registered 129 patients were available for assessment. All of them were found to be clinically inactive and bacteriologically negative.

CH16

RELAPSES DURING LONG TERM FOLLOW UP BY AMONG MULTI BACILLARY PATIENTS TREATED WITH M D T REGIMEN.

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210 patients classified as Lepromatous and Near Lepromatous with a BI of 2.5 or more were admitted to a controlled clinical trail initiated in 1977. The patients were randomly allocated to either a 4 drug regimen (Rif, INH, Clof and Dapsone) or a 2 drug regimen (Clof and Dapsone) for 5 years followed by either Clof and Dapsone or Dapsone alone for a further period of 2 years and subsequently continued with Dapsone or Placebo till 12 years. It was proposed to follow them up till they complete 20 years from the start of treatment. Till date 6 patients out of 138 have relapsed after remaining negative for varying periods. The month of relapse varied from 156 to 209 months after start of treatment. All of them were retreated with National Leprosy Eradication Programme regimen for Multi Bacillary Leprosy (2 discontinued) and they showed good response. The details will be presented..

CH17

Leprosy Relapses after Fixed Duration MDT

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Li Jin-Lan — " " " " "

Between 1986 and 1995, 8307 leprosy patients (MB 5981, PB 2326) from 7 prefectures in the three s-w provinces of China have completed FD-MDT and the relapse rate is 0.19/1000 py for MB and 0.55/1000 py for PB. Further surveillance till end of 1997 in 6 prefectures of 8790 patients (MB 6439, PB 2351), the relapse

rate remains at 0.19/1000py for MB within the limit of 10 years surveillance. In 2351 PB, 4 relapsed within the limit of 5 year surveillance, the relapse rate is reduced to 0.42/1000 py. In the 7 MB relapses, 3 relapsed beyond the WHO specified period of 5 years (mean 5.71 yrs, range 4-8 yrs) and in the 15 PB relapses, all relapses occurred beyond 2 years (mean 7.13 yrs, range 4-10 yrs). Additional data of 320 patients from Kunming Prefecture will be added and the significance of late relapses discussed.

CH18

SURVEILLANCE OF LEPROSY RELAPSE AFTER RIFAMPIN PLUS DAPSONE THERAPY

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Weng Xiao-Man	" " " " "
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Eight hundred forty-six leprosy patients were followed for varying periods (mean 34, range 1-168 months) after being cured with rifampin plus dapsone (R+D), 43 relapses were noticed (MB 30/531, PB 13/315). Increasing significant difference in relapse rates were noticed in MB receiving <12 and >12 months R+D in the 4 different groups with increased duration of dapsone monotherapy prior to R+D. In PB, no such difference can be seen in groups receiving 60-120 and >120 months dapsone before R+D. All diagnosis of relapses were supplemented by laboratory tests and were successfully retreated with FD MDT. The relationship between dapsone and R+D therapy in curing leprosy will be discussed.

CH19

INTERVALS BETWEEN STOPPING RIFAMPICIN-CONTAINING REGIMENS AND OCCURRENCE OF RELAPSE IN MULTIBACILLARY LEPROSY

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Between 1970 and 1992, 1421 multibacillary (MB) leprosy patients were treated with 20 different rifampicin (RMP)-containing regimens; 1325 (93.2%) of them completed the scheduled treatment and had been followed-up for relapse, i.e., seen at least once after stopping treatment. By the end of 1997, 195 relapses, or 14.7% of patients being followed-up, had been diagnosed. Relapse was defined as: i) occurrence of definite new skin lesion(s); and ii) an increase of BI ≥2+ over the previous value at any site. A significant proportion of these relapses were confirmed by mouse footpad inoculation through demonstration of viable *M.leprae*. Mean value of the initial BI, i.e., the BI before treatment with RMP-containing regimen, of the relapsed cases was 4.16±1.09, suggesting that relapse in MB leprosy may be associated with higher initial BI of the patient. Mean interval of relapse, i.e., period of time between stopping treatment and occurrence of relapse (the latter was defined as the mid-point between date of last examination without relapse and first examination with evidence of relapse) was 70±31 months. The information is useful for design the duration of follow-up for relapse after stopping treatment in clinical trials.

CH20

RECIDIVAS EN ENFERMOS DE LEPRA QUE HAN COMPLETADO EL TRATAMIENTO CON MULTIDROGA

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El estudio retrospectivo de las recidivas en pacientes tratados con multidroga esquema OMS, da lugar a cifras que concuerdan con los valores observados en otras publicaciones Sobre un total de 6,614 pacientes en tratamiento a termino, se han presentado 11 recidivas por un 0 16*% De estos, tres pertenecen a formas multibacilares y ocho a paucibacilares Se señala el tiempo promedio que transcurrio desde la terminacion del tratamiento hasta la aparicion de la recidiva y areas de piel donde se localizan las nuevas lesiones

CH21

RELAPSE IN MB LEPROSY AFTER RIFAMPICIN AND OFLOXACIN FOR 28 DAYS - A CASE REPORT

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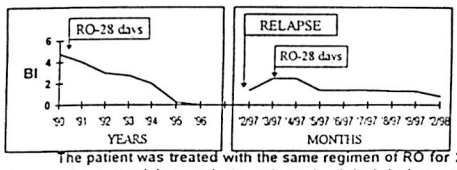
We report on what we believe to be the first case of relapse in multibacillary (MB) leprosy following short course chemotherapy for 28 days with daily doses of rifampicin (R) 600 mg and ofloxacin (O) 400 mg .

The following diagram summarises the events relating to a previously untreated 30 year old male BL-LL patient with initial bacteriological index (BI) of 4.6 who received treatment with RO regimen from 27 December 1990 to 22 January 1991. BI showed gradual decline accompanied by clinical regression. The patient remained negative and sign free from 11 September 1995 (Ganapati 1996;Ganapati et al,1997). Relapse of BL/LL lesions were noticed on 21 February 1997 with a mean BI of 1.3. The case is under investigation for *M.Leprae* viability by mouse foot pad and drug sensitivity etc., the outcome of which is awaited. The patient was HIV negative.



The patient was treated with the same regimen of RO for 28 days under supervision and the relapsed clinical lesions are regressing. Currently the BI is 0.8. The satisfactory response to the same regimen so far indicates the possibility of "persisters" as the cause of relapse and not resistance to the drugs employed. The patient is under continuous observation.

All the remaining 55 MB patients with mean BI of > 3 included in the RO trial have reached a state of skin smear negativity over a period of 6 years. None of these have relapsed.

CH22

BACTERIOLOGICAL CHANGES AND RELAPSE IN 157 MULTIBACILLARY LEPROSY WITH HIGH BI LOAD AFTER WHO/MDT.

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In order to evaluate the late relapse rate of multibacillary leprosy treated with WHO/MDT, the authors investigated the bacteriological changes and relapse rate in 157 MB cases with an average of BI 3.4~3.75 before MDT. Among 157 cases, 65(41.4%) cases have stopped treatment more than 7 years.The rate of smear negativity in 157 cases was 75.16% at the end of 4 years after starting MDT and 97.45% at the end of 5 years. The BI averagely decreased by 0.89 each year. The total of 948 patient/years have been followed up in 157 cases with an average of 6.02 patient/years.There were 2 relapsed cases with a relapse rate of 1.3% or 2.1 cases per 1000 patient/years. The 2 cases relapsed at the end of 3 and 4.5 years after stopping MDT, respectively. The data showed that the relapse rate of MB cases withigh BI load after completion of MDT was not a serious situation. But it is necessary to strengthen the surveillance for MB cases after stopping MDT for collecting the valuable data on relapse.

CH23

VIABILITY OF *M.leprae* ISOLATED FROM MB PATIENTS TREATED WITH WHO/MDT.

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Objective: To assess the viability and drug-sensitivity of *M.leprae* isolated from MB leprosy patients whose BI's had decreased slowly while on Multiple Drug Treatment (MDT).

Subjects: 41 patients who had completed WHO MDT and who had improved clinically, but whose bacteriological index (BI) decreased by less than one log per year, were biopsied and assessed using the mouse-foot-pad assay system. Treatment was stopped and the patients were followed up.

Results: *M.leprae* was isolated from 11 patients. In 2 cases, drug sensitivity could be assessed and the organisms were found to be fully sensitive to all three drugs used in the MDT regimen.

After three years without treatment, 9 of the 11 patients were traced and examined. They were all clinically inactive and had negative skin smears. Of the other two patients, one had died and the other could not be found.

Conclusion: Viable bacilli can be isolated from some patients after completion of WHO MDT, but most patients can eliminate these bacilli without further chemotherapy and do not seem to be at great risk of relapse.

CH24

VIABILITY OF M.LEPRAE IN THE NASAL MUCOSA AND SKIN OF PERSISTENT SMEAR POSITIVE LEPROMATOUS PATIENTS AFTER 2 YEARS OF MDT.

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MDT has played a significant role in the treatment of leprosy. Few studies have investigated the viability of persisting M.Leprae in the nasal mucosa of MB patients who had completed 2 years of MDT, using the mouse foot pad. 11 consecutive lepromatous patients who demonstrated positive skin smears with varying bacterial indices of 2+ to 4+ after completion of a regular course of 24 doses of MDT had their skin and nasal mucosa biopsied. Both biopsied tissues underwent mouse foot pad inoculation into T900r mice and were also studied histopathologically.

Foot pad harvests were done on 6th, 9th and 12th months. Except for one specimen from the skin of a lepromatous patient all inoculations showed no growth of bacteria in the mouse foot pad. Skin histopathology showed a BIG of 1+ to 4+ and a granuloma fraction which varied from 10% to 80%. The nasal mucosal tissue demonstrated atrophy, focal ulceration and stromal collogenization with a BIG of 1+ to 4+. The extent of cellular infiltration varied.

The study strengthens the belief that persistent M.Leprae are not viable after 24 doses of MDT and demonstrates that the nasal mucosa of these patients do not harbour viable bacteria.

CH25

RELAPSED LEPROSY AFTER MULTI DRUG THERAPY PRESENTING IN A HISTOID FORM.

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Histoid leprosy, an unusual variant of lepromatous leprosy, has been known to occur in untreated patients and in patients relapsing after dapsone mono-therapy. The unique occurrence of histoid leprosy in a leprosy patient who had completed treatment with anti-leprosy multidrug therapy is being reported.

