OT&T 6

REVIEW OF KNOWLEDGE AND SKILLS OF TRAINED HEALTH WORKERS IN THE CENTRAL REGION OF NEPAL

Madan Ghimire, Jonathan Quimpo; Gopal Pokhrel, Uddhav Raj Pant, Ram Babu Bista, Kapil Dev Neupane and Rewati Timilsina.

Anandaban Leprosy Hospital, PO Box 151, Kathmandu, NEPAL. E-mail: anandaban@mail.com.np

The Leprosy Mission-Nepal provides training to Basic Health Services (BHS) staff of Nepal's Central Region (CR) using a standard curriculum-based course (CLT-B) and a refresher (CLT-R). A systematic post-training evaluation using a standardised checklist was used from July 2000.

Aim: To assess the levels of post-training core knowledge and skills of BHS staff trained at the Training Centre at Anandaban Leprosy Hospital.

Methods: A post-training evaluation was done in selected Central Region districts, using the same standardized post-training checklist, enrolling a total of 150 staff. Knowledge was assessed by interview and skills by demonstration of procedures. Analysis was done using Epi Info 2000.

Results: Knowledge and skills were correlated with 3 variables: (a) years interval between training and evaluation (1 - 8 yrs); (b) whether they dealt directly with patients post-training (DP+) or not (DP-); and, (c) whether they had CLT-R (R+) or not (R-). Results suggest a decrease in knowledge and skills as the time interval widened (knowledge: 1 yr. (A)= 50% to 8 yrs (H)= 14.3% (p= 0.53)); skills: A= 20% to H= 7% (p= 0.38)). Those dealing with patients appeared to do better (knowledge DP+= 38%, DP-= 20% (p= 0.13); skills: DP+= 17%, DP-= 3% (p= 0.32)). Those who had CLT-R appeared to do better (knowledge: R+= 47%, R-= 30% (p= 0.18); skills: R+= 12%, R-= 4% (p= 0.12)).

Conclusions: This study will help in the planning of future courses, with particular attention to the need, content, timing of refreshers, and the qualifications of participants for each course batch

OT&T 7

TRAINING IN CHANGING CIRCUMSTANCES:

S.A.R. Krishnan

All Africa Leprosy, Tuberculosis and Rehabilitation Centre. ALERT, P.O.Box 165, Addis Ababa, Ethiopia.

All Africa Leprosy Tuberculosis and Rehabilitation Training Centre (ALERT) initiated Leprosy teaching and training during the early 70's to develop manpower to fight against Leprosy in Africa and the rest of endemic countries in the world. Since then many changes in training have taken place at ALERT.

The aim of this study on "Training in changing circumstances" is to observe changes, made in various training related issues by using Alert's annual international training calendar from 1991 till date, statistics on International and National trainee weeks, changes made in training programmes which were offered by ALERT in the past and to plan future training.

The results of the study shows significant changes made in international and national courses, increased the number of trainees weeks in all structured international courses, gradual decrease in all international in service training programmes and a very significant increase of participants in national courses etc. The study relates the present institutional changes in order to challenge and take advantage of the changing circumstances and to improve the international training within and outside ALERT

TREATMENT

OT 1

A COMPARISON OF 12 AND 24-MONTH MDT/WHO REGIMENS WITH MULTIBACILLARY LEPROSY PATIENTS

Sales, A.M.; Sabroza, P.C.; Nery, J.A.C.; Duppre, N.C.; Fialho, M.B.; Gallo, M.E.N.; Sarno, E.N.

Leprosy Laboratory, Oswaldo Cruz Foundation, Rio de Janeiro, R. J., Brazil.

Introduction: The adoption as of 1982 of a standard, fixed-duration, multidrug therapy regimen under the recommendation of the World Health Organization (MDT/WHO) requiring 24 consecutive monthly doses of MDT followed by patient discharge regardless of Bacteriologic Index (BI) was a landmark step in controlling leprosy worldwide. Over time, however, it was seen that duration of treatment proved to be an obstacle for the public health care sector. Short treatment regimens allow for easier patient compliance and, perhaps even more importantly, facilitate the implementation and sustainability of national leprosy programs. Based on a growing body of evidence, in 1998, WHO recommended that MDT be

reduced for multibacillary (MB) leprosy patients to 12 instead of 24 monthly doses.

Objective: To ascertain and compare the bacillary load, grade of disability, and frequency of reactions of a group of MB patients who received 12 monthly doses of MDT to a group who received the full 24-dose regimen and compare both at both the end of one year and the end of two years.

Material and Methods: 213 MB patients who began MDT between 1995 and 2000 were evaluated. Eighty-five patients received the full 24-dose regimen while 128 received treatment for 12 months. The latter group was then examined at the end of the following year. All patients were submitted to clinical and dermatological examinations at the beginning of treatment and at the end of the 12 and 24-month periods, at which time grade of disability and BI were also determined.

Results: At the end of 24 months, the rate of BI decline was almost identical for both groups. Moreover, reactional episode frequency was not significantly different between the two groups.

Conclusion: A reduction in treatment from 24 to 12 monthly doses of MDT did not prejudice BI status in that it similarly declined in both groups of MB patients, and the frequency rate of reactional episodes remained stable.

