

DC69**DIABETIC FOOT REHABILITATION IN
ISTANBUL LEPROSY HOSPITAL**

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Foot ulceration in patients with Diabetes Mellitus is a major public health problem. The minister of health estimates there are 3 million people in Turkey affected by diabetes. 107 male, 77 female total 184 diabetic cases were investigated whom were evaluated in Istanbul Leprosy Hospital. The average age was 61.2, and the average duration of disease was 18 years. 98% of them were seen to have loss of sensation, 17% to have weakness of muscles, 10% have had peripheral vascular disease, 67% of them have ulcers on their feet due to neuropathy, 30% to have local amputation and 2% to have below knee amputation. 5% of the patients have Charcot joint.

We have given them health education about neuropathic foot care and protective shoe.

The poster will show experiences from Istanbul Leprosy Hospital where diabetics can get foot care and rehabilitation.

DC70**EFFECTIVENESS OF PROTECTIVE ORTHOPAEDIC SHOES
IN NEUROPATHIC AND DEFORMED FEET IN LEPROSY**

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The orthopaedic shoe workshop was initiated in our hospital in Bakırköy, Istanbul in 1980. The objective of this workshop is to help prevent foot injuries as a result of loss of protective sensation, also to provide protective and corrective footwear and orthoses to patients with deformities.

681 leprosy patients were studied in this survey and they were evaluated according to their age, sex, level of education the regions they live, as well as the condition of their feet and the type of shoes they required. 74% of these patients were male and 26% were female, the average age was 55.10%. 86% of these cases came from rural areas, 62% were illiterate, 67% of them were unemployed, 30% of them were seen to have loss of sensation, 53% to have claw toes, healed ulcer, drop-foot, 27% to suffer severe disability.

33% of them have had two pairs slippers and protective shoes in a year, 40% have had orthopaedic shoe when they need it, 21% of them wears commercial shoes and we follow them, 2% refuse to use special shoe for them, 4% of them are very old and we give them only orthopaedic slippers for home.

All the other results will be analyzed and the advantages of orthopaedic shoes will be discussed at the congress.

DC71**THREE-YEAR RESULTS OF SELF-CARE AMONG 856 DISABLED PEOPLE
AFFECTED BY LEPROSY**

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The final evaluation results of eyes, hands and feet in the Stage 1 Collaboration Project between MOH and TLMI were summarized. Among 856 people with eye, hand and foot disability, 70% of eye infection (red eye) disappeared, 80% of cracks on hand and foot disappeared, 40% of plantar ulcers healed, 18 wounds on 15 patients' hands healed, and 80% of people affected by leprosy (PAL) formed self-care habits showing that self care was acceptable for PALs and disability could be prevented only if health care and supervision were carried out well and intensively.

DC72**USING NATURAL RESSOURCES**

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Sankuru (Democratic Republic of Congo), is located in the dense tropical rain forest, where people are usually practising traditional medicine.

This is a story of Mr. Dienena, a sixty years old man, known previously as a leprosy healer, and who finally got leprosy.

Many years ago he treated leprosy patients by applying local medicine on the skin, in order to regain normal skin condition. When he found that he was not able to treat properly himself, he came to our clinic where he received proper treatment.

Today he is helping us in finding new cases as a health worker, and is bringing to health units his previous patients for right treatment (MDT) and health education.

In the other hand, we are experiencing the use of a tree resin for the treatment of leprosy ulcers. One of our patients was applying that resin, locally called "TSHO". It's original name is "Austranella", which is as well used by the Catholic church as incense. The substance is known to have a medical effect on wounds. We still need to produce a pharmaceutical ointment, taking in account the guidelines of Dr. Hans Martin Hir's "Topical Medicine". The results obtained by applying the ointment after having soaked and trimmed the ulcer, are encouraging.

Success in healing ulcers requires all the attention of the health worker, to train patients in self-care, changing behaviours in getting family support.

EPIDEMIOLOGY

EP01**SPATIAL DISTRIBUTION OF M. LEPRAE PCR POSITIVE
INDIVIDUALS IN AN INDIA COMMUNITY**

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The problems of identifying sub-clinical infection and those of in vitro cultivation of M. leprae have limited study of the transmission of leprosy infection in endemic communities. Early studies have demonstrated the high rate of discharge of M. leprae from the nose in bacilliferous leprosy patients and the presence of early lesions in the

nasal mucosa. The ability to use polymerase chain reaction (PCR) techniques to identify small numbers of M. leprae now gives potential to study transmission in endemic communities.

A leprosy endemic village (population : 1442) in South-West India where leprosy control activities have been underway for more than 20 years was selected for study. A survey of residents was conducted in 1997 where individuals were examined and nasal swabs taken from 1298 subjects to test for the presence of M. leprae using PCR methods. The house location of old and current patients in the village is known from the leprosy control records. The leprosy cases (old and current) have been plotted on the map of the village along with the location of those identified as having PCR positive nasal swabs. The spatial distribution of cases and PCR positive individuals is presented in this analysis and hypotheses of the transmission discussed based on these findings. Two more villages will be surveyed as part of this ongoing study.

EP02

PATIENT CONTACT IS THE MAJOR DETERMINANT IN INCIDENT LEPROSY: IMPLICATIONS FOR FUTURE CONTROL

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Notwithstanding the elimination efforts, leprosy control programmes face the problem of many leprosy patients remaining undetected. Leprosy control focusses on early diagnosis through screening of household contacts, although this high risk group generates only a small proportion of all incident cases. We explored the extent to which other contact groups contribute to incident leprosy. We examined retrospectively incident leprosy over 25 years in a high endemic village of 2283 inhabitants in Sulawesi, Indonesia by systematically reviewing data obtained from the local programme and actively gathering data through interviews and a house to house survey. We investigated the contact status in the past of every incident case. In addition to household contact, we distinguished neighbour and social contact. Of the 101 incident cases over a 25 years period 79 (78%) could be associated to contact with another leprosy patient. Twenty-eight of those 101 cases (28 %) were identified as household contacts, 36 as neighbours (36%) and the remaining 15 (15%) as social contacts. Three patients had not had a previous contact with another leprosy patient and no information could be gathered from 19 patients. The median span of time from the registration of the primary case to that of the secondary case was 3 years; 95% of the secondary cases were detected 6 years after the primary case. Thus, contact with a leprosy patient is the major determinant in incident leprosy, whereby the type of contact is not limited to household relationships, but also includes neighbour and social relationships. This finding can be translated into a valuable and sustainable tool for leprosy control programmes and elimination campaigns by focussing case detection and health promotion activities not only on household contacts but also on at least neighbours of leprosy cases.

EP03

AN EPIDEMIOLOGICAL STUDY OF *M. LEPRAE* INFECTION AND DISTRIBUTION OF LEPROSY BACILLUS IN THE ENVIRONMENT OF ENDEMIC VILLAGES IN NORTH MALUKU, INDONESIA.Shinzo Izumi¹, Masanori Matuoka², Teky Budiawan³, Noboru Nakata³ and Kesanke Sacki¹ National Leprosarium Oshima Seisho-En, Kagawa, Japan, ² Leprosy Research Center, National Institute of Infectious Diseases, Tokyo, Japan, ³ Ternate Leprosy Hospital, North Maluku, Indonesia.

It is well known that the geographic distribution of leprosy is highly heterogeneous. There are relatively small areas with very high prevalence and incidence. Little is known, however, about the reasons why leprosy is so prevalent in the area. We conducted, therefore, a series of epidemiological survey in such an area to estimate the rate of *M. leprae* infection by serological techniques, and distribution of leprosy bacilli in the environment by polymerase chain reaction. The selected district was North Maluku, Indonesia, where estimated prevalence was 2.5%.

It was found that about one third of the healthy villagers had anti-*M. leprae* specific phenolic glycolipid-I IgM antibodies without evidence of direct contact with leprosy patients, suggesting that epidemiologically important sources of *M. leprae* infection is not the leprosy patient but non-human source(s).

As the first step of searching the possible sources in the living environments, we examined all water sources for washing clothes, bathing and drinking in the villages. It was found that 13 out of 27 samples contain *M. leprae* specific DNA by nested-primer gene amplification technique (PCR). The 347bp PCR product was proved to have the same base sequence with *M. leprae* DNA fragment.

Our results are the first epidemiological observation to suggest that environmental *M. leprae* may play an important roles in the infection of leprosy bacillus and the transmission of leprosy in the endemic areas.

EP04

SEROREACTIVITY OF 102 NONHUMAN PRIMATES TO PGL-I OF MYCOBACTERIUM LEPRAE IN THE REPUBLIC OF BENIN

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Naturally-acquired leprosy prevails in armadillos in the USA, and afflicts mangabey monkeys and chimpanzees in West Africa. Evidence in the US suggests that humans occasionally acquire leprosy from *M. leprae*-infected armadillos or their products. Thus, leprosy can be zoonotic, making the total eradication of leprosy exceedingly difficult. We conducted a serological survey for antibodies to PGL-I of *M. leprae* in nonhuman primates in Benin to obtain data relevant to the question of extrahuman reservoirs of leprosy in West Africa.

All animals originated from the wild and were either pets or sentinels at their owner's residence. Each animal was anesthetized on site with Ketamine via blowgun and drt. After clinical examination, venous blood was taken. No animal died or was injured. Sera were analyzed by a gelatin particle agglutination test (SERODIA-Leprae, Fujirebio Inc Tokyo) for antibodies to *M. leprae* PGL-I. Of the 102 animals the origin of 53 was known; 51 from Benin, 2 from Togo.

Ten animals (9.8%) were positive for antibodies to PGL-I: 9 of 48 baboons (19%), 1 of 23 patas monkeys (4%), none of 31 vervet monkeys. One positive baboon originated from Togo. We found no lesions consistent with leprosy.

We conclude that the data suggest nonhuman primates in West Africa may be reservoirs for *M. leprae*; however, additional studies are needed to establish the specificity of the test employed for PGL-I of *M. leprae* in the animal species examined.

EP05

IMPLICATIONS OF ENVIRONMENTAL MYCOBACTERIAL INFECTIONS FOR THE EPIDEMIOLOGY OF LEPROSY

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Most human populations are exposed to a variety of "environmental" or "atypical" mycobacterial infections. There is much evidence for cross-immunity between different mycobacterial infections, the most obvious examples being the protection by BCG (a derivative of *M. bovis*) against human leprosy, tuberculosis and *M. avium* infections. In addition, animal experiments have shown that exposure of mice or guinea pigs to a variety of different mycobacteria imparts varying levels of protection against subsequent challenge with *M. leprae* and *M. tuberculosis*. Such exposure in natural settings may explain several important features of leprosy, including geographic clustering (reflecting local variations in environmental mycobacterial exposure), regional differences in the observed efficacy of BCG (whose protective action may be masked by the protection provided by other mycobacterial infections) and perhaps also regional differences in disease type (though the evidence here is more speculative). The large number of different species of environmental mycobacteria, and the fact that many are non-cultivable, has inhibited research on this subject, but extensive skin testing in Malawi with a variety of mycobacterial antigens has provided evidence that exposure to agents which share antigens with *M. leprae* imparts protection against leprosy. This paper will examine the global evidence and provide detailed analyses for the involvement of environmental mycobacteria in leprosy.

EP06

EARLY DETECTION BY ELISA AMONG 33 NEW CASES OF LEPROSY IN HOUSEHOLD CONTACTS OF MULTIBACILLARY PATIENTS IN CEBU (1985 - 1997).