A 9-year old boy diagnosed as having borderline tuberculoid leprosy had treatment with dapsone mono-therapy for 3 years followed by 54 pulses of multi drug therapy. After being skin smear negative for 7 years he presented with multiple discrete nodules in the upper and lower limbs and diffuse infiltration of the face. The nodules were non-tender, shiny and firm. Histopathology of one of the skin nodules displayed dense compact granulomatous inflammation composed of spindle shaped macrophages arranged in a whorled pattern in the dermis with numerous clumps of acid fast bacilli that were long and solidly staining. The bacillary index was 5+. The clinical diagnosis of histoid leprosy was authenticated histologically.

This is the first report of leprosy relapsing as a histoid variety after being treated with multi drug therapy. Viability and drug resistance studies on the Mycobacterium Leprae obtained from this patient are being carried out using the mouse foot pad.

CH26

RELAPSE AND RECURRENCE OF LESIONS AFTER MDT IN LEPROSY : CLINICAL, BACTERIOLOGICAL AND HISTOPATHOLOGICAL INVESTIGATIONS OF 56 CASES.

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Fifty six cases of leprosy treated with WHO-recommended Multi Drug Therapy (MDT) were investigated for recurrence of skin lesions. The study included 36 multibacillary (MB) and 20 paucibacillary (PB) cases.

Twenty seven MB cases (75%) and 10 PB cases (50%) were confirmed as relapses. While in all MB cases except 3 the relapse manifested in the form of borderline lepromatous (BL) lesions. All except 2 PB cases relapsed with appearance of borderline tuberculoid (BT) lesions. The precise cause of recurrence of lesions could not be determined in 9 MB and 10 PB cases. Three MB and 4 PB cases had received two full course of WHO-MDT.

The average incubation period for recurrence of lesions was significantly lower among patients who had received fixed duration treatment (6 months for PB and 24 months for MB) as compared to those who had received longer treatment. Forty four percent MB and 55% PB cases had received steroid during and/or after MDT. The MB cases who had received cortico steroid had shorter incubation period for relapse and among PB cases, there was a strong association between steroid intake and presence of viable bacteria. Other interesting observations will be presented and discussed.

CH27

RELAPSES IN MULTIBACILLARY LEPROSY AFTER 2 YEARS TREATMENT WITH WHO-MDT REGIMEN.

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The objectives of this study are to determine the frequency of relapses in MB leprosy patients completing the 2 years WHO-MDT regimen and to determine whether the relapses that occur are due to drug-resistant or to persister organisms.

500 MB patients who completed 2 years WHO-MDT were recruited. They had no previous anti-leprosy treatment, finished the regimen within 24 to 30 months and no anti-leprosy treatment thereafter. Duration of surveillance now range 4 to 11 years which include yearly clinical examinations and skin smears.

Criteria for probable relapse are the appearance of new/active lesions and an increase in BI at least 2+ at any site. Those found with probable relapse were biopsied and tested in mouse footpads or armadillo to confirm relapse. Drug-resistant studies were also done. So far, 6 patients were found to have a probable relapse ranging from 6 1/2 to 10 years after the end of their WHO-MDT treatment.

The clinical and bacteriological characteristics of the patients in the study - their skin smears before and after treatment and during the surveillance period - the clinical, bacteriological, histopathological characteristics as well as the mouse footpad results and the response of the relapse patients to alternative anti-leprosy treatment - will be discussed.

This study is funded by the Pacific Leprosy Foundation, New Zealand and the Sasakawa Memorial Health Foundation of Japan.

CH28

AN ANALYSIS OF RELAPSES AFTER STOPPING MULTIDRUG THERAPY

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Three thousand seven hundred and thirty four leprosy patients (2 768 MB and 966 PB) were treated with MDT. Two thousand four hundred and fourty MB and nine hundred fifty four PB had completed the prescribed course of the treatment. Six cured persons affected by leprosy previously diagnosed as LL were identified as relapses clinically, bacteriologically and pathologically in the surveillance period, 2 of them were confirmed by mouse footpad inoculation. Among 6 relapses, 2 were early relapses and 4 were late ones. The overall relapse rate was 0.25% and the inculation period of the occurrence of relapse was 45, 48, 52, 60 and 80 months respectively. Among 954 PB patients who completed FD WHO MDT, 1 previous PB case was diagnosed as relapse clinically, bacteriologically and pathologically 107 months after completion of the treatment with an overall relapse rate of 0.1% and an incubation period of relapse of 107 months. The authors suggested that FD WHO MDT has been proved effective with a low relapse rate, safe and feasible to use in the field.

CH29

AGRANULOSYTOSIS AND DERMATITIS DURING THE SECOND MONTH OF MDT IN LEPROSY

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Agranulocytosis is a recognised side effect of dapsone. There are many reports of agranulocytosis due to dapsone when used for malaria prophylaxis or treatment of dermatitis herpetiformis. There are only few reports of agranulocytosis during treatment of leprosy.

In treatment of dermatitis herpetiformis agranulocytosis has been estimated to develop in 1 of 240 to 425 patients treated and in malaria profylaxis in 1 of 10 000 to 20 000 persons. In spite of the large number of people treated for leprosy with dapsone the number of reported cases of agranulocytosis is very small. The agranulocytosis develops usually during the first three months of treatment.

Three patients who developed dermatitis and agranulocytosis during treatment with MDT for leprosy are reported. They developed agranulocytosis between 3 and 8 weeks after starting the treatment. One of them had exfoliative dermatitis like dermatitis, but affecting mainly the sun exposed areas of face, arms and ankles. Second had itching rashes all over the body with some scaling. Third had a full-blown exfoliative dermatitis.

The first one had total white blood cell count of 3 000/mm3 of which 10% were neutrophils. His neutrophil percentage normalised in 6 days. The second one had WBC of 8 500/mm3 of which 3% neutrophils. His blood count normalised in 6 weeks. The third one had WBC of only 1000/mm3 and no neutrophils were seen in peripheral blood. He fulfilled also the criteria for dapsone syndrome with enlarged liver, lympadenopathy and exfoliative dermatitis. He died two days later.

CH30

EVALUATION OF MDT DURING PREGNANCY

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Worsening of the disease, intercurrent infections and increased incidence of lepra reactions are the main effects of pregnancy on the women with leprosy. Antileprotic drugs are not contraindicated during pregnancy. Effect of MDT during pregnancy is evaluated.

Total 37 cases of MB leprosy associated with pregnancy were randomized in two groups.

Group A - 21 cases - MDT was given throughout the pregnancy.

Group B - 16 cases - Placebo was given during pregnancy.

In both groups patients were evaluated.

Evaluation	Group A	Group B
1. Disease status	Stable in majoity of cases.	Worsen in majority of cases
2. Incidence of Lepra reaction	Less - 2 had serve ENL in Ist trimester leading to intrauterine death of foetus. MTP was done.	More-5 showed type II reaction in 3rd trimester.
3. Intercurrent Infection	Less	More
4. Outcom of pregnancy	More favourable i) All low birth baby ii) 2 foetus showed brown colouration of skin which gradually disappeared	Less favourable i) All low birth baby ii) 3 patients developed type I lepra-reaction during puerperium.

Incidence of lepra reaction, intercurrent infection were more in group B. Disease status and outcome of pregnancy of group B is less favourable than group A.So MDT should be continued in leprosy during pregnancy.

CH31

HYPERSENSITIVITY SYNDROME TO DAPSONE – AN EPIDEMIOLOGOCAL REVIEW

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Dapsone (4,4' Diaminodiphenylsulfone), commonly used for the treatment of leprosy and cerain chronic inflammatory dermatoses, is now applied extensively in HIV-patients suffering from opportunistic infections. In the literature the various adverse effects of dapsone are well documented. A rather rare side effect of the sulfone is the hypersensitivy syndrome (so-called sulfone-syndrome (HS)) which is potentially life-threatening. However, the real frequency of the HS has long been a subject of controversial speculations. Therefore, in order to ascertain exact data, published cases with HS in the world literature from 1949 – the beginning of epoch-making sulfone treatment – to the end of 1995 were analyzed.
The results reveal a total number of 103 patients with HS, aged 7–76 years (44 female, 45 male, in 14 cases data are lacking). Concerning the global distribution of HS, Asia is most predominant (51 patients) whereas the occurence in the other continents is distinctly lower (Australia: 21, Africa: 1, North-America : 12, Europe: 5 patients). The most frequent indication for dapsone treatment was ieprosy (80 patients) with chronic dermatoses, tuberculosis, other infections or prophylactic use in the remaining cases. Multiple statistical evidence argues against the possibility of a correlation between applied doses of dapsone and occurence or severity of HS. The median of latency (time intervall from commencement of therapy to manifestation of the HS) was 4 to 7 weeks. Nearly all patients had exanthema, fever and/or lymphadenopathy. Most patients additionally showed hapatic disfunctions of varying severity (from elevation of laboratory values and hepato(spleno)megaly to jaundice). In comparison to this, hematological changes were unexpectedly rare (leukocytoses 20,4%, eosinophilia 12,6%, atypical lymphocytes 9.7%). After withdrawl of dapsone and therapy with glucocorticosteroids 79 cases recovered, whereas 16 showed fatal outcome. It could be demonstrated that hepatic coma was the most frequent cause of death. Considering the millionfold use of dapsone all over the world, the HS to dapsone has to be estimated as an extremely rare side effect with recovery in nearly 85% and a mortality of about 15%.

CH32

EVALUATION OF PLASMA CLOFAZIMINE LEVELS IN LEPROSY PATIENTS

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Slow absorption, relatively much slower distribution and longer retention in selective tissues are peculiar features of clofazimine metabolism. Clinical and experimental studies conducted elsewhere have reported that the plasma levels of the drug are not correlated to the dose and length of treatment. There have, however, been no reports on plasma levels of the drug in relation to the present dosage of 50mg daily. A study is, therefore, being made at CJIl, Agra to evaluate plasma clofazimine levels in relation to cumulative intake of the drug mostly as 50mg daily by leprosy patients. With the cumulative drug intake ranging from 1.5 to 26.5g during the period of 1-18 months plasma levels ranged from 0.8-1.0 ug/ml. The mean plasma drug levels were 0.3 and 0.4 ug/ml after 8 and 14 daily doses of 50mg respectively. The plasma drug levels seem to be directly related to cumulative drug intake although the relationship is not so linear. The steady state appears to be reached after about 30-60 daily doses of 50 mg as reflected by plasma drug levels. Our findings on clofazimine pharmacokinetics will be discussed in the light of the relevance of optimising drug administration in the current scenario of chemotherapy.

