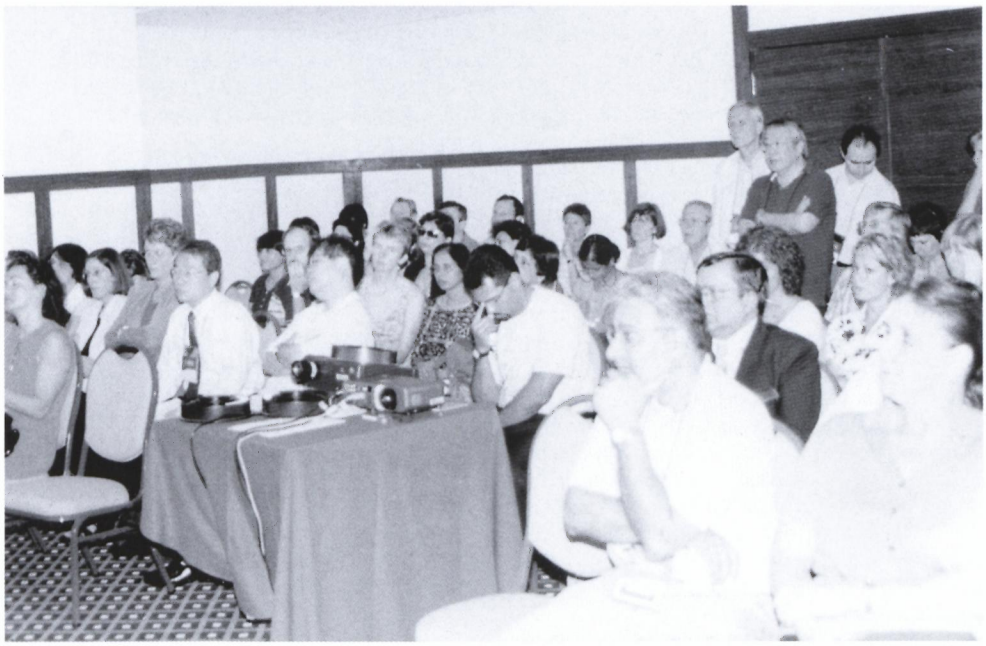
ABSTRACTS OF ORAL PRESENTATIONS



CLINICAL ASPECTS

OCA 1

A LARGE SERIES OF DAPSONE HYPERSENSITIVITY SYNDROME PATIENTS IN NEPAL

Maria Jacob K., Murdo Macdonald and Ruth Butlin.

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

Dapsone Hypersensitivity Syndrome (DHS) is an important although rare complication seen in the treatment of leprosy. It can be very distressing to the patient and in severe forms can even lead to death.

Aim: To review a large series of DHS patients, to be able to recognize and treat this effectively at its initial stages.

Methods: A retrospective study was carried out of a large series of 54 patients affected by leprosy; 47 MB and 7 PB, diagnosed with DHS in the past 11 years. Data of medical history was collected by a review of medical records charts.

Results: Thirty-seven of those affected by DHS in our series were male and 17 female. Time of presentation was usually within 3 months of starting MDT (5 at <1m, 30 at 1-3m, 1 at >3m). The patients presented with a variety of symptoms, the most common of which was dermatitis (74%). All were treated with prednisolone after immediate withdrawal of dapsone. A modified MDT regimen was continued. Eighty per cent of cases recovered fully within one month of starting treatment. A case report on one patient who had a protracted illness and extended stay in the hospital is also presented.

Conclusion: These observations will assist in the clinical management of DHS, and aid its early diagnosis.

OCA 2

ADVERSE EVENTS OF STANDARDISED REGIMENS OF CORTICOSTEROIDS FOR PROPHYLAXIS AND TREATMENT OF NERVE FUNCTION IMPAIRMENT IN LEPROSY: RESULTS FROM THE 'TRIPOD' TRIALS.

J.H. Richardus, S.G. Withington; A.M. Anderson, R.P. Croft, P.G. Nicholls, W.H. van Brakel, W.C.S. Smith.

Department of Public Health, Erasmus University Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands

Aim: Reactions in leprosy causing nerve function impairment (NFI) are increasingly treated with standardised regimens of corticosteroids, often under field conditions. Safety concerns led to an assessment of adverse events of corticosteroids in three trials studying prevention of NFI (the TRIPOD study).

Methods: A multicentre, randomised, double-blind placebo-controlled trial was conducted in leprosy control programmes in Nepal and Bangladesh. Treat-

ment was with prednisolone according to fixed schedules for 16 weeks, starting in one trial with 20 mg/day (prophylactic regimen: total dosage 1.96 g) and in the other two trials with 40 mg/day (therapeutic regimen: total dosage 2.52 g). Minor adverse events were defined as moon face, severe fungal infections, severe acne, and gastric pain requiring antacid. Major adverse events were defined as psychosis, peptic ulcer, glaucoma, cataract, diabetes and hypertension. Also the occurrence of infected plantar, palmar, and corneal ulceration was monitored, together with occurrence of TB.

Results: Considering all three trials together, minor adverse events were observed in 130/815 patients (16%). Of these, 51/414 (12%) were in the placebo group and 79/401 (20%) in the prednisolone group. The relative risk for minor adverse events in the prednisolone group was 1.6 (p=0.004). Complications with a significantly increased risk were acne, fungal infections and gastric pain. Major adverse events were observed in 15/815 patients (2%); 7/414 (2%) in the placebo group and 8/401 (2%) in the prednisolone group. No major adverse events had a significantly increased risk in the prednisolone arm of the trials. No cases of TB were observed in 300 patients which could be followed-up for 24 months.

Conclusion: Standardised regimens of corticosteroids for both prophylaxis and treatment of reactions and NFI in leprosy is are safe when patients are screened for contra-indications before treatment. The risk of minor adverse events was increased in the prednisolone group, but none required stopping of treatment. Major adverse events are rare, and no differences were found between the placebo and prednisolone arm of the trials.

OCA 3

ANTI-PGL I IN THE DIAGNOSIS OF PRIMARY NEURITIC LEPROSY

William R.Faber[1], Samira Bührer-Sekula[2], Linda Oskam[2], Joanne Wildebeest[1], Amir Zamarian[1], Adalberto Santos[3], Haroldo J. Matos[4], Elisabeth P.Sampaio[3], Euzenir N.Sarno[3].

[1]Academic Medical Center and [2]KIT Biomedical Research, Amsterdam, The Netherlands. [3]Fiouruz, Av Brasil 4365, Manguinhos and [4]Bioinformática Médica, State University of Rio de Janeiro, Rio de Janeiro, Brazil.

Primary neuritic leprosy (PN) is difficult to diagnose because skin lesions and bacilli in skin smears are lacking.

It was investigated if the addition of diagnostic tests might improve the decision for the diagnosis PN. In a retrospective study an anti-phenolic glycolipid I (anti-PGL I) Elisa was performed in patients with the clinical diagnosis PN. Anti-PGL I Elisa was positive in 10 out of 44 patients (23 %) with the clinical diagnosis PN. Anti-PGL I Elisa was postive in 4 out of 25 patients in which the histopathological investigation of a nerve biopsy showed non-specific changes or normal histology (total no 36). And was positive in 2 out of 14 patients in which the PCR specific for *M. leprae* from a nerve biopsy was negative (total no 28).