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To assess the value of ELISA in early detection of leprosy we conducted a blinded prospective study among 601 household contacts (age x=29, 267 male, 334 females) of multibacillary cases in Cebu, Philippines. The study started in January 1985. Using the ND-OBSA antigen we found 1.4% of 401 endemic controls (age x=34, 202 male, 199 female) and 91% of 193 multibacillary index cases were ELISA positive. During the study MB patients and their contacts were enrolled as MDT

treatment was started. All contacts enrolled were screened to be free of leprosy. Any contact who developed disease was immediately treated with MDT. The diagnostic team was not given ELISA results. Serum samples were collected at six month intervals until 1989, then another survey was done in 1991. Between 1989 and 1991 and after 1991, passive surveillance was used to detect cases. Of the 601 contacts enrolled 559 were bled and followed for two or more times. The average duration of ELISA follow-up for the 559 contacts was 4.2 ± 1.6 years until 1991. The 33 new cases came from 27/186 households: 6 household had two each and the remaining 21 households one case per household. The average duration in the for development of disease after enrollment was 3.7 ± 3.1 yrs for 15 MB cases and 3.6 ± 1.9 yrs for 18 PB patients. Since the contacts had no sign of leprosy at enrollment and the index patient was on MDT, a contact who became a case was most likely was incubating the disease at intake. The last reported case was detected in 1996 with 9 years in the study as an MB with BI 4.0 and ELISA positive(+) in 1991. In 1994, a second MB case, BI 4.2, was detected after 9 years in the study. He was ELISA(+) at entrance to the study in 1985. These cases have the longest duration in the study prior to the development of disease. The mean duration for household exposure of new cases to the index was: PB 19.3 ± 8.8 yrs and MB 20.5 ± 6.6 yrs, as determined by interview. Of new MB cases 93%(14/15) and 33.3%(6/18) PB cases were ELISA(+). Of these five MB and three PB cases remained ELISA (+) from start of monitoring through 1991. Nine MB and three PB cases became ELISA(+) during the study. Eighty percent of ELISA (+) cases have other contacts in the household that are also ELISA positive. These findings and our earlier studies indicate that the ELISA was effective in identifying the subsets of household contacts who have a very high risk of developing leprosy and an even higher risk of developing multibacillary disease (RR \geq 40) and that being ELISA positive carries a long term risk for developing MB disease. Application of this test to household contacts combined with traditional diagnostic methods could assist control programs in early detection of leprosy and especially multibacillary disease. Application of these findings to chemoprophylaxis is a next step logical step, keeping in mind that the most likely disease to develop in ELISA(+) contacts is MB.

EP07

MONITORING PROPHYLACTIC TREATMENT OF ELISA POSITIVE CONTACTS OF LEPROSY PATIENTS IN CULION.

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Multibacillary leprosy (MB) is difficult to diagnose unless frank signs have occurred, when MB patients are found they are usually detected with high bacterial index (BI) of 3, 4 or 5. This observation suggests that high BI individuals are not recognized as cases of leprosy for some time before signs occur. Since transmission is associated with MB (BL and LL) patients, it is reasonable to assume that among these strongly BI positive incubating cases, some will serve as an undetected reservoir of transmission. The incubation period prior to onset of clinical symptoms is thought to last several years after infection. Since the ELISA based on the PG-I antigen of *M. leprae* is known to be positive in MB patients both before diagnosis, and is also associated with declining ELISA values during treatment, we decided to use this test as a marker for candidates for chemoprophylaxis. In studying 6,837 contacts of leprosy patients Culion, we found positive serology correlated with a high risk of developing leprosy, RR=23(95%CI=12-45). The relative risk of developing MB disease increased among ELISA positive contacts of patients to a RR = 48(17-132). With this background information, we monitored 37 ELISA positive contacts of leprosy patients with the ELISA during preventive chemotherapy in a double blind trial. These contacts had positive ELISAs with OD readings greater than 0.2 on at least two consecutive tests. The treatment group of 19 was given rifampin daily every other month for three months and three doses a week of Clofazimine on alternate months for three months. Dapsone was given daily. The control group of 17 was given a placebo. ELISA monitoring at six month intervals measured OD values within the two groups. The age, sex, starting OD values were similar for both groups. Significant declines in ELISA values were found in the treatment group, compared to the placebo group. Chi square values were: 5.8 at six months, 4.2 at 12 mo. and 5.6 at 18 mo., p=0.03, 0.04, 0.02. No significant changes were found in OD values for the placebo group comparing initial values with 6, 12, 18 month values by Ttest. The Ttest values for the treated group drop significantly at 6, 12, 18 mo., p<0.01, p<0.02 and p<0.01. No side effects were detected with treatment clinically or by monitoring of liver function. These results demonstrate the value of serological selection and monitoring in its application to chemoprophylaxis in leprosy, where there is no other means of identifying incubating disease. These findings also indicate the potential of focal use of the ELISA in eliminating foci of infection in the community.

EP08

DETERMINANTS IN THE DEVELOPMENT OF LEPROSY AMONG HOUSEHOLD CONTACTS OF LEPROSY PATIENTS IN CULION ISLAND, PHILIPPINES

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Observations made from incidence studies among household contacts (HHC) of leprosy patients have established that HHC of

leprosy have the higher risk of developing leprosy infection and disease. To investigate further this data, a longitudinal seroepidemiological survey covering 80% (7547/8508) of the islands accessible population was conducted. One of the objectives of the study is to identify the determinants associated with the development of leprosy among HHC who have intra-familial contact with currently and/or previously infected hansenite. Over the 5 years duration of the study 34/2012 HHC developed clinical leprosy. Sociodemographic profiles and other determinants including positivity to IgM antibody to PGL-1 were analyzed among HHC who develop the disease compared to HHC who did not develop the disease. The following factors were found to be significantly present among HHC who developed leprosy: age when first stayed in Culion, duration of stay in Culion, age of exposure with index case, number of index case in the household and positive serology. This study was able to establish an epidemiological data bank that could be used as a database for designing intervention strategies by the National Leprosy Control Program of the Department of Health in the future.

EP09

MILEP 2: SUB-CLINICAL LEPROSY INFECTION AMONG HEALTHY CONTACTS IN ADDIS ABABA, ETHIOPIA

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With the advent of multi-drug therapy (MDT) for leprosy, the prevalence of the disease has come down tremendously. However, despite effective MDT, the incidence of the disease has remained static in areas where the MDT program has been going on for the last 10 years or more. The possible explanation for the incidence not coming down, could be the presence of people with sub-clinical infections in the community who can serve as reservoirs, of whom only a few become overt clinical cases.

To explore this possible transmission route and also to elucidate the pathogenesis of primary nasal infection in leprosy, pilot studies on a small number of newly diagnosed, untreated leprosy patients (n=20) and healthy contacts or family members of leprosy patients who were released from treatment in the past years (n=15), were conducted. Using polymerase chain reaction to detect *Mycobacterium leprae* DNA from nasal swab material, 2 of the patients and 2 of the healthy contacts were positive.

Anti-*M. leprae* IgA antibody was also detected in saliva by ELISA. Eighty percent (16/20) of the patients and 33% (5/15) of the healthy contacts had Anti-*M. leprae* IgA antibody.

The results of this study to date are consistent with results from the MILEP 2 study in India using similar methods and suggest that such methods may be useful for investigation of transmission and immunity in leprosy in Ethiopia.

EP10

SEROLOGICAL AND PCR MONITORING OF THE EFFECTS OF PREVENTIVE THERAPY AGAINST LEPROSY

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A WHO-Special Action Project for Elimination of Leprosy has been implemented in the Federated States of Micronesia (FSM), in which one dose of rifampin 600 mg, ofloxacin 400 mg, and minocycline 100 mg were given to residents without any sign of leprosy. Serum and nasal swab specimens from the residents were obtained before and on year after one-dose preventive therapeutic drugs and used for detection of antibodies and of *Mycobacterium leprae* by PCR, respectively. Of 1,725 serum samples obtained from three states of FSM before starting preventive therapy, 240 (13.3%) had elevated antibodies to phenolic glycolipid I (PGL-I), the *M. leprae*

specific antigen. The seroprevalence to PGL-I was the highest among the teenage school students (19.1%), followed by the age group of 21-30 years old (15.1%). Surprisingly, 15 (13.3%) of 112 samples from young children (age ≤ 10) were seropositive to PGL-I, indicating the active transmission in the community. Serum samples from 80 students from whom paired sera were obtained before and one year after preventive therapy were analyzed. Among 80 sera, there was no change in the seroprevalence of anti-PGL-I antibodies before and one year after preventive therapy at 23.8%. There were four residents who had seronegative conversion one year after therapy, but other four had seropositive conversion even after preventive therapy. There was also no change in seroprevalence to *M. leprae* soluble antigen and lipoarabinomannan one year after preventive therapy. However, the mean absorbance to PGL-I in seropositive serum samples decreased by 15% one year after preventive therapy. In addition, of 629 nasal swab samples obtained before preventive therapy, 12 (1.9%) were PCR-positive for *M. leprae*, while 9 (1.4%) of 622 samples obtained after preventive therapy were PCR-positive. The results thus failed to show statistically significant decrease in seroprevalence to *M. leprae* antigens and in PCR-positive rate one year after preventive therapy. Further evaluation of long term effects of preventive therapy against leprosy is undertaken.

EP11

ILLUSIONS FROM VISUAL INTERPRETATION OF LEPROSY CONTROL MONITORING DATA

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National Leprosy Eradication Program (NLEP) monitoring statistics routinely collected from leprosy endemic area shows a declining trend in prevalence after the introduction of Multi Drug Therapy (MDT). The assessments based on visual interpretation of NLEP monitoring data or any other data have several pitfalls; therefore the impact on leprosy situations in these areas should be adjudged with extra care. An attempt has been made to examine the leprosy situation and its associations with the type of case detection strategies practiced in different areas.

The data from 3 areas with different case detection strategies has been used for this study. We reanalyzed the same data using in-depth epidemiological analysis and found that Rapid case detection approach covering entire population in short periods is more closely associated with favourable changes in leprosy situations in an area compared to the other areas where conventional total population survey at an interval of 3 years or more are in practice.

Hence the visual approach to the analysis of NLEP monitoring data although seemingly convincing, can be misleading. It is evident from in-depth epidemiological analysis that prevalence though higher in certain areas, the leprosy situations is favourable compared to other endemic areas with different case detection approach.

EP12

RISK OF DEVELOPMENT OF LEPROSY AMONG CULION CONTACTS

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Culion Sanitarium is the oldest existing sanitarium in the Philippines, est. 1906. An island-wide MDT program was started in 1987 and found new cases and prevalence rate of 75/10,000 and 260/10,000 respectively. In 1991 there were 13 new cases, from 1991 to 1997 the average annual number of new cases was 7.9, with 6 new cases in 1997. The population of the Island expanded from 11,070 in 1987 to 18,590 in 1997. In 1997, the incidence was 3.2/10,000 and prevalence 9/10,000. The decline in prevalence was the result of removal of treated cases from registration after MDT and an increase in the over all population by 68%. Most of the population growth was in the community contacts. To investigate the persisting emergence of new cases after the completion of the MDT, occurring at a rate similar to the early 1980's, a new survey was started in 1990 to 1991 covering 90% of stable Culion Island population over 5 years of age. This population was followed from 1991 to 1997. Contacts were placed in two groups: household (HHC) and community (CCC) contacts depending on presence of index cases at home. They were clinically and serologically examined regularly every 6 months. Thirty seven new endogenous cases were diagnosed from 1991-1997: 34(92%) HHC and 3(8%) CCC. A total of 6837 contacts were included in the study of which 54% were female. The contacts were: CCC = 4750 (69.5%) and HHC = 2087 (30.5%). The ELISA was positive for 400 (5.9%) contacts: 118 HHC and 282 CCC. The relative

risk (RR) of HHC developing leprosy was 26 times greater than CCC with a 95% Confidence Interval of (8, 84). The RR of HHC to develop MB disease was 43(6,323) times greater and for PB 17(4,74) greater than CCC. The distribution of ELISA (+) reactions in new cases was: MB 15/20 (75%) and PB 7/17 (41%). The risk of ELISA (+) HHC and CCC of developing any type of leprosy (MB/PB) was RR = 24 (12,45) when compared to ELISA (-) contacts. The risk of ELISA (+) HHC to develop MB disease is 47(17,127) times greater than ELISA negative HHC, with a RR = 15(5,40) for PB HHC. In addition, the risk to develop MB leprosy in ELISA (+) HHC was a RR = 133(52,348) compared to all CCC and ELISA(-) HHC. We found the major risks for developing leprosy were being a HHC and/or ELISA (+). These findings show that household contacts should be a focus of attention of control programs, when ever a new case appears and that most new cases come from households with index cases. The application serology allows the focus of control of transmission to be refined to about 6% of HHC, who are at the greatest risk of developing MB disease.

EP13

ESTIMATING HIDDEN PREVALENCE OF HANSEN'S DISEASE COMBINING TWO RELATED VARIABLES: DIAGNOSIS DELAY AND GRADE OF DISABILITY AT TIME OF DIAGNOSIS

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We have analysed a database of 4142 Hansen's disease (HD) patients, diagnosed in Rio Grande do Sul State (RS), Brazil, between 1970 and 1991. Out of these 4142 cases, 3291 had their grade of disability (GD) evaluated at time of diagnosis and had recorded the information given by the patient about the time elapsed between the beginning of the symptoms and the moment when HD was identified by a physician (diagnosis delay - DD). The mean time, in years, of DD was 1.51 for grade zero of disability, 2.14 for grade 1, 4.46 for grade 2 and 9.64 for grade 3.

