logical steps involved in clinical diagnosis will be described in detail with application in the field work.

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Cl 365

LESSONS FROM THE DELAYED DIAGNOSIS OF LEPROSY IN LONDON, U.K.

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28 patients with a new diagnosis of leprosy have been seen at the Hospital for Tropical Diseases, London in the 3 years 1995-8. We have reviewed their case notes to establish their geographical origin, symptoms, skin signs, and neurological evaluation at presentation. We also noted how many doctors they had seen before the diagnosis of leprosy was made and the incorrect diagnoses made.

54% of our patients came from the Indian subcontinent, but all major leprosy endemic areas are represented. Three patients were Caucasian British but acquired leprosy during long residences in the Indian subcontinent. The median time from onset of symptoms to diagnosis was 3.1 years. The mean time from entry to the UK to diagnosis was 7.9 years.

All types of leprosy were seen. 21 patients had typical skin lesions and 22 had thickened peripheral nerves. 8 patients presented with reversal reactions and 1 with erythema nodosum leprosum.

In 23 cases the diagnosis of leprosy had been delayed. Misdiagnosis as dermatological (7), neurological (6) and orthopaedic/rheumatological conditions (9) was common. 61% of patients had significant nerve damage at the time of diagnosis that required specialist management.

This case series has implications for the development of leprosy services as the leprosy case load diminishes in previous endemic countries. Leprosy patients will no longer present to specialist leprosy services. Doctors in many specialities will need ongoing medical education to ensure that they recognise leprosy.

Conclusion : Leprosy patients outside leprosy endemic areas present to a wide range of doctors. Misdiagnosis can only be reduced if doctors consider the possibility of leprosy in patients from endemic areas with skin rashes, neurological or joint symptoms.

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Cl 374

THE LEPROSY AND THE BURULI'S ULCER ANALOGIES AND DIFFERENCES Dr.Jose

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The analogies and differences of these two Mycobacteriosis are exposed to coincide in belonging to the same bacteria family, in their geographical localization, in tropical and subtropical areas and in affecting populations with faulty socio-economic conditions.

Most notable differences in the Buruli s ulcer are the following : it is possible to cultivate, it has a short period of incubation, its location takes only place in the skin and subcutaneous cellular tissue, the Mycobacterium ulcerans produces an exotoxine, its localization is extracellular and the treatment is eminently surgical.

It must be insisted in the great increase of the Buruli s ulcer and its possible diffusion to other countries mainly in the necessity to avoid the comparition with the leprosy in the negative aspects of commenting that the Buruli s ulcer is not the leprosy of the XXI century.

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Ch 74

EVALUATION OF MULTI-DRUG THERAPY IN URBAN LEPROSY UNIT, PATNA MEDICAL COLLEGE HOSPITAL, PATNA - A 15 YEARS STUDY IN 14,000 CASES

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Elimination of Leprosy from about 95% of the world has become possible due to WHO MDT, PB or MB. 6 months PB MDT & 12 months MB MDT are being evaluated in 14,000 cases of Hansen s disease visiting urban Leprosy Centre PMCH & Leprosy Research Centre, Patna from 1985 to 2000.

DDS daily and supervised Rifampicin once a month in empty stomach was given for 6 months in PB leprosy. Additional Clofaxamine (300 mg. 1st day & 50 mg daily) was given for 2 years (upto 1998) and 1 year after 1998) clinical, bacteriological evaluations were done monthly. Follow-up was done for 2 years in PB and 5 years in MB leprosy.

Droup-outs : 1100, Died: 20, Asked transfer : 280, Completing treatment: 12,600 (PB 7,200 MB 5,400) Male (7,500) Female (5,100) Child (3,200) Adult (9,400). Highest number of cases in 20-30 years of age group, Deformity (15%), Ulcers (6%), Cure rate in PB (97%), MB (94%). Regularity of treatment PB (99%),

MB (91%), Relapse rate PB 2%, MB 5%. Incidence of Type I reaction 8%, Type II reaction 6%. Regularity of treatment was more and deformity reactions were less in MB MDT 1 year. Multi-drug therapy is very effective in Hansen s disease.

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Ch 77

CLARITHROMYCIN IN MULTIBACILLARY LEPROSY

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MB MDT in MB leprosy is very effective but in some cases either Dapsone or Rifampicin or Clofazimine is not well tolerated. In this case Clarithromycin a macrolide, bactericidal drug is as good as Rifampicin alone or in combination.

100 cases of MB leprosy, all adults were randomized in 2 groups :

Group A (50 cases) : WHO MB MDT for 1 yr.

Group B (50 cases) : Clarithromycin (500 mg) daily for 56 weeks.

Clinical & bacteriological evaluations were done monthly for 1 year and then 6 monthly for 5 years.

Drop-outs : A-5 B-0

Completing t/t A-45, B-50

Cured A-44 (98%),B:50(100%)

Replapse rate : A - 0 B - 0

Side effects in both the groups were comparable.

Clarithromycin (500 mg daily) for 8 weeks is a very effective treatment modality for multibacillary leprosy especially for those who may afford it and who don t want to go for routine MDT due to long duration and known side effects of icthyosis and hyperpigmentation.

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Ch 83

ANALYSIS OF MICRONUCLEUS INDUCTION IN LEPROSY PATIENTS WHO ARE UNDER MULTI-DRUG THERAPY

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A cytogenetic study was conducted on peripheral blood lymphocytes of leprosy patients who are under multi drug therapy(MDT). Our previous study showed that there is a DNA damage in leprosy patients who are under MDT. In this experiment micronucleus (MN) test was conducted on the peripheral blood lymphocytes (PBL) of 50 leprosy patients. The result of this study shows that the frequency of lymphocyte with micronucleus (2-4%) was significantly more ($P<0.05$) in leprosy patients when compared to the controls. To assertain the role of antileprotic drugs in the observed DNA damage in leprosy patients an invitro study was conducted using single cell gel electrophoresis assay on human peripheral blood lymphocytes. The lymphocytes were treated with different doses of rifampicin, dapsone and clofazamine for short period (30 min). Dapsone seems to induce DNA damage in human PBL which in not satistically significant at 30 minute of exposure. So we propose to increase the period of exposure up to 2 hours. The results of exposure to longer period in keeping with the human dosage schedule will be presented.

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Ch 136

SIGNIFICANCE OF RECURRENCE OF SKIN AND NERVE LESIONS AFTER MULTI-DRUG THERAPY IN MB LEPROSY

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Introduction :

While implementation of WHO recommended MDT through control programmes has led to excellent progress, an increasing number of follow up studies on patients treated with MDT have however demonstrated viable organisms as well as clinical relapses. Reappearance / recurrence of lesions in treated cases has profound implications for case management, disease transmission and control. It is also speculated that patients receiving prolonged course of steroids may be prone to developing delayed clinical problems which could either be reappearance of lesions or true relapses. Similarly, difficulty in distinguishing clearly on clinical grounds a late reaction from relapse limits the estimation of the magnitude of the problem of true recurrence. In view of this, we are investigating the magnitude of the problem as well as the clinical, bacterial and immunological significance of recurrence of skin and nerve lesions in MDT treated cases.

Methodology :

Treatment records of all patients with a minimum period of 5 years follow-up after MDT, registered in BLP, were taken up for study in a retrospective analysis. The data was collected in a specific format with respect to clinical problems, namely development of new lesions, extension of old lesions, characteristics of skin lesions, duration of follow-up, steroid administration and neurological status. The patients were assessed for clinical, neurological and bacteriological status. The patients were then referred to FMR for investigation, viz assessment of bacterial load, antigen load and drug sensitivity tests.