As the presence of antibodies to *M. leprae* PGL I are supposed to reflect the bacterial load of the patient a positive anti-PGL I may increase the number of patients with the diagnosis PN; as it was detected in this study in one out of 2 patients with a negative PCR and a non-specific histopathology. When considering a field situation where in most cases histopathological investigations and PCR are not performed, detection of antibodies would confirm 23% of the cases.

OCA 4

BCG EFFECTIVENESS TRIAL AGAINST LEPROSY AMONG SCHOOL CHILDREN, IN NORTHERN BRAZIL

Sérgio Cunha,[1,2]; Laura C Rodrigues[2]; Inês Dourado[1]; Susan M. Pereira[1]; Neal Alexander[2]; Maria Yury Ichihara[1,3]; Emilia S. Pereira[4]; Mauricio L. Barreto[1].

Institutions: [1]Instituto de Saúde Coletiva, UFBA/ Bahia/Brazil; [2]London School of Hygiene and Tropical Medicine, UK; [3]Coordenação Regional da FNS na Bahia; [4]Fundação Alfredo da Matta, Manaus, Brazil.

Background: In 1994 the Brazilian Ministry of health recommended a dose of BCG vaccine to schoolchildren aimed to prevent tuberculosis. A trial started in 1996 to estimate the efficacy of such a vaccination in two sites. One of the sites (city of Manaus) is an endemic area of leprosy, and the trial in this site was expanded to estimate protection against leprosy.

Study design: Matched, clustered randomised controlled trial.

Study population: Children aged 7 to 14 years attending state schools.

Objectives.: 1. To estimate the efficacy against leprosy of one dose of BCG vaccine given to school children in a population with a high coverage of neonatal BCG; 2. to estimate the number of individuals that need to be vaccinated to prevent one case of leprosy in school children; 3. To estimate what proportion of all cases of leprosy would be prevented by vaccination in that population; 4. To compare these results with those obtained from vaccination restricted to household contacts.

Methods:. The trial was implemented in 1998. 286 state schools in the city of Manaus, Brazil, were randomised into receiving BCG or not. Identifying in-

formation was collected for 156,331 school children, of whom 72,982 are in intervention schools. Trained nurses examined the right deltoid region to ascertain previous BCG vaccination status. Follow up relies on ascertainement of cases diagnosed at the health services and notified to the reference centre for leprosy. Blindness is guaranteed during linkage and validation of cases. Prophylactic STEROIDS TO prevent nerve function impairment.

OCA 5

BORDERLINE TUBERCULOID LEPROSY: AN IMMUNE RECONSTITUTION PHENOMENON IN AN HIV-INFECTED PERSON

Stephen D. Lawn[1], Diana N. Lockwood[1, 2]
[1]Hospital for Tropical Diseases, Mortimer Market, Capper Street, London, WC1E 6AU UK; [2]Clinical Infection Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK.

Culture-positive pulmonary tuberculosis (TB) and human immunodeficiency virus type 1 (HIV-1) coinfection were diagnosed in a 37-year-old Ugandan male. The plasma HIV-1 load was 120,000 RNA copies/ml and the blood CD4+ T lymphocyte count was 10×10^6/L at the time of diagnosis, indicating marked immunosuppression. The patient responded well to multi-drug antituberculosis treatment and, during the continuation phase, highly active antiretroviral treatment (HAART) was also commenced. Three months after starting antiretroviral treatment the patient developed facial lesions that were clinically diagnosed as borderline tuberculoid (BT) leprosy in reaction and this diagnosis was confirmed histologically. At that time the patient's CD4+ lymphocyte count had increased to 70×10^6/L and the plasma viral load was <50 HIV-1 RNA copies/ml. The temporal association between the commencement of HAART and the development of the skin lesions suggested that the leprosy was a manifestation of immune reconstitution. Such a phenomenon has not previously been reported. However, the occurrence of the BT form of leprosy (indicating marked cell-mediated immunity to *Mycobacterium leprae*) is counterintuitive in the context of marked CD4+ lymphocytopenia. This presentation reviews the current understanding of the relationship between HIV-1 and leprosy.

OCA 6

CHRONIC NEUROPATHIC PAIN IN TREATED LEPROSY

Aki Hietaharju[1], Richard Croft[2], Rezaul Alam[2], Paul Birch[3], Aprue Mong[4], Maija Haanpää[1]

[1]Department of Neurology and Rehabilitation, Tampere University Hospital, Tampere, Finland; [2]Danish Bangladesh Leprosy Mission, Nilphamari, Bangladesh; [3]Cronehills Health Centre, West Bromwich, UK; [4]Chittagong Leprosy Control Project, the Leprosy Mission, Chittagong, Bangladesh

Medical reports on neuropathic pain associated with treated leprosy are scarce. We describe the clinical findings of 16 patients with multibacillary leprosy who had chronic stimulus-independent pain despite finishing their treatment.

The study area was Nilphamari District, northwestern Bangladesh. The patients were recruited for this study with the help of local leprosy workers from four outpatient clinics. The workers were instructed to ask for the following symptoms: burning feet, formication, pricking, biting, or squeezing pain. Altogether, 38 patients were recruited, of whom 16 fulfilled the inclusion criteria and accepted the study protocol. The clinical neurological examination included assessment of tactile, pinprick, thermal, and joint position sensation and tendon reflexes, as well as dynamic and static allodynia. Furthermore, location of pain was recorded by using pain drawings. Thresholds for pinprick sensation were measured by using the weighted needle apparatus, and thresholds for tactile sensation by using Semmes-Weinstein monofilaments.

Pain in all 16 patients was either moderate or severe. It was mainly of burning, tingling or biting quality. Some patients complained electric shock-like pain. The duration of pain varied from two years to more than 20 years. In eight patients (50%) the occurrence of pain was continuous. The distribution of pain and sensory loss was equal in 11 patients (69%), whereas inconsistencies between distribution of pain and sensory abnormalities was found in five cases. Enlargement or tenderness of nerves was noticed in six patients.

Our results indicate that some leprosy patients suffer from neuropathic pain, but further epidemiological studies are necessary to determine the magnitude of the problem. Considering neuropathic pain as one of the medical problems in treated leprosy patients may open new therapeutic avenues in future "care after cure" programmes.

OCA 7

CLINICAL RESPONSE TO CYCLOSPORIN A TREATMENT IN SEVERE LEPROSY TYPE 1 REACTION (T1R) PATIENTS IN NEPAL AND ETHIOPIA.

Sharon N.S. Marlowe, Jukka Knuutilla, Friedbert Herm, Elizabeth Bizuneh, Ruth Leekassa, Diana N.J. Lockwood

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

Green Pastures Hospital, Pokhara, Nepal

ALERT, PO Box 165, Addis Ababa, Ethiopia

Background: Type 1 (reversal) reactions (T1R) are important tissue damaging phenomena responsible for a significant proportion of nerve damage in leprosy. Prednisolone is the principle treatment for reactions but 30 – 60 % patients will not improve. There is a clinical need for a new and better immunosuppressant. Cyclosporin A (CyA) is a potent immunosuppressant that is non-myelotoxic and has been used widely in other immune-mediated diseases for over 17 years. There have been 3 case-reports of the successful treatment of severe and recurrent T1R with CyA.

Aim: To assess the effectiveness of oral CyA in treating severe T1R.