We propose a simplified model to estimate hidden prevalence (EHP), taking into account only 2 strata of GD and expressed by the following formula:

$$EHP = \frac{[(NDC-gd 0/1) \times 2.0 + (NDC-gd 2/3) \times 5.0]}{CGE \times PCP} \quad , \text{ where}$$

NDC-gd 0/1 = mean annual number of newly detected cases, grade 0 or 1;
NDC-gd 2/3 = mean annual number of newly detected cases, grade 2 or 3;
CGE = proportion of newly detected cases with GD evaluated;
PCP = proportion of the population covered by the program;
the values 2.0 and 5.0 correspond to an approximation of the mean time, in years, of diagnosis delay in each respective stratum of GD.

Applying this model to RS data, we have found an EHP of 510 cases.

We have conducted a multivariate analysis, using a logistic regression model: it was observed that, besides DD, other variables, such as clinical form, age group, sex and mode of detection were independent risk factors for having disabilities. In addition, we found two significant effect modification factors: DD vs. clinical form and DD vs. age group. We have performed a more complex model to calculate EHP, with 16 strata, taking into account clinical form, age group and GD from zero to 3. We have found an EHP of 485 cases for RS with this more complex model. This result differs only 5% from that of the simplified model, so, we conclude that the simplified model could be indicated for field uses.

EP14

ARE THE PROPORTIONS OF NEW CASES BY AGE GROUP AND BY CLINICAL FORM USEFUL INDICATORS TO DISCRIMINATE BETWEEN LOW ENDEMIC AND MEDIAN ENDEMIC REGIONS ?

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The relationship between the Mean Annual Detection Rate (MADR) of Hansen's disease and two other epidemiological indicators - Proportion of Newly Detected patients under 15 years old (PR<15) and Proportion of Newly Detected Multibacillary Patients (PRMB) - is analyzed, in order to evaluate the usefulness of these two indicators to discriminate between low endemic regions (LER - with MADR under 0.2/10000) and median endemic regions (MER - with MADR between 0.2/10000 and 1.0/10000).

A database of 4142 cases was studied, corresponding to all Hansen's disease patients diagnosed in Rio Grande do Sul State, Brazil, between January 1970 and April 1991 and notified until April 1994. Out of the 24 geographic regions of the State, 11 could be classified as LER and 13 as MER; subnotification is probably very low, because the control program presents very good operational indicators, covering 100% of the population.

Two kind of analysis were made: 1) bivariate analysis, comparing the distribution of patients, by age group and by clinical form, in the LER group and in the MER group; 2) multivariate analysis (weighted multiple linear regression), using each geographic region as a sample unit, in an

ecological approach. In this multivariate analysis, MADR was the independent variable; PR<15 and PRMB were the dependent variables in two different models, which include many potential confounding factors.

All statistics tests have shown no significance, for $\alpha = 0,05$. In conclusion, this study did not show reasonable evidence that PR<15 and PRMB adequately discriminate between low endemic and median endemic regions; in consequence we should consider alternative indicators to validate the achievement of Hansen's disease elimination goals in those regions where register prevalence is under 1,0 cases/ 10000 inhabitants.

EP15

HISTORICAL SERIE OF THE LEPROSY PREVALENCE ON THE STATE OF AMAZONAS, AN EPIDEMIOLOGICAL AND OPERATIONAL EVALUATION - FROM 1982 TO 1997.

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Leprosy remains endemic within Brazil particularly within the state of Amazonas.

Since the adoption in 1982 of the WHO recommended multidrug therapy (MDT), in the state of Amazonas has been observed variations on its prevalence along 16 years when reached a peak of 24,510 cases, a rate of 128,63/10.000 inhabitants that declined to about 80% if compared to the current prevalence.

In the retrospective study, it was used data of the Amazonas Leprosy Control Program and estimated population based on official census. From those data prevalence rates were calculated and the historical serie of leprosy prevalence described for the state of Amazonas, from 1982 to 1997.

In this study the authors intended to evaluate the influence on behaviour and important leprosy prevalence reduction at the studied area and period due mainly to the introduction and implementation of the MDT with its well-known effectiveness and also some other operational measures carried out such as: elimination of the 2 and 5 years follow up period after the patient released from the MDT regimen for Paucibacillary (PB) and Multibacillary (MB) respectively, later change on the MDT:MB regimen duration period to 24 months, besides norms applied to release defaulter patients from active register recommended by the Brazilian National Coordination of Sanitary Dermatology.

EP16

AN EPIDEMIOLOGICAL ANALYSIS OF LEPROSY FROM 1951-1996, IN SICHUAN

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Sichuan province was one of the most serious leprosy endemic areas in China. Through leprosy surveillance system established in 1990's the authors analysed the epidemiology of leprosy from 1951 to 1996. The results showed that by the end of year 1996, the total number of registered cases was 32 772, the highest incidence rate was 2 441/100 000 in 1958 and then declined gradually. The annual average progressively decreasing speed (AAPDS) of the number of new cases, incidence rate, incidence rate in children, the number of newly detected patients, detection rate, the number of registered cases, registered prevalence rate were 4.7% (sg=0.9534), 5.9% (sg=0.9407), 7.4%, 6.7% (sg=0.9326), 8.1% (sg=0.9195), 11.5% (sg=0.8853), 12.4% (sg=0.8763) respectively. Among newly detected cases the proportion of children gradually reduced year by year with an AAPDS of 2.9% (sg=0.9712), but that of household contacts gradually increased year after year, showing a gradual decline of source of infection the MB rate among new cases, newly registered cases and active cases increased also gradually year after year. The MB rate of children cases was much lower than that of adults ($X=102.7, p<0.01$). The disability rates of two periods of 1986-1990 and 1991-1995 were significantly lower than overall average disability rate of the whole observation period ($X=60.9, p<0.01, X=103.5, p<0.01$). 20-30 age group was the peak of age at onset with an average age at onset of 31.92 years. Average age at onset gradually increased to 34.19 years in the period of 1991-1995. The average delay time of diagnosis was 4.89 years and reduced gradually to 3.24 years in the period of 1991-1995. The authors concluded that 1) the epidemiological status of leprosy in Sichuan province showed an obvious trend of decline, 2) the case-finding activities were improved and intensified year after year, but 3) the disability rate of newly detected cases was still as high as more than 20% in recent years and the average delay time of diagnosis was still as long as 3.24 years suggesting that early case finding was far from satisfactory and more efforts to leprosy control should be made.

EP17

AN EPIDEMIOLOGICAL ANALYSIS OF NEWLY DETECTED LEPROSY CASES IN RECENT TEN YEARS IN HUBEI PROVINCE, CHINA

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An epidemiological study of 964 newly identified patients with leprosy in 1986-1995 was made in terms of year of detection, sex, age at onset, classification, disease duration, clinical skin lesions, disability rate and ulcers, infection sources, case-finding methods, distribution, social, economic and living conditions. The results showed that the annual number of new cases decreased year by year and that of 1995 decreased by 84.3% as compared with that of 1986, the sex ratio was 1.03 to 1 showing no significant change as compared with that of the highest incidence year, the age at onset showed a marked right shift as compared with that in 1960's, and the proportion of children patients among the total number of registered cases decreased from 10% to 3.3%, while that of aged patients (>60 years) increased from 3.4% to 9.5%. The proportion of MB cases among the total number of registered cases increased from 42% in the 1960's to more than 90% in the 1990's, 48.7% of the cases had a disease duration of less than 2 years, the disability WHO Grade II or III rate at diagnosis was 28.3%, much lower than that of 57.62% in 1960's, 39.6% of them were detected by active case-finding modes including clue survey, household contact examination, focus survey, 60.4% of them were detected by passive case-finding methods including case-reporting, making diagnosis in leprosy professional out-patient clinics and general hospitals or health centers, case distribution was uneven, more than 80% of them lived in three previous high leprosy endemic regions, namely Jingzhou prefecture, Enshi prefecture and Wuhan district, incidence rate was closely related to social, economic and living conditions, more than 90% of them came from very poor families with poor living conditions.

Suggestions on how to strengthen future leprosy control and surveillance were made by authors.

EP18

EPIDEMIOLOGICAL STATUS OF LEPROSY AND ITS CONTROL IN BEIJING AREA

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From 1955 to 1996, 125 patients with leprosy were detected in Beijing area. One hundred and six of them were males, 19 were females. As regards their classification, 85 were MB, 22 were PB and 18 unknown due to bad records. The average disease duration was 2.03 years. Among 117 clinically cured cases 15 relapses were identified. There were 6 children (0-14 years) patients. Four cases had not been followed up because of death or unknown reasons. Four active cases remain at present.

Beijing is a non-endemic area of leprosy. The highest incidence period was from 1958 to 1960 and the highest prevalence rate period was from 1958 to 1962. Ninety percent of the registered patients were immigrants from different parts of the country, only 10% of them were natives of Beijing.

Sixty four percent of the mentioned 125 patients were diagnosed by the Institute of Dermatology, the Chinese Academy of Medical Sciences and departments of dermatology of other famous hospitals in 1950s and 1960s and most of the patients were diagnosed in early stage. The profession of the patients in Beijing was significantly different from that in other provinces, 34% were industry workers, 10% were college or university students, 9% were army people and 4% were students from foreign countries, such as Thailand, Myanmar and Indonesia.

The results showed that the periods of the highest incidence and prevalence rates of leprosy in Beijing were similar to those in other provinces of China, and were almost the same to the decrease of both two rates in Beijing area and in remaining areas of the country.

EP19

THE WANING OF LEPROSY ENDEMY IN ARMENIA

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Leprosy on the territory of historical Armenia existed in remote antiquity. The first leprosorium was founded in the end of the third century (290-291). Antileprotic organizational measures, as well as scientific analyses of leprosy epidemiology in Armenia was leaded after 1921. We analyzed the dynamics of incidence and epidemiology of leprosy from 1921 to 1995, on the structure, clinical types, age, gender, cartographic distribution and other epidemiological givens. During the past period 370 primary patients were reported in 111 populated areas. The analysis showed, that peak of incidence

was observed in the first 2-3 decades, after which there was a gradual decrease of the incidence rate, with simultaneous decrease of lepromatous type, as well as incidence among children and adolescents. The last primary patient was registered in 1982. During those seven decades full and obligatory isolation of lepromatous patients and 80% of other types was implemented. Mass and selective inspections of population were implemented, as well as monitoring health of leprocontacts, BCG vaccination of risk groups, dispensary services, and treatment of leprosy cases. The implemented measures, the improvement of socio-hygienic and cultural levels of population brought to the lowering of the activity of leprosy endemy and to its decrease. The organization of antileprotic measures are still being continued.

EP20

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The Incidence of Leprosy among primary school children in central Ethiopia

The study was conducted to appreciate the influence of MDT on the incidence of Leprosy in Central Ethiopia.

The study was conducted in 4 districts of Central Ethiopia with an estimated population of 600,000. From each district 3 to 5 schools were selected by cluster sampling. A total of 6,453 children of 5 to 12 years age range in 15 elementary schools were examined for evidence of leprosy. A public health physician, two dermatologists and one leprosy supervisor were involved in the study. The clinical diagnosis of leprosy was agreed and skin slit smear examination was carried out. Each patient was referred to the nearby leprosy treatment centre for standard WHO/MDT.

The diagnosis of leprosy was confirmed in seven primary school children. Five of them had PB leprosy and two had MB leprosy. All cases were within the age range of 7 and 12. A single patient was female and showed complications of leprosy. 3 patients had indeterminate leprosy and were subjected to regular follow up.

Excluding the 3 cases of early leprosy, the incidence rate in the study group is 10.85 per 10,000 primary school children. This rate is very high in an area where leprosy control programme is operating especially after the introduction of MDT in 1983. There has been no active school survey in the region but the reported passive case detection rate in the region in 1997 is 9.65 per 100,000. Although, MDT has decreased individual sufferings and prevented the emergence of drug resistant strains, it doesn't seem to influence the incidence rate of leprosy. Other measures like effective vaccine have to be included along with MDT if leprosy is to be eradicated in the year 2,000.

EP21

NUMBER OF LEPROSY PATIENTS IN JAPAN
- A SURVEY IN 1995

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In Japan, number of leprosy patients based on WHO criteria had not been reported, which made the international comparison difficult. In December 1995, a nation-wide study to survey all the leprosy patients under medical care was performed. This survey was purposed to provide sound scientific data to the government's council of leprosy prevention law. The law was finally abolished in April 1996.