Results :

Sr. No. Activities Number

1. MB cases registered 1982-1994 2976

2. Records analysed 1852

3. Patients identified having Clinical Events 37 (1.9%)

Continued on next page Observations Observations:

The above analysis showed that a small proportion (1.9%) of treated patients do report with recurrence of lesions, the etiology of which needs to be investigated. However, it appears that true relapses are small in number, though they do occur. The data will be discussed. The bacteriological and immunological significance and their clinical co-relation are being studied and the results are awaited.

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Ch 154

RECENT ADVANCEMENTS IN HANSEN'S MANAGEMENT

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WHO MDT is very effective in the treatment of Hansen s disease, but time required is the only drawback - 6 months / 1 year. Search for shorter duration Antileprotic regimens have yielded good result. Combination of Ofloxacin / Sparfloxacin with Rifampicin kills all living Mycobacteria within 28 days. This becomes possible due to synergism and better tissue penetration.

1200 cases of MB HD, all adults were randomised in 3 groups :

Group A 400 : WHO MB MDT for 1 yr.

Group B 400 : Rifampicin 600 mg Empty stomach +

Ofloxacin (400 mg.) OD = 30 days

Group C 400 : Rifampicin 600 mg OD +

Sparfloxacin 200 mg OD = 30 days

Evaluation was done monthly for clinical activities and bacteriological status. Follow-up was done monthly in group A and 6 monthly in group B & C upto 1 yr. and then 6 monthly in all groups upto 5 years.

Cure rate in Group A was 94%, B 90%, C 86%.

Side effects of Icthyosis & hyperpigmentation were least in Group B. Relapse rate was least in Group A and maximum in Group C. Nausea, vomiting, arthritis were more in Groups B & C. Rifampicin & Ofloxacin combination was most effective due to its shorter duration and less adverse effects and may be given in selected cases not willing to go for routine WHO MDT.

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Ch 217

CHEMOTHERAPY OF LEPROSY IN THE NEW MILLENNIUM

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INTRODUCTION : Though leprosy has afflicted mankind since time immemorial, effective therapy for leprosy became available only after 1946, when Robert Crochane first used dapsone for treatment of leprosy. Subsequently clofazimine and rifampicin were discovered, and in 1981, WHO recommended the MDT regimens for leprosy using these 3 drugs. The MDT regimens proved to be highly effective, having cured more than 8.4 million leprosy patients till the beginning of 1997.

PHARMACOLOGY OF ANTILEPROSY DRUGS : We present a brief overview of clinical pharmacology of the traditional antileprosy drugs mentioned above, as also of the newer ones that have emerged in the past decade, notably ofloxacin and minocyclinc. We also make a brief mention of newer agents that have shown promise in experimental studies.

VACCINES : Recently, a number of vaccines have been tried for leprosy, particularly BCG, M vaccae and M w. We document the results of various studies investigating these vaccines.

NEWER REGIMENS : In the recent years, a large number of alternative regimens combining the newer drugs with the traditional ones have been suggested and tried. Shortening the duration of effective treatment is the main objective sought to be achieved. In addition, these regimens are valuable in cases of resistance to existing drugs, or if the patient is unable to tolerate the existing

drugs. Some of these new regimens have been accepted by WHO as effective and viable. We document the results and conclusions of various studies that have investigated such alternative regimens.

CONCLUSION : The success of WHO MDT regimens have brought us a step closer to elimination and probably even eradication of leprosy. Emergence of newer, shorter, cost-effective regimens with many operational advantages has further given a shot in the arm to leprosy elimination programmes. However, in-depth studies of efficacy of these regimens, as also a long-term follow-up need to be carried out before they are implemented in the field. A judicious use of the advances made in pharmacotherapy of leprosy will indeed make possible the eradication of leprosy in the new millennium.

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Ch 234

A THERAPEUTIC TRIAL OF 'ROM' IN MULTIBACILLARY LEPROSY

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ROM has been advocated as an alternative drug regimen in MB leprosy (WHO 1998). We here present a comparative clinical trial of ROM versus WHO MB MDT in 30 MB leprosy patients.

15 patients (LL-7; BL-6 & BB-2) (Male-13, Female-2) were given daily ROM (Rifampicin 600 mg; Ofloxacin 400 mg and Minocycline 100 mg) for 28 days and thereafter once a month supervised dose for 12 pulses. An equal number of age, sex and class matched controls were taken whose BI closely matched the cases on ROM. These 15 patients received WHO MB MDT as per standard NLEP protocol.

The clinical course of these patients were closely monitored every month using Ramu s Clinical Score and a modified Ramu s score. Slit skin smears were done at start of therapy and repeated every 6 months. Special care was taken to record reactions, neuritis and adverse side effects. Statistical tests of significance were applied to the results.

Results indicate that there is a significant overall clinical response to ROM therapy over WHO MDT. Fall of BI was also quicker with ROM therapy. Reactions (Type I & II) and neuritis were more common in ROM patients. Adverse drug reaction were not encountered in either group.

This study highlights the efficacy of ROM therapy in MB leprosy, its operational ease of administration & the caution regarding reactions with its use as an alternative drug regimen.

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Ch 244

COMPARISON STUDY ON DDS SYNDROME HAPPENED IN DURATION OF MDT AND DDS MONOTHERAPY

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Objective : To study the incidence of syndrome caused by DDS from MDT and DDS - monotherepy respectively.

Methods : To look over the case individual records and look into cases for comfirming the occurrence or DDS syndrome.

Results : 4 cases treated by MDT and 2 cases treated by DDS-monotherepy occured DDS syndrome. Incidence of them were 2.6% (4/153) and 0.098% (2/2044) respectively and showed high significance (P< 0·01).

Conclusion : It is suggested that the cases treated by MDT regimens be carefully observed to find the DDS syndrome and cope with it.

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Ch 258

CLINICAL ANALYSIS OF 12403 RELAPSED LEPROSY CASES IN CHINA DURING 1 9 4 9 -1 9 9 8

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In order to study clinical characteristics and the trend of leprosy relapsed cases after DDS mono-therapy or MDT from 1949 to 1998, the authors analyzed the data on leprosy relapsed cases in China from 1949 to 1998 by computer. The results showed that a total of 12403 leprosy relapsed cases from 1949 to 1998 in China with a cumulative relapsed rate of 3.28%. Among them, 11803 were relapsed after DDS mono-therapy with a relapsed rate of 3. 83% and 236 were after MDT with a relapsed rate of 0. 57%. The relapse rate in previously DDS-treated PB cases with MDT was

higher than that of PB cases only treated with MDT. The relapsed rate in previously DDS treated MB cases with MDT was also higher than that of MB cases only treated with MDT. The rates of disability grade 2 and skin smear positive in relapsed cases were 49.9% and 69.3% respectively. The authors consider that the peak of leprosy relapse after DDS mono-therapy occurred during 1959 1988 which was 20-years after beginning of DDS mono-therapy, it is possible that the peak of relapse after MDT should occur in the next decades .

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Ch 284

A CLINICAL EFFECT OF THE REGIMEN COMBINED WITH DAPSONE, RIFAMPICIN AND OFLOXACIN

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Objective : To study the clinical effects of the regimen consisted of DDS, RFP and Ofloxacin.

Methods : 20 MB cases treated with the regimen and 26 MB cases treated with WHO MDT regimen were compared. In these two groups, WHO criteria in case selection and observation as well as effect judgement were excuted severely. All the treated cases were followed up for 5 years.

