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Images from the History of Leprosy

Missionary work in Chitokoloki, Africa, 1935. Mrs. George Suckling and her assistant are shown with patients at the small, remote hospital in Chitokoloki in what is now Zambia. In this pre-dapsone era, no specific treatment was available and only supportive care could be offered. The image is electronically reproduced from an original black and white print measuring 4 × 6 inches, and was made available courtesy of Mrs. Linda Beer-Kumwenda.
Seroprevalence of HIV Infection among Leprosy Patients in Agra, India: Trends and Perspective

Tahziba Hussain, Shikha Sinha, K. K. Kulshreshtha, Kiran Katoch, V. S. Yadav, U. Sengupta, and V. M. Katoch

ABSTRACT

This study compares the results of HIV seroprevalence, which was carried out in two phases, i.e., 1989 to 1993 and 1999 to 2004. Although the number of leprosy patients screened for HIV infection in the second phase is less (2125) as compared to those screened during the first phase (4025), a rise in HIV infection from 0.12% to 0.37% is certainly disturbing since this area appears to be endemic for both the infections. During the study period, the Out Patient department attendance of a few types of leprosy patients like borderline and borderline lepromatous have risen, whereas others like borderline tuberculoid and polar tuberculoid have declined in the second phase as compared to that of the first phase. The trend over a decade suggests that HIV infection is low among the leprosy patients when compared with other risk groups. Follow-up of these patients at an interval of six months, revealed that none of them downgraded into a severe form of leprosy nor developed ARC or AIDS. In this study, it appears that neither infection precipitated the other. The occurrence of downgradation as well as reversal reactions and neuritis (both chronic and acute) was not observed among the leprosy patients. None of them developed erythema nodosum leprosum reactions. Similarly, the HIV-positive leprosy cases did not develop either AIDS related complex (ARC) or full blown case of AIDS.

RESUME

Cette étude compare les résultats de séroprévalence du VIH, obtenus en 2 phases distinctes : de 1989 à 1993 et de 1999 à 2004. Bien que le nombre de patients testés pour l’infection par le VIH soit moindre dans la seconde phase (2125) que dans la première (4025), une augmentation de prévalence de 0.12% à 0.37% est préoccupante puisque la région étudiée est endémique pour les 2 infections. Pendant la durée de cette étude, si la seconde phase est comparée à la première, la présentation de patients au service de Consultations Externes a augmenté pour quelques types de patients lépreux comme les patients borderline et borderline lépromateux et diminué pour les patients borderline tuberculoides et tuberculo-
loïdes polaires. La tendance dégagée sur une décennie suggère que l’infection par le VIH est faible chez les patients lépreux, comparés à d’autres groupes à risque. Le suivi tous les 6 mois de ces patients indique qu’aucun d’entre eux n’a rétrogradé en une forme sévère de la lépre ou n’a développé le complexe associé au SIDA (ARC) ou le SIDA. Dans cette étude, il apparaît qu’aucune de ces infections ne précipite l’autre. Il ne fut pas observé de déplacement vers le bas le long du spectre immuno-pathologique ou de réactions inverses ou de névrites (à la fois chroniques ou aiguës) parmi les patients hanséniens. Aucun n’a développé de réaction de type érythème noueux lépreux. Concomitamment, les cas de lépre aussi positifs au VIH n’ont développé ni de syndrome ARC ni de SIDA terminal.

India has the largest number of known cases of leprosy and happens to incidentally be endemic for HIV as well. Some of the earlier studies done in North and North-Eastern India did not find any association of HIV infection with leprosy patients (24). A few studies from South Indian states showed a higher prevalence of HIV infection among leprosy patients, but these studies alone do not provide any indication of its association with leprosy (12). Leprosy caused by *Mycobacterium leprae* has an unusually long incubation period, and infection with HIV leads to a profound drop in CD4+ T-lymphocyte count and function and compromises the cell-mediated immune response, as well (19, 25). Earlier studies carried out in this center suggested that 1 per thousand (5/4025 : 0.124%) of the leprosy patients harbored HIV infection. Follow-up of these patients at an interval of six months, revealed that none of them downgraded into a severe form of leprosy nor developed ARC or AIDS (10). Although this study indicated that leprosy is not a risk factor for developing HIV-1 infection, the HIV surveillance studies on this population was continued with a view to assess the risk and find out the trend in an area where both the infections are prevalent. This study compares the results of HIV seroprevalence, which was carried out in two phases; first, from April, 1989 to March, 1993 when HIV infection was being detected in India in different risk group populations to assess the risk among leprosy patients, and then from September, 1999 to March, 2004. This is the first report of a decade of HIV screening of leprosy patients in this region of the country and the longest follow-up of HIV-leprosy co-infected cases.

One of the commonly observed complaints among leprosy patients was pain in the joints. Many studies have proven that microbial agents might trigger the autoimmune phenomenon and induce rheumatoid arthritis (1, 5, 8). In order to find out if arthritis is present in the HIV-leprosy co-infected patients, the sera from these cases were tested for Rheumatoid arthritis (RA) factor. Many risk behaviors as well as the routes of transmission for HIV, Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infection are identical to those for other sexually transmitted diseases (STDs) (1). For this reason, the leprosy sera samples were tested for HBsAg and VDRL simultaneously with HIV.
MATERIALS AND METHODS

Leprosy patients, across the spectrum, i.e., tuberculoid (TT), borderline-tuberculoid (BT), mid-borderline (BB), borderline-lepromatous (BL), lepromatous (LL) and neuritic (N) types, classified, according to Ridley-Jopling criteria (23), attending the Unit-I of the Outpatient’s Department (OPD) of the Central JALMA Institute for Leprosy and other Mycobacterial Diseases (CJILOMD) were included in the study. The leprosy cases in the study were neither newly admitted nor untreated patients, although a few were newly detected cases. For bacteriological determination, the six skin sites used were the two ear lobes and four representative active skin sites, i.e., hand (right arm and left arm), elbow (right and left), back, forehead, and the site of the lesion. In our OPD, four skin sites are routinely used for determination of the bacteriological index (B.I.). The inclusion criteria were: adult leprosy patients between the age group of 16 to 48 yrs. Children and old patients were excluded from the study as it was assumed they were not likely to be sexually active. In order to ensure that the patients were not screened over and over again, their OPD cards were marked, “HIV-Screened.” This helped in excluding the repeat testing of the patients. Blood was collected aseptically from leprosy patients by ante-cubital venipuncture after obtaining pre-informed consent. The sera samples collected after centrifugation at 2500 g were stored at –20°C until the assays were performed. ELISA was done using Genedia HIV-1/2 EIA kit (Greencross, Korea). Those found positive were confirmed by rapid (HIV capillus latex aggregation assay, Trinity Biotech PLC, Ireland) and Western blot assays (WesternBlot, BIO-RAD, NEWLAVBLOT), Nippon Bio-Rad Laboratories, Japan. After post-test counselling, a report was handed over to those found HIV-positive and patient was referred to clinicians for further care and management. To find out any other co-infections, the samples were further tested by HBsAg kit, (Immuno-chromatography test ERBA Hepline, Transasia Bio-Medicals Ltd., Mumbai, India) and VDRL and Rheumatoid Arthritis kits (Carbogen and Rhelax, RF of Tulip Diagnostics (P) Ltd., Bambolim, Goa, India).

RESULTS

The prevalence of HIV-1 infection in leprosy patients was observed in two phases. In phase one, 4025 patients [30 indeterminate (I), 141 polar tuberculoid (TT), 1888 borderline-tuberculoid (BT), 409 borderline (BB), 600 borderline lepromatous (BL), 751 polar lepromatous (LL), 200 N] were screened between 1989 and 1993, out of which only 8 were ELISA positive and 5 were Western Blot reactive. Subsequently, in the second phase from 1999 to 2004, 2125 patients (21 I, 19 TT, 646 BT, 332 BB, 610 BL, 324 LL, 173 N) were screened, out of which 8 were ELISA positive and 5 were Western Blot reactive (Table 1). The variation in the results of the two tests correlated well with the titre of HIV-1/2 antibodies in the sera samples. The strongly positive samples having a high absorbance value, ranging between 1.5 and 2.0, measured in terms of O.D. at 450 nm in an ELISA reader had an excellent pattern of reactivity in Western Blot. The samples with weak or moderate positivity in ELISA, with an O.D. ranging between 0.5 and 0.7, did not react with Western Blot. A rise in HIV infection from 0.124% to 0.376% was observed. Two samples were reactive to HIV-2 by Western Blot. Among all the HIV-positive leprosy patients, there were no other co-infections like Hepatitis B, Syphilis and RA. Out of the 8 HIV-leprosy co-infected patients, 2 each were BT and BL types, 3 were BB and 1 was LL type of leprosy.