OT 2

ANTILEPROSY ACTIVITY OF SOME DERIVATIVES OF DITHIOCARBAMATE

G. Urlyapova, A.D. Daudova

Leprosy Research Institute, Astrakhan, Russian Federation

Despite effective antileprosy drugs available and success of multidrug therapy, searches for new drugs with potent antimycobacterial activity remain to be continued. In mice, experimentally infected with *M. leprae* according to Shepard's method, compounds belonging to a group of dithiocarbamates were investigated for their antileprosy activity. Untreated animals were taken as controls, and DDS as a drug of comparison. Test compounds were introduced per os via probe at doses of 10 and 30 mg/kg five times a week. Mice were sacrified in 7,5 months after inoculation. *M. leprae* counts in soft tissues of foot pads (C.C.Shepard, D.H.McRae, 1968) were (3,91 0,33) $\times$ 10^5 in control animals, (0,27 0,07) $\times$ 10^5 in mice taken dapsone at 10 mg/kg and (0,22 0,04) $\times$ 10^5 in mice received 30 mg/kg, the difference being statistically significant ($p<0,01$). Amount of *M. leprae* in soft tissues of foot pads from animals received compound 1 10026127 at a dose of 10 mg/kg equaled (0,56 0,11) $\times$ 10^5. With 3-fold increase of the dose of the compound average number of mycobacterial cells decrease ten times, and mycobacterial population counted (0,06 0,01) $\times$ 10^5 ($P<0,01$). In mice administered compound 1 10026068 at a dose of 10 mg/kg the number of *M. leprae* was significantly less than in control animals (0,83 0,15) $\times$ 10^5 ($p<0,01$) but higher than in animals introduced dapsone and compound 1 10026127. Three times increase of the dose did not result in decrease of *M. leprae* amount at the site of inoculation (0,77 0,1) $\times$ 10^5. Average number of mycobacteria in foot pads of mice received compound 1 9926126 at a dose of 10 mg/kg was (2,13 0,28) $\times$ 10^5 and at a dose of 30 mg/kg – (1,83 0,2) $\times$ 10^5, being significantly less than in control group ($p<0,01$) but more than in animals received other compounds and dapsone. Thus, the data obtained suggest good prospects of further study of the above compound for antileprosy activity. Among test compounds belonging to dithiocarbamates 110026127 showed the highest activity to inhibit mycobacterial growth.

OT 3

AVALIAÇÃO DA SEGURANÇA, EFICÁCIA E COMPARAÇÃO DE DOSES DE TALIDOMIDA, ADMINISTRADA POR DUAS SEMANAS NO TRATAMENTO DO ERITEMA NODOSO DA HANSENÍASE (ENH)

Gerson Oliveira Penna: Celina M.T. Martelli; Mariane Stefani and Vanize de Oliveira Macedo

Universidade de Brasília em parceria com a Universidade Federal de Goiás com apoio da Celgene Corporatio

Os autores apresentarão e discutirão o protocolo da investigação, aprovado pelo Comitê Nacional de Ética em Pesquisa (CONEP) do Ministério da Saúde, que está sendo desenvolvido em Goiânia e Manaus. Serão enfatizados na discussão os critérios de inclusão, de exclusão, as vantagens do uso da talidomidy em detrimento dos corticosteróides, e sobretudo as perguntas que se buscam responder a partir desse protocolo.

OT 4

CLINICAL PROFILE OF PATIENTS EXHIBITING DRUG RESISTANCE TO MDT DRUGS

Geetha S. Rao, Gift Norman, Gigi J. Ebenezer, Sheela Daniel, P.S.S. Rao

Schieffelin Leprosy Research and Training Center, Karigiri, India

The multidrug therapy (MDT) recommended by the World Health Organization for the treatment of leprosy was designed to prevent emergence of drug resistance, while providing shortened and affordable

treatment required in developing countries. Emergence of drug resistant strains of Mycobacterium leprae could undermine current gains toward global elimination of leprosy. Twenty years after MDT has been in use, there is very little information on the profile of resistance to drugs used in the present MDT regimen. The Schieffelin Leprosy Research and Training Centre (SLRTC), Karigiri has carried out comprehensive leprosy control activities in an entire Taluk (Gudiyatham) since 1955. The institution has facilities to study drug resistance using mouse footpad inoculation (MFP). It receives skin specimens not only from the control area, but from other institutions as well. In a period 1988 - 1998, 122 biopsies from patients belonging to the control area were sent for drug resistance studies using MFP. Of the 122 biopsies 21 (17%) showed drug resistant strains. Of these, 10 (47.6%) were resistant to Dapsone alone and 2 (9.5%) were resistant to Clofazimine alone and 2 (9.5%) to Rifamipicin alone. Five patients (23.8%) were resistant to both Dapsone and Clofazimine and 1 (4.8%) to Rifamipicin and Clofazimine and 1 (4.8%) to Rifampicin and Dapsone. Of the 21 showing drug resistant strains, 9 (42.9%) exhibited primary drug resistance and 12 (57.1%) secondary resistant strains. The demographic information, treatment history and current clinical status of the above patients will be presented.

OT 5

COMBINED 12 MONTHS WHO MDT MB REGIMEN AND *MYCOBACTERIUM w* VACCINE IN MULTIBACILLARY LEPROSY: A FOLLOW UP OF 136 PATIENTS

Bhushan Kumar, Inderjeet Kaur, Sunil Dogra and B. D. Radotra Department of Dermatology, Venereology & Leprology and Department of Pathology*

Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India.