5303 cases were reported from 12 national Hansen's disease sanatoria (4918 cases) and 9 clinics (385 cases), among which WHO-criteria matched patients were 213 (4.0%). Among 213 cases, 23 were fresh MB, 10 were fresh PB, 63 were relapse MB, 25 were relapse PB, and 92 were under treatment more than 5 years and still need therapy. On the other hand, clinically cured cases (based on Japanese criteria in 1988) were 4498 (84.8%), among which grade 2 deformity was observed in 3424, grade 1 in 561, and grade 0 in 513. Remaining 592 cases (11.2%) were between WHO-based patients and clinical cure.

These data indicate that new cases are rare (10-20/year), and 85% of the leprosy patients are relapse or under long time therapy. In addition, overall deformity rate is high, which forces the cured patients to stay in sanatoria.

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EP22

EPIDEMIOLOGICAL TRENDS OF LEPROSY IN CHINA:
1949-1996

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Based on the data of 471,254 leprosy cases from the National Leprosy Surveillance System, the epidemiological trends of detection and prevalence rates in China from 1949 to 1996 were analyzed. The detection rates were higher in 1950s and 1960s with a peak rate of 5.01 cases per 100,000 population in 1958-1959. This rate decreased to less than 1/100,000 in 1980s, less than 0.5/100,000 after 1986 and 0.15/100,000 in 1996. The prevalence decreased from the peak of more than 2/10,000 in 1960s to 0.06/10,000 in 1996. Between 1986 and 1996, a steep reduction in detection rate (66.1%) and prevalence rate (82.3%) can be observed. However, while the prevalence rate continued to decrease in the recent years, the number of the newly detected cases remained steadily ranging from 1,500 to 2,000 with a detection rate of less than 0.2/100,000. In 1996, the WHO elimination of leprosy as a public health problem has been achieved totally in terms of the country or province/region, and in 98.4% of counties or cities. However, the national criteria for elimination of leprosy defined as prevalence rate of less than 1/100,000 remained not to achieve in 337 (13.7%) counties or cities where the active cases accounted to 66.5% of the national load and the special attention for reaching the elimination goal on time will be needed in future.

EP23

LEPROSY IN ASTRAKHAN REGION OF RUSSIA

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Astrakhan region located in the delta of Volga-river to the north of Caspian Sea was and remains the most active focus of leprosy in Russia. With 0.7% population living in Astrakhan region here 40 to 70% of leprosy cases detected in Russia were registered. This fact may be partly explained by ancient centuries-old close economical ties with the countries of SouthEast and Middle Asia and Near East (the Great Silk Way). In total during the period from 1923 (beginning of State Program of Leprosy Control in the USSR) to 1998 about 2800 leprosy cases were registered on the territory of Astrakhan region, more than 90% of them falling on 1923-1962, or by decades: 578 cases - in 1923-1932; 234 - in 1963-1972; 552 - in 1933-1942; 40 - in 1973-1982; 644 - in 1943-1952; 22 - in 1983-1992, 610 - in 1953-1962; and only 8 new cases in 1993-1998. Regular and significant decrease in leprosy incidence, beginning since the 70th years, was achieved through active case-finding and coverage of all the patients with multi-drug therapy (MDT) implemented in the USSR in 1965-1970, regular surveys of leprosy contacts, implementation of preventive chemotherapy, special measures of financial support for leprosy patients and their families, rise in hygienic and sanitary standards. Among leprosy cases detected in the last 25 years women prevail (55%), more than 50% of leprosy cases are over 60 years old and there no children under 14 years old. Duration of incubation period in 75% of all these cases exceeds 10 years. Data Bank on ex leprosy cases is on record since 1923. A retrospective analysis of distribution and activity of leprosy foci is being carried out.

EP24

THE IMPACT ON 12-YEAR MDT ON EPIDEMIOLOGY OF LEPROSY IN JIANGSU PROVINCE

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MDT has been implemented in the whole province of Jiangsu since 1985. By the end of year 1996, a cumulative number of 4 313 cases had received MDT with a coverage rate of 99.17% and a regularity rate of 99.13%. Of these patients, 3 832 cases were cured with MDT. The data of leprosy epidemiology available of a period of 12 years before and after the implementation of MDT were compared. The results showed that the average annual incidence has decreased from 1 011/100 000 to 0 211/100 000, the proportion of children patients (0-14 years) dropped from 4.33% to 2.04% and the average annual prevalence dropped from 26.58/100 000 to 1.46/100 000, all with significant difference ($p < 0.01$). Furthermore, the proportion of MB cases among newly detected patients and that among active cases have increased from 28.97% to 47.53% and from 29.84% to 73.29% respectively. The relapse rate has reduced from 3.05% of cures by DDS-monotherapy to 0.13% of cures by MDT. The authors suggested that a very high coverage rate of MDT, effectively operated case-finding activities, well organized county-township-village network for control and deep-going health education observed in Jiangsu were the explanations of a big difference of the impact of MDT on leprosy epidemiology between this province of China and other reported countries in the world.

EP25

PHRASING TARGET ON PREVALENCE FOR ELIMINATION OF LEPROSY BY 2000 AD - JUSTIFICATION

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There have been conflicting views on phrasing target on prevalence (PR) rather than incidence for elimination of leprosy as a public health problem by 2000 AD. Prevalence is a composite indicator influenced by many factors viz. New case detection, Registration for treatment, Duration of treatment, Regularity of treatment etc.,. The New Case Detection Rate (NCDR) is also depends on case detection activities, knowledge and attitude of people's etc.,. Since it is difficult to obtain precise information on incidence of leprosy of a given area, new case detection rate considered as proxy indicator of incidence. During the initial period of MDT implementation, a rapid fall of prevalence was observed due to the clearance of back-log cases (i.e. PB cases on register for more than one year and MB cases more than 3 year on register). The fall of prevalence in the latter period has been closely related to NCDR. An attempt has been made to examine the influence of NCDR on prevalence by varying the other parameters such as Proportion of MB cases and Treatment Regularity.

Data collected from Tamil Nadu and Andhra Pradesh States of India has been used as empirical data for testing the methodology of analysis. The epidemiological formula $\text{Prevalence} = \text{Incidence} \times \text{Duration of disease}$ is used to study the relationship between PR and NCDR.

If 6 and 24 months duration of treatment for PB and MB cases are continued, the NCDR should be reduced to the level of 1.2 to 0.7 per 10000 population to reach the elimination level prevalence depends on MB proportion among new cases. The target set by WHO on prevalence for elimination of leprosy encompasses both reductions of backlog cases and incidence of leprosy.

EP26

IMPACT OF MDT ON LEPROSY WITH A SPECIAL REFERENCE TO MONOLESIONS AND SMEAR POSITIVITY AMONG THE NEW CASES

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ABSTRACT:

The impact of MDT on the prevalence and incidence rate of Leprosy is studied in a project area of 1 lakh population over a period of 10 years with a special reference to new monolesional cases and those presenting as smear positive cases. The prevalence rate showed a fall from 23 per 10,000 in 1986-87 to 2.6 per 10,000 in 1996-97. The number of cases presenting with single lesion however showed downward trend from 63.69% in 1986-87 to 40.94% in 1996-97. The cases showing smear positivity among the new cases detected showed an ascent from 3.91% in 1986-87 to 6.45% in 1996-97 with a peak of 25% in 1995-96. A similar trend was seen in the analysed figures of the 4 general surveys done.

EP27

EVALUATION OF TEN YEARS OF THE LEPROSY CONTROL PROGRAM IN THE STATE OF SÃO PAULO, BRAZIL- 1986 - 1996

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The prevalence of leprosy in the State of São Paulo, Brazil, shows a declining trend, mainly in the last 5 years. The prevalence was 38,958 registered cases in 1996 and the prevalence rate was 13.01/10,000. The situation observed in 1996 was quite different: the prevalence rate was 2.9/10,000 and the number of the registered cases was 10,013 patients. Although the prevalence of leprosy shows an important decline, the detection trend of new cases has been stable over the last ten years. In 1986, the detection rate was 0.83/10,000 and in 1996 the rate was 0.85/10,000. The proportion of initial clinical types has remained stable over this period. The geographic distribution of leprosy, comparing 1986 and 1996, shows an important change in the prevalence distribution. The number of counties with no patients has increased dramatically. Nevertheless, the geographic distribution of new cases has not changed if one compares 1986 to 1996. The epidemiological factors that influence the maintenance of the detection level during this period is one of the research objective of the surveillance service. Migration is an important factor to be considered. The theme of this presentation is the important reductions in the prevalence and the operational component parts of the elimination program that are responsible for this result. These component parts are: organization of health services to attend the program activities, personnel training, intensification of the educational activities with the community participation and the organization of the State leprosy's surveillance system.

EP28

EPIDEMIOLOGICAL SURVEILLANCE SYSTEM OF LEPROSY RELAPSES - STATE OF SÃO PAULO, BRAZIL, - 1990 - 1997

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The implementation of MDT/WHO in the State of São Paulo, Brazil, started in 1988 as special projects, was fully implemented from 1992 on. The introduction of fixed duration MDT originates a great number of cured cases out of active records. So, many persons were even released with positive skin smear or some cutaneous lesions. After releases, medical teams started questioning the criteria of cure due to the fact that several cases returned with clinical signs suggesting relapses. To avoid premature questioning of the efficacy of the fixed-dose regimen and to get minimum reliable data, the leprosy surveillance has defined a set of procedures. They are: implementation of Regional Reference services, standardized clinical procedures and special standardized forms. This system started in 1995, in an experimental basis, and was effectively adopted from 1996 on. Available information were analyzed since 1990.

In the State of São Paulo, Brazil, from 1990 to 1997, 53,711 patients were released after completion of the treatment. Among those, 27,491 were treated with MDT/WHO regimen, 26,220 were treated with DDS monotherapy or "DNDS regimen". This was the standardized anti leprosy treatment in Brazil since 1975 until the MDT adoption in 1990. It recommended, for the MB patients, Rifampicin daily during 3 months plus DDS daily until the skin smear become negative or the disappearance of the clinical lesions. For the PB patients, it recommended DDS daily for at least 2 years or until the disappearance of the clinical activity. During this same period, 1,035 relapses were notified. Of these, 480 were investigated. Among them, 304 cases were considered relapses. The relapses were classified as: 9 cases were treated with MDT/WHO, 224 were treated with "DNDS Regimen" and 71 were treated with DDS only. The 196 cases discarded as relapses, were diagnosed as Leprotic Erythema nodosum, reversal reactions or some kind of physical disabilities. The operational difficulties to confirm relapses were caused by health services dispersion, troublesome access to references services, and difficulties to get laboratory tests for all patients. Besides that, the clinical and laboratory criteria to confirm relapses are not equally clear to all medical teams. In order to fulfill operational requirements and to settle medical questions, the leprosy surveillance service was motivated to implement a special leprosy relapse study. Preliminary results of this research are prompted in this presentation.

EP29

THE BANGLADESH ACUTE NERVE DAMAGE STUDY (BANDS): DESCRIPTION OF THE COHORT

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BANDS is a prospective cohort study designed to investigate epidemiological, therapeutic and operational aspects of acute nerve function impairment (NFI) in leprosy. It is a unique study with respect to the number of patients included and detail of information gathered prospectively in a cohort of leprosy patients. A total of 2,665 consecutive, newly detected leprosy patients were recruited during 1 year (starting in 1995) in a highly endemic area of Bangladesh with a population of approximately 5.5 million people. This represents a new case detection rate of 0.5 per 1,000 per year.

Risk factors under study include age, sex, leprosy classification (Ridley-Jopling), leprosy group (MB, PB), skin smear result, skin lesion count, mode of detection, distance to clinic, duration of symptoms before diagnosis, NFI (motor and sensory), nerve enlargement, leprosy reactions, pregnancy, delivery, lactation, chronic disease status, and leprosy treatment. The follow-up period is 5 years from the beginning of treatment, with assessments at regular intervals. This includes examination of skin and nerves, nerve function tests and identification of specific risk factors.

An epidemiological description of the BANDS cohort at intake will be provided, together with a discussion of the research questions concerning the occurrence of NFI in leprosy that will be addressed in the study. Results at 24 months follow-up will be presented in different reports.