The predominant clinical features were hypo-pigmented lesions, clawing of fingers and toes, pain, and hand muscle atrophy. Whereas 4 patients had deformity in hands, only one of them reported acute pain. All the patients completed a full course of standard anti-leprosy multi-drug therapy, responded satisfactorily, and were later clinically and bacteriologically negative. The initial bacterial index, prior to treatment, which ranged between 2+ and 3+ became negative on completion of the treatment. Two of the 8 HIV-leprosy co-infected patients (BL, LL) became bacteriologically negative after 6 months and another 2 (BT, BL) became negative after 24 months of treatment (Table 2). We have observed that following treatment, B.I. became negative even in BL and LL cases. The HIV-positive


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<td><strong>I Phase</strong> (N = 4025)</td>
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<td>HIV status</td>
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<td>Borderline- T resembles (BT) 1888 (46.90%)</td>
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<tr>
<td>Tuberculoid (TT) 141 (3.50%)</td>
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<tr>
<td>Indeterminate (I) 30 (0.74%)</td>
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<tr>
<td>Lepromatous- Leprosy (LL) 751 (18.65%)</td>
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<tr>
<td>Borderline- Lepromatous (BL) 600 (14.90%)</td>
</tr>
<tr>
<td>Mid- Borderline (BB) 415 (10.31%)</td>
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<tr>
<td>Neuritic (N) 200 (4.96%)</td>
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*a denotes I Phase of HIV screening of the leprosy patients which was from April, 1989 to March, 1993.  
b denotes II Phase of HIV screening of the leprosy patients which was from September, 1999 to March, 2004.  
EIA = ELISA, WB = Western Blot.  

patients are being followed up at six month intervals. On follow-up, to date none of the patients with HIV-1 infection have progressed into a more severe form of the disease. None of the co-infected cases have been lost so far in follow-up. In these co-infected patients, it is difficult to assess which infection occurred first. Our results indicated that HIV-1 infection does not contribute in any way to the precipitation of serious forms of leprosy.

**DISCUSSION**

It is well recognized that HIV infection constitutes a major risk factor for tuberculosis (TB) and for other mycobacteria, such as *M. avium* and *M. intracellulare*, but there are still uncertainties regarding its association with leprosy. The association between the HIV and tuberculosis and certain other non-tuberculous mycobacterial infections have been established (20, 21). Potential effects of HIV infection on leprosy have been suggested and discussed by several authors but, despite expectations, little interaction has been observed until now (9, 17, 22). Although an association between HIV and leprosy has been described in Zambia (18) and in Tanzania (27, 28), there is some evidence from studies in Mali (15), Ethiopia (6, 7) and in other African countries that HIV infection is not a risk factor for leprosy (14, 16). On the contrary, a few studies carried out in some African countries to determine the association between leprosy and HIV infection suggest that HIV infection is an important risk factor for leprosy (4, 18). Some of these studies had limitations in study design and some found no association between the two diseases (2, 13).

The increase in HIV infection as compared to that of the first phase is disturbing and the mode of transmission appeared to be heterosexual as revealed during the post-test counselling session. None of the co-infected cases admitted to having a homosexual relationship or had a history of blood transfusion. Two of the males had symptoms of STDs at the time of testing.

The trend over a decade suggests that HIV infection is low among the leprosy patients when compared with other risk groups, like TB patients, which is 4.3% (26/600) in Agra (in press). The prevalence and incidence for HIV infection in Agra varies in different groups. Our institute has a Voluntary Confidential, Counselling and Testing Center (VCCTC), a State body of the National AIDS Control Organization (NACO), where screening for HIV infection is carried out routinely from different groups, namely, Volunteers (individuals opting for voluntary HIV testing), HIV-suspected cases referred from different hospitals, female sex workers (FSWs), residents at the Government Protective Home, and cases referred by District Jail and District Magistrate, Agra.
Dec., 2004) revealed that the local prevalence and incidence of HIV-positivity in the area is, 40.31% (156/387) among Volunteers and 43.39% (46/106) among the Referred cases (communicated).

In the second phase as compared to that of the first phase, the OPD attendance of a few types of leprosy patients has risen during the study phase, whereas others have declined. A striking feature which has emerged during the second phase of the study is that there is an increase in the attendance of BB and BL types of leprosy patients, whereas there is a decrease in the BT and TT types of leprosy patients as depicted in Table 1. This could be one of the reasons for the higher HIV-positivity observed among the BB and BL cases. Another one could be attributed to the better control due to multi-drug therapy (M.D.T.) and decreased transmission of \textit{M. leprae}, with new cases dominated by a long period of incubation, in the lepromatous leprosy cases. Although the number of leprosy patients screened for HIV infection in the second phase is less as compared to those screened during the first phase, a rise in HIV infection is disturbing since this area appears to be endemic for both the infections.

Expansion of the HIV epidemic could have a significant effect on the epidemiology of leprosy. In this study, it appears that neither of the infections precipitated the other. The incidence of downgradation, as well as reversal reactions and neuritis (both chronic and acute), was not observed among the leprosy patients. None of them developed Erythema Nodosum Leprosum (ENL) reactions. The total cases of HIV-positive leprosy patients were only thirteen in both the phases (5 in phase I, and 8 in phase II), which have been followed up very carefully and with special care. We have also observed that reversal reactions and ENL did not occur among any of the HIV-leprosy co-infected cases. If the number of cases were more, then probably one might have noted some reversal or ENL reactions. To resolve the issue, a larger study, with longer follow-up is required. Clinical manifestations of lepromatous leprosy cases might be immunologically mediated and these features could be abrogated by HIV infection.

Similarly, the HIV-positive leprosy cases did not develop either AIDS related complex (ARC) or full blown case of AIDS. None of the co-infected cases have been lost so far in the follow-up. This is the first report of a decade of HIV screening of leprosy patients in this region of the country and the longest follow-up of the largest number of HIV-leprosy co-infected cases. Other studies have reported follow-up of very less number of the co-infected cases (11, 26). The underlying mechanism by virtue of which the severity of both the diseases is lowered is not known. The infectious agents and host defences seem to have co-evolved to reach balanced states where virus and host survive. While HIV has not quite yet reached an optimal balance, tuberculosis (TB), leprosy, HBV, HCV in humans or lymphocytic choriomeningitis virus (LCMV) in mice have successfully established persistence (29).

\begin{table}
\centering
\caption{Clinical presentations and bacteriological index among the HIV-leprosy co-infected patients.}
\begin{tabular}{|c|c|c|c|c|c|}
\hline
Clinical findings & Skin Lesions & Nerves & Pain & Deformity & Smear 3+ (Negative after 24 months)  \\
\hline
1 & BL & $>$5 & 5 & Pain & Nil \hline
2 & BL & $>$5 & 4 & Nil & Smear 2+ (Negative after 6 months) \hline
3 & BB & $>$5 & 1 & Nil & Nil \hline
4 & BT & 1 & Nil & Nil & Negative \hline
5 & LL & $>$5 & 4 & Nil & Hand \hline
6 & BB & 1 & 4 & Nil & Hand \hline
7 & BB & $>$5 & 6 & Nil & Negative \hline
8 & BT & $>$5 & 4 & Nil & Hand \hline
\end{tabular}
\end{table}
Although the present study does not show any association between HIV and leprosy, future study is warranted to find out the reasons for cross-protection, if any, at the genetic and molecular level.

Acknowledgement. This study was supported by funds from the Indian Council of Medical Research, New Delhi. Shikha Sinha is a recipient of Senior Research Fellowship of the Council of Scientific and Industrial Research (CSIR). The authors thank Mr. K. L. Verma, Mr. M. M. Alam, Mr. Sushil Prasad, Mr. P. N. Sharma, and Mr. M. S. Tomar of the HIV/AIDS Unit and the entire staff of OPD for their assistance in the study.

REFERENCES


Persister Studies in Leprosy Patients after Multi-Drug Treatment

U. D. Gupta, K. Katoch, H. B. Singh, M. Natrajan, and V. M. Katoch

ABSTRACT

Cutaneous biopsies were collected from leprosy patients who attended the out-patient department of the Institute for treatment at different intervals, i.e., 12 months, 18 months, 24 months, 36 months, and more after beginning the multi-drug treatment therapy (M.D.T.). The patients belonged to the two drug regimens; (i) standard multibacillary (MB) M.D.T. after 12, 24, and 36 months; or (ii) standard M.D.T. + Minocycline 100 mg once a month (supervised) + Ofloxacin 400 mg once a month supervised for 12 months Biopsies were processed for mouse footpad inoculation and for estimating ATP levels by bioluminescence assay as per established methods. Viable bacilli were observed in 23.5% up to 1 year, 7.1% at 2 years, and in 3.84% at 3 years of M.D.T. by MFP and 29.4%, 10.7%, and 3.84% by ATP assay in the M.D.T. group at the same time period, respectively, but not in M.D.T. + Minocycline + Ofloxacin group after one year. The overall percentage of persisters was 5.55% by MFP and 7.14% by ATP assay up to 3 years of treatment.