Results : The active skin lesions disappearing time in the treating group is similar to that of the comparison group The cure period averaged about 39 and 40 months in the treating and comparison groups respectively. There is no leprosy reaction in the treating group but there are 2 cases with leprosy reaction in the comparision group. BI declined averagely 0.78 and 0.76 annually in the two groups respectively and showed no statistical diference (P> 0. 05). Moreover, the treating group has less side effect than the comparison group.

Conclusion : The new regimen has similar effect to WHO MDT regimen but less side effects and good acceptance can effect the regimen to be spread out in the future,especially in the condition of lack of Clofazimine at the grass-roots level.

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Ch 387

DEPIGMENTATION - DELAYED SEQUELAE OF LAMPRENE THERAPY

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The development of depigmented lesions resembling vitiligo in those who had received chemotherapy with MDT was observed. Also it was noted that only those who received chemotherapy with MB MDT regimen presented with these kinds of lesions. The drug lamprene is the only component, which distinguishes the multidrug therapy of MB type from that of PB. Lamprene is a rimino-phenazine dye and is known to cause skin discoloration (pigmentation). The severity of this largely depends on the dose of lamprene and the degree of skin infiltration by leprosy. Discontinuance of the drug leads to clearance of most of the pigment within 6 - 12 months, athough traces may remain as long as 4 years or more. Could it be possible that the depigmentation observed is a delayed sequelae of lamprene therapy? The details of the observed cases will be presented.

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Ch 07

EFFICACY OF ROM IN PAUCIBACILLARY LEPROSY

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A total of 30 Paucibacillary leprosy patients (M 18, F 12) were included in this study, out of which 22 patients presented with single skin lesion and 8 patients had more than one lesion. The clinical profile of these patients and their response to ROM therapy was studied. The response to treatment was assessed using clinical scoring. Clinical classification of these patients were done (BT 27, TT 3) and their immunological status was determined using Mitsuda antigen (Lepromin positivity in 25, Negativity in 4, Not recorded in 2). 18 patients showed borderline tuberculoid histology, 7 tuberculoid and 4 indeterminate histology. AFB was present in the skin biopsies of 5 patients and absent in 25 patients. 4 patients showed clinically and histopathologically features of reversal reaction, and they responded well to corticosteroids. A repeat skin biopsy will be at end of 6 months. The histopathological features and the clinical findings of these patients with reference to the signs of activity and inactivity and the correlation will be discussed.

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Ch 45

SINGLE LESION LEPROSY TREATED WITH ROM - RELAPSING AS PB LEPROSY

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118 patients who had been inducted into a double blind controlled clinical trial comparing ROM treatment for single skin lesion leprosy with WHO recommended PB-MDT were followed up for a period of 36 months. 14 were lost to follow-up. Among the 104 remaining patients, we have noticed 3 non-responders to ROM therapy. The first case was put on 6 months PBMDT to which he responded, but presented with Type-I reaction like features at 36 months follow-up. The second patient was a 15-year-old female who was asymptomatic for 30 months following ROM therapy and then started noticing new patches appearing. Smears were negative. The third patient had deteriorated during the ROM trial; after decoding he was put on PB-MDT to which there was full clinical resolution. This patient presented with new hypopigmented patches in both lower limbs, trunk and face after three years. Since the ROM treatment has now become widely accepted, the authors feel it is important to keep in mind non-responders as mentioned above. The clinical significance of such findings and relevance to anti-leprosy programmes in the present context will be discussed.

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Ch 48

ROM VERSUS PB/MDT IN TREATING PB LEPROSY WITH 2-3 SKIN LESIONS

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51 patients with PB leprosy two to three skin lesions were included in this study. By random allocation 26 had ROM and the remaining had standard WHO PB/MDT. 30% of the patients were biopsied at intake after 6 months and after 2 years. Of these patients, 7 had ROM and d7 had WHO PB/MDT. Clinical improvement was seen in most of the patients in both groups. The histopathological picture showed that there was reduction in granuloma fraction in both categories of patients and bacterial clearance was also noticed in both the groups at the end of two years follow up.

This was part of a multi centric double blind randomised clinical trial which was undertaken to compare the efficacy of the single dose ROM regimen with that of the standard WHO PB/ MDT regimen in the treatment of PB leprosy patients with two to three skin lesions.

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Ch 52

SINGLE DOSE TREATMENT OF PAUCIBACILLARY LEPROSY - OBSERVATIONS ON LARGE LESIONS - A CASE REPORT

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A single dose treatment with Rifampicin (R), Ofloxacin (0) and Minocycline (M) combination (ROM-1) for single skin lesion (SSL) leprosy is being practised and initial experiences on efficacy and delayed clinical problems have been published. Such treatment in PB leprosy with 2-5 lesions is under trial and initial experiences show favourable outcome in terms of clinical regression and.

There is a need to make observations on large single lesions after ROM - 1 in view of apprehension in terms of clinical efficacy of ROM - 1. There is also speculation that relapses / reaction may result in large lesions after ROM - 1. Hence we proposed to make observations on cases of large lesions treated with ROM - 1 in a series of single lesion cases. We present a case report of regression noticed after ROM - 1.

Patient RK M/30 years presented with a hypo-pigmented patch with raised margins on left knee extending with pseudopodia to the medial and lateral side of knee. There was no nerve involvement. BI was negative. He was administered a single dose of ROM. Photographs were taken from various angles to note the course of the lesion during surveillance period in addition to the dimensions of the lesion charted out.

On subsequent follow-up after 6 months the borders were flattened and the lesions appeared faint in appearance and regressing well. The patient will be observed further periodically.

We conclude that one large lesions treated with ROM-1 regimen also show regression and behavior in a similar pattern as the clinical small size lesions. The other cases in the series also continue to show regression. However, longtime observations will be useful to study the course of the disease. 1

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Ch 56

CLINICAL FOLLOW-UP OF 2-5 SKIN LESION PB CASES TREATMENT WITH SINGLE DOSE ROM

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The present study included 31 PB Leprosy patients having only skin lesions (2-5 lesions) treated with single dose ROM under supervision. Clinical description of lesions in terms of number of lesions, hypo-pigmentation, skin thickness, sensory impairment was recorded initially and subsequently every month for 6 months and thereafter every 6 months.

The results of clinical follow up at the end of 6 months, 1 year and 1 and 1/2 years are given below :

Clinical Status Period of Follow up

6 months 1 year 1 and 1/2 years

Regressed 29 (93.5%) 21 (91.3%) 10 (90.9%)

Static 02 (6.5%) 02 (8.7%) 01(9.1%)

Progressed 00 00 00

No. of Patients 31 23 11

The results are comparable with the identical patients on MDT-PB indicating that PB patients with 2-5 skin lesions can be effectively treated with single dose ROM.

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Ch 76

ROM IN 1 - 3 LESION H.D.

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Paucibacillary MDT is very effective in PB leprosy. Recently WHO has introduced ROM IN Monolesion Leprosy. Even in PB upto 3 lesions ROM has been found to be equally rewarding. A comparison has been made to evaluate ROM V/S WHO PB MDT in 1-3 Lesions PB Hansen s Disease.

2,700 smear negative, normal nerve, fresh cases of PBHD in the age range of 15-60 (Male 1,500, Female 1,200) were randomized in 2 groups :

Group A : 1,350 Cases: ROM (Rifampicin 600 mg. Ofloxacin 400 mg,

Minocycline 100 mg), single dose, empty stomach.

Group B : 1,350 Cases: WHO PB MDT (Adult)G months.