Multidrug therapy (MDT) was introduced in the treatment of leprosy in 1980s which lead to a significant change in leprosy scenario at the global level. The success with MDT administered to the MB patients has encouraged leprosy experts to shorten the regimen from 24 months to 12 months. One hundred and thirty six multibacillary patients having BI ≥2 treated with WHO MDT MBR (12 months) on regular follow up were included in the study. Clinical assessment and slit skin smears were carried out in all the patients. At the baseline 69% patients had BI of >3. All patients were also given 4 doses of Mw vaccine at 3 monthly intervals. All patients showed excellent clinical response. A large proportion of patients, 39/42 (92.8%) with BI of ≤3 had become smear negative, whereas, only 10/36 (27.7%) patients with BI between 3.1- 4 and 5/58 (8.6%) highly bacillated patients having initial BI of > 4 had become smear negative at the end of 2 years follow up. Thirty four percent of all reactional episodes and 27% of all nerve function impairments developed in the follow up period after stopping MDT. Relapse rate was 0.36/100 PYAR at 2 years and 1.38/100 PYAR at the end of 3 years follow up. All 4 relapses occurred in patients having initial BI of > 4. All the relapsed patients responded to the retreatment with the same drug combination. Dapsone hypersensitivity, induced urticaria and flu like syndrome were noted in 5, 3 and 1 patients respectively. Although the results of this limited period follow up are satisfactory, a long term follow up in larger number of patients will settle the issue of safety and efficacy of shortened MDT MB regimen and the place of immunotherapy with Mw vaccine in multibacillary patients

OT 6

CYCLOSPORIN A (CYA) PHARMACOKINETICS IN ETHIOPIAN AND NEPALI PATIENTS WITH LEPROSY TYPE 1 REACTIONS (T1R).

Sharon N.S. Marlowe, Terence D. Lee, Atholl Johnston, Diana N.J. Lockwood, David W. Holt

Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel, Street, London, WC1E 7HT, United Kingdom.

St George's Hospital Medical School, London, SW17 0RE

Background: Levels of cyclosporin A (CyA) show high inter-and intra-subject variability as a result of poor oral absorption and also its hepatic metabolism.

Genetic variation and the ability to metabolise CyA differently have been noted in some ethnic groups, but the pharmacokinetics of all ethnicities has not been elucidated.

Aims: To assess inter- and intra- subject variability. To assess the pharmacokinetics of CyA in leprosy Type 1 reaction (T1R) patients. To determine an appropriate dose of CyA to be used. To identify any ethnic variation.

Study: 10 Ethiopian and 10 Nepali patients with severe T1R were recruited. All patients were started on CyA (Indian generic formulation) at 5mg/kg/day. 2 mls blood was taken at intervals (0, 0.5, 1.0, 2.0 2.5, 3.0, 4.0, 5.0, 6.0, 8.0, 12 hours) after the first CyA dose.

Analysis: Concentration of CyA was assayed by liquid –chromatography tandem mass spectrometry. The maximum whole blood concentration (C_{max}) and time of its occurrence (t_{max}) was plotted graphically and the area under the curve (AUC) calculated.

Results: The cyclosporine C_{max} ranged between 328 and 1734μg/L, the t_{max} varied between 1 and 6 hours and the AUC between 1831 and 9704μg/L.h. The

mean C_{max}, 935μg/L and AUC, 5000μg/L.h, and median t_{max}, 2.5h, were similar to those seen in transplant patients at a dose of 5mg/kg. Although variability was high, again it was similar to that of transplant patients immediately following the first dose.

Conclusions: In this small number of Ethiopian and Nepali patients with leprosy T1R, cyclosporin pharmacokinetics are not markedly different from those seen in transplant patients.

OT 7

DAPSONE HYPERSENSITIVITY SYNDROME: SYSTEMATIC REVIEW OF DIAGNOSTIC CRITERIA

Graziela Leta; M Esther dos Santos, M Leide Oliveira.; M Katia Gomes

Federal University of Rio de Janeiro

The awareness of pharmacovigillance is increasing, even in undeveloped countries. In this context, the Dapsone Hypersensitivity Syndrome (DHS), an unusual but potentially serious side effect of dapsone (DDS) which is used in large scale for leprosy treatment, must be considered. Still, there is a consensus about the drug safety. In order to ascertain the diagnosis criteria, a world literature systematic review was done analysing reports from fifteen endemic countries since 1956 to 2001. The authors found 108 reported cases, 96.2 % occurred after 1980. From those, 57.4 % presented complete DHS symptoms - fever, rash, lymphadenopathy, and hepatitis - and 42.6 %, expressed an incomplete form. Fatal outcomes were 12.96 % of the total. An intriguing point is the 9.6% rate of mortality within the group which fulfills the criteria of complete DHS (6/62 patients) and the fact that no statistical association to death or hepatic injury can be attributed. This may express the poor quality of the information collected and reinforces the importance of its reliability.

OT 8

DOUBLE RELAPSE AFTER TREATMENT WITH RIFAMPICIN-CONTAINING MULTIDRUG REGIMENS AMONG MULTIBACILLARY LEPROSY PATIENTS

Samba O. Sow, Abdoulaye Fomba, Issa Traore, Augustin Geudenon, Pierre Bobin, Jacques Grosset, Baohong Ji

Centre National d'Appui à la lutte contre la Maladie du Mali (CNAM), BP 251, BAMAKO, MALI

We present herewith 12 cases of multibacillary (MB) leprosy who had relapsed twice after treatment with various rifampicin (RMP)-containing multidrug regimens. Because these patients were derived from different cohorts, it is difficult to define the denominator for calculating the frequency of double relapse.

Relapse was defined as followings: i) occurrence of definite new skin lesions and/or reactivation of pre-existing lesions; and ii) the bacterial index (BI) at any single site was found to have increased by at least 2+ over the previous value, or the new lesions had a BI greater than that in any pre-existing but non-reactivated lesions.