RESUME

Des biopsies cutanées furent prélevées à intervalles successifs (12, 18, 24, 36 mois et plus) de patients hanséniens traités au service de consultation externe de l‘Institut, après mise en œuvre de la polychimiothérapie (PCT). Les patients furent répartis en 2 types de PCT : (i) PCT multibacillaire standard après 12, 24 et 36 mois et (ii) PCT standard + Minocycline 100 mg une fois par mois (prise contrôlée) + Orofloxacine 400 mg une fois par mois en prise contrôlée pendant 12 mois. Les biopsies furent préparées pour le test d‘inoculation à la patte de souris (IPS) et pour l‘estimation des niveaux d‘ATP par bioluminescence selon des méthodes bien établies. Des bacilles viables furent observés dans 23,5% des biopsies jusqu‘à 1 an ; 7,1% après 2 ans et 3,84% après 3 ans de PCT par le test IPS et 29,4% ; 10,7% et 3,84% par test de l‘ATP pendant les mêmes temps après PCT, respectivement, mais pas chez le groupe PCT + Minocycline + Orofloxacine après 1 an. Le pourcentage global de patients avec bacilles persistants était de 5,55% d‘après le test IPS et de 7,14% d‘après le test à l‘ATP après 3 années de traitement.

RESUMEN

Se trabajó con pacientes con lepra que acudieron al Instituto para su tratamiento. Los pacientes se asignaron a dos grupos, uno que recibió la poliquimioterapia (PQT) estándar para lepra multibacilar (MB) y otro que recibió la PQT estándar combinada con Minociclina (100 mg mensuales) y Ofloxacina (400 mg mensuales), ambas drogas administradas de manera supervisada por 12 meses. De cada paciente se tomaron biopsias de piel a los 12, 18, 24 y 36 meses o más, después de haber iniciado el tratamiento. Las biopsias fueron procesadas para su inoculación en la almohadilla plantar del ratón (APR) y para la medición de sus niveles de ATP por bioluminiscencia, de acuerdo a métodos ya establecidos. En el grupo tratado con PQT se observaron bacilos viables en el 23% de las biopsias a un año del seguimiento, en el 7.1% de las biopsias a los 2 años, y en el 3.8% a los 3 años usando la técnica de la APR, y en el 29.4%, 10.7% y 3.84% de las biopsias usando el ensayo de ATP, a los mismos intervalos de tiempo. En las biopsias de piel del grupo tratado con PQT + Minociclina + Ofloxacina no se observaron bacilos después de un año de tratamiento. El porcentaje global de “persistentes” fue de 5.5% por el ensayo de la APR y de 7.14% por el ensayo de ATP a los 3 años del tratamiento.

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In pre-multi-drug therapy (M.D.T.) era, persistence of drug sensitive Mycobacterium leprae and emergence of drug resistant mutants despite prolonged therapy with DDS was reported to be the cause of treatment failures in lepromatous patients. With the introduction of rifampicin, it was expected that in addition to a rapid decrease in the infectivity of multibacillary (MB) cases, the above problems would also be taken care of if drugs were used alone or in combination. With the M.D.T. of leprosy, the results have been satisfactory as it has been generally effective in reducing the viable load as well as duration of treatment in MB cases. However, the persistence of drug sensitive viable organisms has been demonstrated after varying durations of treatment at different sites by several workers. These persisting bacilli have special significance as they have the potential of causing relapse in MB cases after M.D.T. This study has been initiated to gain an overview of this problem and follow the recent trends in multibacillary cases treated with M.D.T.

**MATERIALS AND METHODS**

One hundred twenty six biopsies from ninety six borderline lepromatous (BL)/polar lepromatous (LL) patients attending the outpatient department of Central JALMA Institute for Leprosy and Other Mycobacterial Diseases were included in this study. The age of the patients ranged from 16 to 60 years. All these patients did not suffer from any chronic disease like diabetes mellitus, tuberculosis, hypertension, etc., and showed no clinical evidence of resistance. The patients belonged to the two drug regimens: (i) standard MB M.D.T. after 12, 24, and 36 months; (ii) standard M.D.T. + Minocycline 100mg once a month (supervised) + Ofloxacin 400mg once a month (supervised) for 12 months.

Before starting the treatment, these patients were examined in detail, clinical findings were charted and recorded, and smears were taken from different sites for calculation of bacterial index (B.I.). At the start of therapy, the average B.I. ranged from 2 to 5+ for regimen 1 (mean 3.6), and from 1 to 4+ for regimen 2 (mean 2.2). The biopsies were processed for mouse footpad inoculation and bacillary ATP assay as used earlier by us.

**Mouse footpad inoculation.** The footpads were homogenized and the bacterial enumeration was done as described by D’Arcy and Rees. A batch of five random bred BALB/C mice was taken and each hind mouse footpad was inoculated with 0.03 ml suspension containing 5000 to 10,000 bacilli. The bacilli were harvested at six months and eight months (50% at each stage) after inoculation and acid–fast bacilli (AFB) were counted. The footpad pools were used for enumeration of the bacilli. The percentage of viable persisters being low, even a 10-fold increase in the harvest count was taken as evidence for bacillary growth.

**ATP assay.** The biopsies were processed, bacillary ATP was extracted and assayed as per the technique standardized in our laboratory. ATP levels were estimated and expressed as pg/million of AFB. Cultures were set up in the final preparation to rule out contamination with any cultivable mycobacteria or any other organism.

**RESULTS**

The details of specimens showing viability after different durations of M.D.T. by mouse footpad as well as ATP are presented in Table 1. Out of 126 biopsies, 71 biopsies belonged to patients treated with standard M.D.T. regimen while 55 biopsies belonged to patients treated with standard M.D.T. + 100 mg of Minocycline + 400 mg of Ofloxacin once a month (supervised). After one year of treatment, out of 17 biopsies (MDT), 4 were found to be positive for viable M. leprae by mouse footpad and 5 by the ATP method while out of 55 biopsies belonging to M.D.T. + Minocycline + Ofloxacin group, none was found to positive. The range of B.I. of these patients were 2 to 5+ (average 3.60) and 1 to 4+ (average 2.2), respectively. By the mouse footpad method, the Fisher exact test of viability of M. leprae at one year between regimen 1 (4/17) and regimen 2 (0/55) is highly significant (p = 0.002). Similarly, by the ATP method, the Fisher exact test of viability of M. leprae at one year between regimen 1 (5/17) and regimen 2 (0/55) is highly significant. The results from the percentage of patients with viable bacilli at all time periods from regimen 1 (7/126) with viable bacilli from regimen 2 at one year is statistically significant (p = 0.02).
Similarly, out of 28 biopsies from patients who had M.D.T. up to 2 years, 2 biopsies showed AFB counts by mouse footpad and 3 were positive for bacillary ATP. The mean B.I. of these biopsies ranged from 1 to 5+ (average 2.6). Further, out of 26 biopsies from patients who had taken up to 3 years of M.D.T. or more, 1 biopsy showed positivity by mouse footpad as well as by ATP assay. Statistically, the differences between the two methods were non–significant. The B.I. of the patients ranged from 1 to 3+ (average 1.81). Overall, out of 126 biopsies included in this study, 7 (5.55%) showed evidence of viability by mouse footpad, whereas 9 (7.14%) showed positivity by ATP bioluminescence. The results of quantitative relationship between bacillary ATP and mouse footpad showed that when ATP levels were in the range of 0.36 to 3.59 pg/million, both techniques were equally good (positives were 7/126). However, two cases whose bacillary contents were in the range of 0.039 to 0.04 pg/million bacilli did not show growth by mouse footpad (Table 2).

The correlation of initial B.I. and M. leprae viability after chemotherapy was analyzed and is presented in Table 3. At one year of treatment with standard M.D.T., it was observed that in biopsies in initial B.I. up to 2+, no viability was observed by either of the method. Further, in biopsies with initial B.I. of 2 to 3.9+, viability was observed in 4/53 (7.55%) and 5/53 (9.4%) biopsies by mouse footpad and ATP, respectively. However, in biopsies with initial B.I. of 4+ and more, higher viability was observed [3/13 (23.1%) by MFP, and 4/13 (30.8%) by ATP]. The differences in viability in biopsies between group 2 to 3.9+ and 4+ and more, the differences were significant.