Criteria for Cure :

Reduction in size, colour, infilteration, disappearance of lesions, improvement in sensation.

Grading : 3 to 0 (15 to 0 Score)

Follow-up : Monthly (6) then 6 monthly (5 years)

Drop-outs : Group A 14 (10%), Group - S : 7 (5%),

Cured Cases : A:1,309(98%), B:1,317(98%)

Relapse & side effects in Group A & B were equal.

ROM in PB Hansen s disease upto 3 lesions is comparable with traditional WHO PB MDT.

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Ch 93

A SINGLE DOSE SUPERVISED REGIME FOR PAUCIBACILLARY LEPROSY

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An ideal regimen for treating leprosy is supervised single dose therapy making it 100% patient-compliant with several operational advantages. In an effort to extend the scope of ROM regimen for single lesion leprosy, we compared the efficacy of standard WHO-MDT for paucibacillary leprosy (control group) with a regimen of rifampian 600 mg + sparfloxacin 400 mg + minocycline 100 mg + clarithromycin 1000 mg given as a single supervised dose. The patients selected had a maximum of 3 lesions which could include a single thickened nerve. The number of patients in each group was 15. A monthly evaluation for 6 months and then at 3-monthly intervals was done in respect to the size of the lesion, discoloration of skin, induration and sensory deficit and the improvement was graded over a score of 0-4 for each of these 4 parameters, 4 being the maximum improvement. Histopathological evaluation of skin lesions (in all patients) and nerves (66.6% patients) was done. At 12 months, the net % improvement in the study group was 66.9% while in the group receiving WHO-MDT-PB was 55.14% and the response was comparable statistically in both the groups ($P>0.05$). In the study group 66.70% patients showed a

marked improvement while 40% patients in the WHOMDT group showed a comparable response. This single dose treatment could have tremendous operational advantages as well as be more patient friendly.

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Ch 149

EFFICACY OF SINGLE DOSE ROM FOR SINGLE LESION PB LEPROSY

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AIMS AND OBJECTIVES : To evaluate the efficacy and safety of a combination of Rifampicin plus Ofloxacin plus Minocycline administered as a single dose for single lesion paucibacillary leprosy.

MATERIALS AND METHODS : 30 skin smear negative paucibacillary patients having only one skin lesion were treated with a single dose of ROM (rifampicin 600mg + ofloxacin 400mg + minocycline 100mg) after a complete clinical, histopathological and bacteriological evaluation. Patients were examined once every month for 6 months, then at the end of 12 months and 18 months. At the end of 18 months, complete clinical and histopathological examination was repeated.

RESULTS : Of the 26 patients who completed 18 months follow up, complete clinical cure was seen in 12(46%), marked clinical improvement was seen in 12(46%), and treatment failure was seen in 2(7%) patients. None of the patients had any significant adverse effects, or any signs of reaction. Before treatment, 20 out of the 26(77%) patients showed a granulomatous infiltrate on histopathological examination, while at the end of the study, 5 out of 26(19%) patients showed a granulomatous infiltrate. There was a definite reduction in granuloma fraction in all except one patient.

CONCLUSION : Single dose of ROM (rifampicin 600mg + ofloxacin 400mg + minocycline 100mg) is almost as effective as the standard WHO/PB/MDT for the treatment of single lesion PB leprosy. It is easily acceptable, cost effective, safe and easy to administer. It is particularly useful in patients whose follow up is not guaranteed.

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Ch 184

RELAPSE RATE IN SINGLE DOSE TREATMENT IN PAUCIBACILLARY LEPROSY

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A single dose treatment with rifampicin(R), ofloxacin(O) and minocycline(M) combination (ROM-1) in SSL-PB leprosy is being practised and initial experiences on efficacy and delayed clinical problems have been published by the authors. Such treatment in PB leprosy with 2-5 lesions [PB (2-5)] is under trial and initial experiences have been also reported by the same authors. Both these groups showed late clinical problems such as occurrence of new lesions, persistence of lesions and relapses in addition to reactions. There is a need to define and quantify delayed clinical problems in the field, which are to be diagnosed and managed as relapses or reactions and to interpret their significance in relation to patients who benefited from ROM - 1 in SSL-PB and PB (2-5) groups.

A treatment period cohort observation of ROM - 1 treated 620 SSL-PB and 282 PB (2-5) patients yielded 35 late clinical problems other than reactions. The period of follow up ranged from 6 months to 48 months. The mean period of follow-up is 2.4 years in SSL - PB and 2.1 years in PB (2-5) leprosy groups. 28 clinical problems were treated with a standard course of steroids out of whom 14(50%) showed good clinical response. 8 out of the remaining 14 who did not respond to steroids were diagnosed as relapses. The mean incubation period for these relapses is 2.4 years.

Relapse Rate in ROM - 1 treated PB leprosy

Events SSL - PB PB (2 -5) Total

No. of patients followed up 620 282 902

Person years follow-up 1480 600 2080

No. of patients with delayed 17(2.7%) 18(6.4%)* 35(4%) clinical problems (11.5/1000 py) (30/1000 py) (16.8/1000)

No. of patients relapsed 04 (0.64%) 04 (1.42%)** 08 (0.9%)

(2.7/1000 py) (6.7/1000 py) (3.8/1000 py)

* $p < 0.05$ ** $p > 0.05$

Continued on next page Overall 99% of the patients received the benefit of this single dose of treatment. This study showed that ROM single dose in patients with 1 to 5 lesions of PB leprosy group is quite effective and the delayed clinical problems could be managed in the field satisfactorily. The relapse rate is less than the rate in PB leprosy treated with WHO-MDT. This confirms of an observations on a smaller group made earlier.

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Ch 375

COMBINATION OF RIFAPENTINE-MOXIFLOXACIN-MINOCYCLINE (PMM) FOR THE TREATMENT OF LEPROSY

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Despite the great success of standard MDT regimens, newer regimens are required that are more efficient and operationally less demanding. One of the concerns with regard to MB regimen is that it is difficult to persuade patients to comply with the self-administered daily dapsone and clofazimine, which are required to ensure elimination of spontaneously occurring rifampin (RMP)-resistant mutants before stopping chemotherapy. Hence, resistance to RMP may develop among MB patients if the daily component is not taken regularly. The risk of resistance might be significantly reduced if a monthly administered, fully supervisable MDT regimen were developed, so that all of the components could be administered once monthly under supervision. The combination RMP-ofloxacin (OFLO)-minocycline (MINO), or ROM, is the first monthly administered, fully supervisable MDT regimen. However, compared with that of RMP, the bactericidal activities of both OFLO and MINO are rather weak; the combination OFLO-MINO (OM) was significantly less active than was RMP alone, and combination ROM was no more bactericidal than was RMP alone. To increase further the efficacy of a monthly administered, fully supervisable MDT regimen, it would be desirable to substitute more powerful bactericidal agents for the components of ROM.

The objectives of the experiment are to measure the bactericidal activities against M.leprae of various new drugs and combinations in mice, and to compare these with the activities of established drugs. Bactericidal activity was determined by proportional bactericidal technique in mouse footpad system. Administered in five daily doses of 100 mg/kg, HMR 3647 and clarithromycin killed, respectively, 90.0% and

74.9% of viable M.leprae, but the difference did not attain statistical significance between the two macrolides.Administered as a single dose, moxifloxacin (MXFX) 150 mg/kg killed 92.1% of viables, more bactericidal than OFLO in the same dosage and displayed the same level of activity as RMP in a dosage of 10 mg/kg; the combination MXFX-MINO (MM) was more bactericidal than OM; rifapentine (RPT) in a dosage of 10 mg/kg killed 99.6% of viable organisms, more bactericidal than RMP in the same dosage, and even more active than the combination ROM, which killed 95.0% of viables; the combination RPT-MXD(-MINO (PMM) killed 99.9% of viable bacilli, and was slightly more bactericidal than RPT alone, indicating that the combination PMM showed an additive effect against M. leprae. These promising results justify a clinical trial among lepromatous patients, in which the combination MM is being compared with OM, and PMM with ROM, in terms of efficacy and tolerance.