EP30

NERVE FUNCTION IMPAIRMENT AND REACTIVE EVENTS IN A PROSPECTIVE COHORT OF LEPROSY PATIENTS AT 24 MONTHS' FOLLOW-UP

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The Bangladesh Acute Nerve Damage Study (BANDS) is a prospective cohort study aimed at investigating the epidemiology of acute nerve function impairment (NFI) in leprosy, its risk factors and response to treatment. A total of 2,665 new leprosy patients have been recruited in the cohort. This paper reports on the results of follow-up at 24 months.

Incidence, timing and severity of episodes of NFI and other reactive phenomena will be presented and discussed. The contribution of the various risk factors under study will be analysed by means of regression analysis. The risk factors include age, sex, leprosy classification (Ridley-Jopling), leprosy group (MB, PB), skin smear result, skin lesion count,

mode of detection, distance to clinic, duration of symptoms before diagnosis, NFI (motor and sensory), nerve enlargement, leprosy reactions, pregnancy, delivery, lactation, chronic disease status, and leprosy treatment.

EP31

SENSITIVITY AND SPECIFICITY OF SIMPLE METHODS OF CLASSIFYING LEPROSY WITHOUT THE USE OF SKIN SMEARS

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Over the past few years a number of simplified methods of classifying leprosy into Paucibacillary (PB) and Multibacillary (MB) disease have been developed and recommended. Classification is of importance to the selection of the MDT chemotherapy to be used to treat patients. The simple methods are important where basic health or primary health workers who have had minimum training in the diagnosis and treatment of leprosy. Methods which do not require the use of skin smears are also important for use in situations where skin smears are not available or can not be performed reliably. However it is important to know the sensitivity and specificity of these new methods in order to understand the size and direction of any misclassification.

Data from a cohort of 2665 consecutive, newly diagnosed leprosy patients recruited over one year in an area of north west Bangladesh were analysed. These patient data contained the results of skin smears at diagnosis, Ridley-Jopling classification and details of the numbers and distribution of nerve and skin lesions. The WHO 1983 MB/PB classification was used as the gold standard and different methods based on counting skin lesions assessed. In this data set a cut off of 6 skin lesions misclassified a small percentage of smear positive patients. Varying the number of skin lesions required to diagnose MB affects the sensitivity and specificity of the method.

EP32

MOTOR IMPAIRMENT WITHOUT SENSORY IMPAIRMENT IN LEPROSY

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The classical picture of peripheral nerve impairment in leprosy is that sensory impairment develops first, followed by motor impairment and in the established peripheral nerve damage there is both sensory and motor deficits. This is usually explained by the stating that sensory nerves are more susceptible to pressure and inflammation so that sensory deficit appears first. However a number of studies report, although not always commenting, on the fact that some patients have motor impairment with out sensory impairment.

We have analysed a dataset of 2665 consecutive, newly diagnosed leprosy patients from north west Bangladesh which included detailed nerve function assessments using the modified 5-point MRC scale for motor assessment and the ball point method of assessing 12 standard points on each palm and 11 standard points on the sole. The data set shows that 15% of patients have some sensory impairment and 12% have some degree of motor impairment and indeed there are patients who have motor with no sensory loss in the same nerve trunk as reported in other studies. These findings may be explained by differential recovery between motor and sensory fibres, misdiagnosis, or the insensitivity of sensory testing or they may hold clues to the pathogenesis of nerve damage in leprosy.

EP33

FACTORS IN DELAYING DIAGNOSIS AND TREATMENT OF LEPROSY - FINDINGS FROM THE BANDS STUDY

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It is generally held that early diagnosis and treatment of leprosy leads to better outcome of treatment, particularly in terms of nerve function impairment. It is therefore important to recognise the factors which are associated with delay in diagnosis of leprosy and to understand the underlying issues.

Each of 2665 consecutive, newly diagnosed leprosy patients in a field project in north west Bangladesh was asked about the duration of skin lesions and the duration of nerve damage at detection. Around 55% reported that the lesions present for up to one year prior to diagnosis where 9% reported that the lesions had been present for more than 5 years. The delay in diagnosis has been analysed by factors such as age, sex, classification, and disability so that the characteristics of those with long delays to diagnosis can be described. These data can also be used to identify true incident cases from so called backlog cases. The validity of self reported delay to diagnosis can be challenged, with possible under-estimation in those reported only short duration of lesions.

EP34

GENDER, CASE DETECTION AND DISABILITY IN LEPROSY IN BANGLADESH: A TREND ANALYSIS

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A trend analysis is presented of all newly detected leprosy cases over a 18-year period (1979 to 1996) in a highly endemic area of Bangladesh. A total of 23,678 new cases were registered, with an average of 860 new cases per year in the first 12 years, and increasing to around 3,000 newly detected cases in 1996. This increase primarily reflects intensified case finding efforts.

The male:female ratio decreased from 2.5 to less than 1.5, and annual new case detection rates per 10,000 general population increased from 3 to 6 and from 1 to 4 for males and females respectively. The proportion of newly detected cases with MB leprosy decreased over time, from 60% to 10% in males and from 45% to 5% in females. The proportion of newly detected cases with disability also decreased over time, from 65% to 20% in males and from 55% to 10% in females. The decline was primarily attributable to decline in grade 2 disability.

Together with more or less equal benefits of the intensification of case finding in terms of disability for males and females, these data also show an overall reduction in the gap in case detection between males and females. But comparison of the age-specific new case detection rates reveals that in the period 1991 to 1996, females in the age between 15 and 29 years were considerably under-represented compared to males in the same age group. This is probably due to the particular sociocultural circumstances of Bangladesh, where (young) women are less likely to report possible symptoms of leprosy in fear of not being able to get married, or to be divorced.

EP35

MILEP 2: USE OF PNA IN HIGH THROUGH-PUT PCR FOR *M. LEPRAE* DETECTION

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As part of the MILEP 2 study, a large survey of the mucosal immunology of leprosy, we have developed a procedure for the detection of small numbers of *M. leprae* bacteria on the nasal mucosa, utilising polymerase chain reaction (PCR) coupled with a specific, sensitive and robust detection strategy which uses novel peptide nucleic acid (PNA) probes. This study (funded by E.C. grant IC18-CT96-0047), follows on from the MILEP 1 study previously undertaken by our group (Ramaprasad *et al.*, *Lep. Rev.* 68 301-315 (1997)).

The MILEP 2 survey team from Richardson Leprosy Hospital, Miraj, collected samples from all inhabitants of a nearby village. Two nasal swabs, sampling the dorsal surface of the nasal mucosa, were obtained from each individual; over 1200 subjects have been tested in the study to date. PCR analyses of material from nasal swabs were performed in the Stanley Browne Laboratories of Richardson Hospital. Reactions were performed using "Ready-to-Go" PCR beads (Pharmacia, UK), under conditions similar to those recommended by the manufacturer. The PCR strategy is specific for the proline rich antigen (*pra*) gene of *M. leprae*: in our hands, DNA equivalent to as few as 5 bacteria could be detected by this method (de Wit *et al.*, *J. Clin. Microbiol.* 31, 502-506 (1993)). Confirmation of the presence of *pra*-specific amplicons was achieved using a fluorescein-labelled PNA probe (Perspective Biosystems, UK) complementary to an internal sequence of the *pra* gene. PCR products were heat denatured in the presence of this probe and allowed to anneal. The DNA-PNA complex was bound to streptavidin-coated 96 well plates by virtue of biotinylation of one of the PCR primers. This was followed by colourimetric detection of binding of the PNA probe to the PCR product by HRPO conjugated anti-fluorescein antibody.

By this method, it was apparent that approximately 5% of individuals in the clinically normal population tested were positive for nasal carriage of *M. leprae*; this is in agreement with previous studies. Studies of these "PCR positive" individuals are continuing, to ascertain the progression of their *M. leprae* PCR status over time.

EP36

THE EPIDEMIOLOGY OF *M. LEPRAE* PCR POSITIVITY IN AN ENDEMIC COMMUNITY - PRELIMINARY FINDINGS FROM THE MILEP2 STUDY

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The MILEP2 Study is an investigation into transmission of leprosy and protection within leprosy endemic populations. The study is funded by the European Commission and is a partnership including researchers in India, Ethiopia, United Kingdom, the Netherlands and Norway. The development of laboratory methods for the detection of small numbers of *M. leprae* on nasal mucosa utilising polymerase chain reactions (PCR) coupled with a specific, sensitive and robust detection strategy have been established in both India and Ethiopia. Details of the techniques are presented elsewhere.

The initial part of the study is to conduct surveys of endemic villages, examining all inhabitants and collecting nasal swab and saliva samples, in both India and Ethiopia. The target is to examine 3 500 individuals over the first year of this 4 year project. A total of over 1200 have been recruited into the study so far and we have preliminary analysis of the first 600 samples available. The percentage of the population who are PCR positive is around 5% which is similar to that found in previous studies in India and Indonesia. The rates appear higher in women than in men. There are few positive under the age of 15 years and over the age of 65 years. The PCR positivity rate is slight lower in those who have a BCG scar but further analysis of the effect of age and BCG is to be undertaken. The rate of PCR positivity in household contacts is around four times higher than the rate among non-household contacts.

These findings are the result of preliminary analysis of the initial results from this large scale investigation. Further analysis are being undertaken but the initial results reveal some important and interesting features of the epidemiology of *M. leprae* in nasal mucosa in a population. The potential significance of these findings will be discussed.

EP37

MILEP2: DEFINITION OF LEPROSY TRANSMISSION AND PROTECTION WITHIN LEPROSY ENDEMIC POPULATIONS

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The incidence of leprosy in many endemic countries has remained stable despite the success of MDT in reducing the prevalence of the disease. Studies of transmission of *M. leprae* infection have been limited due to the inability to cultivate the organism *in vitro*. The recent development of sensitive polymerase chain reaction (PCR) methods for the detection of small numbers of *M. leprae* should enable the estimation of infection rates within a population. Saliva IgA responses can also be used to reflect exposure to *M. leprae*. The laboratory methods for these techniques have been established during a previous European Commission funded project in India (MILEP1).

The presentation will describe the design of a 4 year project in India and Ethiopia which will use these established techniques to study the transmission of *M. leprae* and protective immunity in endemic populations.

The objectives of the study are: To establish the relationship between *M. leprae* infection and the development of immunity in a community in which multiple drug therapy (MDT) has been used for more than 10 years; to elucidate the pathogenesis of primary infection in leprosy; and to develop and test a chemotherapy based intervention strategy for the interruption of leprosy transmission.

Three villages in India and one in Ethiopia were selected and matched for socio-economic status and size. Complete household surveys for detection of leprosy and BCG status are being performed and two Nasal swabs and saliva sample collected from each member. ENT examination and nasal biopsy is being performed on all PCR positive subjects, follow-up will continue for 3 years.

EP38

A CLUSTER OF CASES OF HANSEN'S DISEASE IN MARSHALLESE RESIDING IN HAWAII

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Hansen's disease has been endemic in Hawaii since the 1830's. Following initial importation, the disease became well established in the native Hawaiian population. Since the middle of the twentieth century, the number of cases in Hawaiians and the number of cases acquired in Hawaii have fallen progressively and in recent years the vast majority of cases have been imported. Two major factors have determined the sites from which cases come. These are 1) the number of immigrants coming from a particular country and 2) the prevalence of Hansen's disease in that country. While screening of immigrants for communicable disease may eliminate the importation of some cases of Hansen's disease, several factors limit the effectiveness of this type of screening. Among these are the nonspecific appearance of some of the skin lesions, the appearance of lesions long after exposure and infection in many individuals, and the long period of time required for successful treatment. Most of Hawaii's cases in the last few decades have come from the Philippines, with the next largest number coming from Samoa. In the last decade, however, an increasing number of cases have come from other Pacific island nations.

The Republic of the Marshall Islands had a prevalence rate of 15.5 cases of Hansen's disease per 10,000 and a case detection rate of 20.4 per 10,000 in 1996. This nation of 55,000 residents signed a Compact of Free Association with the United States of America in 1986. Under this compact, Marshallese citizens are free to travel to the U. S. without any health screening. Hawaii is the preferred destination for Marshallese travelling to the U.S. and the port of entry for many of those who settle elsewhere.

In 1996 a case of Hansen's disease was identified in a 19 year old Marshallese man hospitalized on the island of Hawaii. Contact investigation revealed a number of individuals with skin lesions suspicious for Hansen's disease. The Hansen's Disease Community Program of the State of Hawaii Department of Health established a program to screen Marshallese residents of nearby communities. The screening of about 235 people detected 11 cases of Hansen's disease confirmed by clinical findings and skin biopsy. This report gives details of that investigation.