**DISCUSSION**

M.D.T. campaigns have led to a major decline in the prevalence of leprosy. However, it continues to be an important public health problem in many parts of the world. Despite the regular administration of M.D.T., live bacilli persist in a section of leprosy cases. A number of workers have demonstrated these live persisters by growth in mouse footpads inoculated by M. leprae in pre-M.D.T. (13,14), as well as post-M.D.T. era (5, 9, 16, 17, 18). W.H.O. and the some national agencies such as in India have recently recommended that treatment in MB cases be stopped after 1 year of treatment. In this study, 23.5% of the specimens showed growth by mouse footpad while 29.4% of the specimens showed growth by ATP assay in patients treated with conventional M.D.T. after 1 year of treatment (Table 1). On the other hand, none of the specimens showed growth by mouse footpad as well as ATP assay in patients treated with M.D.T. + Minocycline + Ofloxacin, clearly indicating that addition of Minocycline and Ofloxacin in the treatment regimen was quite effective as no viable persisters were detectable after 1 year of treatment (7). However, in the present

<table>
<thead>
<tr>
<th>Duration of treatment</th>
<th>Range and average BI at the time of biopsy</th>
<th>MFP+(%)</th>
<th>ATP +%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(1)</td>
<td>(2)</td>
</tr>
<tr>
<td>6 months to 1 yr of treatment</td>
<td>3.6 (2–5+)</td>
<td>44/17 (23.5%)</td>
<td>0/55 (0%)</td>
</tr>
<tr>
<td>&gt;1 yr to 2 yrs of treatment</td>
<td>2.55 (1–5+)</td>
<td>2/28 (7.1%)</td>
<td>1/26 (3.84%)</td>
</tr>
<tr>
<td>&gt;2 yrs to 3 yrs of treatment</td>
<td>1.81 (1–3+)</td>
<td>1/26 (3.84%)</td>
<td>1/26 (3.84%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>7/126 (5.55%)</td>
<td>9/126 (7.14%)</td>
</tr>
</tbody>
</table>

BI: Bacteriological index; MFP: Mouse Footpad; ATP: Bioluminescence assay; (1) conventional MDT; (2) Conventional MDT +Minocycline 100 mg once a month supervised + Ofloxacin 400 mg once a month supervised; (3) Overall.
study as well as in other studies live bacilli have been demonstrated after one year of treatment with conventional M.D.T. Out of the 17 specimens in the up to one year M.D.T. group, 6 had received M.D.T. for 6 months out of which one showed growth (having initial B.I. of 5+), and 11 received M.D.T. for 1 year and growth was seen in 3 patients (having initial B.I. of 4+ and more, and 3 to 4+ after one year of treatment). These observations clearly indicate that there is a potential risk associated with stopping the therapy at one year mainly in such patients who are having high initial B.I. However, the adequacy of one year treatment in such cases can only be known after experience of follow-up studies become available. Up to 2 years of M.D.T. (13 to 24 months), 2 out of 28 biopsies (7.1%) showed growth in mouse footpad and significant ATP was detected in 1 out of 28 (10.7%) of the biopsies. In patients who had taken M.D.T. from 25 to 36 months, 1 out of 26 (3.84%) biopsies was positive by both, i.e. mouse footpad as well as ATP assay. Overall, 7 out of 126 (5.55%) and 9 out of 126 (7.14%) biopsies by mouse footpad and ATP assay were observed to be positive which are in agreement with earlier reports where persister rates of 9 to 16% varying periods of MDF have been reported (5, 6, 9, 10, 20). On the other hand, much higher persister rates has also been reported by Shetty, et al. (16, 17, 18) in nerves and skin of leprosy patients. There has been good concordance between viability determination by mouse footpad and ATP when ATP levels were in the range of 0.36 to 3.59 pg/million but when ATP levels were lower mouse footpad failed to detect any positivity as reported earlier by Gupta, et al. (5).

In the present investigation, the patients of standard M.D.T. were on continuous M.D.T. until smear negativity (at least 2 years). It is difficult to foresee how these patients would have behaved if they had been on one year fixed duration M.D.T. Persisters have been reported to be the cause of relapses after 4 to 9 years in well conducted drug trials with adequate follow-up (12). There are reports which suggest that patients with high pretreatment M. leprae loads are at higher risks of relapse if the treatment is stopped after 2 years W.H.O.-M.D.T./Fixed Duration Therapy compared to patients treated till point of smear negativity (13). Further, it is apparent that in biopsies with initial B.I. of 1 to 1.9, the M.D.T. alone or in combination with minocycline and ofloxacin, no viable organisms were observed. But when the initial B.I.s were 2 to 3.9+ or = 4, the percentage of specimens showing viable organisms increased (7.55% and 22.1% by mouse footpad and 9.4% and 30.8% by ATP). All the specimens in which viable organisms could be demonstrated beyond one year had the initial B.I. of ≥ 4+ (Tables 1 and 3). Other studies at our institute have also shown that highly bacillated cases dropping out of treatment up to 12 to 18 months had higher relapse rates (14). These cases are very small proportion of all leprosy cases as <2% of current cases have B.I. of 3+ or more (unpublished data by Katoch, et al.). It will be interesting to observe the progress

<table>
<thead>
<tr>
<th>ATP content (pg/million)</th>
<th>Positive by ATP</th>
<th>Positive by MFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.36–3.59</td>
<td>7/126</td>
<td>7/126</td>
</tr>
<tr>
<td>0.04–0.359</td>
<td>1/126</td>
<td>0/126</td>
</tr>
<tr>
<td>0.02–0.039</td>
<td>1/126</td>
<td>0/126</td>
</tr>
<tr>
<td>Total</td>
<td>9/126</td>
<td>7/126</td>
</tr>
</tbody>
</table>

**Table 2.** Quantitative relationship between ATP content and positive growth in mouse footpad.

**Table 3.** Correlation of initial B.I. and M. leprae viability after chemotherapy.

<table>
<thead>
<tr>
<th>Initial B.I.</th>
<th>No. of biopsies</th>
<th>MFP+</th>
<th>ATP+</th>
</tr>
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<tbody>
<tr>
<td>1–1.9+</td>
<td>60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–3.9+</td>
<td>53</td>
<td>4(7.55%)</td>
<td>5(9.4%)</td>
</tr>
<tr>
<td>4–5+</td>
<td>13</td>
<td>3(23.1%)</td>
<td>4(30.8%)</td>
</tr>
<tr>
<td>126</td>
<td></td>
<td></td>
<td>9</td>
</tr>
</tbody>
</table>
of such patients after stopping M.D.T. at other centers where M.D.T. is being given. Further, there is a need to carry out surveillance studies in larger number BL/LL patients to know the trends of persisters as well as the resultant relapses.

Acknowledgment. Authors are thankful to Ishaat Ali, R. S. Gupta, Asha Ram, V. K. Mathur, Thakur Das, and Noel Crispin for clinical and technical support. The gift of some of the reagents from LEPRRA, U.K. is gratefully acknowledged.

REFERENCES
Comparative Evaluation of Immunotherapeutic Efficacy of BCG and Mw Vaccines in Patients of Borderline Lepromatous and Lepromatous Leprosy

Tarun Narang, Inderjeet Kaur, Bhushan Kumar, Bishan Dass Radotra, and Sunil Dogra

ABSTRACT

Background. Even after 12 months of multi-drug therapy (M.D.T.) multibacillary (MB) therapy patients with high bacterial index (B.I.) continue to harbor dead bacilli and viable persisters, which lead to immunological complications such as recurrent reactions and late relapses, respectively. To achieve faster killing of viable bacilli and clearance of dead bacilli, various immunotherapeutic agents (vaccines and cytokines) are being evaluated as an adjunct to M.D.T.

Aims and objectives. To evaluate the role of BCG and Mw vaccines in the immunotherapy of leprosy.

Materials and methods. Sixty untreated leprosy patients with a BI = 2 were randomly allocated to three treatment groups of twenty patients each. Group A patients received World Health Organization (W.H.O.) (12 months M.D.T.-MBR) and BCG intradermally (10^5 live bacilli /per dose). Group B patients were administered 12 months M.D.T.-MBR and Mycobacterium w (1 × 10^8) killed bacilli as first dose and 0.5 × 10^8 /dose in subsequent doses. Group C received 12 months M.D.T. MBR with 0.1 ml of normal saline as placebo. All the groups received 4 doses of vaccine or normal saline repeated at three monthly intervals. The patients were periodically monitored by clinical (Ramu’s score), bacteriological (slit skin smear), and histopathological (skin biopsy) parameters, six monthly during and one year after completion of M.D.T.

Results. The mean reduction in clinical scores in BCG and Mw groups was significantly more when compared to controls. At 12 and 24 months, the patients in BCG group had significantly greater reduction in Ramu’s score as compared to those in the Mw group. BI declined by 2.40 units/year in patients receiving BCG, 2.05 units/year in the Mw group and 0.85 units/year in the control group. Although the incidence of type 1 reactions was apparently more in the BCG and Mw vaccinated groups, the incidence of type 2 reactions, neuritis and development of new deformities was less as compared to the controls.

Conclusions. In our study, BCG exhibited slightly better and faster effect on bacteriological clearance and clinical improvement as compared to Mw vaccine in borderline lepromatous (BL)/ polar lepromatous (LL) patients with a high initial B.I., however, their effect on histopathological (decrease in GF) improvement was comparable. Both the vaccines were well tolerated. Immunotherapy can be a useful adjunct to the shortened (12 months) M.D.T. MB regimen to decrease the risk of reactions and relapses in highly bacilliferous BL/LL patients.