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Ch 388

A STUDY OF INCIDENCE OF RELAPSE IN MONOTHERAPY AND MULTI-DRUG TREATMENT

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The incidence of relapse rate in leprosy patients amongst those given monotherapy were campared with patients given Multi Drug Treatment. In Kolhapur District during 1990-95, 1998 patients were treated with monotherapy and during 1995-2000, 2557 patients were given Multi Druy Treatment. In patient treatment with monotherapy 59 (2.95%) showed relapse & only 4 (0.14%) patients showed relapse while on Multi Drug Treatment regimen.

It was also noted that conversion from infectious to non infectious occured in shorter period in Multi Drug Treatment compared to monotherapy also regularity is of paramount importance in preventing relapse.

In conclusion, relapse rate was very low & deformities reduced in Multi Drug Treatment if regular schedule is metaculously followed.

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Ch 44

CASE REPORTS OF RELAPSES AFTER MB-MDT Dr.(Mrs.)

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Multi-drug therapy was initiated in India in the early 1980s. Following this, thousands of leprosy patients

have been treated and released from treatment. Richardson Leprosy Hospital with a control area of 2.7 lakhs and a much larger catchment area has treated and released from control many thousands of cases. The numbers of relapse cases observed have been very low. Nonetheless, the rare reports of relapses which are highly bacilliferous are a cause for concern. While MDT has presumably reduced transmission within society, highly bacilliferous presentations of relapse cases have been observed by us. We report here four cases that relapsed. All patients received strictly supervised treatment. The first two cases received the standard 24 dose WHO recommended MB-MDT. One of them reported back 15 years after RFT with BL leprosy in Type-I reaction; the other reported with diffuse infiltration and one nodule on the abdomen with BI 4+ on the nodule. The third patient received closely monitored WHO recommended MB-MDT doses for over 5 years (prior to the fixed duration treatment era). After an intervening smear negative period of 9 years, he reported as a full-blown leproma. The last case had received 17 pulses of WHO recommended MB-MDT and had to discontinue treatment for side effects. He was consistently smear negative for 13 years but reported with unequivocal bacteriological relapse with one site reading BI = 4+.

Studies on relapse rates and risk of relapse have been done by many researchers. The concern that this paper raises is the risk that highly bacilliferous cases of relapse can pose for society in an age that is talking about the eradication of leprosy. The clinical and laboratory findings and subsequent clinical course of these cases will be detailed and discussed.

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Ch 54

RELAPSING MULTIBACILLARY LEPROSY - A NEW DIMENSION TO TRANSMISSION IN URBAN AREAS

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It is too well known that a bacterial disease cannot be eradicated by chemotherapy alone. Several factors still have to be considered in breaking the chain of transmission. Besides hidden untreated skin smear +ve cases, the contribution of patients relapsing with MB leprosy with +ve skin smears (irrespective of their classification) has not been adequately documented. Though relapses are few in relation to the number, this phenomenon brings a new dimension to the hidden aspects of transmission of leprosy, particularly in densely populated cities.

In our experience only one case relapsed 8 years after RFT out of 416 MB cases whose initial BI was more than 3+ and who were followed up for periods ranging from 5 to 13 years. (Table - 1) On the other hand, it is also true that sporadic relapses eluding attention keep reporting voluntarily, well beyond the specified surveillance periods posing a threat of transmission (Table - 2, Fig.l-9).

Table - 1. Relapses in relation to duration of follow-up

Treatment No. of Follow-up after RFT patients

5-8 9-12 13-16 years years years

FDT-24 76 43 26 7 FDT-12* 45 37 8

TOTAL 121 80 34 7

*FDT- Fixed Duration Therapy-1 patient has relapsed

Continued on next page Table - 2: Relapses in relation to mean duration

Treatment Number of Mean duration after relapses RFT

MDT >24# 12 11 1/12 years FDT - 24 5 9 4/5 years FDT - 12 1 8 years ROM - 1 2 2.10 years RO 3 3 years

Many patients in this group had received MDT for many years beyond the period of skin smear negativity (Some were on DDS monotherapy prior to MDT). Relapses seem to occur as indicated in the following schematic diagram.

Treatment period 24 months

1234567 1415

* Period of risk of relapses necessitating mop-up

s 12 mts

Short course Chemotheraphy

s* Unfortunately it is during this period that 1) there is a severe lack of field manpower and

2) patients are likely to be missed in highly urbanized. It is a paradox that at the most crucial stage after induction of the treatment, the programme loses its hold on the disease owing to reasons of logistics when the disease management demands serious attention and substantial financial support. If retrieval is not planned, one may never understand the course of this chronic disease and as a consequence, the very soul of leprosy work will be lost.

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Ch 66

RELAPSED AFTER NDT - AN EXPERIENCE IN WARDHA DISTRICT

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MDT was introduced in Wardha District in 1981 and till March 2000, 42,598 cases were treated with MDT and declared RFT. Among these cases, relapses were reported in some cases during the period of surveillance. Some more cases reported themselves after the period of surveillance. Thus, a total of 47 (1%) such relapsed cases were found during the period from 1981 to 2000. Reversal reaction was ruled out in all these cases.

In order to understand the profile of the relapsed cases, the 47 cases were analysed with regard to age, sex, type of leprosy, number of lesions, type of lesions, time interval between RFT and relapse, bacteriological status, etc.

Relapse was found both among paucibacillary and multibacillary cases. The majority of the relapse cases were from these with flat lesions. It may be observed that most of the relapsed cases were from the age group of 26 to 45 years at the time of re-registration. These was no case of relapse within 6 months after RFT and a significant proportion of cases relapsed between 6 and 12 months after RFT. It is important to note that nearly a third of the cases relapsed after 36 months and among them, PB and Mb cases were equal. This emphasises the need for a longer watch of the cured cases.

The paper presents detailed discussion on the above findings.

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Ch 75

MDT IN MB LEPROSY : EVALUATION OF 1 YEAR VERSUS 2 YEARS

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2 years MB MDT has changed global scenario of leprosy. Now it has been seen that as all living bacilli (AFB Leprae) are killed within one year of treatment MDT can be stopped at one year in MB HD. All dead bacillia are removed without treatment and BI becomes zero in due time even after stopping treatment at one year. There are many advantages of stopping the treatment at one year.

8,000 cases of MB Hansen s Disease were randomised in 2 groups :

Group A : 4000 cases WHO MDT for 2 years

Group B : 4000 cases : WHO MB MDT for 1 year

Drop-out : Group A : 50, Group B : 20

Completing T/T A : 3,950; B : 3,980

Cases were evaluated for clinical activities. Bacteriological Index & Morphological Index monthly, follow-up six monthly (A: 5 years, B : 6 years)

At the end of 2 yrs & 6 yrs, cure rates were comparable in both the groups. Relapse rate were equal in both the groups. Side effects were more in group A.

1 year WHO MB MDT in MB Leprosy is better than 2 years MB MDT.