EP39

CLINICAL RISK FACTORS IN LEPROSY REACTIONS: AN EPIDEMIOLOGICAL REVIEW OF RECORDS FROM NORTHERN THAILAND

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A previous small study of selected new cases suggested that leprosy patients who develop erythema nodosum leprosum (ENL) have an earlier age of disease onset than patients who develop reversal reactions (RR) or no reaction. To confirm this and look for other possible risk factors affecting leprosy reactions, we analyzed medical records of all 7881 patients seen at McKean Hospital, Chiang Mai, Thailand, from 1965 through April, 1996. Of the 7881, 4324 received care entirely at McKean, and 4241 (98.1%) had complete data. Of the 4241, 21.8% developed ENL, 10.0% developed RR, and 68.1% had no reactions. The median (25th-75th percentiles) age of leprosy onset for patients who developed ENL: 22 (14-34) years, RR: 30 (18-45) years ($P < 0.0001$), and no reaction: 29 (17-43) years ($P < 0.0001$ compared to ENL, $P = 0.34$ compared to RR). Moreover, as the median age of onset steadily increased from 18 (12-26) years in the 1950s to 34 (23-44) years in the 1990s ($P < 0.0001$ for trend), the proportion developing ENL declined steadily from 41.5% of patients with leprosy onset in the 1950s to 11.9% of patients with leprosy onset in the 1990s. The proportion developing RR increased steadily from 7.7% of those with leprosy onset in the

1950s to 16.0% of those with leprosy onset in the 1990s ($P < 0.0001$ for both trends). As expected, the incidence and types of reactions were related to leprosy type and severity: Only 8.9% of those with paucibacillary leprosy developed any reactions (0.9% ENL, 8.0% RR), while 55.1% of those with multibacillary leprosy developed reactions (42.4% ENL, 12.7% RR) ($P < 0.0001$). Among patients with no deformities, 16.6% developed ENL and 11.9% developed RR, while among those with at least 1 grade 2 limb deformity, 21.8% developed ENL but only 7.0% developed RR ($P < 0.0001$). There was no relationship between sex or between family history and incidence (or types) of reactions. We conclude that the risk of RR and ENL is strongly related to age of leprosy onset which is changing over time; to type and severity of leprosy; but not to sex or family history. The age relationship may point to important clues regarding the pathogenesis and epidemiology of leprosy.

EP40

EPIDEMIOLOGICAL SURVEILLANCE OF THE OCULAR DISABILITIES IN LEPROSY, SÃO PAULO STATE, BRAZIL

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Evaluation of available data on the ocular disabilities of registered leprosy cases in 1989 in the State of São Paulo, Brazil, revealed a need to change the criteria of diagnosis of such disabilities to improve its sensibility at the time of detection. Since 1990, the Leprosy Program together with the Ophthalmology Service intensified training in the detection, prevention and treatment of the ocular disabilities. At the same time a group of experts designed new standardization of the procedures and criteria for grading ocular disabilities based on WHO guidelines. The suggested changes were also adopted by the National Leprosy Control Program of the Ministry of Health of Brazil.

To evaluate the new criteria, data recorded on São Paulo State Leprosy notification forms was analyzed for the years 1989, 1993 and 1996.

There was notification on 3,210 leprosy cases in 1989. Of these, there were 72 (2.2%) with ocular disabilities, of which 20 (1.1%) were PB and 52 (3.8%) were MB cases. In 1993, there was notification on 2,927 leprosy cases of which 40 (3.0%) were PB and 90 (8.1%) were MB cases. The number of cases notified in 1996 was 2,915. Ocular disability was present in 164 (6.9%) of which 48 (3.7%) were PB and 116 (10.7%) were MB cases.

The increase in number of cases with ocular disabilities (from 1989 to 1996) reflects the result of changes in criteria and the notification forms to document ocular disability, as well as training of personnel. Increases were primarily noted in Grade I (corneal hypostesia) and Grade III (visual acuity less than 20/200). The MB cases showed a greater proportion of ocular disability than the PB case ($p < 0.005$).

EP41

RELATIONSHIP OF THE LEPROSY PATIENTS IN TURKEY

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Leprosy seems to be an interfamilial disease in Turkey. Many patients has ancestors affected with leprosy in the past stories. On the other hand it is a typical fact to get married among the patients. In this study we wished to learn the relationship of the patients and male female ratio in a given group.

We have already datas of the 2607 leprosy patients who are alive and who are under the control of the our center at the end of the 1997 (Male=1695 (65.02 %), Female=912 (34.98 %)). If we documentate at the previously registered patients this number comes to 5298. When we examine them, 3449 are male (65.10 %) and 1849 are female (34.90 %).

Among this group we were able to find information about the familial relationship of only 1481 patients.

In this study we are giving the documentation of the relationship of this 1481 cases as a model in Turkey.

EP42

RAPID GEOGRAPHICAL INFORMATION ASSESSMENT FOR LEPROSY SURVEILLANCE IN LARGE URBAN AREA

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In the present study, a georeferenced leprosy surveillance system was built-up in a large urban setting of central Brazil to define cut-off levels of endemicity and to establish inner city migration patterns. Six hundred newly detected leprosy cases were interviewed to record their socioeconomic status, rural-urban origin and residential history in the last 10 years. Rates were calculated according to district level and the threshold for discriminating high risk areas were defined by exploratory data analysis and by the distribution of the pediatric cases. Our results showed that most of the leprosy cases were city residents in the last decade despite of their rural origin, suggesting infection transmission within the city. Around 33% of the cases had changed addresses in a decade in a well defined centre-periphery flow. The exploratory method used in this paper through the graphic representation of stem & leaf and box-plot allowed to discriminate pocket areas inner city taking into account the variability of the local leprosy rates. The appropriateness of this methodology was to provide rapid assessment of leprosy critical areas, feasible for leprosy control interventions.

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EP43

MONITORING THE LEPROSY ELIMINATION PLAN IN BRAZIL

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A decreasing trend in the prevalence rate of leprosy was observed in Brazil only after the introduction of the WHO /MDT implementation in 1990. This paper analyzes prevalence rate, and its utilization in monitoring the progress towards leprosy elimination in Brazil. Since this indicator is influenced by changes of definitions, comparisons from different endemic countries or different periods of time within the same country calls for caution. In Brazil, the current prevalence rate of 6.34/100,000 inhabitants could be considered high as compared to rates from other countries, but it is important to note that defaulters and patients being treated with old regimens are kept in the active registers, while in some other endemic countries they are not.

EP44

LA LÈPRE EN ALGÈRIE

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La lèpre ne constitue pas un problème de santé publique en Algérie. En un siècle, de 1822 à 1987, 250 cas maximum ont été répertoriés, 75 cas seulement étaient algériens dont 61 cas contractés en Algérie.

En 1987(1)(2), nous avons rapporté un cas supplémentaire de lèpre autochtone chez un homme de 45 ans habitant la région de Tlemcen, à 70 km de la frontière marocaine et qui n'avait jamais quitté le pays.

En 1988, nous avons observé à Tlemcen (ouest Algérie) deux autres cas (une femme de 33 ans et un homme de 39 ans), Algériens travaillant au Mali depuis plusieurs années.

La lèpre autochtone a toujours été rare en Algérie.

Si l'existence d'un foyer ancien en Algérie a toujours été reconnue, les cas sporadiques de l'ouest Algérie et particulièrement la région de Tlemcen, méritent l'attention des leprologues. La lèpre Algérienne a-t-elle été principalement une lèpre d'importation. Les échanges multiples avec d'autres pays limitrophes ne risquent-ils pas d'augmenter sa fréquence?

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EP45

A STUDY OF 97 LEPROSY CASES FROM KNOWN PATIENTS' HOUSEHOLD CONTACTS IN WUWEI COUNTY, ANHUI

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Wuwei county was a mid-endemic area of leprosy that reached the target of basic eradication of leprosy in 1994. By the end of 1995, 902 leprosy have accumulatively been detected (MB 284 and PB 618; female 161 and male 741). There were 97 cases of attacked household contacts (MB 45 and PB 52; female 29 and male 68) involving 44 families, among them the female percentage (29.9%) and MB percentage (46.4%) were significantly higher than that of other non-household leprosy patients (17.8% and 31.5% respectively). Though the detection rate of new patients has been decreasing gradually, the household patients show a relatively increasing trend. The household patients diagnosed in the recent 10 years made up 30.6% of all newly detected ones during the same period, significantly higher than that 10 years ago (9.3%). The author emphasized the importance of regular surveillance of household contacts of known patients in detecting early leprosy in low-endemic situation.

EP46

LEPROSY DISEASE IN MINORS 15 YEARS OF AGE AND UNDER THE INFLUENCE OF DETECTION PROCEDURES ON CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS. Duppre NC, Nery JAC, Garcia CC, Pereira RAM, Sarno EN. Leprosy Laboratory, Oswaldo Cruz Foundation, Av. Brasil 4365 - Mangunhos, Rio de Janeiro - RJ, Brazil.

The clinical characteristics of leprosy in childhood are similar to those in adulthood but with certain peculiarities. It is known that children constitute a high risk group in families with MB leprosy patients because of greater risk of contagion by *M. leprae*.

One-hundred-twenty (120) leprosy patients between the ages of 0 to 14 were included in this study. Their clinical and epidemiological characteristics were analyzed according to detection procedure and then divided up into two groups, as follows: **Group 1:** Detection through examination of household contacts; and **Group 2:** Passive detection (self-referral or referral by others).

Among the 51 children included in this group 28 (58%) were from 0 to 9 years of age, 44 (86%) developed paucibacillary forms, 16 (36%) of whom presented the Infantile Nodular form. Among those whose degree of disability was evaluated 35 (97%) presented 0. **Group 2:** 49 (68%) of the 69 children included in this group were between the ages of 10 and 14. Twenty-three (33%) developed multibacillary forms, and the disability grading for 11 children (17%) was between 1 and 3.

The examination of household contacts made it possible to diagnose children in the 14-and-under age group and to detect early forms of leprosy, including the Infantile Nodular form (IT single lesion children)

EP47

ANALYSIS OF 512 CHILDREN WITH LEPROSY

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512 children suffered from leprosy had been detected during the period of 1950 to 1995 in Hunan province, among them 470 cases (91.8%) were detected before 1985 and 42 cases (8.2%) after

1985 (including 1985). The proportion of children patients with a disease duration of less than 2 years was 66%. Most of the cases (59.6%) were household contacts of known leprosy patients and the main source of infection was active MB cases. The illiteracy rate of children cases was 42%, and 73.1% of them were unable to go to school after diagnosed as leprosy patients. The first skin lesion more frequently appeared in MB and PB cases was erythema with a frequency of 43.7% and 38.1% respectively. The main location of the first skin lesion was face (42.2%) in MB and upper limbs (30.7%) in PB. The Grade II and III disability rate was 31.8%. There were remarkable differences between MB/PB value, detection rate of early leprosy, modes of case detection, incidence of household contacts, illiteracy rate, rate of deprivation of education after diagnosed as leprosy and Grade II and III disability rate of children with leprosy identified before and after 1985.

EP48

THE EPIDEMIOLOGY OF LEPROSY AND ITS CONTROL IN TIBET

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Tibet Autonomous Region was previously a medium leprosy endemic area with an endemic history for more than 1400 years. Leprosy patients were identified in 58 of 75 counties (cities).

Through comprehensive leprosy control activities implemented for more than 30 years, especially with the introduction of WHO MDT since 1987, the prevalence and incidence rates reduced from the highest (0.60‰ in 1980 and 12.62/100,000 in 1970) to 0.027‰ and 0.20/100,000 in 1997 respectively. No children cases were detected in the recent 3 years. The proportion of county and village with registered leprosy patients also remarkably dropped by 63.7% and 82.5% respectively. Epidemicity of this disease has been effectively controlled from the whole autonomous region point of view. By the end of the year 1997 there were only 66 active cases in the whole region.

EP49

GENETIC MARKERS IN LEPROSY

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Of late, the significance of genetic mechanism in leprosy has been highlighted to account for the unexplained vagrancy of its incidence in endemic population. The epidemiological studies of the disease have contributed in this regard to some extent. Our previous studies on blood groups, Dermatoglyphics and other genetic markers have shown the association with leprosy in one way or the other. In the present study, we have taken two important genetic markers Taste deficiency for phenyl-Thio-Carbamide (P.T.C.) and Colourblindness in order to find the association, if any, of these markers with leprosy. For the Taste deficiency for P.T.C., 409 leprosy patients (212 BL/LL type and 197 TT/BT type) were compared with 200 normal healthy individuals taken as controls. For the incidence of Colourblindness 600 leprosy patients (311 BL/LL Type and 289 TT/BT type) were compared with 199 controls.