Study: This is a closely monitored pilot study. Patients with severe T1R were recruited in Nepal and Ethiopia and given an Indian generic preparation of CyA at 5mg/kg/day. 40mg of prednisolone was given for the first 5 days until CyA blood concentration reached a steady state. A clinical severity scale (CSS) was used to identify patients severe enough to enter the trial and the CSS was also used to monitor the response to CyA treatment. Patients were either in-or out-patients. CyA treatment was given for 3 months. Patients had regular assessments (during and after treatment) according to the CSS and were also examined and tested for CyA related side-effects.

Results: The effects of CyA on nerve function impairment, skin and systemic signs will be reported and any side-effects seen. The effficacy of CyA and prednisolone will be compared in each location (Nepal and Ethiopia) using retrospective T1R data on prednisolone use.

OCA 8

CYTOKINE EXPRESSION IN THE SKIN AND BLOOD OF SEVERE LEPROSY .TYPE 1 REACTIONS TREATED WITH PREDNISOLONE AND AZATHIOPRINE.

Sharon N.S. Marlowe, Niraj Shrestha, Rakesh Manandhar, Murdo Macdonald, Paul Roche, Saroj Khanolkar-Young, Diana N.J. Lockwood

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

Anandaban Leprosy Hospital, PO Box 151, Kathmandu, Nepal

Aim: To compare the cytokine production in skin lesions and blood of severe Type 1 Reaction (T1R) Nepali leprosy patients taking azathioprine and or prednisolone. To relate these findings to the clinical state of the patients and the dose of drug administered.

Study: 40 patients with severe T1R were recruited. 21 were treated with 3 months of azathioprine at 3mg/kg/day plus a 2 month reducing course of prednisolone starting at 40mg (AP). 19 patients were treated with a 3 month reducing prednisolone course starting at 40mg (P).

Results: Cytokine production (tumour necrosis factor, interleukin-10 and gamma-interferon) in whole blood assay was assessed by ELISA at day 0 and weeks 2, 8 and 16. 2 skin biopsies were taken from each patient to cover the whole time period (day 0, and weeks 4, 6, 8, 12 and 16). Immunohistochemical staining and semi-quantitative grading for tumour necrosis factor, interleukin-10 and interleukin-2 was carried out on the skin biopsies.

Comparisons will be made between the effects of AP and P treatments on patients' clinical status and cytokine production.

OCA 9

DIFERENCIAS – SIMILITUDES DOS MICOBACTERIOSIS LEPRA – ULCERA DE BURULI

Dr. Gómez Echevarría, José Ramón, Director Médico Lepra Sanatorio San Francisco de Borja.

Sanatorio San Francisco de Borja

03791 FONTILLES (ALICANTE) ESPAÑA

Teléfono: 96 558 33 50; Fax: 96 558 33 76; E-mail: ptorres@fontilles.org

Tras su experiencia de trabajo en Lepra y en Ulcera de Buruli en la región del lago Kassou, distritos de Sakassou y Bouq en Costa de Marfil, el autor intenta recoger las diferencias y similitudes entre ambas enfermedades de origen bacteriano.

OCA 10

ERITEMA NODOSO HANSÊNICO, PERFIL CLÍNICO E IMUNOPATOLÓGICO A PARTIR DE 90 PACIENTES ESTUDADOS EM GOIÂNIA.

Jackeline Gomes Guerra, Lia Cândida Miranda de Castro, Celina Maria Turchi Martelli, Mariane Martins de Araújo Stefani, Maurício Barcelos Costa, Gerson Oliveira Penna.

Introdução: O eritema nodoso hansênico (ENH) é um evento imunológico freqüente responsável por hospitalização e incapacidade física em pacientes com hanseníase Borderline Lepromatosa e Lepromatosa (BL e LL). No nosso meio há poucas informações disponíveis sobre essa patologia.

Objetivo: O presente estudo busca estudar características clínicas, epidemiológicas, histopatológicas, sorológicas e terapêuticas de pacientes com ENH atendidos em serviços de saúde de referência para hanseníase com o objetivo de caracterizar a demanda do ENH no atual contexto da eliminação da hanseníase.

Material e método: Estudo de série de casos de ENH recrutados no período de agosto de 2000 a janeiro de 2001 no Centro de Referência em Diag-

nóstico e Terapêutica (CRDT) e Hospital de Doenças Tropicais Anuar Auad (HDTAA) em Goiânia/GO. Foi preenchida ficha padronizada com dados epidemiológicos, clínicos e terapêuticos, posteriormente analisados. Foi coletada biópsia de pele para histopatologia e amostra de sangue para sorologia de anticorpos anti- PGL I, cujos resultados foram comparados com os de pacientes MB sem ENH.

Resultados: Foram incluídos 58 pacientes com ENH e 32 com hanseníase BL ou LL sem ENH. Os pacientes com ENH eram predominantemente do sexo masculino (58,6%), forma clínica LL (81%) e faixa etária média de 34,5 anos. Mais da metade dos pacientes com ENH apresentaram sorologia positiva para anticorpos IgM anti- PGL I, embora com títulos inferiores aos dos pacientes MB sem ENH. À histopatologia, a presença de infiltrado neutrofílico, paniculite, vasculite e agressão neural foram estatisticamente significantes nos pacientes com ENH ($p<0,001$). O primeiro episódio de ENH ocorreu durante o tratamento específico em 66% dos pacientes e foi tratado com corticosteróide em 77,6% dos casos.

Conclusão: Pacientes com ENH apresentaram sorologia positiva para anticorpos anti PGL- I e alterações histopatológicas estatisticamente significantes quando comparados com pacientes BL e LL sem ENH. Há a necessidade de ficha padronizada específica para coleta de dados do ENH para melhor avaliação dos seus aspectos clínicos, epidemiológicos e terapêuticos.

OCA 11

ESTUDIO SEROEPIDEMIOLÓGICO DE LEPRA. PROVINCIA CAMAGÜEY. AÑO 2000- 2001.

Nieves Atrio Mouriño. Dra. Maria Leticia Costa García

* Especialista de segundo grado en Dermatología. Jefa del grupo Provincial de Dermatología. Jefa del Programa de Lepra en la Provincia.

**Especialista de primer grado en Medicina General Integral.

Centro Provincial de Higiene y Epidemiología General Gómez No. 5 Camagüey Cuba.

La Lepra, representa un problema de salud universal; la lucha contra la enfermedad necesita la incorporación de todos los mecanismos demostrados para el control como son: el diagnóstico precoz, preclínico o muy temprano, mediante pesquisa a poblaciones consideradas de riesgo con un examen Dermatoneurológico, estudio Serológico y tratamiento oportuno con MDT. En base a ello se realizó un estudio de intervención para conocer el comportamiento de la infestación por el Microbacterium leprae durante los años 2000-2001 en la provincia de Camagüey.

El universo poblacional estuvo constituido por todas aquellas poblaciones donde se notificó 1 caso de lepra durante estos años. Se realizaron 15 131 pruebas serológicas a la población de riesgo en aquellos municipios con una prevalencia de la enfermedad superior a $1 \times 10\,000$, a los cuáles se le aplicó una encuesta. Las variables a analizar fueron: edad, sexo, raza, escolaridad, ocupación, lugar de procedencia, causas del pesquisaje, examen Dermatoneurológico, fecha y resultado de la Baciloscopia, Lepromina y tratamiento recibido, así como seguimiento serológico. Si la prueba serológica resultó por encima del nivel de corte (0,300), se le realizó Baciloscopia y Lepromina. Aquellos casos con respuesta inmunológica negativa recibieron tratamiento profiláctico y seguimiento serológico por un año. Este trabajo tuvo como principal objetivo conocer el comportamiento de la infestación por el Micobacterium leprae en la Provincia de Camagüey.