CH33

Evolution of the leprosy problem in Anjouan (Comores) after 17 years of intensive treatment

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From 1981 to 1989 leprosy patients were treated with intensive treatment regimens: PB cases receiving 10 weekly doses of 600 mg RMP and MB cases 2 months daily RMP, ETH, DDS followed by 10 months RMP 1/7 + ETH, DDS 7/7. Cure rate for PB was > 95%. MB patients represent more than 4000 patients-years of FU. Ten relapses (0.25%) were observed after 71, 98, 120, 129, 132, 144, 153, 176 and 190 months respectively.

From 1989 on PB treatment was R600 C1200M 200 in a single dose. MB: R600, Oflo 400, Clo 100 7/7 + Mino 1/7 for 6 weeks - cure rate of PB is over 85%. MB represents 535 PYrs of FU (mean duration 4.05 yrs). No relapses were observed.
The yearly detection rate of cases from 1981 to 1997 for PB has remained remarkably stable, but the proportion of patients with ≤ 3 lesions increased. PB patients also presented earlier after the first symptoms of disease, the detection of MB diminished slightly during the last 3 years.
Diagnostic skin biopsies revealed 5% MB, 58% PB and 37% no leprosy.

Conclusion:
1. Short term combined treatment of both PB and MB with excellent results is realizable.
2. Some treatment regimens applied in the past give rise to relapses after 10 years and more.
3. Although intensive chemotherapy was given during 17 years, the detection rates show some improvement only during the last 3 years, and PB patients show up at an earlier stage.

CH34

LONG TERM FOLLOW UP STUDY OF 140 LEPROTICS TREATED BY M.D.T.

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Since the recommendation of the W.H.O. to use the M.D.T. for Leprosy control in 1982, it was applied to a group of Leprosy cases collected from a Skin & Leprosy clinic situated down-town Cairo.

Methods: All cases were examined clinically & bacteriologically, routine lab. Exams done. Colored slides were taken to all cases during the follow up.
The ages ranged between 5 & 75 years, with about 75% of the cases occurring in the age group between 5 & 40. The cases were classified according to the Riddly Jopling scale as follows: TT 12, BT 50, BL 29, LL 47. 76 cases (54.2 %) were multibacillary.

Reactions: 48 cases of which 29 were E.N.L. & 19 reversal reaction cases.

E.N.L.: was recurrent in all the cases inspite of regular M.D.T. 19 of the cases were followed for more than 2 years, while 9 cases were followed for more than 5 years. In 5 cases new crops of small red tender nodules continued to appear for more than 4 years after starting treatment.

Reversal Reactions: 9 out of the 19 cases were followed for more than 2 years. Recurrence of reaction occurred only in 2 cases.

In one case of L.L., the disease relapsed 2 times during the observation period of 15 years. The second relapse occurred shortly after sudden death of his wife.

CH35

CLINICO-BACTERIOLOGICAL FOLLOW UP OF SMEAR +VE MDT DEFAULTERS

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We have earlier observed bacteriological response in smear +ve MB cases defaulted after 6-12 months of MDT, similar to that in the comparable pts having taken 2 years MDT.

In the present study, we tried to follow up 182 smear +ve leprosy patients who were registered from 1986 to 1990 and defaulted at variable period before completion of MDT for 24 months.

On repeated visiting in 1997, it was revealed that out of 182 cases, 15 were found expired, 17 had taken treatment elsewhere, 36 left area permanently, 81 could not be traced due to incomplete address, while remaining 33 (18%) could be examined clinically and bacteriologically.

Out of these 33 cases, 12(37%) and 20(60%) had initial BI up to 2+ and 2.1 to 4+ respectively. 19(57%) took MDT up to 6 months, 8(24%) for 7-12 months and 6 for 13-23 months. Their initial skin lesions varied from patchy infiltrations to disseminated nodular lesions.

Clinico-bacteriological check up carried out of all these cases revealed complete regression of all skin lesions and bacteriological negativity examined in three skin smears.

CH36

OUR EXPERIENCE WITH ANOTHER MULTIDRUG THERAPY REGIMEN FOR LEPROSY

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In San Francisco between 1979 and 1994, 125 new lepromatous leprosy patients (51 BL and 74 LL) were treated with a regimen of 100 mg dapsone and 600 rifampin daily. Patients ranged in age from 9 to 77 (mean 37) and included 44 Mexicans, 44 Filipinos, 23 Southeast Asians, 7 Pacific Islanders, 3 Indians, 2 Chinese, 1 Korean, and South American. Rifampin was maintained for at least a year and often until skin smear negativity (average 5 years, range 1-15 years), while dapsone was continued indefinitely. Prior to therapy patients were highly bacilliforms with a BI of generally 4+-6+. Significantly M. leprae from pretreatment skin biopsies were found uniformly fully sensitive to dapsone (0.0001% in mouse diet) and sensitive to rifampin (0.01%). Patients were seen initially six times annually and no less than twice annually with skin smears from

the 6 disparate sites being performed generally every two years. On this regimen all patients improved clinically with rapid resolution of leprous infiltrates. Skin smears also improved with most becoming negative in 2-5 years and all eventually attaining smear negativity. The total duration of follow-up of these patients ranged from 5-15 years (averaging 9.4 years) and patients were followed an average of 4.1 years (range 1-15 years) following smear negativity. Adverse events were not problematic and occurred at anticipated frequencies. No patient during the course of follow-up was observed to develop new leprous infiltrates, a rising BI, or become skin smear positive after once being rendered negative. Thus this regimen was found to be reliably effective in treating BL and LL leprosy patients.

CH37

FIXED DURATION MULTI-DRUG THERAPY IN LEPROSY - A PRELIMINARY FOLLOW UP REPORT

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The main question currently needing an answer is whether the frequency of relapses in multibacillary leprosy will be more after fixed duration multi-drug therapy for 24 months (FDT - 24), and after the currently recommended (WHO, 1997) duration of 12 months (FDT - 12). This question assumes importance because of a few relapses reported amongst patients with an initial BI of >4.0 after FDT - 24 (Jamet et al, 1995).

We report our observations on 50 patients with BI ≥ 3.0, 36 of whom had BI ≥ 4.0 who were examined beyond a minimum period of 5 years after release from FDT - 24 and FDT - 12. None of the patients were clinically active and their skin smears were negative. In other words none of them relapsed.

Treatment group	Number of patients	Duration of follow-up after RFT		
		5-8 yrs	9-12 yrs	13-16 yrs
FDT - 24	28	9	17	2
FDT- 12*	22	20	2	0
TOTAL	50	29	19	2

*This investigation was started in 1990. These patients will be undergoing long-term follow-up

If we include to this sample, the defaulter study sample of (1) 41 patients (Ganapati et al, 1992) and (2) 33 patients reported recently by Bhatki (1997) whose BI was ranging between 1+ and 5+, consolidated observations on relapse in Bombay sample alone extend up to a total of 124 patients, out of whom none has relapsed till today. All the patients have remained negative.

Recent questionnaire study (WHO,1997) of 761 patients also indicates that patients dropping out of treatment after 24 months of MDT behave in a manner comparable to those who have taken treatment for 12 months or less in respect of reaching skin smear negativity. Such observations do not however rule out the possibility of stray relapses.

CH38

EVALUATION OF WHO MDT IN TRIBALS OF BIHAR - A STUDY IN 18000 LEPROSY CASES

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Total Cases - 18,000

Completing treatment -	16, 620 (Drop - outs - 1200 Died - 30, Asked Transfer - 150).
PB/MB	7840/8780
Male/Female	9830/6790
Children/Adult	1:3
Highets no. in	20 - 30 age group
Incidence of deformity	12%
Incidence of trophic ulcer	5%

Treatment schedule WHO MDT : PB 2 drugs (6 months) MB 3 drug (24 months) Follow - up : 6 monthly PB (2 years), MB (5 years).

Cure rate	PB - 98%
	MB - 94%
Regularity of treatment	PB - 95%
	MB - 90%
Relapse rate	PB - 5%
	MB - 4%
Incidence of Type - 1 reaction	8 %
Type - II reaction	6%

WHO MDT is most effective even in leprosy of tribals.

CH39

COMPARISON OF 1 & 2 YEARS MULTIDRUG THERAPY (WHO) IN MB LEPROSY - A STUDY OF 3740 CASES.

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Dr. R. N. Mishra, Prof. Dr. Mathura Prasad

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The morphological index becomes 0 within one year of MB MDT in majority of leprosy cases. The Bacteriological index (accounting for all living, dying & dead bacilli) may remain positive even after 2 years of continuous MDT, but becomes negative with out any further treatment. Old approach of treatment till bacterial negativity was changed to a fixed duration chemotherapy of 2 years. It has been observed that if MDT is stopped at 1 year and cases kept in regular follow-up, the cure-rate is comparable with the series on 2 years treatment. A comparison between 1 year and 2 year MDT regimens in MB leprosy cases is being made.

3740 MB cases age range (15-70 years), 2700 males 1040 females) were randomized in 2 groups.

Group A - 2800 cases (2190 males 610 females)

Group B - 940 Cases (510 males 430 females)

Cases lost during treatment & follow-up were A-110 & B-20.

Cases completing the evaluation A-2690 & B- 920.

Cases were evaluated monthly for clinical activities and BI, MI, SFG. Follow-up was done 6 monthly for 5 years in group A & 6 years in group B. At the end of 2 years and 5 years there was no significant difference between the 2 groups. Relapse rate was equal in 2 groups (2.5%) side effects (Ichthyosis, Lipofuschinosis) were less in group B. WHO MB MDT fixed duration Chemotherapy can be recommended for one year.