Investigations reveal that both TT/BT and BL/LL type of leprosy patients differ significantly from controls with regard to the frequencies of Tasters and Nontasters in them. On the other hand, no significant difference was observed between patients and controls with regard to the frequencies of colourblindness. Yet another important finding was that 2 TT/BT type of female patients (out of 56 TT/BT female patients) were colourblind.

EP50

LEPROSY IN INFANCY: HUCFF-UFRJ (RIO DE JANEIRO, BRAZIL) STATISTICS (1990-7)

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INTRODUCTION - Regarding number of leprosy cases Brazil ranks second in the world. Epidemiological indicators, as of 1995 (Brazilian Ministry of Health), are: prevalence rate: 8.82/10,000 population; detection rate: 2.30/10,000 population; detection rate below-age-fifteen: 0.63/10,000 population. All these data are thought of as high according to WHO standards.

OBJECTIVE - To investigate clinical, histopathological, bacteriological and epidemiological patterns within the below-age-fifteen leprosy patients group treated in HUCFF (University Hospital), a reference center for Rio de Janeiro metropolitan area.

METHODS - Transverse survey of below-age-fifteen patients records, treated in HUCFF from 1990 to 1997.

RESULTS - 26.08 percent were multibacillary. In 65.2 percent the index case was unknown. 43.47 percent came from "Baixada Fluminense", a group of poor dormitory towns in the neighborhood of Rio de Janeiro, and 40 percent were from the same district as our hospital - both areas considered endemical ones. Two cases came from "Vila do João", a shantytown close to our hospital. Both were investigated in their homes and surroundings, and it has been possible to determine the index cases (one in his own family, and the other one in the neighborhood, both Lepromatous leprosy).

CONCLUSION - The epidemiological studies point out that one of the main indicators in order to define a risk area for leprosy is the detection rate among below-age-fifteen. Considering leprosy incubation period (2-6 yrs.) every diagnosed case in this age range should result in epidemiological investigation of origin area and near home focuses research.

MOTIVE OF PRESENTATION - Discussion of these results, based upon bibliographical data.

EP51

THE DETERMINATION OF IgM ANTIIPHENOLIC GLYCOLIPID-1 ANTIBODIES IN CURED LEPROSY PATIENTS

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In order to develop a surveillance approach to be effectively used in the field, this study was carried out in 8 high, medium and low endemic counties to determine IgM anti-phenolic glycolipid-1 antibodies in 359 leprosy cases cured with DDS monotherapy and to assess its role may have to play in predicting leprosy relapses. Positivity of IgM antibody to ND-O-HSA-ELISA (OD value ≥ 0.16) is regarded as a hazardous factor. During the three years of monitoring 14 relapsed cases were detected including 12 in IgM positive group and 2 in the negatives, and the relapse rates were 26.09% and 0.65% respectively. The relative hazard degree was 40.17. The sensitivity and specificity of the test for MB were 91.6% and 90.16% respectively with a relative hazard degree of 70.28, and those for PB were 50%, 89.54% and 7.80. The results showed that the antibody has been disappearing gradually in cured individuals as time goes on. The authors consider that those who had gone through longer time after cure with higher IgM level or with an IgM level suddenly elevated after its reduction should be given a more careful attention and more longer time for surveillance.

EP52

THE DYNAMICS OF LEPROSY PATIENT'S FAMILY AND EPIDEMIC FOCUS OF LEPROSY - A PRELIMINARY ANALYSIS

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Six hundred and seventy three patients with leprosy from 524 families and 310 villages were detected from 1958 through 1996 in Nandan County, Guangxi Autonomous Region.

The results showed:

- a significant familial clustering infection of leprosy;
- that transmission and occurrence of clinical leprosy in households is likely hereditarily and that in general population probably related to geographical and environmental factors;
- that the highest space transmission scope was an increase of 16.4 families and 11.04 villages and remarkably reduced after effective control;
- a longer interval (9.18-21 years, geometrical average: >5 years) between the occurrence of secondary case(s) and that of the index case in patient's family and epidemic focus of leprosy indicating that both patient's family and epidemic focus of leprosy should be recognized as priorities for leprosy control.

EP53

ANALYSE DE LA TENDANCE TEMPORELLE ET DE LA DISTRIBUTION SPATIALE DE LA LÈPRE DANS LA VILLE DE RECIFE - ÉTAT DE PERNAMBUCO - BRÉSIL

Auteur - Magalhães, M.C.C.

Entre les états brésiliens, celui de Pernambuco, situé dans la région nord-est du Brésil, présente une situation des plus atypiques étant donné sa croissante tendance à une épidémie prévalent de 12,93 / 10000 habitants, tandis que les autres états présentent cette tendance décroissante. Les taux de détection sont de 3,55 / 10.000- habitants contre 1,45 / 10.000 habitants moins de quinze ans après.

La concentration urbaine et les conditions socio-économiques de cet état font que 90% des cas se concentrent en zone métropolitaine de Recife, avec une population de 45% du total de l'Etat.

Face à cette réalité sévissante, on a essayé d'étudier, dans le présent travail, certains indicateurs, comme par exemple le coefficient de détection de la maladie en moins de 15 ans, par local de résidence, en cherchant à identifier les événements dans lesquels ce phénomène-là intensifierait les actions de contrôle.

Ce travail, à travers une recherche opérationnelle, analyse la tendance temporelle de la Lèpre et utilise les techniques du système d'Information Géographique, que permet de vérifier la variation spatiale des cas de Lèpre à Recife, en relation aux aspects opérationnels des services de santé et de la condition socio-économique de la population.

EP54

INCIDENCE RATES AND USE OF A LOGISTIC REGRESSION MODEL TO CHARACTERISE RISK FACTORS IN A COHORT STUDY. Matos, HJ, Duppre, N, Alvim, MFS, Vieira, LMM, Sarno, EN, Struchiner, CJ.

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Leprosy household contacts have a greater risk in developing leprosy than general population. In a recent study (1993), Chanteau et al. have calculated a risk ratio of 30.8 for acquiring leprosy in household contacts in comparison to general population. So, contacts surveillance is as necessary as understanding basic mechanisms related to the transmission and developing of frank disease. In fact both become important in a perspective of control and in an effort to eliminate this disease.

The main objective of this study was to answer to the following question: Among a set of factors, which are most important to influence development of disease in a cohort of household contacts? This way, a dynamic cohort of leprosy household contacts has been followed since 1987, at Department of Leprosy from Fundação Oswaldo Cruz, in Rio de Janeiro. Up to now, this cohort includes 2225 subjects, and a set of data have been collected, from three levels of analysis: family, person and individual immunologic status. The present study analyses data from 1987 to 1991. In this period a total of 670 healthy contacts have been followed. Incidence rate, in person year of follow-up was calculated as 0,01694 at the end of observation time. Nevertheless, there was variation in this rate related to the time of follow-up for each subject in the cohort. For subjects at the end of the first year of follow-up, for instance, the incidence rate was 0,06385; in contrast if we consider all subjects up to the end of the second year of follow-up it was 0,03299; up to end of the third year it was 0,02370, up to the fourth it was 0,018622, and as was mentioned, up to the end of the period of observation it was 0,01694. For modelling risk from these data, it was proposed a stepwise multivariate logistic regression model. The software used was EGRET®. In this model, co-prevalent cases have been included, totalling 758 contacts. In the final logistic regression model, the risk of developing leprosy was related to a negative Mitsuda cutaneous test (the cut-off adopted was that recommended by WHO, as 3,0 mm), with OR of 3,093 (CI95% = 1,735-5,514), also it was related to a previous vaccination with BCG, OR of 0,3802 (CI95% = 0,2151-0,66719), and finally it was related to a multibacillary clinical form of primary case (either BB, BL or LL), with OR of 2,547 (CI95% = 1,249-5,192). Although this model is dependent to a set of assumptions, among these cut-offs used, it shows that both, sufficient amount of bacilli, as well as specific immunologic status are useful indicators of risk of developing leprosy in a cohort of household contacts.

EP55

FOLLOW-UP OBSERVATION OF THE ONSET AGE DISTRIBUTION IN KOREA, NEPAL AND HAITI

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**Anandaban Hospital (previous), RN, Nepal

It is widely accepted that the high ratio of child leprosy suggests that leprosy is still endemic there.

K. Saikawa had carried on the follow-up survey of the age specific distribution in Okinawa prefecture since just after the retrocession from the U.S.A., comparing with the other part of Japan. He traced how the pattern of the age specific distribution changed with the lapse of time. His conclusion is that the peak of the curve shifts toward the

right (to older ages) accompanying with a decrease of new cases. The peak splits into one or two lower peaks and the curve becomes bimodal. A. Obara et al. also observed a similar phenomenon in Korea. On the other hand, there are different patterns in other areas, as S.K. Noordeen mentions in his article. The patterns in Nepal and in Haiti are different from ones observed in Japan and in Korea, where the elimination of leprosy has been achieved relatively in a short time. In the areas where leprosy is chronically endemic, the peak at ages below 14 (child leprosy) persists rather for a long time.

Impression: These different patterns look to reflect the endemicity in each area related with socio-administrative backgrounds.

EP56

THE PREDICTIVE VALUE OF NERVE ENLARGEMENT FOR NERVE FUNCTION IMPAIRMENT IN LEPROSY

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The presence of nerve enlargement is considered as almost pathognomonic for leprosy. Suspected leprosy patients are usually examined for the presence of enlarged nerves, yet little is known about the sensitivity and specificity of this sign as indicator of nerve function impairment (NFI) in leprosy. The development of disabilities can be prevented successfully by treating recent NFI with corticosteroids. It is therefore important that NFI in leprosy patients is diagnosed easily, safely and effectively in field conditions. Palpation of peripheral nerves is a simple, cheap and safe test. This study examines its effectiveness as a diagnostic tool for NFI.

Included in the study are 2,665 new leprosy patients who were recruited in the Bangladesh Acute Nerve Damage Study (BANDS). This is a prospective cohort study aimed at investigating the epidemiology of acute NFI in leprosy, its risk factors and response to treatment. All patients were examined for the presence of enlarged peripheral nerves and sensory and motor function impairment at the time of diagnosis and at 12 months follow-up.

Nerves included in the study are the ulnar, median, radial, common peroneal, and posterior tibial. The following values will be presented and discussed: 1) the predictive value of nerve enlargement for the presence of NFI, and 2) the predictive value of nerve enlargement for the occurrence of NFI within the following 12 months.

EP57

THE EFFECTIVENESS OF THE BCG-ID VACCINE AMONG HOUSEHOLD CONTACTS OF MULTIBACILLARY LEPROSY PATIENTS - A RETROSPECTIVE STUDY. Duppre NC, Nery, JAC, Wanzeller SH, Mattos H, Sarno EN, Struchiner CJ. Leprosy Laboratory - Oswaldo Cruz Foundation, FIOCRUZ, RJ - Brasil.

The degree of protection conferred by the BCG-ID vaccine against leprosy continues to be investigated worldwide. Studies are constantly being carried out to evaluate the degree of protection that BCG confers against both leprosy and tuberculosis. In this connection, it has regularly been demonstrated that BCG provides a more consistent protection rate against leprosy (20 to 80 %) than against tuberculosis (0 to 80%). The present study was developed in the Clinical Unit of the Leprosy Laboratory, Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, RJ, BRAZIL. The health care center takes care of leprosy patients from all over the State of Rio de Janeiro who have been referred either by doctors or other patients.

Six hundred-twenty (620) contacts of MB leprosy patients were included in the study, 468 of whom had a BCG scar (exposed to BCG) and 152 did not (not exposed to BCG), all between the ages of 0 to 28.

These contacts were introduced into the study at different times from June 1987 thru December 1992. Medical exams were carried out on these contacts for a consecutive five-year period as of the date of the first examination at the clinic.

The results showed a cumulative rate of infection of 7.05% among those exposed to BCG and 15.13% among those that had not been exposed to BCG. A variation in the incidence rate was seen during the five years the contacts were under surveillance. In the first year, the incidence rate for those with a BCG scar was 0.49/100 persons versus 4.07/100 without a BCG scar. In the second year, the rate was 0.41/100 for those with a BCG scar as opposed to 1.08/100 for those without.