De las 15 131 resultaron por encima de nivel de corte 185, de estas fueron Lepromino negativas 29, enfermos de Lepra 4 y se trataron 29. En el seguimiento serológico se mantuvieron con igual cifra o inferior el 100 %.

OCA 12

FACTS AND FALLACIES OF CORTICOSTEROID TOXICITY IN LEPROSY - AN EXPERIENCE WITH MORE THAN 1000 PATIENTS IN 10 YEARS.

D.S.T. Sugumaran

Sacred Heart Leprosy Centre, Sakkotai, Kumbakonam, Tamilnadu, India- 612 401

Corticosteroids are used in various complications of leprosy like Leprosy Reactions (Type I and Type II), Neuritis and Quiet Nerve Paralysis (QNP). Most of these complications are due to immunological hypersensitivity response to *M. leprae* antigens. Corticosteroids act in a three pronged approach to control the symptoms of reacitons as well as prevent nerve damage. Even when there is evidence of nerve function loss corticosteroids can reverse the function loss and restore useful function in the majority of leprosy patients if the function loss is of less than 1 year duration. Some patients will need prolonged courses of corticosteroids because of their tendency to have prolonged and recurrent episodes of reactions or neuritis. Hence it is inevitable that some patients will develop one or more adverse effects of corticosteroids. Some of the side effects are mild and transient (moon face, acne etc.) while some are serious and life threatening (Secondary infections like tuberculosis, peptic ulcer perforation, diabetes etc.). Some side effects are neither mild nor life threatening but potentially disabling (osteoporosis, cataract, glaucoma).

While the side effects are alarming, the Doctor has to continue corticosteroids for the leprosy patients when indicated tackling the adverse effects as well as controlling the leprosy reactions and neuritis.

The present paper will furnish the incidence and implications of corticosteroid toxicity in the proper perspective without any prejudice so that clinicians will be able to understand and tackle the problem without fear thereby extending the maximum benefit to the patients. The problems and their solutions will be discussed with graphs and tables.

OCA 13

HISTOLOGIA DA ÁREA PERILESIONAL EM PACIENTES PORTADORES DE HANSENÍASE TUBERCULÓIDE E DIMORFA REACIONAL.

Joel C. Lastória, D.V.A. Opromolla, Raul N. Fleury, Alexandra P. Bononi, Karina G. Pedroso, Carlos R. Padovani., Mariângela A.E. Marques.

Depto de Dermatologia da F. M. de Botucatu- UNESP

A hanseníase, de acordo com o sistema de classificação adotado pelo VI Congresso Internacional de Leprologia, 1953, apresenta duas formas polares, clínica e imunologicamente distintas: o tipo virchoviano e o tuberculóide. Apresenta ainda dois grupos instáveis, o indeterminado e o dimorfo. Em todas elas, exceto na indeterminada, a evolução crônica pode ser interrompida por surtos agudos, denominados de tuberculóide reacional (TR), dimorfo reacional (DR) e, quando na virchoviana, de eritema nodoso. Na tentativa de diferenciar os TR dos DR, os autores avaliaram a histologia da área lesional e perilesional em 17 pacientes com forma TR e DR durante o surto reacional e observaram que nos pacientes TR não houve alteração histológica da pele perilesional em 100% dos casos, enquanto que nos pacientes DR, 60% deles apresentaram infiltração nesse local, muito embora sem que houvesse diferença estatística, talvez pelo tamanho amostral. Com esses resultados, não podemos afirmar quanto à diferença entre estas formas pela histologia da região perilesional clínicas mas, no entanto, quando houver infiltrado perilesional, este paciente não deve pertencer ao grupo TR.

OCA 14

HISTOPATHOLOGICAL STUDY ON EXPERIMENTAL LEPROSY IN TUPAIAS (*Tupaia belangeri yunalis*)

Wang Heying, Liu Jihe, Yu Lingchong, et al.

Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, National Center for STD and Leprosy Control, Nanjing 210042

In order to explore new experimental leprosy in tupaias. Ten tupaias were infected with 5.0104–2.67107 *M. leprae* by different routes, intravenous and subcutaneous (fore and hind foot pads, nose, ears) or intratesticular inoculation. These animals were scarified 373–786 days after infection, the average time were 546 days. Large patches of leprous granulomatous infiltration, containing a large number of acid fast bacilli (AFB) were found at the inoculated sites by histopathological examination. The morphologic indices (MI) of most AFB were greater than 40%, and the bacterial indices (BI) ranged 5+–6+. The dermal nerves showed "onion skin-like" ± appearance and were severely destroted with large numbers of AFB and globi. It looks like borderline lepromatous leprosy in tissue sections. The bacilli in the foot pads of tupaia increased up to 5.97109/g of tissue. According to the histopathological observation and bacteriological determination, it is proved that experimental leprosy model in tupaia has been established.

OCA 15

IMMUNOHISTOCHEMISTRY, *IN SITU* HYBRIDIZATION AND *IN SITU* PCR IN THE HISTODIAGNOSIS OF EARLY LEPROSY.

Mohan Natrajan, Kiran Katoch and V.M. Katoch.

Histological confirmation of the clinical diagnosis of early lerosy using conventional histopathological techniques is possible only in a fraction of the cases. The present study was done to assess the role of immunoperoxidase techniques, *in situ* hybridization and *in situ* PCR in the histodiagnosis of leprosy where conventional histopathology fails.

Forty four cases showing a non-specific pathology on routine histopathology and, which were negative for AFB were chosen for the study. Immunostaining for mycobacterial antigen using an indirect immunoperoxidase technique and the streptavidin-biotin system, revealed the presence of antigen in 10 of 44 cases (22.7%) cases. *In situ* hybridization using digoxigenin labelled oligonucleotides gave positive signals in a further 13 of 33 cases (39.3%). Finally, the use of *in situ* PCR in resulted in positive signals in 6/11 cases (54.5%) which were negative by in situ hybridization.

The technical feasibility and limitations and the usefulness of these procedures will be presented.

OCA 16

INOCULATION OF *M. leprae* IN RIGHT FOOT PAD IN MICE AND ITS CONTRALATERAL EFFECT ON THE NEUROFILAMENTS OF SCIATIC NERVE

M.P. Save[1], V.P. Shetty[1], KT Shetty[2] and N.H.Antia[1]

[1]The Foundation for Medical Research, 84-A R.G.Thadani Marg, Worli, Mumbai 400 018, India Tel: 91-22-4934989, Fax: 91-22-4932876

frchbom@bom2.vsnl.net.in

[2]National Institute of Mental Health and Neurosciences, Bangalore.