CH40

THE EFFECT OF MDT FOR 27 MONTHS AND POST-TREATMENT SURVEILLANCE FOR 11 YEARS IN MB LEPROSY CASES

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Since February of 1983, 47 active MB patients have been regularly treated with RFP, B663 and DDS for 27 months with satisfactory clinical, bacteriological and histopathological improvements and with mild side effects. MDT was also effective in controlling type II leprosy reaction. After stopping MDT, the clinical symptoms continuously subsided and BI steadily fell down. In the sixth year after stopping MDT, all cases became skin smear negative, and the histopathological inflammatory infiltration also gradually subsided in the 11-year period of surveillance. Except 4 cases who died of non-leprosy cause, all the remaining 43 cases met the China's criteria of clinical cure and no relapse occurred. It indicated that MB leprosy patients could be definitely cured with short-term MDT regimen. Extensive implementation of FD WHO MDT has been proved very important in reaching the goal of basic eradication of leprosy in China by the end of year 2000.

CH41

A LONG-TERM OBSERVATION OF THE EFFECT OF MULTIDRUG THERAPY IN LEPROSY IN LIANGSHAN AND PANGZHIHUA

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From 1984 to 1997, 1 229 MB and 775 PB leprosy patients were treated with FD WHO MDT in Liangshan Yi Autonomous Prefecture and Panzhihua City, Sichuan province, China. Two hundard and twenty eight out of 775 PB patients, together with 1 229 MB cases were treated with FD WHO MDT - MB regimen and followed up for a minimum of 5 years. 537 PB patients wre treated with FD WHO MDT - PB regimen and followed up for a minimum of 2 years. Among 1 066 MB patients completed treatment with MDT, 1 053 (98.7%) patients remarkedly improved and 13 (1.22%) improved clinically with an overall efficiency rate of 100%. In a period of 5 years after stopping MDT, the cumulative skin smear negativity rate of MB patients previously untreated with DDS monotherapy and those treated previously was 95.31% and 98.25% respectively. Ninety nine and point one per cent of those patients with a BI of < 3.0 and 91.8% of those with a BI of ≥ 3.0 before MDT became skin smear negative. Among 758 PB patients with skin lesions before MDT and completed MDT, skin lesions completely subsided in 69.52% of patients treated with MDT PB regimen and in 75.98% with MDT MB regimen. There was a close correlation between the number of skin lesions and the therapeutic effect of MDT ($p<0.01$). And among PB patients with BI positive before MDT, the skin smear negativity rate after completion of treatment was 95% and 97.7% respectively in patients completed treatment with MDT MB regimen and MDT PB regimen. Among 205 patients with reactions (Type I 135, Type II 70) during MDT and surveillance, reactions occurred in 112 patients (54.63) in the first year of MDT. Four patients (borderline tuberculoid 1 and lepromatous 3) were diagnosed as relapses with a incubation period of relapse of 45, 48, 52 and 107 months. The relapse rates of MBand PB were 0.71/1000 py and 0.28/1000 py respectively. The results showed that FD WHO MDT regimens have been proved effective with a low relapse rate, safe and feasible to use in the field.

CH42

Evolution sous polychimiothérapie du statut neurologique des malades hanseniens nouvellement dépistés

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Les auteurs présentent les résultats, à 30 mois, d'un suivi longitudinal, par des bilans neurologiques standardisés et répétés, de cohortes de malades nouveaux cas de lèpre mis en traitement polychimiothérapie (PCT). Les résultats concernent 87 de 121 malades dépistés et traités.

Le facteur déterminant dans l'évolution du statut neurologique des malades en traitement PCT est la survenue ou non d'une réaction lépreuse.

Chez 55 malades n'ayant jamais présenté une complication lépreuse (Réaction Reverse (RR) ou Erythème Noueux Lépreux (ENL)), l'évolution du statut neurologique est favorable dans 98% des cas : la polychimiothérapie stabilise et même améliore certaines lésions nerveuses (probablement les plus récentes). Cette constatation souligne l'intérêt d'un dépistage et d'un traitement précoces de la lépre et dans ces conditions, le rôle certain de la PCT dans la prevention des invalidités.

Chez 32 malades ayant présenté une complication lépreuse sévère, l'évolution du statut neurologique est surtout fonction du délai écoulé entre l'installation des troubles - qu'elle soit brutale ou progressive - et l'institution d'un traitement par corticostéroides. Le délai « idéal » est inférieur ou égal à 90 jours. Dans cette condition, l'évolution du statut neurologique des malades est favorable dans 80% des cas. Par contre, pour un délai supérieur à 90 jours, l'évolution du statut neurologique n'est favorable que dans 42% des cas. Cette constatation pose le problème de la mise en œuvre d'une stratégie efficiente pour le dépistage précoce et la prise en charge adéquate des névrites lépreuses qu'elles accompagnent ou non une réaction lépreuse cliniquement évidente. Dans cette optique, l'une des activités essentielles de cette stratégie serait la pratique systématique chez tous les malades dépistés d'un bilan neurologique trimestriel, notamment pendant la première année de suivi au cours de laquelle survient la majorité (74%) des épisodes réactionnels.

CH43

A CASE FOR TREATING ALL SINGLE LESION PB LEPROSY PATIENTS

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This paper presents evolution of single lesion PB leprosy without treatment from a retrospective study of 144 untreated single lesion PB cases detected during the AMPLE programme in Muzaffarpur district of Bihar between September 1992 and January 1993. The study was done as no treatment was started after detection for various reasons even after 18 months.

Self healing was seen in 63.8% of these cases. The age and sex correlation was not significant though lesions on the upper and lower limbs healed more than those on the trunk and face. Of the remaining 36.2%, 22.4% remained stationary while 13.8% deteriorated. 0.7% of the patients who did not self heal developed deformity.

The large percentage of self healing raises the issue of the relevance of treatment but the study highlights the significant percentage who did not self heal. As there are no definite indicators to which lesions self heal and which do not, the paper proposes that all single lesion PB leprosy patients be given treatment.

CH44

SURVEILLANCE OF 994 CURES BY DDS MONOTHERAPY RE-TREATED WITH MDT

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In Xinjiang Autonomous Region , 994 cures by DDS monotherapy (MB 581, PB 413; male 596, female 398) have completed re-treatment by MDT for one year with a surveillance period of 5-11 years from 1986 to 1992 and no relapse occurred.

One hundred and ninety five relapsed cases were detected from 1978 to 1986 among those cures who did not receive re-treatment with a relapse rate of 11.14%, but from 1987 to 1995 there were only 68 relapses with a relapse rate of 0.72%. There was a significant difference between relapse rates in two groups.

During the period of re-treatment with MDT, side effects occurred in varying degrees, but disappeared spontaneously or only with general treatment not having influence to complete the course of MDT.

CH45

EFFICACY OF SINGLE DOSE ROM FOR THE TREATMENT OF SINGLE LESION PB LEPROSY
-24 months follow up from the date of intake.

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A multicentric double-blind controlled clinical trail was carried out to compare the efficacy of a combination of rifampicin 600mg plus ofloxacin 400 mg plus minocycline 100mg (ROM) administered as single dose with that of standard six-month WHO/MDT/PB regimen. The duration of study from the day of intake was 18 month. The trail has been carried out by single lesion Multicentre Trail Group, Action Programme for the Elimination of Leprosy, World Health Organisation.

105 cases who have completed treatment under the above trail at leprosy control area of The Leprosy Mission, Champa, India, were further followed up for another six month.The follow up assessment after 24 months from day intake has shown that ROM is almost as effective as the standard WHO/MDT/PB in treatment of single lesion PB cases.

CH46

MINOCYCLINE USED IN LEPROSY CAUSES LONGTERM MARKED BLUE PIGMENTATION IN SKIN LESIONS

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Two patients from S.E.Asia with borderline leprosy were treated with minocycline as multidrug therapy. Both quickly (within two months) developed marked blue pigmentation in their skin lesions which continued in both cases for over two years despite cessation of the drug.

The first patient was treated with minocycline in conjunction with rifampicin and clofazimine, because she had glucose 6 phosphate dehydrogenase deficiency precluding the use of dapsone. When the minocycline was stopped, she was continued on dual therapy of rifampicin and clofazimine.

The second patient was treated with standard multidrug therapy (rifampicin, clofazimine, dapsone), and developed marked red pigmentation due to clofazimine, which worried him. He was therefore switched from clofazimine to minocycline whereupon his

skin lesions became dark blue. This blue pigmentation had not completely faded even after two years.

This marked pigmentation due to minocycline may preclude extensive use of this drug in leprosy, particularly in fair-skinned races.

CH47

EIGHT-YEAR SURVEILLANCE OF 481 PB LEPROSY CASES WITH DDS AFTER COMPLETION OF WHO MDT REGIMEN

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This article reported the effect of MDT in 481 paucibacillary leprosy cases. All cases have completed fixed duration of regimen of 6 months, 44 (9.15%) of them were released from treatment, 437 (90.85%) cases continued DDS monotherapy after MDT until all active skin lesions completely disappeared or skin smear became negative. Twenty eight cases of them even continuously treated with DDS monotherapy for as long as 36 months. The surveillance period ranged from 7 to 10 years with an average of 8 years, no relapse and reversal reaction occurred. The results showed that it is necessary for PB leprosy cases to have a continuous treatment with DDS after completion of FD WHO MDT of 6 months.

CH48

FIELD TRIAL OF OFLOXACIN DRUG REGIMENS IN MULTIBACILLARY AND PAUCIBACILLARY LEPROSY. PRELIMINARY RESULTS.

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From September 1992 to July 1994, 100 MB and 142 PB leprosy patients have bib included in the trial. A 1 month regimen of daily Rifampicina and Ofloxacin is compared with the standard WHO/MDT regimens in a multicenter double blind study. 98 MB and 136 PB patients have already completed the first 4 weeks of treatment. 94 MB and 133 PB patients have completed the prescribed course of treatment and are under surveillance. The clinical results are good and the incidence of side effects were low. 3 patients were decoded and dropped from the study because of severe side effects. Only one of these patients was receiving ofloxacin.

The PB cases will be follow for at least 5 years and the MB patients for at least 7 years. During surveillance period three patients, 1 MB and 2 PB, were clinically diagnosed as relapse cases. Mouse foot inoculation was performed with specimen from skin biopy of the MB patient. These 3 cases started adequate MDT and are progressing.

This investigation received financial support from UNDP / World Bank / WHO Special program for Research and training in Tropical Diseases (TDR)/DAHW.

CH49

LEPROSY REACTION IN MULTIBACILLARY LEPROSY PATIENTS AFTER 2 - YEAR MULTIDRUG THERAPY .