The durations of the first treatment with RMP-containing multidrug regimens ranged from a single dose to 2 ± 4 months. Patients began treatment with a mean BI of 4.2 ± 1.0. At the end of treatment, despite none of the 12 cases were BI negative, the BI continued to decline after stopping treatment and became negative in 9 cases after 5 ± 3 years of follow up. The first relapse occurred 6 ± 3 years after completion of treatment. The major clinical signs of relapse were occurrence of macules in 2 cases, diffuse infiltration in 4 cases, nodules and/or lepromas in 6 cases; with a mean BI of 4.1 ± 1.2. All relapses have been confirmed by histopathology, and viable *M. leprae* were demonstrated from skin biopsies of 10 cases by mouse foot pad inoculation; drug susceptibility test indicated that all 10 strains of *M. leprae* remained susceptible to RMP. All relapsed cases were retreated with WHO/MDT regimen for 24 months, and administration of the monthly doses was supervised at our institute. At the end of 24 months of treatment, none of the 12 cases were BI negative, but after 4 ± 2 years of follow-up, 8 of them became BI negative.

The second relapse occurred at 6 ± 1.5 years after stopping treatment with WHO/MDT. The major clinical signs of relapse were macules in 3 cases, nodules and/or lepromas in 9 cases, with a mean BI of 4.3 ± 0.9. Again all relapses were confirmed by histopathology, and viable *M. leprae* were demonstrated in skin biopsies of 8 cases by mouse foot pad inoculation; all 8 strains of *M. leprae* remained susceptible to RMP. After the second relapse, all these patients were treated with another course of MDT for 24 months; they are being followed-up, and so far without any sign of relapse.

The results clearly confirmed our earlier findings that MB relapse does exist, and in certain patients, they may even relapse more than once. The results also clearly indicate that after treatment with any RMP-containing regimen, the average incubation period of MB relapse is at least five years after stopping treatment; therefore, attempt to detect individual relapsed case and to define the magnitude of MB relapse, patients must be followed up with a minimum duration of five years after stopping treatment.

OT 9

DRUG RESISTANCE IN THE TREATMENT OF LEPROSY -STUDY IN THE RELAPSED CASES FOUND IN SANATORIA

Masako Namisato; Mamoru Matsubayashi; Masaaki Higashi; Motoaki Ozaki; Masanori Matsuoka; Yoshiko Kashiwabara and Hideoki Ogawa

National Sanatorium Kuryu-Rakusenen 647, Kusatsu-machi, Gunman-ken, 377*L*-1711, Japan

Amagasaki Prefectural Hospital

Leprosy Research Center, National Institute of Infectious Diseases

Department of Dermatology, Juntendo University School of Medicine

We studied 14 relapsed cases of leprosy that have once cured with various anti-leprosy drugs. Genomic DNA was prepared with *M. leprae* isolates harvested from skin biopsy samples. Mutations of genes involved in resistance to DDS, RFN and OFLX were examined. Mutations related to DDS-resistance were found in 9 out of 11 cases, the same to RFP were found in 9 out of 11, and the same to OFLX were found in 2 out of 3. Seven cases had mutations related to 2 or 3 drugs. In many cases, these drugs were given with small dosage. No mutation was found in the cases without history of administration of particular drug(s). The method used in this study is considered to be a trustable and effective to find drug-resistance. Application of simple molecular tests to assess the drug-related mutations in *M. leprae* may offer another strategy to the leprosy control in the endemic areas where the decrease in the new case incidence has not been apparent. (This work was supported by an Emerging and Remerging Infectious Disease Promotion grant from the Ministry of Health, Welfare and Labor in Japan.)

OT 10

EFICACIA DE LA PENTOXIFILINA COMO COADYUVANTE TERAPÉUTICO DE LAS VASCULITIS NECROTIZANTES EN REACCIONES REVERSALES (T1)

Giménez, Manuel F.

Centro Dermatológico. Ameghino 1205. (CP 3500) Resistencia- Chaco Argentina.

Dentro de los episodios reaccionales (ER), la reacción Tipo1 conocidad con las denominaciones de reacción reversal(RR), reacción de reversa, reacciones limítrofes ó reacción dimorfa; predomina en enfermos de lepra dimorfa o borderline, usualmente ¨upgrading¨; causadas por un incremento de la inmunidad mediada por células (CD4 activadas, elevación de IL2, y aumento de IFNã y del Factor de necrosis tumoral alfa(FNTá). Clínicamente se expresa por edemas acrales, infiltración de lesiones, aparición de lesiones nuevas, neuritis, neuralgias, disestesias y vasculitis necrotizantes.El daño neural se debe al edema, la infiltración del axón por el granuloma la trombosis de los vasa-nervorum y la fibrosis post-inflamatoria.

El tratamiento convencional es continuar con la Poliquimioterapia (PQT) si aún no completó el esquema OMS, agregar precozmente corticosteroides y se han ensayado aumentar la dosis de clofazimina, también inmunosupresores (azatioprina) y ciclosporina A. La pentoxifilina (Ptx) se ha usado con éxito en la Reacción tipo 2 ENL y en el fenómeno de Lucio en Lepras difusas.

Nosotros realizamos el tratamiento asociado de corticosteroides y Ptx en cuadros de severas vasculitis necrotizantes que aparecieron en el curso de reacciones reversales en lepras dimorfas y que no cicatrizaban con el uso convencional y prolongado de corticosteroides. Presentamos tres pacientes en los que utilizamos una dosis de 1200 mg.diarios con una mejoría evidenciable en la cicatrización de las ulceras en las primeras 4 semanas de tratamiento. Paralelamente se observó un mejoramiento de la neuralgia. Los efectos inmunopatológicos de la Ptx justifican su uso en éstos cuadros

OT 11

ENSAIO TERAPÊUTICO: AVALIAÇÃO DA ASSOCIAÇÃO DE OFLOXACINA COM RIFAMPICINA POR 28 DIAS EM PACIENTE DE HANSENÍASE VIRCHOVIANA.