Mouse is a well established animal model for leprosy. The sciatic nerves of mice inoculated in both the hind foot pads with viable (VML) and heat killed *M. leprae* (HKML) showed the loss of immunoreactivity to phosphorylated epitopes of NF heavy chain (using SMI 31 antibody) in WB analysis of Triton X-100 insoluble cytoskeletal preparation. These observations were corroborated by the abnormal immunostaining pattern of affected nerves and ultrastructural changes such as compaction and arraying of filaments particularly in atrophied fibers as well as at the S-L cleft region. It was also noted that HKML cause NF alterations earlier however transient, than the VML. The observations were suggestive of a role for cellular component(s) of *M. leprae* in triggering the onset of such degenerative changes.

The question then was; what is the effect of unilateral *M. leprae* inoculation on the contralateral side? Further experiments were carried out using a similar protocol. Adult Swiss White mice were inoculated into the right hind foot pad with $1x10^4$ acid fast bacilli (both VML and HKML). Both left and right sciatic nerves were biopsied at regular intervals starting from one week till 12 month. Changes in the Rt and Lt sciatic nerves were compared.

Results showed a) qualitatively similar contralateral effect with both VML and HKML inoculation. b) The changes were of smaller magnitude as compared to ipsilateral side c) There was some difference in time kinetics. These results have far reaching implications on the mechanism of nerve damage in leprosy.

OCA 17

INTRAOCULAR LENS IMPLANTATION IN MULTIBACILLARY AND PAUCIBACILLARY LEPROSY PATIENTS.

Ebenezer Daniel and Sheena Koshy

Schiefellin Leprosy Research and Training Center, Karigiri, Vellore District, Tamilnadu, India – 632106.

Pre-operative, operative and post-operative ocular complications in 48 eyes of 39 leprosy patients who underwent standard extra-capsular cataract extraction and posterior chamber intra-ocular lens implantation, by the same surgeon, during 1997-1998, were studied retrospectively. 17 were male and 22 female. 13 (33%) were pauci-bacillary (PB) while 26 (67%) were multi-bacillary (MB) patients. 3 patients were smear positive at surgery. Grade II deformity that included claw hands, absorbed fingers, saddle noses and foot drop were present in 64% of the patients. None had any previous intra-ocular inflammation although 1 patient had had Type I reaction and 5 patients, Type II reaction. Pre-operative complications like corneal opacities (3 eyes) and lagophthalmos (5 eyes) were not associated with lowered vision post-operatively. No significant operative complications were encountered except in one eye where there was a posterior capsular tear. 17 eyes (35%) developed uveitis of 3+ or more in the immediate post-operative period but abated with routine topical steroid eye drops. 6 months after surgery 7 out of 47 eyes (15%) had developed posterior capsular opacities (PCO). The amount of uveitis and PCO were similar to those reported in non-leprosy patients. There were no significant differences ($p>0.05$) in the visual acuity outcomes or ocular complications when MB patients were compared with PB patients. Post-operative complications were not significantly different in smear positive patients compared with smear negative patients. Visual outcomes in the 23 eyes followed up at 2 years after surgery were 6/18 or higher except in one eye which had sustained severe injury 1 year after surgery. IOL implantation in leprosy patients has definite advantages and given the right management, is reasonably safe.

OCA 18

LEPROSY TRANSMISSION AND MUCOSAL IMMUNITY IN HOUSEHOLD CONTACTS OF SUBJECTS WITH NASAL PRESENCE OF *M. leprae*

Ravindra R Kamble, Dr. R.S. Jadhav, Miss A. Fernando, Miss V.S. Shinde, Mrs. S.P. Madhale, Dr. V. K. Edward, Dr. J.R. Rao and Prof. W.C.S. Smith on behalf of MILEP-2 Study Group*

Stanley Browne Research Laboratories, Richardson Leprosy Hospital, Miraj, Maharashtra-416410. Tel. No Off: 0233-211213 Fax: 0233-211708 E-mail: sblabtlm@vsnl.com

Multi Drug Therapy of leprosy has helped to bring down the prevalence rate, but the new case detection rate has not decreased in the endemic areas. A study was designed to look at the transmission and the development of mucosal immunity. In the present study, 3034 individuals from three villages in Miraj taluka in the State of Maharashtra, India were initially screened. Out of which a cohort of 154 subjects was identified as the household contacts of 42 individuals carrying *M. leprae* in their nose (PCR-C), and then followed up in a six monthly follow-up. Presence of *M. leprae* on the nasal mucosa in subjects studied was identified by Polymerase Chain Reaction (PCR) and mucosal immunity was detected by measuring the salivary anti-*M.leprae* IgA antibodies (sML-IgA) using ELISA. An average of 75% of the subjects (PCR-C) were positive for sML-IgA throughout the three follow-ups. sML-IgA positivity was higher in females than in males. Throughout the year, 65-80 % of the total subjects tested showed sML-IgA response. 3 subjects from PCR-C group were found to be PCR positive in the first follow-up, which became negative in the second follow-up. Subjects in all the age groups showed sML-IgA response. The response between BCG vaccinated and non-vaccinated individuals did not show any difference. In the follow-up studies it was observed that in the PCR-C group, two out three subjects were PCR positive in the summer season unlike the rest of the population,

which showed peak of PCR positivity in the monsoon. It is possible that close contact may play a role in transmission. Follow-up studies with shorter intervals can shed more light on the mechanism of.

OCA 19

LOW BONE MASS IN PATIENTS WITH PROLONGED REACTIONAL EPISODE.

Ximena Illarramendi, José Augusto Costa Nery, Euzenir Nunes Sarno.

Laboratório de Hanseníase, Departamento de Medicina Tropical, Instituto Oswaldo Cruz, FIOCRUZ, Av. Brasil 4365, Rio de Janeiro, RJ. CEP. 21045-900, Brasil.

Reactional episodes may recur after lowering the doses or ending the various treatments. Generalized osteoporosis has been reported during reactions and prolonged use of steroids could increase the risk for suffering it. In a previous study in treated leprosy patients, taking prednisone (PDN) resulted in 4 times higher risk of radiography diagnosed osteopenia. We evaluated 22 patients treated for multibacillary leprosy (10 females, 12 males) aged 23-49 years with prolonged reactional episodes. Bone mineral density (BMD) of the lumbar spine, the proximal femur and the distal radius was determined by dual X-ray absorptiometry using a LUNAR® densitometer. Erythema nodosum leprosum with neuritis was the most frequent form of reaction recorded (81%). The patients had been taken PDN among other drugs during an average of 39 ± 18 months. The mean daily dose received was 28.6 ± 13.1 mg/day. A positive significant correlation was found between the BMD measured at the different sites (femur/spine r=0.565 p=0.008; femur/radius r=0.678 p=0.001; spine/radius r=0.452 p=0.04). Osteoporosis was found in 5 patients (3 female, 2 male, 3 at age 20-29 years) in the spine and one also in the radius. Osteopenia was seen at 52 sites. No association was observed with sex or having a positive bacilloscopic index. For increasing cumulative dose of PDN lower z-scores were found in the femur (r=-0.45 p=0.04). The expected reduction of bone mass with age was not observed in this group of patients. The lowest mean values were observed in the lowest decade. In spite of the high daily doses of PDN received, few cases of osteoporosis were observed. Spinal osteoporosis could be a result of the prolonged use of steroids, but low bone mass at other sites could also be due to the reactional episode itself.

OCA 20

MARCADORES CLÍNICO-LABORATORIAIS AUXILIARES NO MONITORAMENTO DO ERITEMA NODOSO HANSÊNICO

Martins, A.B; Simão, J.C.; Foss, N.T.; Souza, C.S.