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In this prospective study 337 multibacillary (MB) leprosy patients treated with the standard 2- year multidrug therapy (MDT) had been followed for 7 years to establish the frequency ,timing, and clinical features of leprosy reactions, mainly after treatment.

Patients from 1987 to 1992 where included in the study, all of them without previous specific treatment. Clinical and skin smear examination were done once a year and histopathological examination was performed in selected cases .

During surveillance period 102 (33%) patients developed leprosy reactions of whom 68 (67%) have already had reaction episodes during treatment. All reactions cases were treated only with steroid or talidomide and had showed satisfactory clinical and laboratory results.

Relapse cases have not been detected among the group of patients who developed reactions but within the group without reaction, 1 patient had relapsed after 6 years treatment. Mouse foot inoculation with specimen from skin biopsy of this patient was performed for evaluation of organisms viability and for drug sensitivity. Immediately after that the patient were retreated with the standard MDT and is improving.

CH50

ANTI PGL-1 LEVELS IN MULTIBACILLARY LEPROSY PATIENTS TREATED WITH OFLOXACIN COMBINED DRUG REGIMENS

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In this double blind study IgM antibodies against phenolic glycolipid-1 (PGL-1) were measured in the serum of 100 multibacillary (MB) leprosy patients, receiving ofloxacin containing combined drug regimen or the standard multidrugtherapy (MDT). The patients were included in the trial from September 1992 to July 1994 and all of whom had not previously been treated. IgM anti PGL-1 antibodies were determined by ELISA method.

Before treatment ,100% of the patients were reactive to antigen PGL-1. During treatment the IgM antibodies levels decreased significantly but slowly. There was a decline in IgM anti PGL-1 of about 37% from the starting level to the end of treatment. After 3 years follow up there were no significantly difference on antibodies titers detected in both groups .

During follow up period 1 patient were clinically diagnosed as relapsed case and the code was broke. Mouse foot inoculation with specimen from skin biopsy of this patient was performed for evaluation of organisms viability and for drug sensitivity. Immediately after that, the patient started the standard MDT and is improving.

CH51

AN ANALYSIS OF 1 313 CURED LEPROSY CASES WITH MODIFIED WHO MDT REGIMEN IN JIANGSU PROVINCE

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This article reported the results of 1 313 MB cases cured with MDT regimen (RFP 1200mg, B663 300mg once monthly surpervised and B663 50mg , DDS 100mg daily self administered) until active skin lesions completely disappeared and skin smear became negative two times with an interval of 3 months. Patches and plaques disappeared by 85.97% and 76.64% respectively after two year's trentment, nodules and difuse infiltration slower. There was a significant difference of BI values before and during MDT. BI during MDT gradually reduced and became skin smear negative after 72 months' treatment (Cox-Stuart test $p<0.05$). Reactions occurred in 18.82% and 5.60% ($p<0.05$) and desability rate was 57.88% and 4.70% before and during MDT respectively ($p<0.05$). This MDT regimen has been proved effective for every case. The shortest duration of treatment was 24 months and the longest was 74 months with an average of 41 months. The surveillance was conducted by leprosy staff. One hundred and seventy seven cases have been monitored for 8 years and 16 cases for 10 years with an average follow-up period of 65 months. No relapse case was detected during surveillance period. This study revealed that it would be better to release MB cases from MDT treatment until the skin smear became negative and active skin lesions entirely disappeared.

CH52

MULTIPLE DRUG RESISTANCE IN LEPROMATOUS LEPROSY - A CASE REPORT

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We report on what we believe to be the first documented case of multiple drug resistance in a lepromatous leprosy patient treated with WHO-MB-MDT in combination with daily ofloxacin for 28 days. The following diagram summarises the events relating to a 45 year old male patient with initial BI of 6.00 who had received dapsone for many years and had florid lesions of LL on examination in January 1991. He was treated with WHO-MB-MDT from 17 January 1991 to 27 March 1993 along with ofloxacin 400 mg daily for 28 days during the initial period. BI showed gradual decline accompanied by clinical regression marked by a few episodes of type II reaction.

In Vitro tests	•						
Resistance Tests	■	▲					
BI	6.00		4.00				- ve
Ofloxacin	-						
Rifampicin	.....						
Clofazimine	———						
Dapsone	———						
	1991	1992	1993	1994	1995	1996	1997

• Viability(+++):17.1. 91; ■ RFP&DDS resistance:17.1. 91; ▲ OFL resistance: 27.1.92

Studies revealed multiple drug resistance (MDR) to dapsone, rifampicin and ofloxacin by In vitro investigations using FDA, Fc receptor, EA resetting techniques as well as by mouse foot pad tests as reported by collaborating laboratory specialising in these tests. However continued administration of these drugs as per current recommendations resulted in bacterial decline and clinical regression. Patient continues to show smear negativity and has shown no signs of clinical relapse for the past 6 years, revealing lack of co-relation between viability, drug sensitivity and clinical behaviour. We believe that the laboratory evidence of MDR alone need not be considered as an indication for switching over to alternative drugs, unless there is definite clinical worsening of the disease and rise in BI.

CH53

REGRESSION OF CLINICALLY ACTIVE LESIONS AFTER SHORT COURSE CHEMOTHERAPY IN LEPROSY

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With the advent of short course chemotherapy (SCC), clinical problems associated with residual skin lesions are assuming importance. The continuation of anti-bacterial chemotherapy beyond the recommended periods is often practised by physicians and leprosy programme managers. Though this may have only a placebo effect, patients are made to believe that therapy is needed for continued clinical regression. The ideal method of management of such patients through counselling techniques is still a subject matter of research. This problem is more keenly felt in the era of SCC with newer drugs, than with WHO-MDT. An attempt was made to assess the magnitude of the problem posed by patients left with symptoms after being released from treatment (RFT) in various research trials based on rifampicin (R), ofloxacin (O) and minocycline (M).

Clinical status at RFT and at sixth month follow up was assessed in 122 patients who received different regimens viz. ROM single dose(ROM-1) and RO-28 days treatment and ROM intermittent treatment(3,6 and12 months).

REGIMEN	No. of patients	CLINICAL STATUS			
		RFT		After 6 months	
		Active	Inactive	Active	Inactive
RO - 28 days	20	8(40%)	12(60%)	6(30%)	14(70%)
ROM - 1	47	43(91%)	4(9%)	8(17%)	39(83%)
ROM - 3 - 6 - 12	55	18(33%)	37(67%)	4(7%)	51(93%)
Total (%)	122	69(56.5%)	53(43.5%)	18(14.8%)	104(85.2%)

It is seen that clinical regression continues irrespective of regimens followed. This indicates the imperative need for devising suitable counselling techniques, to avoid currently practised advocacy of chemotherapy beyond RFT on empirical lines.

CH54

IS THERE A NEED TO RETREAT PB LEPROSY WITH MDT AFTER ROM? - A CASE REPORT

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Concepts of chemotherapy in leprosy have recently undergone a phenomenal change. Trials on intermittent therapy using rifampicin, ofloxacin, and minocycline (ROM) are underway in many parts of the world. Such drug regimens generally do not consider the clinical parameters for deciding the duration of chemotherapy. However many clinicians often resort to different regimens or re-introduce the same treatment for the following reasons:

a) Patients are not satisfied unless all clinical signs disappear.
b) Lesions persist for a long time even after adequate treatment.

We present, the details of an adult male patient who reported to us with 5 skin lesions. He was diagnosed as PB and was treated with ROM intermittent regimen for 3 months. Patient was released from treatment (RFT) after 3 months and kept under surveillance. On a visit to his native place in Uttar Pradesh 19 months after RFT, he was started on WHO-PB MDT by a private practitioner as he did not find any improvement in the skin lesions. Having taken three months MDT, he came to us with persisting skin lesions which were still there when last seen in February 1998. No new lesion or any significant clinical changes were detected when he reported.

Treatment Summary												
Dapsone					———							
Rifampicin	•	•	•			•	•	•				
Ofloxacin	•	•	•									
Minocyclin	•	•	•									
	S	O	N	D		Ju	A	S	O	N	D	Ja	Fe
	1995				96	1997						1998	

We conclude that the continuation of treatment with other regimens had no effect on the clinical regression and it is necessary to counsel the patients and reassure them against over treatment.

CH55

GRANULOMA REGRESSION AFTER 'FDT' IN LEPROSY - A LITERATURE REVIEW

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The basic misconception about the Fixed Duration Therapy (FDT) in paucibacillary leprosy is that the persistence of granuloma, which takes its own time to regress indicates continuation of treatment. To allay the fears of those who are concerned about the withdrawal of chemotherapy after a fixed duration of 6 months in PB leprosy in the face of persisting granuloma, we summarise selected observations arising from two publications on histopathological (HP) studies in BT leprosy.

	JOB et al (1997)	EBENEZER et al (1997)
No. of PB patients	30	37
HP confirmed as BT	22	24
Active after 6 months	11	8 *
Active after 1 year	4	No follow up
Active after 18 months	3	No follow up

Recommendations	
JOB et al (1997)	EBENEZER et al (1997)
1.To identify the high risk groups at the onset i.e. patients with multiple and large lesions, tender nerves & obviously active lesions at Release from treatment (RFT) .	1.Emphasise for HP examination on patients undergoing research studies for confirmation and proper classification.
2.To follow up these patients for longer periods like 2 - 5 years .	2.Need for sequential HP and longer follow up in patients with active lesions at RFT .
3.Intervene with anti-inflammatory drugs or chemotherapy if necessary.	

* These patients are showing continued regression of the granuloma without further treatment . (Ebenezer, personal communication)

Except in a small proportion of cases , the granuloma continues to regress pointing out that beyond the optimum period for which chemotherapy is administered to achieve bacterial kill , the maintenance of granuloma is triggered mainly by the presence of antigens . How this stimulus can be overcome is a subject matter for basic research .

CH56

CLINICAL TRIAL OF SPARFLOXACIN IN LEPROSY PATIENTS

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Seven male patients (age range 20-33 years) with leprosy took mainly 100 mg or 200 mg of sparfloxacin(SPFX) in the evening. Therapeutic effects were determined by clinical, bacterial, or histopathological findings. The study patients took SPFX from a few months to one year. 100 mg SPFX daily obtained excellent clinical, bactericidal and pathological improvement in a few weeks. We did experience reversal lepra reaction in one case. No other side effects of SPFX were observed. It seems that a few months of SPFX therapy is enough to treat leprosy, and combined therapy with clofazimine and DDS should be considered as lepra reaction and resistant bacterias are indicated. We followed the patients for only a few years, and a long term follow-up study of the patients will be necessary for complete eradication of the disease.