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Ch 85

A STUDY OF RELAPSED CASES IN SEVAGRAM CONTROL UNIT

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Sevagram Leprosy Control Unit has been the first Control Unit in the country, started in 1952. Since then has treated a total of 2011 cases amongst which 62 (3.1%) cases have relapsed. All the cases that exhibited active signs after completion of prescribed treatment as per the particular regimen are treated as relapse on clinical grounds only.

In order to understand the profile of relapsed cases in the control unit, a retrospective analysis of the data of the last 48 years, i.e. since inception till 2000 has been conducted and the results presented in the paper.

The initial observation of the data shows that MDT has brought down the relapse rate from

3.6% to 1.2%, the relapse rates are less among children (2.2%) and females (2.3%). Among those relapsed over the period, 91.9% are from pre MDT era and 8.1% are from MDT era. The data also shows that 10.1% of the cases with 1.0 initial B.I. did relapse, whereas the relapse rate is lesser among the cases with 2+ and above, and still lesser among the -ve cases. The paper also intends to explore association if any, between the relapse and socioeconomic characteristics of the patients.

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Ch 182

PROFILE OF RELAPSES IN A SELF-DRAWN LEPROSY OUT-PATIENT CLINIC

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Dhoolpet Leprosy Research Centre is a self referred out-patient research clinic. Over a period of 20 years (1979-1999) 16,745 patients were registered for treatment in the clinic and given monotherapy until 1984 and WHO MDT thereafter. Only cases who had taken either prolonged monotherapy or adequate WHO MDT were considered. Multibacillary relapse was defined as a BI increase 2+. Paucibacillary relapse as new active lesions that were not reactional.

During this period, 14 male patients presented with new lesions. These patients records have been analyzed with regard to their classifications, past treatment and duration & nature of relapse.

Most of the patients were in the age group of 15-45 years; the duration of relapse was >2 years in 74% of the patients (AV 5.5 years). 8 patients (57%) of the patients had taken Dapsone monotherapy in the past; 4 patients (29%) relapsed after completion of a PB MDT course. A proportion of the patients relapsed after having had a combination of Monotherapy follow by either PB or MB MDT. About 1/3rd of the patients had irregular treatment prior to the relapse.

8 patients (57%) relapsed with an identical classification, 4 patients (29%) relapsed with upgrading disease whereas only two patients downgraded on relapse. Histological confirmation of relapse was available in 8 patients (57%). 6 patients who relapsed had a history of reactions (Type I & II) in the past and 5 patients had a reaction during the course of relapse. There were fewer neuritis in the relapsed patients.

We found few true PB relapses. Differentiation of relapse from reaction was frequently difficult. Prospective clinical and histoiogical studies of these post treatment episodes are needed to define diagnostic features and optimum clinical management.

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Ch 190

EVALUATION OF POST-RELEASED FROM CONTROL MULTI BACILLARY (RFC-MB) LEPROSY PATIENTS IN SATARA DISTRICT

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MDT Project was started in July 90 in Satara District. The prevalance rate of leprosy was 61/10,000 population at 1990 and P.R. is 3.2/10,000 population at Dec. 98. There are 2166 MB RFC patients in Satara District at present. Routinely RFC patients are not followed and we do not have knowledge about the present status of RFC patients and his family members.

Therefore, we have decided to evaluate the RFC patients by directly contacting them by NLEP staff, and to collect the information by questionnaire method. The questions considered disease status of patients, their contacts, health consciousness and health education amongst the RFC patients.

We have contacted 960 RFC patients and the study analysis shows that,

1] 99% patients are inactive & 1% RFC patients are having active lesions.

2] The healthy contact have developed PB/MB leprosy disease amongst 17% of family members.

3] RFC patients have received only 6% follow-up during post RFC period

INFERENCE :-1] Healthy contacts of MB patients having more risk of developing disease. Therefore healthy contacts of MB patients must be checked periodically.

2] MB patients should be followed yearly because 1% RFC patients have chance of active lesions.

3] Intensive health education should be given to patients and relatives during the treatment, surveillance and post RFC period which is inadequate.

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Ch 203

A LONG TERM FOLLOW-UP OF MULTIBACILLARY LEPROSY PATIENTS WITH HIGH

B.I. TREATED WITH WHO MULTI-BACILLARY REGIMEN FOR A FIXED DURATION OF TWO YEARS

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Forty six newly detected previously untreated MB patients with a BI 3 who received MDT for 2 years were followed up for a total duration of 424 person years and a mean duration of

9.26 ± 2.98 years. The BI of the patients continued to fall and all the patients, except one, reached skin smear negativity. MDT was well accepted and well tolerated.

Relapse which was defined as increase in the BI of 1+ or more with or without clinical evidence of activity was diagnosed in only one patient. He was started on a 2nd course of MDT to which he responded favourably. MDT for a fixed duration of two years for MB patients as recommended by WHO is vindicated.

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Ch 207

RISK FACTORS PREDISPOSING TO RELAPSE IN LEPROSY : RETROSPECTIVE ANALYSIS OF 78 MB AND 59PB CASES PRESENTING WITH RELAPSE

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A total of 78 MB and 59 PB cases of leprosy, presenting with relapse after the release from treatment, were analyzed with a view to find common risk factors if any associated with relapse. Only cases confirmed as relapses were included in this analysis. Factors analyzed were :

1. Pretreatment clinical presentation to include class and bacteriological status.

2. Type and duration of antileprosy and any other treatment received.

3. History of reaction and neuritis and its management.

4. Concurrent infection/s if any.

5. History of contact past and present.

Forty two (54%) of MB and 29 (49%) of PB cases, had received one of the WHO recomended regimen fixed duration multi drug therapy (FDT). Thirty (38%) MB cases and 25 (42.3%) PB cases had received DDS monotherapy prior to MDT or had extended (>2years) MDT (NON FDT). Six MB and five PB cases had received only monotherapy.Therefore majority of relapse cases were from FDT group. Another important finding was, 29 MB and 23 PB cases had received corticosteroids along with MDT. It was noted that cases receiving corticosteroids as well as FDT had a significantly lower incubation period of relapse (IPR). Combination of FDT and steroids, there was further lowering of IPR suggesting poor killing of M.leprae to be the cause of relapse in these cases. On relapse, eighty percent of MB cases and 48% of PB cases scored positive in the mouse foot pad test system, thus establishing the presence of viable M.leprae.

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Ch 331

THE EFFECTIVENESS OF WHO ONE-YEAR MULTI-DRUG THERAPY FOR MULTIBACILLARY LEPROSY

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The objective of the study was to identify the effectiveness of 1 year multidrug therapy (MDT) for multibacillary leprosy patients. The subjects enrolled in the study were leprosy patients, either with a positive bacteriological index (BI), or with a negative BI and more than 5 skin lesions. 49 new cases of leprosy were recruited from four skin clinics in Thailand between 1st January and 31st October, 1998. Each patient was given the MDT (MB) regimen for 12 doses within 18 months. The assessment before starting the treatment included clinical, bacteriological and histological findings. The primary outcome of the assessment at the end of treatment period was clinical inactivity. There were 41 cases who attended the study completely. Thirteen of these (31.7%) were clinically inactive at the end of treatment. All 32 positive BI cases showed a decrease in their bacteriological index. Also, 23 cases whose histological findings were reported showed resolving histology. There were 9 cases (21.9 %) with ENL, 10 cases (24.4 %) with RR and 12 cases (29.3 %) with neuritis. The authors need to follow up the study for a longer period in order to detect any cases of relapse or clinical improvement.