João Carlos Regazzi Avelleira, Larissa Mitraud Alves, Francisco Reis Vianna, Alfredo Marques Boechat, Raul Negrão Fleury

Instituto Estadual de Dermatologia Sanitária do Rio de Janeiro.

Introdução: O esquema poliquimioterápico (PQT/OMS) representou notável progresso na luta contra o *M. leprae*. Entretanto, novas drogas continuam sendo testadas, com o objetivo de aumentar a eficácia destes esquemas, e diminuir o tempo de tratamento. As quinolonas são derivadas do ácido nalidíxico, que tiveram atividade antibacteriana aumentada com a introdução de um átomo de flúor no anel quinoleico. Agem inibindo a enzima responsável pelo enovelamento do DNA bacteriano. A quinolona com melhores resultados contra o *M.leprae*, foi a Ofloxacina.

Material e métodos: Paciente do sexo masculino, de 54 anos, que apresentava quadro clínico compatível com Hanseníase Virchoviana: face e pavilhões auriculares infiltrados, madarose, tubérculos disseminados, extremidades edemaciadas e com sensibilidade diminuída. A hipótese de Hanseníase foi confirmada

pela baciloscopia positiva e histopatologia. Em regime hospitalar o paciente foi tratado por 28 dias com 400 mg de ofloxacina, e 600 mg de Rifampicina em dose diária supervisionada. Recebeu alta e passou a ser observado pela clinica, histopatologia e baciloscopicamente por um período de 2 anos, sem nenhuma medicação específica. Foi posteriormente foi introduzido no esquema PQT/MB/OMS.

Resultados: A evolução do paciente mostrou, gradativa desinfiltração do tegumento, redução do tamanho e número dos tubérculos, acompanhado de baciloscopia decrescente, após a suspensão do tratamento, enquanto o índice morfológico mostrava ausência de bacilos íntegros.

Comentários: O esquema Ofloxacina e Rifampicina mostrou ação eficaz contra o *M.leprae*, apontando a possibilidade de que a associação entre as duas drogas possa potencializar a poliquimioterapia antihansenica

OT 12

LEPROSY PATIENTS DESERVE A PROPER FOLLOW-UP!

Ben Naafs

Dept. Dermatology Leiden University Medical Centre (LUMC) and IJsselmeerziekenhuizen Emmeloord/Lelystad, The Netherlands; Instituto Lauro de Souza Lima (ILSL) Bauru SP Brazil; the Regional Dermatology Training Centre (RDTC) Moshi, Tanzania; c/o Gracht 15 8485 KIN Munnekeburen, The Netherlands

During a recent GAEL meeting it was proposed to treat all leprosy patients, independent of classification, with six months MB-MDT. It was suggested to hand out blister packs for six months at the time of diagnosis, cautioning the patient to report back when complications occur. From public health point of view it is essential that infectious leprosy patients are made non-infectious. The presently proposed treatment will certainly do so in over 95% of the patients, thus satisfying i nfectiologists.

Nerve damage and as consequence deformities lead to the leprosy stigmata. In over 30% of the patients this damage will occur during and even after the proposed new treatment regime. The patient will be disappointed and the reputation of the leprosy control program damaged. However adequate treatment could have been instigated, provided a careful follow-up was available. To neglect such a follow-up and to believe that a patient after only one contact with the health worker will report back in time is at least naive. Simple methods of follow-up which can be handled by the peripheral health worker and which can detect early and treatable damage are available. In this presentation these will be presented.

OT 13

MANAGEMENT OF REACTIONS IN LEPROSY

Ben Naafs

Dept. Dermatology Leiden University Medical Centre (LUMC) and IJsselmeerziekenhuizen Emmeloord/Lelystad, The Netherlands; Instituto Lauro de Souza Lima (ILSL) Bauru SP Brazil; the Regional Dermatology Training Centre (RDTC) Moshi, Tanzania; c/o Gracht 15 8485 KN Munnekeburen, The Netherlands

Nerve damage leadingto impairments is still the major problem in the course of a leprosy infection. Were it not for this damage, leprosy would be a rather innocuous skin disease, whereas even today it is one of the most feared diseases, often associated with social repercussions. Since there is no change in the number of detected cases and if any, it is an increase, leprosy will remain one of the main causes of peripheral nerve damage. Nerve damage may occur before anti mycobacterial treatment, during treatment and even in patients released from treatment.

In borderline leprosy (BT, BB and BL) such damage usually develops during a so-called reversal reaction (RR), type I leprosy reaction. When this happens, the peripheral nerve trunks at specific sites may become swollen and tender and may show deterioration of function, which is generally rather gradual, taking weeks or even months to become irreversible. Occasionally, severe nerve damage may occur overnight.

In lepromatous leprosy (BL, LLs and LLp) the damage may take years to develop or may increase suddenly during a reactional episode, called erythema nodosum leprosum (ENL), type II leprosy reaction. Since lepromatous leprosy is a generalised disease other organs may be involved as well, skin, joints, lymphnodes, eyes, testicles, liver and kidney. The patient can be extremely ill and the reaction may become chronic.

Reactions must be diagnosed early and treated appropriately if permanent disability is to be avoided. Ideally the reactions should not occur at all, being prevented by treatment. To achieve this, it is of utmost importance to understand the mechanisms behind reactional states and principles of management. This will be discussed, taking the latest developments in account

OT 14

OFLOXACIN BASED REGIMENS IN LEPROSY – LONG-TERM OBSERVATIONS

R. Ganapati, V.V. Pai, C.R. Revankar, H.O. Bulchand and S. Kingsley

Bombay Leprosy Project, Sion-Chunabhatti, Mumbai – 400 022, India

The inclusion of Ofloxacin in regimens in leprosy for research trials (RO and ROM) and recommendation of ROM as a single dose for the treatment of PB Single Skin Lesion Therapy (SSL-PB) formed a landmark in the chemotherapy of leprosy.