Divisão de Dermatologia da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo

Grande parte das complicações da Hanseníase é decorrente das reações hansênicas. O eritema nodoso hansênico (ENH) demonstra efeitos de acentuada formação de imunocomplexos.

Objectivos: Avaliar a freqüência de alterações clínico-laboratoriais em amostra de doentes com ENH. Enumerar os exames laboratoriais relevantes para o monitoramento das reações hansênicas

Casuística e Métodos: Procedeu-se levantamento e análise retrospectiva de prontuários-médico dos doentes assistidos no Ambulatório de Hanseníase, HCFMRP. Verificou-se registro da investigação clínico-laboratorial em 24 prontuários de doentes em vigência de reação tipo ENH.

Resultados: No total de 24 doentes, 50% eram do sexo masculino. Dos doentes avaliados, 80,9% apresentaram elevação de proteína C-reativa. Em 8 doentes, o nível de mucoproteína foi normal e o α - ácido glicoproteína (α-AGP) elevado em todos. Na avaliação de enzimas hepáticas, 58,3% apresentaram algum tipo de alteração: γGT estava elevada em 47,6%, TGP em 25% e TGO em 20,8%. Verificou-se redução da albumina sérica em 30,76% e a de proteína total em 12,5% dos doentes. Foi observada leucocitose em 50% dos doentes e anemia em 62,5%, sendo que 4 apresentaram valores eram inferiores a 7,0 mg/dl. Em 54,2% havia febre; em 33,4% artralgia; em 12,5% hepatomegalia; em 8,4% esplenomegalia; em 16,7% adenomegalia; em 25% sinais clínicos evidentes de neurite.

Conclusões: Nossos resultados confirmaram a relevância de avaliação multissistêmica, indicando alta percentagem de doentes com elevação da proteína C-reativa sérica, sugerindo esta medida como parâmetro de monitoramento da reação hansênica. Salienta-se que as alterações de enzimas hepáticas, particularmente, as canaliculares e os distúrbios hematológicos que devem ser investigados nos episódios de ENH.

OCA 21

OCULAR COMPLICATIONS OF LONG-TERM ORAL CORTICOSTEROID THERAPY IN PATIENTS WITH LEPROSY REACTIONS

Monica Jeha Maakaroun M.D. and Aldemar N.B. Vilela de Castro M.D.

Hospital São Geraldo/UFMG - Av. Alfredo Balena, 190 - Belo Horizonte/MG and, Sanatório Santa Izabel/FHEMIG – Betim/MG - BRASIL

The use of systemic or topical ophthalmic corticosteroids is an established risk factor in the development of ocular hypertension and/or posterior subcapsular cataract. Dermatologists often prescribe long-term oral corticosteroid therapy in the treatment of leprosy reactions and ocular side effects have not been reported yet.

There were 31 patients (mean age 36,8 ± 13,0 years) with leprosy reactions studied. All patients were receiving oral corticosteroid therapy (prednisone) for a mean duration of 18,7 ± 10,1 months. The dose range was 5 to 60 mg (mean dose, 19,8 ± 11,8 mg) by the time of the ophthalmologic examination. Of the 62 eyes, 14 (22,6%) showed ocular hypertension and 12 (19,4%) had posterior subcapsular cataract formation. Regular eye examinations are recommended for all patients during the entire course of long-term oral corticosteroid therapy to minimize ocular side effects and to prevent iatrogenic visual loss.

OCA 22

PREVALENCE AND CHARACTERISTICS OF NEUROPATHIC PAIN IN 303 PATIENTS WITH LEPROSY.

Patrick R.N.A.G. Stump, Rosemari Baccarelli, Lúcia H.S.C. Marciano, José R.P. Lauris, Somei Ura, Marcos Virmond, Manoel J. Teixeira.

Instituto Lauro de Souza Lima, CP 3031, Bauru - SP, Brasil, CEP 17034-971

Aim of investigation: This study aims to contribute to the knowledge of neuropathic pain prevalence in leprosy.

Methods: A total of 303 leprosy patients attending at Lauro de Souza Lima Institute and the Infections Disease Center were evaluated (58.7% lepromatous, 25.7% borderline, 13.9% tuberculoid and 1.7% indeterminate). All patients underwent neurological examination with special focus on the occurrence of pain, its localization, duration, installation, intensity (verbal scale) and quality (McGill Pain Questionnaire).

Results: Neuropathic pain was present in 174 (57.4%) patients. It occurred before (73.0%) or at the moment of evaluation (27.0%). Pain lasted more than six months in 138 (79.4%) and installed as bursts in 84 (48.3%) cases out of the 174 cases. It affected one or more peripheral nerve territories totalizing 291 territories, ulnar nerve in 101 (58.0%), tibial nerve in 48 (27.6%), polyneuropatic distribution as glove in 47 (27.0%) or sock 47 (27.0%). Pain was present at the moment of evaluation in 47 (27.0%) patients. It was moderate or severe in 41 (87.2%), constant in 30 (63.8%) and remitted in only 9 (19.1%).

Conclusions: Neuropathic pain is an important, frequent and lasting occurrence in leprosy. It is also a disabling condition that can lead to poor quality of life by itself. The low frequency of remitted pain suggests the need to a better approach of antalgic therapy in leprosy. There is also a need to develop a national study to quantify the prevalence of neuropathic pain in Brazil and to discuss the need of a national politic to implement antalgic therapy in leprosy.

OCA 23

PROPHYLACTIC STEROIDS TO PREVENT NERVE FUNCTION IMPAIRMENT IN LEPROSY: A RANDOMISED CONTROLLED TRIAL (TRIPOD 1)

A.M. Anderson, W.H. van Brakel, S.G. Withington, R.P. Croft, P.G. Nicholls, J.H. Richardus, W.C.S. Smith.

International Nepal Fellowship-RELEASE, PO BOX 28INF-RELEASE, PO BOX 28, Pokhara, Nepal

aanderso@inf.org.np

Aim: It was investigated whether treatment with low dose prednisolone for the first four months of multidrug treatment (MDT) would reduce the incidence of leprosy reactions leading to nerve function impairment (NFI), in patients with multibacillary (MB) leprosy at diagnosis.

Methods: A multicentre randomised, double-blind, placebo-controlled trial was conducted in leprosy control programmes in Nepal and Bangladesh. Eligible patients had a confirmed leprosy diagnosis, were between 15 and 50 years old, were starting MB MDT for the first time and did not require steroids for other reasons. Subjects were randomised to prednisolone 20 mg per day for 3 months, tapering during the 4th month, or placebo. Nerve function was monitored monthly. The main trial outcome was the percentage of patients needing full-dose steroid treatment for Type 1 reaction (RR), type 2 reaction (ENL), NFI or neuritis, assessed at 4, 6, 9 and 12 months from the start of the treatment.

Results: 636 patients were enrolled; 312 (49%) in the prednisolone arm and 324 (51%) in the placebo arm. There is a significant preventive effect of prednisolone at 4 and 6 months, but this is not sustained to the 12th month. At the end of the treatment phase, the relative risk of a poor outcome given placebo compared with prednisolone is 3.93 (95% CI 2.13-7.25). At 12 months there is still an increased relative risk, but the effect is not significant (RR 1.31, 95% CI 0.95-1.81)

Conclusion: Prophylactic treatment with steroids of MB patients starting on MDT with the given dose and duration prevents NFI at 4 and 6 months after the start of treatment, but the effect is not sustained at 12 months.