New anti-leprosy drugs such as SPFX must be required in the treatment of MDT-resistant bacilli for the eradication of leprosy. Furthermore, SPFX should be examined for inclusion in a MDT regimen for the treatment of leprosy.

SPFX is a strong bactericidal agent against M. leprae, and a promising drug to treat leprosy. Skin involvement of all patients decreased or disappeared within a few months. The bacterial index of skin smears also decreased.

CH57

ACTIVITY OF MINOCYCLINE AGAINST M.LEPRAE IN MICE AND ITS EFFECTS ON LEPROMATOUS PATIENTS

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The paper reported the activity of minocycline against M.leprae in mice and its effects on multibacillary leprosy cases in the short-term clinical trial.The results showed that using the kinetic method,the growth delay of M.leprae in the foot-pads of infected mice was 144 days after treated with 25mg/kg minocycline daily by gavage 5 times weekly over a period of 60 days. Fourteen multibacillary leprosy patients were treated with 100mg/day minocycline for 3 months. The clinical improvement such as softening and flattening of the nodules and plaques in the patients was found as early as 1 week after treatment. At the end of the trial, significantly clinical improvement was found in all patients. The average morphological index decreased from 8.29±3.29% before therapy to 0% at the end of the trial, and the average bacteriological index, from 4.48± 0.52 before therapy to 4.18±0.60 at the end of the trial. Of 8 cases detected by mouse foot-pads test, no viable M. leprae were found in 4 cases after one month's treatment and in all cases after 2 months' treatment. Two cases developed mild ENL and one developed mild skin reversal reaction during the trial. All the patients had silght brownish pigmentation on the exposed skin lesions, but the patients tolerated the drug well during the trial. The authors suggest that minocycline is effective and safe for treatment ofleprosy and it can be used in leprosy chemotherapy.

CH58

TREATMENT OF PB LEPROSY USING A MDT REGIMEN CONTAINING CLOFAZIMINE

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While WHO MDT for paucibacillary (PB) leprosy has been generally effective, there have been problems of residual activity, late reactions and relapses. Clofazimine (CLF) is a proven anti-leprosy drug which is well accepted in Indian population. This study is aimed at investigating the therapeutic efficacy of addition of clofazimine to current MDT in PB patients. In this study, 300 smear negative (99 TT, 173 BT and 28 Indeterminate) patients were randomely allocated to 2 regimens :(i) Regimen I was the WHO advocated therapy for PB patients (ii) Regimen II was the above regimen plus 50mgs of clofazimine daily. Treatment was stopped in both the regimens after 6 months. The CLF containing regimen (Regimen II) was well tolerated and there was no adverse reaction. There was lesser residual activity in the CLF containing regimen at the time of stopage of therapy which was more apparent after 2 years of post treatment follow-up. Two patients from the WHO regimen have relapsed whereas there have been no relapses in the CLF containing regimen in the follow-up period. Late reactions were observed in 8 cases in control group and in 1 case in CLF containing regimen.

CH59

AN ANALYSIS OF 119 RELAPSED LEPROSY PATIENTS IN CHAOHOU CITY

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From 1956 to 1995, in Chaozhou City with a population of 1.4 million (1995), a total of 2 728 leprosy patients (MB 558 and PB 2 170) has been found. Of whom 1 998 cases (MB 418, PB 1580) cured with DDS monotherapy and 119 relapses, including 51 MB (2.2%) and 68 PB (4.3%), occurred with an overall relapse rete of 6%. Four cases relapsed twice and one case three times, actually there were 125 relapses with a relapse rate of 6.3%. Among 11 MB and 246 PB with DDS monotherapy for 1 to 3 years, 2 (18%) and 30 (12%) relapses were diagnosed respectively, out of 92 MB and 219 PB with 3-5 year treatment 5 (5.4%) and 9 (4.1%), and of 315 MB and 1115 PB with 5-10 year treatment 44 (14%) and 29 (2.6%) relapses occurred respectively. Among the 119 relapsed cases, 20 (16.8%) occurred less than 2 years after cure, 24 (20%) in 2 to 5 years, 35 (29.4%) in 5 to 10 years and 40 (33.6%) more than 10 years. In other words, one third or more of relapses occurred 10 or more than 10 years after cure. Thirty eight MB (75%) and 56 PB (82%) relapses have been cured once again with DDS monotherapy. New disabilities or exacerbation of existing disabilities developed in 13 cases (10.9%). Four and 18 of original T relapsed cases became lepromatous type and borderline group respectively, and two of original lepromatous type relapsed cases became borderline group. Since 1985, WHO MDT has been introduced and implemented, 108 cases have been cured with it and no relapse occurred up to now.

CH60

SINGLE DOSE MULTI DRUG THERAPY FOR THE TREATMENT OF SINGLE LESION PB LEPROSY

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A double blind controlled clinical trial was done with the objective of determining efficacy of single dose (Rifampicin, Ofloxacin and Minocycline - ROM) regimen with standard regimen WHO-PB MDT. Untreated PB leprosy patients with single skin lesion only were included. They were followed up for 18 months after completion of prescribed MDT – including placebo. 108 patients completed the treatment. Clinical status was assessed with scoring system for individual clinical aspects like size, appearance, infiltration, sensory deficit, etc.

Lesion had completely disappeared in 38% of those who received WHO-PB MDT and it was 45% in those who received ROM regimen. Overall improvement observed was 75% in WHO regimen whereas in ROM regimen it was 84%. None of the patients developed lepra reactions. Three patients developed drug related side effects in WHO regimen. None of the patients deteriorated in both the groups. Single dose regimen seems to be equally effective in comparison to standard WHO regimen of 6 months duration in single lesion PB leprosy.

CH61

EPIDEMIOLOGICAL SURVEY AND GENETIC IMPACT OF MULTIDRUG THERAPY IN LEPROSY PATIENTS AT COIMBATORE

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The clostogenic effect of the antileprotic drug correlated with the physical condition and environmental factors. Epidemiological data was collected from 150 patients undergoing multidrug therapy, at CULES. MB cases are more than the PB cases. Thirty patients (22 MB & 8 PB) were selected for chromosomal study. The peripheral blood lymphocyte culture showed higher frequency of chromosomal aberration. The PB cases showed maximum chromosomal abnormalities. In both PB and MB cases the large chromosome was involved in the chromosomal aberrations. Among the 30 patients, 24 of them are from consengunous family and 22 of them belong to MB cases and 2 belong to PB cases. They come under the age group of 10-60 years, 24 of them are male patients and most of them are chain smokers and alcoholics. The occupation of many of the patients were agriculture. The genetic disorder seen in the patients may also be influenced by environmental factors.

CH62

COMPARATIVE STUDY OF TWO DRUG REGIMEN AND THREE DRUG REGIMEN IN PAUCIBACILLARY LEPROSY.

Sixty two paucibacillary cases were randomly selected within the age group of 8-80 years, and put on two different multidrug regimen for 6 months. Regimen I was according to WHO (1982) recommendations consisting of Dapsone daily and six once a month rifampicin. In regimen II in addition to above two constituents, clofazamine was added 50mg per day in adults and doses according to body weight in children. The efficacy, acceptability and side effects of MDT were observed for a period of one year. Clinical and histopathological assessment was done, on completion of MDT and there after every 3 months up to end of one year in all cases. A comparative evaluation of effects of two multidrug regimen in paucibacillary leprosy patients is reported. Addition of clofazamine over WHO (1982) recommended regimen appears to have marginal benefit with regard to period of inactivation, disease regression and incidence of reactions.

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CH63

AMINOGLYCOSIDES AS AN EFFECTIVE THERAPY FOR MYOBACTERIAL SPECIES.

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A study performed on tuberculous patients previously treated with several courses of chemotherapy but remain sputum positive, draw the attention of using other drugs.

In vitro susceptibility testing using ofloxacin (0.5 -1 microg/ml) Norfloxacin (0.5 - 1 microg/ml) Kanamycin 2-4 microg/ml and Amikacin (0.5-2 microg/ml) Mycobacterium tuberculosis shows marked sensitivity to these drugs. Marked improvement (in vivo) of many of the chronic cases was noticed and some became sputum negative.

Trials are now going on using the floroquinolones and aminoglycosides after being mixed with Microbacter leprea and injecting in laboratory animals.

The significance of the results and effects of the aminoglycosides on Mycoba. Leprea will be reported and discussed.

CH64

COHORT RESULTS OF 383 RELEASED LEPROSY PATIENTS (MB).

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In order to evaluate the magnitude of relapses and their risk factors associated, a study both current and retrospective was undertaken. In a total of 383 MB patients with BI > 2+ and never treated before, released after 3 recent national treatment schemes (MDT/OMS 1, fixed duration MDT2 and previous national scheme-DNDS) were submitted to clinic and laboratory exams.

The average of treatment term under DNDS scheme was 5 times higher than fixed duration MDT which was 26.43 month longer. Although the fall in BI average showed some differences according to high BI, clinic form, and treatment scheme, the follow-up evaluation (49,62 to 58,17 months) didn't show any significant differences A group composed by the 3 schemes still presents positive smears (14%).

The relapse result was 0.33 in the MDT and 1,18/100 patients years observation in DNDS. The results of ELISA test applied to 155 patients and 182 health controls detected 12% of positivity in the control group and 52.25% in patients groups (6,2% MDT1, 76,5% MDT2 17,3% DNDS).

Two risk group for surveillance were defined: one with positive smears and positive ELISA (32 patients)and another one composed by patients with ELISA levels (>0,800) and also positive smears (7 LL and 1 BL). Both groups present less reactions during and after treatment. A prospective study is need in order to confirm this association.

CH65

TITLE: Effect of Hydnocarpus on wound healing

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INTRODUCTION: Hydnocarpus has been replaced by other chemotherapeutic agents which have a better mycobactericidal effect. However none of the currently used antileprosy drugs have been reported to have a positive effect in would healing. Anecdotal reports claim that leprosy patients who have been given hydnocarpus capsules orally have shown more rapid wound healing.