Table I – ROM single dose for PB leprosy

Group	Fl.up in Months	Occurrence of clinical problems * after ROM treatment						
		0	12	24	36	48	60	72
SSL-PB	Total cases	843	635	479	352	208	75	11
	Problem cases	0	6	10	8	3	1	0
2-5 PB	Total cases	347	286	222	131	55	6	0
	Problem cases	0	16	9	6	1	1	0

* These do not include reactions, which formed 4% in SSL – PB and 7% in 2 – 5 PB cases.

The pattern of clinical problems in the two groups indicates lack of any correlation between the problems encountered and the chemotherapy interventions adopted. All clinical problems including reactions are manageable. Relapse rate is less than the reported rates with PB-MDT.

Table II – Reaction rate in patients receiving intermittent ROM therapy for varying durations.

TYPE	ROM – Intermittent Therapy			Standard WHO MDT		
	Number	Reaction	%	Number	Reaction	%
MB	415	99	24	379	90	24
PB	595	74	12	513	27	5

RO: BI decline

It has already been documented that the rate of decline of BI after RO over 8 years is identical to MB MDT (WHO) administered for 24 or 12 months (Ganapati et al, 1997). Continued follow-up of a total sample of 189 patients confirms these observations.

Table III – RO – 28 days: Relapse

Number of patients	189
Number of patient years of follow-up	1020
Number of relapses	8 (4.2%)
Relapses per 100 patient years	0.70

RO group is associated with relatively far higher risk of relapse than expected. The rates however compare favourably with those encountered in Tuberculosis.

OT 15

PANCITOPENIA OBSERVADA DURANTE POLIQUIMIOTERAPIA PARA MHD-T, REVERTIDA COM A SUSPENSÃO DA DAPSONA

Ana Regina Coelho de Andrade; Andréa Machado Coelho Ramos; Marcelo Grossi Araújo; Marilda Helena T. Brandão

Hospital das Clínicas da Universidade Federal de Minas Gerais. Alameda Álvaro Celso, 55 Santa Efigênia- Belo Horizonte MG CEP 30150-260. adermato@hc.ufmg.br

Relata-se a ocorrência de pancitopenia em paciente portadora de hanseníase dimorfo-tuberculóide,em tratamento com poliquimioterapia (PQT) esquema 2 (rifampicina, dapsona e clofazimina). A paciente fazia uso prévio de ácido valpróico, hidroclorotiazida e amilorida, enalapril, amitriptilina e diazepam. O quadro hematológico instalou-se subitamente, no segundo mês de tratamento, quando o hemograma revelou hemoglobina de 6,5g%, 48.000 plaquetas e o leucograma 4.900 leucócitos com desvio escalonado à esquerda com a presença de 10% de blastos. A PQT foi suspensa imediatamente, e não obstante a paciente tenha mantido o uso dos outros medicamentos, o quadro reverteu-se e na terceira semana já estava normalizado. A impressão diagnóstica foi de pancitopenia secundária a drogas, em resolução. Considerando os efeitos hematológicos da dapsona, foi reiniciada a PQT sem a mesma. O seguimento da paciente com hemograma mensal desde novembro de 2001 não tem mostrado novas alterações hematológicas.

OT 16

PERSISTÊNCIA DE BACILOS EM PACIENTES DE HANSENÍASE MULTIBACILARES APÓS 12 DOSES DO ESQUEMA PQT/OMS. RESULTADOS PRELIMINARES

João Carlos Regazzi Avelleira, Francisco Reis Vianna, Larissa Mitraud Alves, Alfredo Marques Boechat, Suzana Madeira.

Instituto Estadual de Dermatologia Sanitária, Rio de Janeiro e Instituto Lauro de Souza Lima, Bauru, São Paulo

Introdução: Recentemente o Ministério da Saúde, baseado nas conclusões da reunião de peritos em Lepra da OMS, recomendou que o esquema poliquimioterapico para tratamento da hanseníase, em pacientes multibacilares poderia ter sua duração reduzida para 12 doses.

Material e métodos: Participaram do trabalho, 4 pacientes do sexo masculino, virgens de tratamento, com diagnóstico clinico, e confirmação baciloscópica e histopatológica de hanseníase virchoviana, realizado no ambulatório do Instituto de Estadual de Dermatologia. Todos os pacientes apresentavam índice baciloscópicos maiores que 5, com presença de bacilos íntegros, em todos os casos. Foi instituído em todos o tratamento com o esquema padrão PQT/OMS para Multibacilares (Rifampicina em dose mensal supervisionada, Dapsona e Clofazimina autoadministradas diariamente), com duração de 12 doses, que todos os pacientes concluíram em 12 meses. Ao término do tratamento foram retirados através de biópsia, material para inoculação em camundongos no Instituto Lauro de Souza Lima, Bauru/SP, conforme a técnica de Shepard.

Resultados: Foi constatada a presença de crescimento de bacilos álcool ácido resistentes em apenas um paciente dos 4 que haviam sido inoculados.

Discussão: Os estudos apresentados em que foram baseadas as recomendações para a diminuição da duração do tratamento, fundamentam-se principal-

mente na possibilidade que o novo esquema seja eficaz na grande maioria dos pacientes multibacilares. No entanto, é real a possibilidade de que entre pacientes com carga bacilar elevada, um grupo venha a recidivar. Uma melhor avaliação destes achados deverá ser realizada com o aumento da amostra.