OCA 24

PROPHYLACTIC STEROIDS TO PREVENT NERVE FUNCTION IMPAIRMENT IN LEPROSY: THE EFFECT OF PRE-EXISTING NEUROPATHY OBSERVED IN THE TRIPOD 1 TRIAL

W.H. Van Brakel, A.M. Anderson, S.G. Withington, R.P. Croft, P.G. Nicholls, J.H. Richardus, W.C.S. Smith.

TLM Research Resouce Centre, 5 Amrita Shergill Marg, New Delhi – 11003

Aim: To assess whether prophylaxis with low dose prednosolone during the first 4 months of MB MDT will result in at least a 50% reduction in the number of patients experienceing Type 1 Reaction (T1R)

leading to nerve function impairment (NFI) compared to those receiving placebo treatment. This report describes the effect of pre-existing neuropathy on the outcome.

Methods: A multicentre randomised, double-blind, placebo-controlled trial was conducted in leprosy control programmes in Nepal and Bangladesh. Eligible patients had a confirmed leprosy diagnosis, were between 15 and 50 years old, were starting MB MDT for the first time and did not require steroids for other reasons. Subjects were randomised to Prednisolone-prednisolone 20 mg per day for 3 months, tapering during the 4th month, or placebo. Nerve function was monitored monthly. The main trial outcome was the percentage of patients needing full-dose steroid treatment for Type 1 reaction (RR), type 2 reaction (ENL), NFI or neuritis, assessed at 4, 6, 9 and 12 months from the start of the treatment.

Results: 636 patients were enrolled; 312 (49%) and 324 (51%) in the prednisolone arms, respectively. Pre-existing NFI older than 6 months was present in 153 subjects (24%). A striking difference was observed in the effect of the prophylaxis between these subjects and those without pre-existing NFI. In the former group, there was no significant difference between the treatment and placebo group at any point during follow-up, while in the latter, a strong protective effect was present at 4 months, relative risk 6.7 (2.7–16.7), gradually declining to 1.45 (0.97–2.18) at 12 months.

Conclusion: Prophylactic steroid treatment did not prevent reactions or NFI in those with pre-existing neuropathy. A strong protective efffective effect was observed in those without NFI during and directly after the prophylaxis, but this was not sustained during the 8 months of post-prophylaxis follow-up. The pathophysiological mechanism of reactions and neuropathy appears to be different in both groups.

OCA 25

STUDIES ON MECHANISM/S OF SILENT NERVE DAMAGE IN LEPROSY WITH SPECIAL EMPHASIS ON BIOCHEMICAL BASIS OF AXONAL ATROPHY

V.P. Shetty[1], M.P. Savel, K.T. Shetty[2] and N.H.Antia[1]

[1]The Foundation for Medical Research, 84-A R.G.Thadani Marg, Worli, Mumbai 400 018, India Tel: 91-22-4934989, Fax: 91-22-4932876; E-mail: frchbom@bom2.vsnl.net.in

[2]National Institute of Mental Health and Neurosciences, Bangalore.

Pathomechanism/s of silent nerve damage in leprosy is not known. A morphological feature commonly seen in leprous nerves was the presence of atrophic axons. Question that remained was why and how such atrophic changes occur. A further study therefore was carried out to understand the structural and biochemical basis of axonal atrophy in leprous nerves. Since axonal caliber is governed by the C-terminal phosphorylation of high molecular wt. Neurofilaments (NF-H and NF-M) it was hypothesized that there may be involvement of the same following infection with *M.leprae*. In order to test this hypothesis, the state of NFH phosphorylation was studied in leprous nerves using immunohistochemistry, SDS-PAGE, WB technique (using SMI-31 antibody) and correlated with morphological changes. Both human and experimental mouse sciatic nerve model are used for the study. The results indicate that there is disturbance in the phosphorylation mechanisms of neurofilaments in leprous nerves in contrast to controls. It is also noted that the bacterial antigens play a crucial role in triggering these changes It is suggested that the observed hypo-phosphorylation of NF proteins could be the factor behind the Silent Neuropathy that precedes clinically demonstrable manifest hypo-anesthesia and anesthesia.

OCA 26

THE DEFORMED FOOT: CORRECTIVE ARTHRODESIS IN LEPROSY IN NEPAL

Mark Macdonald, Malcolm Stoney and Richard Schwartz

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

Nerve invasion by leprosy bacteria commonly results in neurologically impaired lower limbs. Denervation to external and internal structure can lead to stress fractures, collapse and recurrent ulceration. This commonly presents as a foot with change of normal anatomy and function. In a foot which has concurrent loss of normal protective sensation, the risk of further damage is high. The aim of corrective osteotomy and arthrodesis is to restore the foot to as close as possible to the normal anatomical foot, to fit conventional footwear and to decrease recurrent ulceration.

Aim: To review the results of corrective arthrodesis surgery performed over a twenty-year period at two major tertiary leprosy referral centres in Nepal

Methods: Data was collected by review of medical records of all patients who had undergone an arthrodesis of the foot or ankle at Anandaban Green Pastures Hospitals between 1980 and 2000. Types of procedure, methods of fixation, post operative complications and fusion rates were reviewed, as was the incidence of recurrent ulceration.

Results: 116 corrective arthrodesis were performed in 107 patients (73 male, 34 female) There was a 13% infection rate and six patients required a further procedure. 16% failed to fuse but in some cases the fibrous ankylosis was adequate for stability. 63% avoided further admissions for recurrent ulceration after the procedure. The complication rate was high but in line with that of the literature.

Conclusion: These results indicate that corrective arthrodesis is helpful in reducing recurrent ulceration secondary to deformity, but that occasionally further procedures such as soft-tissue reconstruction must be considered. Corrective arthrodesis will also enable the patient to wear normal footwear in most cases. Arthrodesis in those with recurrent acute neuropathic symptoms can also prevent further bone and joint destruction.

OCA 27

THE INFIR COHORT STUDY: ANALYSIS OF RELIABILITY AND NORMAL DATA FROM THERMAL SENSORY TESTING

Peter Nicholls, Wim H. van Brakel, Loretta Das, Alex Mathew, Sujai K. Suneetha, Rupendra S. Jadhav, Pranava Maddali, Diana N.J. Lockwood, Einar Wilder-Smith and K.V. Desikan

Aim: The INFIR Cohort Study aims to find clinically relevant predictors of nerve function impairment (NFI) and reactions.

Design: A multi-centre cohort study of 300 multibacillary patients, followed for two years.

Methods: Staff in the field centres were trained, reliability testing of the key techniques was done and normal reference data were collected. The test methods include Thermal Sensory Assessment using the Medoc TSA II Neuro Sensory Analyzer, a computer-based system that logs warm and cold detection thresholds by nerve in a data base. After training, staff at each centre completed paired bi-lateral assessments of some 60 leprosy patients, assessing cold and warm thresholds on ulnar, median, radial cutaneous, posterior tibial and sural nerves. Having established adequate reliability, we proceeded with collection of data to assess normal detection thresholds for warm and cold sensation. We recruited consenting volunteers, without signs of neurological disorders or diabetes, from amongst individuals not affected by leprosy attending the hospital outpatient department. Data were collected on people in four age groups of 75 individuals each, 10-30, 31-40, 41-50 and 51-60 years, with equal sex distribution within each group. For both reliability and normal data analysis of thermal sensation we extracted data from the Medoc data base and completed the analyses using Excel and STATA. For the reliability study, analysis followed the method of Altman and Bland.