RESUME

Contexte. Même après 12 mois de polychimiothérapie (PCT), des patients multibacillaires (MB) avec index bactérioscopique (IB) élevés continuent à avoir des bacilles morts ou des bacilles viables et persistants, qui mènent fréquemment à des complications immunologiques comme des réactions récurrentes ou des rechutes tardives, respectivement. Afin d’atteindre une éradication plus rapide des bacilles viables et une élimination plus rapide des bacilles morts, des agents immuno-thérapeutiques variés (vaccins et cytokines) sont en cours d’évaluation, comme compléments à la PCT.
Buts et objectifs. Évaluer le rôle des vaccins BCG et Mw dans l’immunothérapie de la lèpre.

Matériels et méthodes. Soixante patients hanseniens encore non-traités, avec IB de 2, furent attribués en aveugle à 3 groupes de traitements de 20 patients chacuns. Le groupe A reçut la PCT pour patients MB de 12 mois recommandée par l’OMS et une injection intradermique de BCG (10^5 bacilles vivants par dose). Au groupe B fut administré 12 mois de PCT-MB et Mycobacterium w (1 × 10^6 bacilles morts en primo-injection et 0,5 × 10^8 en injections de rappel). Le groupe C reçut PCT-MB pendant 12 mois et 0,1 ml de liquide physiologique comme placebo. Tous les groupes ont reçu, tous les 3 mois, 4 doses de vaccins ou bien du liquide physiologique normal. Un suivi clinique (score de Ramu), bactériologiques (test du suc dermique) et histopathologiques (biopsies cutanées) des patients fut effectué tous les 6 mois pendant le traitement puis 1 an après la fin du traitement par la PCT.

Résultats. La réduction moyenne des scores cliniques des groupes traités au BCG ou à Mw fut significativement plus importante que celui du groupe contrôle. A 12 et 24 mois, les patients du groupe BCG avaient une réduction plus importante du score de Ramu que le groupe Mw. L’IB a diminué de 2,40 unités par an chez les patients ayant reçu le BCG, 2,05 unités par an dans le groupe Mw et de 0,85 unités/an dans le groupe contrôle. Bien que l’incidence des réactions de type 1 fût apparemment plus élevée dans les groupes vaccinés au BCG et Mw, l’incidence des réactions de type 2, les névrites et le développement de nouvelles déformations a été moindre chez les vaccinés que chez les contrôles.

Conclusions. Dans cette étude, le BCG a démontré un effet plus rapide et plus important en terme de clairance bactériologique et d’amélioration des signes cliniques que le vaccin Mw chez les patients lépromateux borderline (BL) ou les patients lépromateux polarisés (LL) avec un IB initial élevé. Cependant leurs effets sur l’aspect microscopique (diminution de la fraction granulomateuse GF) restaient très comparables. Les 2 vaccins furent tous deux fort bien tolérés. L’immunothérapie peut être très utile comme traitement complémentaire à la PCT-MB abrégée à 12 mois, pour diminuer le risque de réactions et de rechute(s) parmi les patients BL/LL fortement infectés par les bacilles de Hansen.

RESUMEN

Panorama. Los pacientes multibacilares (MB) con índices bacterianos (BI) altos siguen teniendo bacilos muertos y bacilos viables persistentes aún después de 12 meses de tratamiento con PQT, lo que conduce a complicaciones inmunológicas tales como reacciones recurrentes y recaídas tardías, respectivamente. Para acelerar la muerte de los bacilos vivos y la eliminación de los bacilos muertos se están evaluando varias vacunas y citocinas como agentes inmunoterapéuticos.

Metas y objetivos. Evaluar el papel de las vacunas BCG y Mw en la inmunoterapia de la lepra.

Materiales y Métodos. Sesenta pacientes con lepra sin tratamiento y con un BI = 2, se asignaron, a azar, a 3 grupos de tratamiento de 20 pacientes cada uno. El grupo A recibió la PQT de la OMS para lepra MB por 12 meses y BCG intradérmicamente (10^5 bacilos vivos por dosis). El grupo B recibió la PQT de la OMS para lepra MB y Mw (1 × 10^8 bacilos muertos como primera dosis y 0,5 × 10^8 en las dosis subsecuentes). El grupo C recibió 12 meses de PQT-OMS-MB y 0,1 ml de solución salina como placebo. Todos los grupos recibieron 4 dosis de vacuna o de salina a intervalos de 3 meses. Los pacientes fueron evaluados periódicamente usando parámetros clínicos (escala de Ramu), bacteriológicos (examen de linfa cutánea) e histopatológicos (en biopsia de piel).

Resultados. Los grupos tratados con BCG y con Mw evolucionaron mejor que los pacientes del grupo control. Dentro de los pacientes vacunados, los del grupo BCG mostraron una reducción en la escala de Ramu significativamente mayor que los pacientes del grupo Mw. El BI mostró una disminución de 2,4 unidades/año en los pacientes con BCG, de 2,05 unidades/año en el grupo Mw, y de 0,85 unidades/año en el grupo control. Aunque la incidencia de reacciones tipo I fue aparentemente mayor en los grupos vacunados con BCG y Mw, la incidencia de reacciones tipo 2, neuritis y nuevas deformidades, fue menor que la observada en el grupo control.

Conclusión. En nuestro estudio, el grupo vacunado con BCG mostró una mejor y más rápida evolución clínica y bacteriológica que el grupo vacunado con Mw, y esto ocurrió tanto en los pacientes BL como en los pacientes LL con altos BI; sin embargo, la mejoría histopatológica (disminución en la fracción granuloma) fue comparable en ambos grupos. Ambas vacunas fueron bien toleradas. La inmunoterapia puede ser un complemento útil a la PQT-MB de duración acortada (12 meses) para reducir el riesgo de reacciones y recaídas en los pacientes BL/LL altamente bacilíferos.
Leprosy continues to be a public health problem in seventeen endemic countries of the world. Since the inception of M.D.T. in 1982, there has been 85% reduction in global prevalence of leprosy. The prevalence of leprosy in India has fallen from 57 per 10,000 in 1981 to 3.3 per 10,000 in 2003 (3), but India still accounts for 78% of all the leprosy cases in the world, and its elimination program is of major importance for global leprosy control.

The duration of M.D.T. regimen for MB leprosy was reduced to 12 months by the W.H.O. Expert Committee on Leprosy in 1997 (34); however, information regarding efficacy and safety of shortened MB regimen (12 months) is very limited at present. There are reports of relapses in MB patients treated with fixed duration treatment (FDT) from some centers, especially in patients with higher B.I. (6, 11, 21, 32). Patients in the lower spectrum, i.e., BL/LL leprosy, have partial or complete lack of CMI, which is responsible for persistence of dead as well as live bacilli even after adequate therapy. A variety of possible factors which have been postulated for deficient cell mediated immunity are: genetic constitution, primary fault in T-cells and macrophages, inappropriate suppressor cell activity, and abnormal antigen presentation (26). In these cases the dead bacilli and their antigens and viable persisters lead to immunological complications such as recurrent reactions and late relapses, respectively. To achieve faster killing of bacilli and clearance of dead bacilli as well as possible alteration of immunological unresponsiveness in these patients, immunotherapy in the form of vacccines and cytokines has been tried.

Antigens of various mycobacteria have been observed to cross-sensitize the immune response to M. leprae and this might help in augmenting CMI in leprosy. Prominent among these are BCG (16), BCG plus killed M. leprae (3), Mycobacterium w (Mw) (9, 14, 15, 16, 23), and Indian Cancer Research Center (ICRC) bacillus (3). Many studies have confirmed the immunotherapeutic efficacy of Mw vaccine, but very few have evaluated the efficacy of BCG or compared BCG and Mw vaccines. Katoch, et al. (16) compared the immunotherapeutic efficacy of BCG and Mw vaccines in MB patients and found both to be effective however; patients were given M.D.T. until smear negativity in their study. Present study, was designed to compare the immunotherapeutic efficacy of BCG and Mw vaccines in BL/LL leprosy patients treated with fixed duration (12 months) W.H.O. M.D.T. MBR.

MATERIALS AND METHODS

Sixty untreated bacteriologically positive multibacillary leprosy patients (BL, LL) with a B.I. ≥ 2, age more than 12 years, attending the Leprosy Clinic of Post Graduate Institute of Medical Education and Research, Chandigarh, India were randomly allocated in 3 groups of twenty patients each.

All patients received W.H.O. M.D.T. (MBR) for one year. In addition, the first group (group A) was given BCG vaccine (0.1 ml/dose, containing 10^5 viable units of BCG; BCG vaccine laboratory, Guindy, Chennai, India). Group B received Mw vaccine (1 × 10^8 killed bacilli in the first dose and 0.5 × 10^8/dose in the subsequent doses), and group C was administered normal saline 0.1 ml intradermally as control. The patients in groups A, B, and C received four doses of BCG, Mw vaccine and normal saline, respectively, at three month intervals. Informed consent was taken from all the patients before inducting them into the study. Patients who were pregnant, in type 1 lepra reaction, and those who had any immunodeficiency disorder or were taking immunosuppressive therapy, were excluded from the study.