OT 17

RELAPSES AMONG LEPROSY PATIENTS TREATED WITH 2 – YEAR MULTIDRUGTHERAPY.VIABILITY OF THE ORGANISMS AND DRUG SUSCEPTIBILITY.

Maria da Graça S. Cunha, Suzana Madeira, Paula F. Bessa Rebello e Silmara N. Pennini.

Fundação de Dermatologia Tropical e Venereologia "Alfredo da Matta" Rua Codajás nº 24, Cachoeirinha – CEP 69.065-130, Manaus - Amazonas - Brazil.

In this prospective study multibacillary (MB) leprosy patients were treated with 2- year multidrug therapy (MDT) and had been followed up for 8-10 years after released from treatment (RFT). The relapse rate was the most important parameter for assessing the efficacy of the therapeutic regimen. The viability of *M. leprae* organisms and drug susceptibility had been tested whenever clinical relapse was detected.

From 1987 to 1992, 424 MB leprosy cases where included. None of the patients had been treated previously and all had bacterial index (BI) of at least 2+ in any site. Relapse was suspected on the appearance of new lesions of multibacillary leprosy and if the BI at any site was found to have increased by at least 2+ over the previous value. The demonstration of viable *M. leprae* and drug susceptibility were tested by mouse footpad inoculation. Simultaneously the patients who relapsed had been retreated with the standard 2-year MDT for MB leprosy.

Treatment was completed for 337 patients and during surveillance period 6 cases of relapse were detected. The relapse rate was 1.78% and the shortest interval between the end of MDT and the occurrence of relapse was 70 meses. The available results of drug susceptibility testing of the organisms recovered from the relapsed lesions were susceptible to both rifampin and dapsone. Clinical improvement was observed in all 6 patients and the mean BI continued to decline after patients had been retreated. No further relapses have been detected during the same period.

OT 18

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

Cellona, R.V., Balagon, M.F., Dela Cruz, E.C., Abalos, R.M. and Walsh, D.S.

Leonard Wood Memorial Leprosy Research Center, P.O. Box 727, Cebu City 6000, Philippines.

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 persister organisms using the mouse-footpad technique of Sheppard.

500 MB leprosy patients who completed the 2 years WHO-MDT regimen were recruited sequentially and followed up. Duration of surveillance now range from 8 to 15 years. Surveillance includes yearly clinical examinations and skin smears. Criteria for probable relapse are the appearance of new/active lesions and an increase in BI of at least 2+ at any site compared to the lowest BI taken at the same site. Those with probable relapse are biopsied and tested for growth in mouse footpads to confirm relapse. The organisms are then passaged to groups of mice given the 3 drugs composing the WHO-MDT regimen to determine whether the relapse is due to drug-resistant or persister organisms.

So far, 15 patients were found to have a probable relapse occurring 6 to 12 years after the end of their WHO-MDT regimen. No relapses were noted within 5 years after end of treatment. Twelve of the 15 relapsed patients with complete mouse footpad test results were all due to persister relapse. There were no drug-resistant relapses.

The clinical, bacteriological and histopathological characteristics of the patients in the study including the mouse footpad results will be discussed

OT 19

RESULTADOS PRELIMINARES DE COORTE DE PACIENTES MULTIBACILARES TRATADOS COM 12 MÊSES DE POLIQUIMIOTERAPIA MB/OMS.

Gerson Oliveira Penna; Ana Maria Costa Pinheiro; Lucas Nogueira and Daniela Cardoso

Trabalho desenvolvido no Hospital Universitário da Universidade de Brasília UnB

Os autores apresentarão e discutirão os resultados preliminares de uma coorte aberta de pacientes multibacilares tratados com esquema poliquimioterápico preconizado pela Organização Mundial de Saúde por 12 meses.

OT 20

RESULTS OF POST ROM (SINGLE DOSE) FOLLOW-UP OF 332 SINGLE SKIN LESION (SSL) CASES IN THE N, S, T WARDS OF GREATER MUMBAI, INDIA

Sachin R. Salunkhe, Joy Mancheril, P.R. Dewarkar, and A. Antony Samy

ALERT-OIndia, B-9 Mira Mansion, Sion (West), Mumbai - 400 022, India

ROM has been introduced as an effective short-term Chemotherapy for SSL cases to reduce the period of treatment in leprosy elimination campaigns. ALERT-INDIA in its leprosy control areas of Greater Bombay has treated 332 SSL cases from Jan. 1998 to Dec. 1999. Of these 302 cases have been followed up for 24 months and the remaining 30 cases have been followed up for 18 months. Ten of these cases presented a clinical picture that warranted further treatment. Five of these were confirmed histo-pathologically. These cases were put on regular PB MDT for 6 months, and subsequently showed good clinical improvement. Hence we confirm satisfactory results of single dose ROM therapy in majority of SSL cases and also suggest proper surveillance to detect cases that do not im prove clinically.