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Ch 339

EARLY DETECTION AND MANAGEMENT OF LEPROSY

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Leprosy is a common disease. In this study all patients attending the outpatient department of skin were examined. All the cases of skin discolouration nerve thickening, etc. were taken up for examination and out of a total number of 597 (five hundred ninty seven) cases, a total number of 48 (fourty eight) cases of leprosy detected. In this eight cases belong to SSL group, thirty two cases belong to TT group while only eight cases were of LL group. Period of this study was from June '97 to June 2000.

Management of these cases started immediately after detection of disease and supervisory dosage given according to M.D.T. schedule. Two cases of deformaties referred to higher institution for constructive surgery.

All of these patients were called for follow-up at monthly interval and every patient was cooperative enough with the author to take regular M.D.T. schedule. Combination of rehabilation therapy and occupational therapy were given so the patients could earn their own income and not remain dependent on others. Basic aim is that leprosy patient should have normal social life, proper health & education given.

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Ch 09

IS PENTOXIFYLLINE AN ALTERNATIVE DRUG IN THE TREATMENT OF ENL?

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This study (single blind controlled clinical trial) was undertaken to determine whether Pentoxifylline is an alternative therapy for the management of ENL reactions and to study the clinical response in BL and LL patients undergoing acute inflammatory re-actional episodes. According to present knowledge Pentoxifylline (PF) could be useful in ENL reaction because it interferes on the level of TNF factor-alfa and decreases leukocyte response to IL-I which are probably associated in the development of ENL reactions.

26 patients (22 M, 4 F) (22 LL, 4BL) suffering from ENL reactions who satisfied the criteria for inclusion and exclusion were randomly allocated to two groups. 13 patients received Prednisolone 30 mg/day and Pentoxifylline 400 mg tid and 13 patients received Prednisolone 30 mg/day and Placebo 1 tid. Both groups received the same dose (30 mg) of Prednisolone which was tapered over a period of four weeks. Pentoxifylline was prescribed for a period of four weeks. The same dosage schedule was followed for placebo group. MDT was continued without alteration in both the groups Clinical assessment was performed every two weeks for a period of three months. Response to treatment was assessed objectively with the predetermined clinical parameters and the intensity of the reaction was graded by allotting scores to the severity of the clinical manifestations of the reaction.

8 patients in the trial group needed additional corticosteroids and 10 in the placebo group received additionalsteroids to control reactional episode. The results are equivocol and will be discussed.

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Ch 34

A CRITICAL APPROACH FOR CHEMOTHERAPY IN LEPROSY

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Efficacy of the different therapeutic agents against leprosy bacillus (LB) is assessed either by the results of human trials or effects seen in the mouse footpads (MFP). Various exo-vivo or in vitro substitutes of the in vivo assay procedures have been developed. Essentially, all these methods aim at detecting viability of the leprosy bacilli. However, the greatest snag in most of these methods is an uncertainty that LB is growing in these test systems; if the LB could not grow and actively metabolise test substrates then differences between stationery LB and dead cultures of LB will become negligible and the results of antibiotic susceptibility unreliable. On the other hand, if it is assumed that the LB is growing in these in vitro test systems, then, their in vitro cultivation would also become possible, Unfortunately, it was not. Another limitation of such in vitro methods.is failure to take into account the copious production of arthrospores and blastospores by the LB, commonly considered as degenerate cells or non-descript coccoid bodies. Both of these influence antibiotic susceptibility of the LB.

The cultivation of LB in vitro has helped overcome the problems of such assay. Numerous nutritional, enzymological, biochemical, immunological (PGL-I, lepromin), antigenic tissues (mycolates), nucleic acids, molecular-biological characteristics, pathogenicity and all other criteria. had conclusively proved the total identity of the two.

There are some intrinsic limitations of drugs being effective against LB. This is primarily because of presence of blastospores of the LB. These can resist high doses of most of the drugs, and are capable of surviving within the host tissues for very long time as spores. Most drugs, therefore, in effect act as bacterio- (lepro-) static agents even if their general character is as a cidal agent with respect to vegetative cells of lepra bacilli and other bacteria. This explains rapid develop-

ment of drug-resistance with respect to most drugs used now, occurence of relapse and reversal reactions linked with bacterial growth. These findings inevitably lead to the conclusion that for effective/complete cure of leprosy, sporicidal drugs, singly or in combination should be used.

Present knowledge shows that there are not many successful sporicidal drugs; more over, the spores (blastospores) of LB have many unique characters : these can resist higher temperatures and very high gamma and UV radiations, suggesting that the LB-spore walls may be exceptionally impregnable to noxious agents. In a comparative study of pentavalent antimony viz-a-viz conventional antileprosy drugs, the former showed marked superiority. Results were based on MFP versus in vitro cultures.

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DISTRIBUTION AND RETENTON OF CLOFAZIMINE IN MICE

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Clofazimine (3-(p-chloroanilino)-(p-chlorophenyl)-2,10-dihydro-2-isopropyliminophenazine) is an antinycobacterial agent which has been in use since 1962 in the treatment of leprosy and it is administered orally at doses of up to 300 mg/d in the form of a microcrystailine suspension in an oil-detergent base. In the present study, distribution and deposition of clofazimine in mice has been investigated following administration of the drug with or without Isoniazid (p.o.) for a period of 15-30 days. Clofazimine was administered at a dose of 500 ug (equivalent to 20 mg/kg body weight).

Varions tissues (liver, spleen, lung, small intestine, heart, kidneys, muscle, mesentric fat, lymph nodes, foot pad and nerve) were analysed for clofazimine content. High levels were observed in tissues having reticulo-endothelial components (53 - 263 ug/g wet tissue). In other tissues, the levels were relatively lower. There was a significant amount of the drug in the foot pad and the pooled nerve tissue showed detectable amount of the drug. The pooled plasma presented drug levels of 0.5 - 0.8 ug/ml. Tissue levels were found to be increased with the duration of drug administration.

Simultaneous administration of isoniazid and clofazimine resulted in reduced levels of clofazimine in tissues like small intestine to different extents. The mechanism of the interaction remains unclear and needs to be investigated.

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MANAGEMENT OF TYPE II LEPROSY REACTION - A NEW APPROACH

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Type II reaction in leprosy is not uncommon these days. Traditional method of treating type II reaction in absence of Thalidomide is to continue MB MDT and start with 50 mg. Prednisolone and tapering gradually (every month by 10 mg). This may be good in some cases but most of the cases become worse with this treatment. Clofazimine 300 mg. daily for 1st month followed by 200 mg & 100 mg. in next 2 months along with same regimen of Prednisolone (no other ALT) has been shown to be very much effective in controlling episodes of reaction.100 cases of Type II lepra reaction were randomized in 2 groups.

A (50) MB MDT 1 year + Prednisolone 50 mg daily tapering (1 yr) by

10 mg every month.

B (50) Clofazimine (100 mg.)3 x 1 = 1 month, 2 x1 x1 month

1 x 1 = 1 month followed by routine MDT for 1 yr + Prednisolone as in group A

Clinical & bacteriological evaluation & cure criteria were as per WHO guidelines.

Recurrance of reaction

Group A - 40 (80%)

Group B - 5 (10%)

If routine WHO MB MDT is withheld for first 3 months and Clofazine with Prednisolone is given in high doses, reactions of leprosy are controlled in a better way.