Patients were classified according to the Ridley-Jopling classification (10) and diagnosis in all patients was confirmed by histopathology. During and after M.D.T. treatment, activity of the disease was routinely assessed clinically by Ramu’s clinical scoring system (12) (minimum score = 0 and maximum = 28). A detailed history including symptoms and occurrence of reactions and findings on physical examination were recorded for all the patients, initially monthly for one year and every 3 months later on. Type 1 reaction (reversal reaction) was diagnosed on noting visible changes in the existing lesions in the form of erythema, swelling (edema), presence of subjective feeling of warmth, tingling sensations and or local tenderness, or appearance of new lesions, associated with or without constitutional symptoms. Type 2 reaction was diag-
nosed on the basis of presence of constitutional symptoms of varying degree like fever, aches, joint pains, bony tenderness with characteristic evanescent lesions of erythema nodosum leprosum (ENL) associated with or without specific organ involvement like eye, testis, kidney, etc. Only neuritis was diagnosed by the presence of persistent and demonstrable tenderness in the nerves (thickened or not) in the absence of any evidence of inflammation in the leprosy lesions but with nerve function impairment. Tenderness of nerves in the presence of inflamed skin lesions of type 1 or type 2 reaction was considered to be part of the reaction. Patients with deformities were classified according to W.H.O. grading of 1998(34).

Slit-skin smears were taken initially, and then every 6 months from the same sites. Skin biopsy was also repeated from the same site after 6, 12, and 24 months of starting treatment for histopathologic evaluation. The biopsies were graded as LL, BL, borderline (BB), or borderline tuberculoid (BT) based on the characteristic distribution of various types of inflammatory cells as well as the character, location, and extent of granuloma. Biopsy was classified as non-specific infiltrate (NSI) if there was no evidence of a granuloma, absence of acid-fast bacilli (AFB) and presence of minimal and scattered peri-appendageal lympho-histiocytic infiltrate in different parts of dermis. The results were also compared in respect to clearance of dermal granuloma(s) by measuring the estimated reduction in granuloma fraction (GF) (i.e., fraction of dermis occupied by the granuloma(s) and clearance of acid-fast bacilli) (6).

All the patients were followed up for two years. The data was analyzed and the therapeutic efficacy of the vaccines compared using the paired “t” test.

RESULTS

The mean age of the patients in all the groups was similar. Maximum number of patients were in the age range of 18 to 40 years. A majority of the patients in all the groups were males (46/60, 76%). Group A had 8 (40%) LL, 10(50%) BL, and 2 (10%) patients of histoid leprosy. In group B there were 10 (50%) LL, 9 (45%) BL, and 1 patient with histoid leprosy. Group C had 12 (60%) LL, and 8 (40%) BL patients. The clinical scores, B.I., and GF were analyzed and it was observed that the patients in the three groups were almost comparable by all these parameters.

All the patients exhibited reduction in clinical scores with therapy. The mean reduction in clinical scores in both groups A and B was significantly more at 6 and 12 months when compared to group C (p <0.05). At 24 months the patients in group A still had significantly greater reduction in clinical score but the difference between groups B and C was not statistically significant (Figs. 1a and 1b). The difference between groups A and B was not significant at 6 months, but at 12 and 24 months the patients in group A had significantly greater reduction in the score as compared to group B (p <0.05). (Table 1).

The fall in B.I. was significantly more in groups A and B (p <0.01) at 6, 12, and 24 months when compared to group C. On comparing the BCG and Mw groups the mean decrease in B.I. was more in the BCG
group (p <0.01) at 12 and 24 months (Table 2). At the end of two years, 14 (70%) patients in group A were smear negative as compared to 13 (65%) in group B and 6 (30%) in group C. Almost all the patients showed a rapid decline in morphological index (M.I.) during treatment. None of the patients showed solid staining bacilli at the end of 12 months.

All the patients showed reduction in GF but it was more marked in group A when compared to group C at 12 months (p <0.05) (Table 3). In relation to the reduction in GF, the difference between the groups B and C, as well as the groups A and B, was not significant (p >0.05) at any time during the study (Figs. 2a and 2b).

Histological upgrading from LL to BL was seen in 8/12 (66.6%) patients in the BCG group, 7/11 (63.6%) patients in Mw group and 5/12 (41.6%) patients in the control group. Upgrading from BL to BT disease was seen only in the vaccine treated groups. These changes were seen in 1/10 (10%) patient in BCG group and 3/9 (33.3%) patients in Mw group. At 24 months, near complete clearance of granulomas and AFB with histological picture suggestive of non-specific infiltrate was seen in 17 (85%) patients in the BCG group, 12 (60%) in the Mw group, and 6 (30%) in the control group.

A majority of patients in each group had experienced one or more episodes of reaction before starting antileprosy treatment. However, only those reactions which occurred in the previous two years (frequency and degree of severity was also noted) were considered for comparison in post-treatment statistical evaluation. History of type 1 reactions was present in 4 (20%) patients in group A, and 3 (15%) patients each in groups B and C. During the course of study, the number of patients who experienced type 1 reaction were 6 (30%), 6 (30%), and 4 (20%) in groups A, B, and C, respectively. There was an apparent but not statistically significant increase in the incidence of type 1 reactions in groups A and B, as compared to group C. However, majority of these reactions were mild and were managed with anti-inflammatory drugs (NSAIDS).

During the period of study, there was a significant decrease in the incidence of type 2 reactions in group A (p <0.05). The inci-

| TABLE 1. Clinical scores (mean ± S.D.) before and after treatment. |
|--------------------------|----------|----------|----------|----------|----------|----------|----------|
|                          | At 6 months | At 12 months | At 24 months |
|                          | Score      | Reduction  | Score      | Reduction  | Score      | Reduction  |
| Baseline                 |            |            |            |            |            |            |
| A                        | 16.55 ± 3.60 | 11.90 ± 2.42 | 4.65 ± 2.05 | 8.30 ± 2.70 | 8.25 ± 2.63 | 4.60 ± 1.84 |
| B                        | 15.50 ± 3.7  | 11.8 ± 2.78  | 3.70 ± 1.92 | 10.05 ± 2.68 | 5.45 ± 2.58 | 6.65 ± 1.66 |
| C                        | 16.20 ± 5.06 | 14.65 ± 4.92 | 1.55 ± 1.19 | 12.60 ± 4.75 | 3.60 ± 1.46 | 8.45 ± 2.52 |

Fig. 2(a). Pre-treatment LL patient in BCG group—diffuse granulomatous infiltration in dermis. GF = 80%. (H&E × 55).

Fig. 2(b). Post-treatment (same patient at 12 months)—almost complete clearance of granulomas. GF = 5%. (H&E × 55).
Table 2.  **Bacteriological index (mean ± S.D.) before, during and after treatment.**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>At 6 months</th>
<th>At 12 months</th>
<th>At 24 months</th>
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</thead>
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<tr>
<td></td>
<td>Score</td>
<td>Reduction</td>
<td>Score</td>
<td>Reduction</td>
</tr>
<tr>
<td>A</td>
<td>4.00 ± 0.85</td>
<td>2.35 ± 1.08</td>
<td>1.65 ± 1.18</td>
<td>1.60 ± 0.91</td>
</tr>
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<td>B</td>
<td>3.80 ± 0.95</td>
<td>2.45 ± 1.25</td>
<td>1.35 ± 0.93</td>
<td>2.05 ± 1.09</td>
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<tr>
<td>C</td>
<td>3.50 ± 1.05</td>
<td>3.20 ± 0.95</td>
<td>0.30 ± 0.47</td>
<td>2.65 ± 0.87</td>
</tr>
</tbody>
</table>

D
cidence of type 2 reaction decreased in all the
groups after starting therapy; the decrease
was from 45% (pre-treatment) to 15% (post-
treatment) in group A and from 45% to 20% in
group B, whereas in Group C there was
hardly any change, from 40% to 35%, and 4
(20%) of the patients in group C continued
to have recurrent episodes throughout the
study period. The decrease in the incidence
of type 2 reactions in groups B and C was
not statistically significant.

At the beginning of the study, positive his-
tory of neuritis was present in 8 (40%), 7
(35%), and 9 (45%) patients in groups A, B,
and C, respectively. After starting treatment,
the incidence of neuritis decreased in all the
patients. In group A, 2 (10%); group B, 3
(15%); and in group C, 6 (30%) patients ex-
perienced neuritis as part of reactions. How-
ever, the decrease in the incidence of neuritis
was statistically significant only in group A.
All the patients with neuritis were managed
with systemic steroids, NSAIDS and rest.

Grade 2 deformities like claw hand, foot
drop, and trophic ulcers were present in 4
(20%) patients in group A and 5 (25%) each in
groups B and C. None of the patients in
groups A and B developed any new defor-
mities nor was there any further deteriora-
tion in the deformity status, whereas in
group C, 3 (15%) patients developed new
deformities during the study period, (claw
hand = 2 and foot drop = 1).