In view of these reports a pilot experimental study has been undertaken to demonstrate the effect of hydnocarpus in experimentally inflicted wounds on male Wistar rats. The wound healing effect of hydnocarpus is studied with reference to the collagenation, wound contraction and epithelialisation phases of healing. The results of this pilot study will be elaborated and the possible mechanism/s of the action highlighted.

Hydnocarpus could be a useful adjunct in the chemotherapy of leprosy.

CH66

SIGNIFICANCE OF "VIABLE" M.LEPRAE IN TREATED MB LEPROSY PATIENTS

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Detection of viable *M.Leprae* by sensitive laboratory techniques in patients who have completed MDT is generally

interpreted as an indication for re-treatment with MDT or administration of even newer drugs. We present case reports of two multibacillary (smear + ve) patients under observation since 1990-91 as potential candidates for relapse.

Case I: Patient DS diagnosed as LL (BI: 3.75) in 1979, remained absent from 1980 to June 1988. In 1988, (BI: 4.8) he received WHO - MB - MDT from July 1988 to June 1990. Biopsy of skin and nerve in April 1990 showed regressing LL. BI of 4.3 at release from treatment (RFT) reached zero over 5 years. Skin and nerve biopsies at RFT revealed growth of *M.Leprae* in the mouse foot pad. Patient has not relapsed so far.

Case 2:Patient CS diagnosed as LL with pulmonary tuberculosis (B1 : 5.2) in January 1980 was incompletely treated with anti-tuberculosis treatment. In 1988 after 8 years absence BI was 4.0 and patient received WHO -MB - MDT for 2 years from March 1988. At RFT BI was 3.0. Biopsy of skin and nerve at this stage showed regressing BL. BI was negative in 1994 and growth of *M.Leprae* was reported in the mouse foot pad. Patient has not relapsed so far.

Conclusion:

In both these cases, we are presumably dealing with dormant "persisters" which have not multiplied leading to clinical and bacteriological relapse. However, in view of stray reports of late relapses in patients with high BI, we advocate observation of such patients for a longer period.

CH67

RELAPSES AFTER MULTIDRUG THERAPY IN LEPROSY RESPOND TO RETREATMENT

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Leprosy like any other myco-bacterial disease cannot be devoid of relapses. We report our observations on a profile of leprosy relapses after WHO-MB-MDT encountered over a period of 15 years since MDT was introduced.

15 MB (+ve) cases treated with WHO - MB - MDT have so far relapsed (MB+ve → MB+ve). 11 cases had received extended MDT regimen i.e. beyond 24 months and 12 had also received dapsone monotherapy prior to receiving MDT. Initial BI of relapsed cases was 1 to 4.6 (>3.0 in 10). Skin smears were negative at RFT except one case. All the cases remained clinically inactive and bacteriologically negative during surveillance . Relapses were observed after a period of 4 to 13 years after RFT.

Relapses were confirmed by clinical, bacteriological and histopathological investigations. All were HIV negative. In 6 cases mouse foot pad studies showed growth of viable bacilli. On re-treatment with WHO - MB - MDT, all the cases responded well. These relapses, we consider, are due to the 'persister' bacilli rather than to development of drug resistant strains to all the drugs employed, which is a very rare phenomenon.

Relapse in leprosy is generally considered to be due to multiple drug resistance and clinicians often resort to newer drugs or arbitrary regimens. We believe that the relapses after MDT should be managed with the same course of treatment.

CH68

AN ASSESSMENT OF EFFICACY ON MULTIDRUG THERAPY AMONG 795 MULTIBACILLARY LEPROSY PATIENTS IN SHANDONG PRVINCE, CHINA

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Multidrug therapy (MDT) for leprosy was started in Shandong Province, in 1986 and the duration of treatment required before 1991 was as long as until all active sin lesions completely disappeared and/or skin smear became negative. In this paper the authors analysed the efficacy of the regimen with which 795 MB caces were treated.

Out of the 795 leprosy cases, 388 were newly diagnosed or relapsed cases without previous treatment or only treated less than 6 months before MDT(group A), and 407 cases were same cases mentioned but previously treated with DDS monotherapy for a certain period of time before MDT (group B). The average BI value in group A was 2.9 before MDT, among them, BI > 3.0 in 206 cases and BI< 3.0 in 182 cases. The average BI value in group B was 2.2 before MDT, among them, BI > 3.0 in 88 cases and BI<3.0 in 319 cases. The average time needed to reach the negativity of skin smear was 46.5 ± 20.8 months for newly diagnosed and 45.1 ± 26.2 months for relapsed cases in group A, while that needed for becoming negative of skin smear was 44.7 ± 22.2 months for newly diagnosed and 43.9 ± 26.6 months for relapsed cases in group B. There was no statistical significance regarding the time needed to reach skin smear negativity among mentioned 4 categories of patients.

A further analysis showed a close correlation between the time needed to reach skin smear negativity and BI before starting MDT, more than 50 months were needed for patients with BI > 3, while less than 48 months for the patients with BI<3 before MDT. The higher the BI value before MDT, the more time needed to reach negativity of skin smear would be. When these patients were divided into groups by an increase of BI value in an order of 1+, the difference of time needed to reach skin smear negativity was very significant among these groups. Relapses were also monitored annually after completion of MDT and no relapse was detected in a total of 5233 person years of follow up. The authors believed that the regimen were very effective in treatment of MB cases with a very low relapse rate, although they understand that not all MB cases should be treated until skin smear became negative.

CH69

DELAYED CLINICAL PROBLEMS IN SINGLE LESION PB LEPROSY AFTER SINGLE DOSE ROM TREATMENT

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Single dose treatment of single lesion PB leprosy with a combination of rifampicin (R), ofloxacin (O) and minocycline (M) is being practised gradually by the leprosy programmes. Delayed occurrence of clinical problems like new lesions / relapse have not yet been documented.

We report here a patient who was treated with ROM single dose(ROM-1) for a single lesion PB leprosy in November 1994. The following table summarises the events relating to a 45 years old female patient with a raised single lesion PB leprosy on left forearm.

ROM-1	Surveillane completed	One new lesion appeared + old lesion in Type I reaction	Steroid 40mg	No change in new lesion
30.11.94	30.5.96	24.12.96	19.11.97	16.2.98

In December 1996, she reported with reaction of old lesion along with a erythematous and raised new lesion on dorsum of left foot. She was treated with chloroquine. Skin biopsy of both lesions showed tuberculoid granuloma negative for AFB. In November 1997, 40 mg steroid was started to differentiate between type-I reaction and relapse. The old lesion on forearm showed regression. However, the new lesion did not show any change except slight change in erythema. The patient is under steroid to decide about possible relapse.

Very rarely such clinical problems are also encountered after WHO -PB treatment.

CH70

OFLOXACIN CONTAINING COMBINED DRUG REGIMENS IN THE TREATMENT OF MULTIBACILLARY LEPROSY

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The results of Ofloxacin containing combined drug regimens in the treatment of 60 multibacillary leprosy cases from January 1989 to February 1998 are reported. The objective of the trial is to compare the antileprotic property of

ofloxacin and rifampicin in multibacillary leprosy patients and to study the killing rate of *M. leprae* by ofloxacin and rifampicin before mass treatment can be recommanded.

The complications and side-effects of ofloxacin and rifampicin were of a mild nature and both drugs were well tolorated. Moderate to marked clinical improvement was noticed in a short period with Ofloxacin containing regimens in multibacillary Leprosy patients. No persisters were detected in any of the 33 specimens (of mouse footpads) that had been obtained after treatment for 6 months. Ofloxacin if added to the currently used WHO recommended MB-MDT regimen may shorten the duration of treatment. Ofloxacin, therefore, may be considered as a suitable alternative in suspected/proven Rifampicin resistant case and where Rifampicin is contraindicated.

The results were evaluated on the basis of the clinical conditions, mycobactericidal effectiveness, signs of drug toxicity and side effects.

CH71

ACTIVITY OF MINOCYCLINE AGAINST M.LEPRAE IN MICE AND ITS EFFECTS ON LEPROMATOUS PATIENTS

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The paper reported the activity of minocycline against M, leprae in mice and the effects of minocycline on multibacillary leprosy cases in a short-term clinical trial. The results showed that using the kinetic method, the growth delay of M. leprae in the foot-pads of infected mice was 144 days after a treatment with 25mg/kg minocycline daily by gavage 5 times weekly over a period of 60 days. Fourteen multibacillary leprosy patierts were treated with 100mg/day minocycline for 3 months. The clilical improvements such as softening and flattening of the nodules and plaques in the patients were found as early as 1 week after starting treatment. At the end of trial, significant clinical improvement was found in all patients. The average MI decreased from 8.29 ± 3.29% before therapy to 0% at the end of trial, and the average BI from 4.48 ± 0.52 to 4.18 ± 0.60. Of 8 cases tested by mouse foot-pad one month after starting treatment, viabie M. leprae was not detected in 4 cases, but after 2 months' treatment, viable M. leprae were not detected in all cases. Mild ENL and one mild skin reversal reaction developed in 2 and 1 cases respectively during the trial. All patients had slight brownish pigmentation on exposed skin lesions, but the patients tolerated the drug well during the trial. The results suggested that minocycline was proved effective and safe against leprosy and could be used in leprosy chemotherapy.

CH72

REACTION TO RIFAMPIN IN THE TREATMENT OF LEPROSY (MDT/WHO) RECORDED IN THE RIBEIRÃO PRETO REGION

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The objective of the present report was to describe the adverse reactions attributed to the use of rifampin at the recommended monthly dose of 600 mg for the treatment of leprosy (MDT/WHO), recorded from 1992 to 1996 in the Ribeirão Preto region.
Fourteen cases, 7 men and 7 women aged 16 to 64 years, nine of them multibacillary and five paucibacillary, were observed. Fifty percent of these patients, all of them multibacillary, had been previously submitted to treatment (600 mg rifampin/day/3 months and 100 mg sulfone/day/5 years). Symptoms characteristically started 35 minutes to 3.5 hours after the ingestion of the supervised rifampin dose. We observed more than one organ or system were frequently involved. Among the adverse reactions, acute renal failure (ARF) and hepatitis predominated: 5 cases of ARF, 2 of them isolated and 3 associated with hepatitis; 5 confirmed and 3 suspected cases of hepatitis; one case of disseminated intravascular coagulation associated with hepatitis; one case of purpuric thrombocytopenia with possible hemolytic anemia; and 3 cases of flu-like syndrome. Eleven patients were cured, two developed mild to moderate chronic renal failure, and one patient died.
We emphasize the frequency of the combined involvement of various organs and the importance of the early recognition of adverse reactions to rifampin.