In the third year, 0.13/100 with a scar became infected with the disease versus

1.44/100 without. In the fourth year, however, the incidence rate was zero for both groups and remained so in the fifth year of surveillance. As a whole, the protection rate conferred by BCG-ID provided a greater degree of protection against the multibacillary forms (BB/BL/LL), which was 85.6% (53.8 - 95.5%) than against the paucibacillary forms (HI/IT/NI/NT), which was 52.6% (23.0 - 70.9%). Moreover, it was shown that other factors contributed to contraction of the disease. These factors included the presence of two or more MB patients in the family, type of relationship of the household contact with the patient (s), and the number of inhabitants per room in place of residence.

EP58

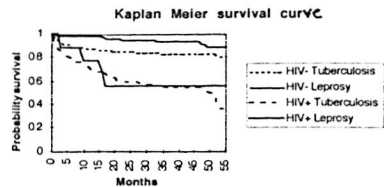
IMPACT OF HIV INFECTION ON SURVIVAL OF LEPROSY AND TUBERCULOSIS PATIENTS IN MWANZA, TANZANIA
 J. van den Broek, S. Mfinanga, C. Moshiro, R. O'Brien, et al
 Royal Tropical Institute, Amsterdam, The Netherlands

Long term survival of 120 consecutively diagnosed leprosy and 561 tuberculosis patients, with and without HIV infection, enrolled in 1991 in Mwanza Tanzania, after 56 months observation, was as follows:

Leprosy: 5 patients died during and 5 after treatment. The mortality of leprosy in this cohort was 33% (3/9) for HIV+ and 6% (7/111) for HIV- patients. Death after treatment occurred in HIV negative patients only. The risk of dying was significantly associated with HIV infection (HR 8.3, 95% conf. int. 1.9 - 35.6), controlling for age group, sex and disability grading. In this study, HIV infection was associated both with MB disease and mortality.

Tuberculosis: 56 died during and 51 after treatment. Mortality of tuberculosis in this cohort was 35% (51/146) for HIV+ and 13% (56/415) for HIV- patients. The risk of dying was significantly associated with age group above 35 years 1.5 (95% conf. int. 1.03 - 2.1), and HIV infection 3.7 (95% conf. int. 2.6 - 5.2).

Kaplan Meier survival analysis for HIV- and HIV+ leprosy and tuberculosis patients, adjusted for age group, sex, disability grading (for leprosy) and type of tuberculosis (for tuberculosis) was as follows:



Conclusion: leprosy and tuberculosis patients with HIV infection have a high mortality: in leprosy during the treatment period and in tuberculosis both during the treatment period and the years following.

EP59

MODELLING THE PREVALENCE OF PERSONS AFFECTED BY LEPROSY IN TANZANIA
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Variables used in a model to estimate the burden of leprosy disabled grade 1+2:

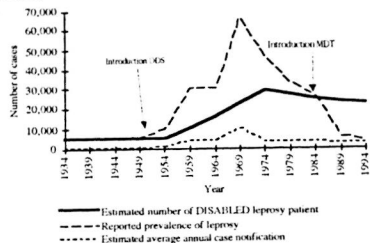
- registered leprosy prevalence since 1934;
- leprosy case notification, derived from registered prevalence;
- proportion disabled grade 1+2 among new cases (ND);
- age group specific disabled grade 1+2 among new cases;
- worsening (W) and improving (I) disability during and after R/;
- age group specific mortality rates (m) per 10 year age group.

Model: the disabled prevalence (DP) equals the sum of survivors (S) and new or additional disabled, in 10 year age groups (t) and over 10 year periods (t):

$$\sum_{i=1}^n DP_{(t+i)} = \sum_{i=1}^n S_{(t,i)} + \sum_{i=1}^n ND_{(t+i)}$$

given that
$$S_{(t,i)} = \left\{ DP_{(t-1,i)} - I_{(t,i)} + W_{(t,i)} \right\} \cdot e^{-10m_{(t,i)}}$$

Result:



Conclusion: the proportion of disabled among new cases and their age distribution, everything else kept equal, are the most important determinants of the level and trend of disabled prevalence.

EP60

HOUSEHOLD CONTACTS STILL AT HIGH RISK ?

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Multi Drug Therapy (MDT) programme with WHO recommended treatment regimen has given the hope of early case detection and rendering a leprosy patient especially Multi Bacillary (MB) non infective within a short duration. Hence duration of exposure for household contacts to infection is expected to be remarkably less when compared to MB leprosy patients on DDS monotherapy. During the period from 1984 to 1994, a total of 360 MB (previously untreated & skin smear positive) leprosy patients were treated with Multi Drug Therapy (MDT). The household contacts were examined once year. The incidence of leprosy among these contacts was about 14 per 1000 PYR during the first three years of surveillance. It declined to 4.6 per 1000 PYR during 7th, 8th and 9th years. Overall incidence of leprosy among all these household contacts was 9.8 per 1000 PYR. Other factors like duration of the disease, coprevalent cases, etc will be discussed. The incidence during Dapsone monotherapy period was reported to vary between 4.2 per 1000 to 29.5%. Though it was less during MDT, still the incidence seems to be high. Combined chemotherapy seems to be effective in reducing disease transmission among household contacts. But still the incidence is higher when compared to that of total population. Effective intervention needs to be introduced to reduce the risk of contacts developing leprosy.

EP61

EPIDEMIOLOGICAL CHARACTERISTICS OF LEPROSY IN LOW ENDEMIC AREAS ALONG THE MIDDLE-LOWER REACHES OF YANGTZE RIVER

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Jiujiang city, administratively divided into 14 counties and districts, was a low endemic area. The prevalence has dropped from 0.222 ‰ in 1971 to 0.03 ‰ in 1995 and the average incidence rate for every 5 years from 0.32/100 000 to 0.02/100 000 having reached the goal of basic eradication of leprosy. By the end of 1995, 167 leprosy patients have been diagnosed, most of them lived in the south part of this city. The age at onset of the disease was 8-74 years including 15 cases of less than 15 years. The average detection age, average age at onset, the proportion of MB patients amongst newly detected cases and average median time of delay increased as the time goes on. Seventy (41.92%) of 167 registered patients were immigrants mainly living in 7 counties/districts along railway and arterial highways. The index cases of 86 counties/districts of above mentioned seven were immigrants.

Early casefinding has been the key of leprosy control particularly in low endemic area. It needs participation of the whole health system and its personnel. Clue survey is considered as the best mode of case detection, which largely depends upon the quality of training of personnel at peripheral level and their conscientious service for the community.

EP62

THE CHARACTERISTICS OF EPIDEMIOLOGICAL DISTRIBUTION AND STRATEGY DURING THE PERIOD OF POST ELIMINATION OF LEPROSY

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Seven counties of Wuzhou prefecture with a population of 3 672 300 and an area of 20 113 97 kilometers in the East Guangxi Autonomous Region where leprosy was medium endemic were selected for investigation. One thousand two hundred and eight three leprosy patients have been detected in 788 of 16 756 villages. Every five years from 1956 through 1955 was considered as an endemic period for observation. The method consist in linear correlation analysis and multiple regression coefficient test using average incidence of each period (AIP) as independent variable, unknown-cause incidence (UCI)×, incidence by extra-familial infection (IEFI) and incidence by familial infection (IFI) as dependent variables. The results showed that as regards the average period incidence (API), there is a significant correlation between UCI, IEFI and IFI, a very significant dependence relation between UCI and no linear regression correlation between IEFI and IFI indicating a potential change from coexistence of incidence by irregular UCI and incidence by extra-familial and familial clustered infection to clustered incidence by extra-familial and familial infection. It also demonstrated that intimate and repeated contacts with patients still remain as a risk factor of familial incidence and of extra-familial incidence as well.

※ Occurrence of clinical leprosy by an unidentified source of infection

EP63

LEPROSY IN ASTRAKHAN REGION OF RUSSIA

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Astrakhan region located in the delta of Volga-river to the north of Caspian Sea was and remains the most active focus of leprosy in Russia. With 0,7% population living in Astrakhan region here 40 to 70% of leprosy cases detected in Russia were registered. This fact may be partly explained by ancient centuries-old close economical ties with the countries of South-East and Middle Asia and Near East (the Great Silk Way). In total during the period from 1923 (beginning of State Program of Leprosy Control in the USSR) to 1998 about 2800 leprosy cases were registered on the territory of Astrakhan region, more than 90% of them falling on 1923-1962, or by decades:

578 cases - in 1923-1932;	234 - in 1963-1972;
552 - in 1933-1942;	40 - in 1973-1982;
644 - in 1943-1952;	22 - in 1983-1992;
610 - in 1953-1962;	

and only 8 new cases in 1993-1998. Regular and significant decrease in leprosy incidence, beginning since the 70th years, was achieved through active case-finding and coverage of all the patients with multi-drug therapy (MDT) implemented in the USSR in 1965-1970, regular surveys of leprosy contacts, implementation of preventive

chemotherapy, special measures of financial support for leprosy patients and their families, rise in hygienic and sanitary standards. Among leprosy cases detected in the last 25 years women prevail (55%), more than 50% of leprosy cases are over 60 years old and there no children under 14 years old. Duration of incubation period in 75% of all these cases exceeds 10 years. Data Bank on ex leprosy cases is on record since 1923. A retrospective analysis of distribution and activity of leprosy foci is being carried out.

EP64

LEPROSY IN KARAKALPAKSTAN. PROSPECTS FOR ITS ERADICATION

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For Karakalpakstan leprosy is an ancient heritage, but regular efforts towards leprosy control were initiated since 1933 after national health protection and leprosy service had been organized. To intensify antileprosy activity in 1962 Karakalpak Leprosy Control Branch of Uzbek Institute for Study of Dermatovenereology was opened and two outpatient clinics and six leprosy units were organized. Since 1957 active case-finding through regular sample and mass surveys with annual coverage of up to 100 000 inhabitants were carried out, identified foci of leprosy were put under surveillance with chemotherapy of both leprosy cases and their contacts, and just in 1960-1964 these efforts resulted in finding 490 new leprosy cases. Rates of leprosy incidence sharply contrasted between north and south parts of the country. Thus, in 1960 when the highest rate of total incidence for the country was observed (30,4 per 100 000) it was 43,7 in the north districts, approaching 185,6 in Muinak while in the southern parts it reached only 2,8 per 100 000. This difference is due to various factors, including genetic, besides living and economical conditions (Abdirrov Ch.A. et al., 1973, 1977). Successful combined chemotherapy resulted in gradual decrease in leprosy incidence. By 1980 a tendency towards sporadic incidence began to be observed, ranging from 0,83 to 0,7 per 100 000 in 1987. In recent years only single cases of leprosy have annually been registered in the north territories, and Karakalpak focus acquired features of disappearing endemicity. Meanwhile, difficult ecological and economical situation, long incubation period, absence of antileprosy vaccine and high susceptibility of a part of the population to leprosy could induce burst of leprosy incidence on Karakalpak territory.

EXPERIMENTAL

EX01

A GLOBAL STRATEGY FOR BASIC BIOMEDICAL RESEARCH ON LEPROSY ERADICATION.

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Basic biological research on *Mycobacterium leprae* and on the immunology and pathogenesis of leprosy conducted over a period of the past 20 years has contributed little to the present optimistic state of global leprosy. Indeed, proceedings from the recent historical joint workshop of ILEP and WHO/LEP (July 1997) made no mention of a role for such research in identification/confirmation of the still appreciable numbers of new leprosy cases, or in gauging the extent of sub-clinical leprosy in the community, or in the ultimate eradication of the disease. Yet, there is the need for new diagnostic and epidemiological tools, for a deeper understanding of the bacteriological and immunological basis of pathogenesis, perhaps resulting in new treatment for reactions, for probes and assays for drug resistance and, possibly, for a vaccine for ultimate eradication of the disease. Those principles are still the driving force behind small, poorly funded but

enthusiastic and well coordinated research groups throughout the world. Recent watershed meetings in Bangkok (March 1996) and Addis Ababa (February 1998) have identified disease-related issues to be addressed, most promising immunological and molecular approaches to follow, and shared centralized resources required to fulfill the mission. The International Leprosy Congress provides the ideal forum for the exposition and promulgation of a shared, interdisciplinary, interdependent global research strategy.

EX02

ANALALIES IN NEUROFILAMENT PROTEINS: SOME HUES TO MOLECULAR MECHANISM OF PASSIVE NERVE DAMAGE IN LEPROSY.

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Mechanisms of nerve damage in leprosy remains very poorly understood. In a recent morphological study, it was noted that, a