All the patients in group A developed an
erythematous papule at the site of BCG vac-
cination, which progressed to shallow ulcer
and healed spontaneously with scarring.
Three patients in this group developed sec-
ondary infection of the ulcer with associated
regional lymphadenopathy and required a
course of antibiotics. Similarly, in the Mw
group as well, all the patients developed
erythema and induration or an inflammatory
papule at the injection site, and in 15 (75%)
of these patients ulceration occurred which
healed spontaneously within 3 to 4 weeks.
No systemic complications were noted fol-
lowing vaccination with BCG or Mw.

All patients tolerated M.D.T. well except
for the occurrence of dapsone syndrome in
three patients (2 in group A and 1 in group
B), who recovered completely following
withdrawal of dapsone.

**DISCUSSION**

Multidrug therapy (M.D.T.) has been a
very successful development in the treat-
ment of leprosy. However, most of the pa-
tients in the lepromatous spectrum were
still harboring dead bacilli at the end of two
years of treatment with M.D.T., indicating
their poor ability to clear the bacilli. Im-
munotherapy with vaccines, drugs and cy-
tokines could be useful in these patients in
the very specific role of augmenting the
CMI leading to faster killing of *M. leprae*
and clearance of dead bacilli, thereby re-
ducing the risk of relapse and reactions.

There are many reports in the literature,
which show that the immunological unre-
sponsiveness to bacillary antigens of *M.
leprae*, in multibacillary patients (BL, LL)
may be altered by various immunological
approaches (3, 7, 9, 13, 14, 15, 16, 22, 23). Although
the precise mechanism of action of these
vaccines is yet unknown, certain assump-
tions can be put forward based on the above
studies and results of other clinical trials.
Mw and BCG vaccines are able to override
the immunological non-responsiveness to
bacillary antigens in multibacillary patients
by generation of cross-reactive Th₁ type of
clones and amplification of IFN-γ produc-
tion with a concomitant decrease in levels
of TNF-α and IL-10.

In our study, the reduction in the clinical
scores was significantly more marked in the
BCG and Mw treated groups as compared
to controls (M.D.T. alone) at 6 and 12
months (p <0.05), however, BCG resulted
TABLE 3.  
Granuloma fraction (GF) (mean ± S.D.) at baseline and after treatment.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>At 6 months</th>
<th>At 12 months</th>
<th>At 24 months</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Score</td>
<td>Reduction</td>
<td>Score</td>
<td>Reduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>55.75 ± 21.04</td>
<td>32.00 ± 18.52</td>
<td>10.25 ± 10.81</td>
<td>45.50 ± 16.05</td>
</tr>
<tr>
<td>B</td>
<td>55.00 ± 22.47</td>
<td>29.00 ± 0.04</td>
<td>13.75 ± 12.55</td>
<td>41.25 ± 16.69</td>
</tr>
<tr>
<td>C</td>
<td>55.25 ± 23.92</td>
<td>35.00 ± 7.91</td>
<td>22.75 ± 14.09</td>
<td>32.50 ± 14.18</td>
</tr>
</tbody>
</table>

Narang et al.: Immunotherapy with BCG and Mw Vaccines

in greater reduction in the clinical scores as compared to the Mw at 12 and 24 months (p <0.01). All the previous studies on Mw vaccine have also reported significant clinical improvement due to faster clearance of bacilli (9, 14, 15, 30, 33, 35).

The average decline in B.I. with M.D.T. has been reported to be 0.57 to 1.01 units/year (1). In our study, bacterial indices declined by 2.40 units/year in patients receiving BCG, 2.05 units/year in Mw group, and 0.85 units/year in the control group, the fall becoming more apparent in immunotherapy groups at 6, 12, and 24 months. The decline in B.I. was significantly more in the BCG treated group when compared to Mw treated group. The differences between BCG and Mw vaccine groups observed by us are not in consonance with the observations made by Katoch, et al. (16) who found the fall in B.I. to be significantly more in the Mw-treated group at 12, 18, and 24 months. The decline in B.I. was significantly more in the BCG treated group when compared to Mw treated group. The differences between BCG and Mw vaccine groups observed by us are not in consonance with the observations made by Katoch, et al. (16) who found the fall in B.I. to be significantly more in the Mw-treated group at 12, 18, and 24 months (p <0.05) as compared to the BCG group.

Faster reduction in bacterial load and changes in the cellular composition of the granuloma(s) from lower to higher spectrum and reduction in the granuloma fraction, observed in all of our patients in groups A and B reflects the upgrading of CMI following vaccination. Similar histological/immunological upgrading has also been reported in all previous studies (9, 14, 15, 30, 33, 35). Katoch, et al. (16) showed better histological improvement and immunological upgrading with Mw vaccine when compared to BCG, but in our study the difference between the two vaccine groups was not statistically significant for these parameters.

Leprosy reactions have a great significance in the course of the disease. Although the incidence of ENL appears to have fallen with the introduction of M.D.T., still a majority of patients with high smear positivity are tormented by recurrent episodes of ENL (17, 25). The incidence of type 2 reactions decreased in all our patients after starting therapy but it was more in the BCG treated group. Reduction in the incidence of type 2 reactions following immunotherapy has been observed in other studies as well. (9, 16, 25, 27, 30, 33).

Incidence of reversal reactions in MB patients treated with M.D.T. alone is reported to vary from 9% to 41% in hospitalized patients (20, 25). In majority of the earlier studies and as observed by us although there is an apparent increase in the incidence of reversal reactions in patients treated with Mw /BCG vaccines as compared to the group given M.D.T. alone, it did not achieve statistical significance (9, 14, 15, 16, 27, 28).

During the follow-up, it was reassuring to note that there was a lower incidence of neuritis in the vaccine treated groups [BCG = 2(10%); Mw = 3(15%)] as compared to the figure of 30% for the control group. This is in consonance with an earlier study by Talwar, et al. (30) where the control group had significantly more episodes of neuritis compared to the vaccine group. However, the decrease in the incidence of neuritis was statistically significant only in the BCG group.

A steady fall in the deformity rate among new cases has been observed following the introduction of M.D.T. since 1980 (4,28), but patients can have further deterioration of their existing deformities during treatment and thereafter due to increased incidence of reactions and neuritis (24). In our study none of the patients in the vaccine treated groups developed any new deformity or deterioration of the pre-existing deformity, but in the control group 3 (15%) patients developed grade 2 deformities. Similar observations have been made after immunotherapy with Mw vaccine by Sharma, et al. (30) and with BCG + killed M. leprae by Convit, et al. (7).

The vaccines were well tolerated and only local complications like ulceration and
mild secondary infection were seen. No systemic complications developed following administration of either of the vaccines. Development of ulceration and scarring which were hardly of any consequence have also been reported in earlier studies (9, 15, 16, 23, 30, 33). Three patients developed dapsone syndrome, which is certainly a very high incidence for dapsone hypersensitivity. This was probably a chance occurrence, however such an observation of rising incidence of dapsone hypersensitivity in the last two decades has been made by workers from other parts of India (18, 24). Dapsone was stopped in all these patients, they were given the vaccines as per schedule and none of them developed any other complications.

Ours is the only study after Katoch, et al. (16) where BCG and Mw have been compared. In the study by Katoch, et al. (16), M.D.T. and vaccines (at 6 month intervals) were administered until the patients attained smear negativity whereas in our study all the patients received M.D.T. (MBR) for one year and 4 doses of vaccines at intervals of 3 months.

We observed that BCG combined with M.D.T. produced better bacteriological clearance, faster clinical improvement as well as significant reduction in the incidence of neuritis and type 2 reactions than Mw, although both the vaccines were almost comparable in the histological upgrading. Katoch, et al. (16) reported better histological upgrading and bacteriological clearance with Mw. It is difficult to decide as to which biological parameters should be given more significance (bacteriological or histopathological) in evaluating the immunotherapeutic efficacy of a vaccine. Histopathological improvement seems to follow bacillary clearance but they can occur simultaneously and are inter-related but may not exactly follow each other. Immunological investigations like lepromin test, serology, cytokine assays and lymphocyte transformation tests as well as bacillary ATP measurement, macrophage based assays or DNA/RNA probes which directly measure the immunological upgrading and killing of viable bacteria, respectively, may provide a better answer to some of these questions; however, the results have not always been unequivocal.

Although no exact cause can be attributed to the observed better efficacy of BCG vaccine in our study, the following hypothesis can be proposed: different immunostimulatory response of BCG in different groups of people similar to the wide range of its prophylactic efficacy in different trials (20% to 80%) (25), shorter interval between the doses, and the fact that BCG contains live attenuated bacilli (whereas Mw contains killed bacilli) hence they multiply and stay for longer period in the patient and may continue to augment the immunostimulatory/immunomodulatory action of BCG vaccine. These hypotheses can only be confirmed by studying these vaccines in large number of patients who are followed up for longer periods and by using a combination of better investigative immunological tools as stated above.

At present, based on the results of our study and the previous similar studies on BCG and Mw vaccines, we can conclude that both these can prove to be important immunotherapeutic tools in the management of BL/LL patients with high smear positivity. In the present scenario of decentralization of leprosy services, reduction in the duration of MB treatment to 12 months, with no strict slit skin smear monitoring and absence of rather essential long term follow-up, BCG appears to be a better option than Mw because it is cheap and easily available.