CH73

POTENTIAL APPLICATION OF MOLECULAR BIOLOGY IN FIELD TRIALS OF ANTI-LEPROSY VACCINES.

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Leprosy is a Chronic granulomatous disease caused by ***Mycobactrium leprae***. "A unique relationship exists between immunology and central nervous system that governs the principle of clinical application in Homoeopathy. The immune system is not confined to single site in the body : rather governed by central motor nervous system, immunocytes and their secreted molecules traffic within and among lymphoid organs and various body compartments. Hence a highly complex system of communication has developed among the various cell types in the immune system. Homoeopathic medicines determine the pattern of chemical transformation in biological system, catalysed by specific proteinaceous macromolecules called 'enzymes'. The antigen combining regions of most of the high affinity antibodies are encoded by immunoglobulin genes which acquire somatic mutations. Serum levels of the immunoglobulins generally are normal in tuberculoid leprosy patient, whereas polyclonal hypergammaglobulinemia is a common feature of lepramatous leprosy. The homoeopathic medicines like *Hura braziliensis* and *Hepersulf* have been found to cause reduction in lymphoid swelling and levels of gamma globulins. These medicines irreversebly bind to collagens and are, therefore, are targeted to the infected cells.

Hura braziliensis and ***Hepersulf*** proposed to be new antileprae drugs, having recently met first phase of clinical trials. The initial results are promising, however, further studies are still awaited.

CH74

RELAPSES AFTER MDT (ISOPRODIAN-RMP)

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Of 2,743 Hansens patients being treated with MDT (Isoprodian-RMP) at Km 81 during Jan 1/87 through Dec 31/95, we have detected four relapses by MB patients and one by a PB patient. The control period, after the MB patient was released from treatment, was 5 years; and for the PB patient, 2-3 years. The observation is that the relapses by MB is presented between 7-10 years after release of MDT, and none during the conventional control period. The relapse rate in this period is, therefore, globally 1.8/1000.

CH75

RELATIONSHIP BETWEEN THE LEVEL OF PGL-IgM ANTIBODY AND RELAPSE IN CURED LEPROSY PATIENTS

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In 1 515 cured leprosy patients (MB 917,PB 598) from 20 countis in Shandong Province, the level of PGL-IgM antibody was monitored for five years. The patients with positive PGL-IgM antibody were randomly diveded into two groups. First group was purely followed (group A) and the second group (group B) was treated with MDT for one year. The patients with negative PGL-IgM antibody were followed as group C. All the patients were examineted clinically and bacteriologically once a year for five years. At the end of the study, relapse rates in three groups were compared.

The results showed that in the first year of monitoring, the positive rate of PGL-IgM antibody gradually increased in patients at the pole of tuberculoid leprosy towards the pole of lepromatous leprosy, and the shorter the time after cure , the higher the positive rate was. In the period of 5 years, 20 relapsed cases were detected: 16 (11.4%) in group A, 1 (0.71%) in group B and 3 (0.24%) in group C. The relapse rate was higher in those with positive PGL-IgM antibody than those with negative. ($p<0.001$). Treatment with MDT had significant impact on the relapse in this study ($p<0.001$).

The authors concluded that: 1) there was a tendency in leprosy patients with positive PGL-IgM antibody to develop relapse after termination of DDS monotherapy; 2) blood spot method for monitoring of PGL-IgM antibody was feasible for use in the field; 3) treatment with MDT was very effective to prevent those with positive PGL-IgM antibody from relapse.

CH76

TWELVE -YEAR SURVEILLANCE OF 657 CURED PERSONS AFFECTED BY LEPROSY RE-TREATED WITH MDT

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From 1983 through 1988, 657 MB patients clinically cured with DDS monotherapy together with BI of 2 or more at any site smeared previously were re-treated with RFP, B663 and DDS in combination. Four hundred and eighty seven of them were males and 170 were females. Their age ranged from 17 to 70 years and their disease duration ranged from 1 month to 39 years. Cured individuals not re-treated were used as control for this trail.

All patients were administered RFP and B663 1 200 mg each once monthly with supervision and DDS 100 mg daily self-administered. This treatment was continued for 12 months and was completed within a period of 15 months. Six hundred and twenty cases (94.37%) of them completed regularly the prescribed course but 37 did not due to the occurrence of side effects or complications. Exclusive of 2 who died and 1 migrated out of Shanghai after completion of re-treatment, the remaining 654 were followed up for a period of 7-12 years (494 cases for more than 12 years) and the total follow up period was 8 926 person years, no relapses occurred. But there were 23 identified as relapses among the 137 control individuals, giving an overall relapse rate of 16.79% and an average annual relapse rate of 1.29%. The authors suggested that for a more reliable conclusion, these cases should and will be followed up until 20 years after completion of re-treatment.

CLINICAL

CL01

MARKERS FOR REACTION

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Serum samples were taken before reaction, at reaction and during antireactional treatment in a prospective study.

The following markers were studied: TNFα, produced predominantly by macrophages (normal value < 40 pg/ml); IFNγ, produced by activated T cells (normal value < 15 pg/ml); neopterin, produced by macrophages activated by IFNγ (normal value < 10 nmol/ml) and soluble TNFα receptor (= sTNFαr normal value <1.5 ng/ml).

Four patients with reversal reaction (RR) and one patient with several episodes of ENL and one episode of neuritis were studied.

TNFα , IFNγ and neopterin were simultaneously increased in two and TNFα , IFNγ in the other two RR. Levels decreased or normalized during antireactional treatment with prednisone.

Only TNFα was increased at ENL on two occasions; on the third occasion i.e. an exacerbation of ENL during prednisone treatment given for a neuritis TNFα level was normal.

sTNFαr levels varied but were increased in nearly all samples.

In general, patients in reaction showed elevation of markers investigated. Laboratory markers may be helpful to support the diagnosis of reaction in leprosy patients.

CL02

NEUROLOGICAL ASSESSMENT OF A COHORT OF CHILDREN BORN TO MOTHERS WITH LEPROSY AND HEALTHY CONTROLS (A9 STUDY) - 1. CLINICAL AND CONVENTIONAL TESTS

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In a prospective (1975-1997) study (A9) of mothers with leprosy and healthy controls, and their children, 15/99 of children were found to have very early leprosy at puberty (1990). Despite MDT 13/15 showed new nerve damage (1993). In 1993, 40% of the A9 cohort who had easily palpable/slightly enlarged nerves without suspicious skin lesion showed early neurodysfunction. The aim of this study was to investigate if early nerve enlargement was a prodromal sign of leprosy.

Subjects: A9 cohort children: 85 (51 females and 34 males); distribution according to leprosy status of the mother multibacillary leprosy (MBK:47), paucibacillary leprosy (PBK:22) and non-leprosy (NLK:16). [K=kids!]. Control group: no known family or household leprosy contact (NKLCK:18).

Nerve enlargement: The A9 cohort had 45% with early/definite nerve enlargement (MBK 55%, PBK 36%, NLK 54%) compared with 25% NKLCK. Male:female ratio for nerve enlargement was 25:17, except in MBK (11:12). The ulnar nerve was the most frequently enlarged.

Sensory and motor nerve impairment (graded sensory testing (STG) and voluntary muscle testing (VMT)): A9 cohort had i) 32% sensory nerve impairment (MBK 40%, PBK 29%, NLK 14%) compared with NKLCK 13%, and ii) 12% motor nerve impairment (MBK 12%, PBK 14%, NLK 7%) compared with NKLCK 7%.

Nerve Conduction Velocity: measurements in 30 children who had evidence of neurodysfunction were all within limits of normal for the reference laboratory.

CL03

NEUROLOGICAL ASSESSMENT OF A COHORT OF CHILDREN BORN TO MOTHERS WITH LEPROSY AND HEALTHY CONTROLS (A9 STUDY) - 2. TESTS OF SMALL NERVE DYSFUNCTION

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The aim of this study was to see whether neurodysfunction could be detected before irreversible nerve damage had occurred in the A9 cohort and healthy controls. The Thermal Threshold Tester (Triple-T: Medelec Ltd (see poster)) detects small nerve dysfunction in thinly myelinated A (cold) and unmyelinated C (heat) fibres. The Laser Doppler blood flow meter (MicroFlo DSP: Oxford Optronix (see poster)) assesses function in autonomic (vasomotor) unmyelinated C fibres by recording skin blood flow response to inspiratory gasp (LD-IG) and cold challenge (LD-CC) in tips of index and fifth fingers.

Triple-T: The A9 group had significantly increased hot and cold thermal thresholds (MBK 70%, PBK 70%, NLK 75%) indicating small fibre damage compared with NKLCK (18%).

LD-IG and LD-CC: LD-IG showed abnormal traces with established and subclinical nerve damage. The fall from resting blood flow (baseline) to the lowest point of the curve in response to LD-IG and LD-CC is expressed as % of the baseline. The mean LD-IG and LD-CC % fall in index and fifth fingers showed no differences between A9 and control groups. The percentage of children having i) abnormal LD-IG were MBK 22%, PBK 19%, NLK 17%, NKLCK 37%; ii) abnormal LD-CC were MBK 38%, PBK 33%, NLK 36%, NKLCK 33%.

CL04

ASSESSMENT OF THE A9 STUDY NERVE FUNCTION TESTS, HYPOTHESIS AND APPLICATIONS FOR LEPROSY ERADICATION

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The prospective (1975-1997) study (A9) of mothers with leprosy and healthy controls, and their children, showed 15/99 of children with very early leprosy at puberty (1990). Despite MDT 13/15 showed new nerve damage (1993), while 40% of the A9 cohort with easily palpable/slightly enlarged nerves without suspicious skin lesion showed early neurodysfunction. In 1997 70% of the cohort had abnormal thermal thresholds, 32% had sensory impairment and 12% motor impairment. These findings from a well documented cohort are indicative of a significant level of as yet undiagnosed subclinical leprosy among teenagers and young adults in the "leprosy villages", potentially explosive and crippling in the event of widespread immunosuppression.