Results: We found good agreement between paired assessments for both warm and cold detection thresholds. From the analysis of normal data we present age group-specific thresholds within each sex group. Because of the skewed nature of the data we discuss the need to compute these from log-transformed data. Implications of our findings are discussed.

Conclusion: The investigations described show that thermal detection thresholds in hands and feet can be reliably tested and quantified in a leprosy-endemic population

OCA 28

THE INFIR COHORT STUDY: INVESTIGATING PREDICTION, DETECTION AND PATHOGENESIS OF NERVE DAMAGE AND REACTIONS IN LEPROSY

Wim H. van Brakel, Peter Nicholls, Loretta Das, Alex Mathew, Sujai K. Suneetha, Rupendra S. Jadhav, Pranava Maddali, Diana N.J. Lockwood, Einar Wilder-Smith and K.V. Desikan

TLM Research Resource Centre, 5 Amrita Shergill Marg, New Delhi – 11003 - wvbrakel@mail.com

Aim: To find clinically relevant predictors of nerve function impairment (NFI) and reactions, to determine which method(s) of nerve function assessment are most sensitive in detecting peripheral neuropathy, to study the pathogenesis of peripheral neuropathy and reactions and to create a bank of biopsy specimens and sera, backed up by detailed clinical documentation.

Design: A multi-centre cohort study of 300 multibacillary (MB) patients, followed for two years.

Methods: All newly registered MB patients requiring a full course of MDT are eligible. MB patients are defined as those who are smear positive and/or have 6 or more skin lesions and/or have two or more nerve trunks involved. A detailed history is taken, including an activities of daily living assessment, and physical and neurological examinations are done. Peripheral nerve function is evaluated at each visit using sensory and motor conduction testing, quantitative thermal sensory testing, electronic vibrometry, dynamometry, Semmes-Weinstein monofilaments (SWM) and voluntary muscle testing. The study outcome for sensory and motor impairment uses the latter two tests as the 'gold standard'. Other outcomes are Type 1 and 2 reactions and neuritis. A severity scale is used to grade the severity of the latter three outcomes. All subjects have a skin biopsy at registration, repeated at the time of an outcome event. At that time a radial cutaneous or sural nerve biopsy is also taken. The biopsies are being examined using a variety of immuno-histological techniques to detect cell populations and cytokine production. Blood sampling for immunological testing is done at every 4-weekly clinic visit. Samples are frozen in liquid nitrogen and transported by train to the designated laboratories. A specimen bank has been set up at the Blue Peter Research Centre in Hyderabad.

Results: By February 2002, 230 subjects had been enrolled. Enrolment is expected to close in Spring 2002. Reliability studies of the neurophysiological tests have shown good results. Details of some of the methods will be presented.

OCA 29

THE LINK BETWEEN FACIAL PATCHES AND LAGOPHTHALMOS OCCURRENCE DURING TYPE 1 REACTION IN LEPROSY

Diltor V.A. Opromolla, Rosemari Baccarelli, Somei Ura, Marisa Goebel, Cassio Ghidella.

Instituto Lauro de Souza Lima, CP 3031, Bauru - SP, Brasil, CEP 17034-971

Aim: This study aims to investigate the relationship between facial patches and lagophthalmos occurrence during Type 1 reaction in leprosy.

Methods: The charts of paucibacillary leprosy patients attended at Lauro Souza Lima Institute (ILSL) in Bauru - SP, Brazil, were reviewed for facial patches due to Type 1 reaction and for recent zygomatic temporal branches damage of the facial nerve. Facial patches were divided into "significant" patches (more than three centimeters in diameter, located on the zygomatic region and/or around the eye) and "other" patches (smaller than three centimeters in diameter and/or located elsewhere in the face). This study was divided in two categories: retrospective (patients attended at ILSL from 1983 to 1993) and a prospective part (patients attended at ILSL after 1993). To be part of this study the patient should not be using steroids during the reaction course.

Results: In the retrospective category, the majority of patients were already using steroids when they were studied. This also occurred in the prospective category, but in a smaller percentage. Overall, 7.5% of the patients studied were not using steroids and did not have lagophthalmos when they were examined throughout the course of the reaction.

Conclusions: The lagophthalmos is not a mandatory condition in the presence of facial patches due to Type 1 reaction therefore, there is no need to use the steroids as a profilatic if there is no damage in the zygomatic temporal branches of the facial nerve.

OCA 30

USE OF AZATHIOPRINE IN THE TREATMENT OF LEPROSY TYPE I REACTIONS

Rachel Hawksworth, Sharon Marlowe, Ruth Butlin, Maria Jacob K, Murdo Macdonald, Peter Nicholls and Diana Lockwood.

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

Type I reactions (T1R) are acute inflammatory episodes which occur in about 30% of non-polar leprosy patients. The standard treatment of these reactions is with corticosteroids (prednisolone). However, these often need to be given for long periods of time and so the risk of side effects is therefore considerable.

Aim: To reduce the overall steroid dose by the use of azathioprine as an adjunct treatment in severe T1R, and to document the safety profile of azathioprine in leprosy.

Methods: A total of 40 T1R patients were recruited between June 2000 and September 2001. The test group received azathioprine at a dose of 3mg/kg/ day with a reduced course of steroids, while the control group received the semi-standard WHO 12 week prednisolone course. Patients were assessed at intervals during and following the treatment course using a severity grading which included appraisal of skin, systemic and nerve signs, and also VMT and ST assessments.

Results: During the six months of monitoring, 23 patients required extra prednisolone (13 in the azathioprine plus prednisolone group and 10 in the prednisolone only group). Results will be presented of a comparison between the clinical outcomes of skin, systemic and nerve indicators in the two treatment groups.

Conclusion: Azathioprine has been shown to be a safe drug for use in leprosy. Our evidence indicates that it may be a useful steroid-sparing agent in leprosy, but further studies in this regard are required.

OCA 31

ZONAS CUTÁNEAS INMUNES A LA LEPRA

Dr. José Terencio de las Aguas

Es evidente el dermotropismo del *Mycobacterium leprae* por la piel, y lo abundante y frecuente de estas lesiones, sin embargo hay zonas cutáneas que nunca o excepcionalmente son afectadas por la Lepra, como son las regiones inguinales, pubis, genitales masculinos y femeninos, axilas, cuero cabelludo, palmas y plantas.

Se expone nuestra experiencia personal durante 49 años en unos tres mil enfermos y nunca hemos observado lesiones en axilas, genitales e ingles, pero sí aunque no son frecuentes en cuero cabelludo, palmas y plantas, y pubis, y casi todos en pacientes LL y BL siendo las lesiones clínicas maculas infiltradas y nódulos.

Más excepcionales son las Reacciones en las lesiones de estas zonas, habiendo observado algún caso de Eritema Nodoso en cuero cabelludo y genitales masculinos.

Curiosamente, no obstante, la preferencia del *M. leprae* por las zonas más frías y periféricas del cuerpo, poco suelen ser afectados el cuero cabelludo, genitales, palmas y plantas.