OT 21

SCENAR-THERAPY FOR LEPROSY PATIENTS WITH CHRONIC NEURITIS

E.I. Shats, O.A. Bezrukavnikova

Leprosy Research Institute, Astrakhan, Russian Federation

Scenar (Self-Controlled Energoregulator) devices are portable autonomous electric apparatus operating in the mode of biological feedback circuit with a patient. The operation of the device is based on a physical factor representing an individually modulated electric signal similar to nervous impulse in its form. Advantages of scenar-therapy include non-invasiveness, a wide spectrum of indications, and absence of age limitations. General course of treatment consists of 10-15 procedures on alternate days. If necessary, treatment courses may be repeated after three-four weeks. Treatment of peripheral nerve damages, especially chronic ones remains to be an urgent problem. Methods of therapy available are of little effect. The results of scenar-therapy of 20 patients with leprosy (12 males and 8 females) aged 30-65 years and suffering from chronic peripheral neuritis are presented. Before treatment patients complained of sharp pains in extremities, thickening and painfulness in ulnar and peroneal nerves at palpation, amiotrophies and flexion contractures of fingers. Against the background of scenar-therapy arresting of painful syndrome and increase in muscle strength (by 10% in average) was noted. All the patients noted a significant improvement of their general state, appetite and sleep. Electropuncture testing of biologically active points located in zones under stimulation performed before and during scenar-treatment revealed increase in nerve conduction suggesting functional improvement of peripheral nerves

OT 22

TRATAMENTO ÚNICO PARA PACIENTES DE HANSENÌASE.

Gerson Oliveira Penna; Ana Maria Costa Pinheiro; Lucas Nogueira and Daniela Cardoso.

Trabalho desenvolvido no Hospital Universitário da Universidade de Brasília UnB

Os autores apresentarão e discutirão o protocolo de investigação aprovado no Comitê de Ética em Pesquisa (CEP) da Universidade de Brasília, que objetiva instituir tratamento Poliquimioterápico - Multibacilar - padronizado pela Organização Mundial da Saúde, para todos os doentes de hanseníase independentemente da forma clínica.

Medicamentos utilizados: Todos os pacientes - Independentemente da forma clínica - receberão Rifampicina 600 mg/mês, Dapsona 100 mg/dia e Clofazimina 300 mg/mês e 50mg/dia.

Tempo de Tratamento: Todos os pacientes - Independentement da forma clínica - serão tratados por seis meses

Serão discutidos:

— o critério de inclusão, que será baseado unicamente na definição clínica de Caso de Hanseníase;

— a justificativa para a não utilização de nenhuma das classificações de pacientes de hanseníase para fins terapêuticos;

— os parâmetros de acompanhamento;

— o uso da baciloscopia como parâmetrp de acompanhamento laboratoril

— a dificuldade para estabelecer *Gold standart* laboratorial

OT 23

TREATMENT OF MB LEPROSY PATIENTS UINSG CONVENTIONAL AND NEWER DRUGS MINOCYCLINE AND OFLOXACIN

Kiran Katoch, M. Natrajan, V.D. Sharam, H.B. Singh, U.D. Gupta, V.M. Katoch and Raj Kamal

Centrla JALMA Institute for Leprosy (ICMR), Taj Ganj, Agra, India

This study has been carried out to study the effect of regimen comprising of conventional drugs used in MDT along with newer drugs like Minocycline and Ofloxacin. One hundred, untreated, smear positive

BB, BL and LL patients were treated with a regimen comprising of supervised, 600mgs of Rifampicin, 300mg of Clofazimine, 100 mg of Minocycline and 400mg of Ofloxacin once a month in addition to 50 mg of Clofazimine and 100mg of Dapsone daily for 12 months. The treatment was then stopped and patients were followed up on placebo. This study reports the follow-up of these patients up to 5 years after stoppage of therapy. The drugs were well tolerated, there was a good clinical response and there was no case of treatment failure during the treatment period. At the end of one year of treatment 25 of the 70 (patients available for follow-up) were still smear positive. No bacterial growth was observed in the foot pad of mice and no bacillary ATP was detected in the tissue biopsies one year after therapy. The patients continued to progress satisfactorily, and by 2 years only 4 patients were still smear positive. However 4 patients have relaped in the follow-up of 5 years. The results have been compared with patients treated with WHO MDT for one year. The details findings and their implications in the therapy of leprosy of MB patients will be discussed.

OT 24

ULTRA-HIGH DOSE COBALAMIN FOR TREATMENT OF LEPROSY NEUROPATHY

Márcia R. Jardim; Ximena Illarramendi; Patrícia S. Penna; José A.C. Nery; Nádia Duppre; Euzenir N. Sarno

Neurological damage may persist after completion of multidrug therapy (MDT). Corticoidsteroids have been proved successful for the improvement of recent motor deficit but are little effective for sensitive alteration.

Objective: An open controlled clinical trial was done in order to evaluate the effects of ultra-high dose of cobalamin (Cb) for persistence of motor and/or sensory nerve deficit after MDT and steroid treatment.

Method: Nineteen patients (13 males, 6 females) aged 44 ± 16.7 years were divided into 2 groups of treatment: 10 patients (treatment group) received 1000μg of intra-muscular Cb, 3 times per week, and 9 patients (controls) received 1 dose of Cb per month. Clinical and nerve conduction (ENMG) evaluations were performed by 2 neurologists before, at 3 months (only clinical) and after the 6 months of treatment.

Results: Nine patients were MB and 10 patients were PB. Grade of disability 0 was present in 60% of the patients, but 27% had GD 2 at the end of MDT. Muscle strength and vibratory sensation were little affected but improvement was observed in twice the number of nerves on thermal, tactile and pain evaluation in the treatment group compared to the controls. In addition, significant worsening of sensation was observed in the control group (pain $p=0.026$; tactile $p=0.006$; thermal $p=0.031$). On ENMG, the evaluation of the amplitude of motor and sensory conduction showed worsening of twice the number of nerves in the control group than in the treatment group and a slight improvement was seen in the latter.

Conclusion: Axonal nerve lesions diagnosed by ENMG have a slower recovery than clinical alterations. In this preliminary study we observed some beneficial effects of the use of ultra-high doses of Cb for the treatment of peripheral neuropathy.