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IMMUNOTHERAPY OF LEPROSY : ANALYSIS OF 8-10 YEARS FOLLOW-UP RESULTS

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During the recent years there have been radical changes in the therapy of leprosy. Advent of MDT has changed the outlook completely and from a life long treatment in BL/LL cases, we have reached the stage of fixed duration treatment. While overall results have been good, persisters and resultant relapses in a section of MB cases, persistent clinical activity in PB and continued high incidence rates indicate the need for improvement. With a view to improve the treatment in highly bacillated MB cases, we had initiated immunotherapy trials about 10-12 years back. Highly bacillated BL/LL cases were allocated to three gropus. To one group MDT and six monthly intradermal injections of Mycobacterium were administered. To the second group, MDT and BCG was administered using the same protocol whereas the third group received MDT & distilled water placebo and served as control. These patients were monitored clinically, bacterioiogically (BI, ATP, mouse foot pad) and histopathologically for histological changes as well as clearance of bacilli and granuloma. Analysis of data at different stages showed clear benefit in terms of enhanced killing and clearance of bacilli as well as faster granuloma clearance. These patients have completed 8-10 years of follow-up. Analysis of these results as well analysis of data from other groups show clear promise to the addition of immunotherapy to MB leprosy. PB cases treated with ultrashort regimens could be other candidates in which immunotherapy need to be tried and followed-up.

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MULTICENTRIC CLINICAL TRIAL OF PREDNISOLONE IN THE TREATMENT OF TYPE-1 REACTIONS IN LEPROSY

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Prednisolone has been widely used in the management of Type-l reactions in leprosy, but its dosage and duration have not been standardized. A randomized double blind controlled clinical trial with continuous enrolment of individuals was carried out in order to assess and compare the feasibility and therapeutic effects of three different regimens of corticosteroids: high dose, low dose and high dose short duration. The treatment duration was 5 months followed by 7 months of surveillance. Recovery of nerve function, recurrence of Type 1 reaction, requirements of additional steroids and long term assessment of physical disability due to Type-1 reaction were the outcome measures. This study was conducted in 6 centres in India and the enrolment of patients began in August 1997. A triple blind analysis revealed that there were no significant differences especially in terms of additional steroid requirements. There were no adverse side effects warranting withdrawal from the study. Detailed analysis and recommendations are given based on the study results.

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Ch 107

EFFICACY OF ROM THERAPY PLUS CONVIT VACCINE IN PB LEPROSY PATIENTS

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The recent WHO multicentric field study on the treatment of paucibacillary leprosy patients with single skin lesion (SSL) by single dose of ROM brought new hope to those who are engaged in the eradication of leprosy from India. Being encouraged by the WHO report, we undertook the present hospital based study. We found that SSL in the PB leprosy patients attending our hospital were morphologically and histopathologically heterogenous. The histological spectrum ranged from indeterminate through TT toBT leprosy and most patients had BT leprosy. This indicates that the field study of WHO is perhaps different from our hospital based study and hence it is not camparable. Ninty fresh untreated PB leprosy patients with SSL were included in the present study. Children, pregnant women,lactating mothers and patients with any thickening nerves were excluded from the study. All patients were bacteriologically negative but lepromin reactive. The patients were divided into two groups after proper matching for morphology and histological status of SSL. The test group included 60 patients and control group of 30 patients. The test group was given single dose of ROM at start and two injections of low dose Convit vaccine, one at the start and the other at the end of three months. The control group was given only single dose of ROM at the start. Both groups were clinically followed for six months and then retested for histological, bacteriological and lepromin status. Thereafter, they were followed monthly for another six months. In the test group, SSL resolved in 33.4%, regressed in 48.3% and remained active in 11.3% patients while granuloma disappeared in 70% cases. Only one case developed neuritis and in another patient, the disease relapsed. On the other hand, SSL in the control group resolved, regressed and remained active 13.3%, 63.3% and 23.3% cases respectively, while granuloma disappeared in 53.3% cases. In seven patients, the disease course went down hill; of them, two developed neuritis. Thus, the outcome of ROM plus vaccine therapy was marginally superior to that of ROM therapy alone.

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DOES CLOFAZAMINE PROTECT THE DNA DAMAGE INDUCTED BY DAPSONE?

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In the present experiment the clastogenic effects of antileprotic drugs (rifampicin, dapsone and clofazamine) used in multi drug therapy (MDT) were studied on mice bone marrow cells and spermatogenial cells. Seven groups of mice were administered with antileprotic drugs (separately and in combination) for 60 days. The dose and the combination of the drugs were selected on the basis of human dosage as recommended by WHO. The administration of drugs adopted the Continuous technique (WHO 1979). Except rifamipicin treatment in all other treatment groups, the incidence of chromosomal aberrations (CA) was significant ($p<0.01$) when compared with controls. Dapsone treatment resulted in higher incidence of CA when compared to the mice treated with rifampicin or clofazamine. The incidence of CA was rnore in combined drug treatment than in single drug treatment. Similarly R+D treatment resulted in more CA (27.4%) than R+D+C (18.7%) treatment. It is suggested that clofazomine counteract the effect caused by dapsone. It needs further study.

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MULTIPLE DOSE PHARMACOKINETICS OF CLOFAZIMINE

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Clofazimine (3-(pchloroanilino)- 10-(p-chlorophenyl)-2,10- dihydro- 2- isopropylimino phenazine) is an effective antileprosy drug. It is a part of the multi drug therapy (MDT) for leprosy and is given at a dose of 50 mg daily. Slow absorption, relatively much slower distribution and longer retention in selective tissues are significant features of clofazimine metabolism. Clinical and other experimental studies conducted at CJIL, Agra and other laboratories have suggested a not-so-linear relationship between the drug dosage and the plasma levels of the drug and so the therapeutic monitoring of clofazimine on the basis of plasma levels has not been possible. Further studies conducted in leprosy patients who attended the clinics of CJIL have thrown light on the multiple dose pharmacokinetics of clofazimine, With seven daily doses of 50 mg clofazimine the oral availability of the drug as defined by the area under plasma concentration - time curve (AUG 0-12 h)was 4.40 ug/ml.h while it was 6.8 ug/ml.h after fourteen daily doses. The basal plasma levels were 0.34, 0.52, 0.70 and 0.80 ug/ml respectively after 8, 15, 30 and 60 doses respectively. The peak plasma levels were obtained at &12 hours after drug intake. Limited studies on the urinary ercretion of clofazimine have shown that as much as

0.20 % of the daily dose of the drug was excreted in 24 h in unchanged form. Parallel studies on metabolic disposition of clofazimine in mice have showed that the drug accumulation attained saturation in tissues like fat where the drug remainer dissolved in the fat whereas the drug deposition still continued in other tissues where the drug is deposited as crystals. The findings of this ongoing study and their relevance in the treatment of patients with leprosy will be discussed at length.

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CHEMOTHERAPY OF LEPROSY IN MOROCCO

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After the development of MDT, we have actually entered the era of full-blown leprosy control, having the promising results of this regimen. However, along with the remarkable decrease in the prevalence rate, some anxious subjects have been discussed.

The most arguable point is the terms of chemotherapy; i.e. the current fixed duration of MDT or single dose of ROM without obligatory follow-up after the completion of chemotherapy. Another subject of concern is the definition of MB and PB. Insufficient treatment caused by the misdiagnosis may precipitate relapse.

Through the 3-year study of leprosy control in Morocco, we could learn another alternative strategy to conquer this disease. At present, the prevalence and incidence are well below the global target and we hardly imagine that leprosy was highly endemic in 1980 having the estimated prevalence of 0.75-1.5%. We will present the unique system of leprosy control that brought successful decline of new cases in this country.

The most unique point of Moroccan system is the combination of short-term intensive regimen and sub-