Problems in field implementation may be patient selection; as SSS is not being done so B.I. cannot be used as a criterion. Studies have shown that number of lesions/ thickened nerves or extent of disease (number of body areas involved) may be used to predict smear positivity (19,31). Based on these criteria bacilliferous multibacillary (BL/LL) patients can be offered benefits of immunotherapy. Other problem that needs to be addressed is, training of health workers in diagnosing and identifying patients with multibacillary disease. As far as the supply and administration of vaccine is concerned, BCG vaccine is freely available in all the health centers in India (supplied under Universal immunization program of Government of India), and the health workers are well trained to administer the vaccine so there should not be any operational difficulty to add BCG vaccine to our ongoing National Leprosy Elimination Program (NLEP).
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Prevalence of Leprosy in Agra District (U.P.)
India from 2001 to 2003\textsuperscript{1}

Anil Kumar, Anita Girdhar, and B. K. Girdhar\textsuperscript{2}

ABSTRACT

Leprosy prevalence has reportedly declined all over the world, but six countries, including India, are still endemic for the disease. India alone contributes about 60% to the world’s leprosy case load, with the major share from its northern states. The present study done in Agra district was based on a randomly-selected sample of over 10% of the population, spread across 300 villages and 16 urban units of the district. A house-to-house survey was conducted from July 2001 to July 2003 in all the 26 selected panchayats (300 villages), all the 11 block headquarters which have an urban component, and 5 (out of 20) localities in Agra city.

A population of 361,321 persons was examined for leprosy. A total of 592 leprosy cases [new and cases yet to complete a full course of multi-drug therapy (M.D.T.)] were found, giving a prevalence rate of 16.4/10,000 population. Although the overall prevalence was found to be similar in both rural and urban areas, there were pockets with high prevalence. More cases were detected in the eastern side of Agra (31.4/10,000 in Fatehabad and 28.5/10,000 in Bah Tahsils). Overall, the multibacillary (MB) leprosy rate was 22.3% and the child leprosy rate 8.4%.

Of the 592 cases, 523 (88.3%) were new untreated cases, giving a new case detection rate of 14.5/10,000. The MB rate was 17% (89/523), and the child leprosy rate was 8.4% (44/523) among the new patients. The grade 2 deformity rate was found to be 4.8% (25/523) among these cases. The duration of disease among new cases was 32.3 months as compared to 48.1 months among prevalent (registered) cases (i.e., patients who had been diagnosed earlier and had yet to complete a full course of M.D.T.). The large number of undetected cases found in this survey suggests the need for continued intensive health education campaigns and case detection activities.

This study highlights the fact that a large number of leprosy cases go undetected in the present integrated system which is mainly based on voluntary reporting of cases.

RESUME

Il est rapporté que la prévalence de la lèpre est en diminution partout dans le monde. Cependant six pays, l’Inde y compris, sont encore endémiques pour la maladie. A elle seule, l’Inde contribue pour environ 60% des nouveaux cas à l’échelle mondiale, avec la partie la plus importante dans les états du Nord. La présente étude, réalisée dans le district d’Agra, fut réalisée sur un échantillon pris au hasard de plus de 10% de la population, s’étendant à travers plus de 300 villages et 16 unités urbaines du district. Une enquête de maison en maison fut menée entre juillet 2001 et juillet 2003 dans l’ensemble des 26 panchayats sélectionnés (300 villages), l’ensemble des 11 centres urbains et 5 (parmi 20) localités de la ville d’Agra.

Un échantillon de 361 321 personnes fut examiné pour la présence de la lèpre. Un total de 592 cas de lèpre [nouveau ou des cas n’ayant pas encore complétés leur PCT] fut détecté, donnant un taux de prévalence de 16,4 cas pour 10 000 habitants. Bien que la prévalence globale fut déterminée être similaire entre les zones urbaines et les zones rurales, des poches de prévalence importante furent découvertes. Plus de cas furent détectés dans les quartiers Est de la ville d’Agra (31.4/10 000 à Fatehabad et 28.5/10 000 à Bah Tahsils). Globalement, le taux de lèpre multibacillaire (MB) était de 22,3% et le taux de lèpre pédiatrique de 8,4%.

Parmi les 592 cas, 523 (88,3%) étaient des nouveaux cas n’ayant pas encore été traités, se traduisant par un taux de détection de nouveaux cas de 14,5/10 000. Le taux de lèpre MB était de 17% (89/523), celui de lèpre des enfants de 8,4% (44/523) parmi les nouveaux patients. Parmi ces cas, le taux de déformations de grade 2 était de 4,8% (25/523). La durée de la maladie parmi ces nouveaux cas était de 32,3 mois, comparé à 48,1 mois parmi les cas

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prévalent déjà enregistrés (c.-à-d. les patients qui ont été diagnostiqués auparavant mais qui n’ont pas encore terminé leur traitement de PCT). Le nombre important de cas non détectés dans cette étude d’épidémio surveillance suggère qu’il existe encore un besoin important de campagnes intensives d’éducation sur la santé et la lèpre et d’activités de détections de nouveaux cas.

Cette étude stresse qu’un grand nombre de cas de lèpre reste non détectés après la mise en œuvre du système actuel intégré, qui repose principalement sur la déclaration volontaire des cas.

RESUMEN

La prevalencia mundial de la lepra ha disminuido notablemente en los últimos años pero 6 países, incluyendo la India, se mantienen con alta endemia. La India sola contribuye con cerca del 60% de los casos de lepra en el mundo y su mayor aportación proviene de sus estados norteños. El presente estudio, realizado en el distrito de Agra, se hizo sobre una muestra seleccionada al azar que incluyó a más del 10% de la población de Agra distribuida en 300 poblaciones rurales y 16 comunidades urbanas. La encuesta, casa por casa, se realizó de julio del 2001 a julio del 2003 en las 300 poblaciones rurales, en 11 municipios y en cinco (de 20) localidades de la ciudad de Agra.

Se examinaron 361,321 personas, encontrándose un total de 592 casos de lepra [casos nuevos y casos que debían completar su tratamiento con PQT-OMS], con una tasa de prevalencia de 16.4/10,000 habitantes. Las tasas de prevalencia en las regiones rural y urbana fueron similares pero se detectaron focos de alta prevalencia. La mayoría de los casos se detectaron en el lado oriental de Agra (31.4/10,000 habitantes en Fatehabad y 28.5/10,000 en Bah Tahsils). La tasa global de lepra multibacilar (MB) fue del 22.3% y la tasa de lepra en niños fue del 8.4%. De los 592 casos de lepra, 523 (88.3%) fueron casos nuevos no tratados, lo que significa una tasa de detección de 14.5/10,000. Entre los pacientes nuevos, la tasa de lepra MB fue del 17% (89/523) y la tasa de lepra infantil del 8.4% (44/523). También en estos casos, la tasa de deformidad de grado 2 fue del 4.8% (25/523). La duración de la enfermedad entre los casos nuevos fue de 32.3 meses en promedio, mientras que en los casos prevalentes registrados ésta fue de 48.1 meses. El gran número de casos nuevos descubiertos en esta encuesta, sugiere la necesidad de continuar con las campañas de educación y de detección de casos de lepra. Por otro lado, el estudio subraya la baja eficiencia en la detección de casos del programa integrado actual, el cual se basa principalmente en el reporte voluntario de los casos.

METHODS AND MATERIALS

Agra district has 6 Tahsils (talukas)—5 predominantly rural and 1 mainly urban. Each of the rural Tahsils is divided into blocks. These blocks are subdivided into nyay panchayats (judicial units) and each nyay panchayats (referred to as panchayats in the text) has a cluster of villages under its jurisdiction. About 65% of the 3.3 million in the total population of Agra district lives in the urban areas, while the remaining 35% live in villages. Of the 65% of the population living in urban areas, 50% live in Agra city and the rest 15% reside in smaller towns, mainly the block headquarters (urban) of the rural tahsils. Within Agra city, almost three quarters of the population live in underdeveloped or semi-developed crowded colonies with minimal open space and poor civic amenities.

The rural part of the Agra district is comprised of 94 panchayats spread over 13
blocks in 6 tahsils. For the purpose of this study, 2 panchayats from each block were randomly selected and all the villages and households in the selected panchayats were included for the survey. In addition, the urban population from 11 blocks headquarters (in the remaining 2, there being no town) and 5 (out of 20) localities in Agra City have likewise been surveyed. In all 361,321 persons—128,819 (35.7%) in rural and 232,502 (64.3%) in urban areas—were examined for leprosy.

A house-to-house survey was conducted between July 2001 and July 2003. All the members present in each of the households at the time of survey were shown picture cards and briefed about early symptoms and signs of leprosy and then physically examined by a trained paramedical worker (PMW). The population examined included all those who were present. Experienced supervisors and medical doctors confirmed the suspect cases later. The coverage (examined population) was about 70% of the total population living in these areas.

Once the patient was diagnosed as having leprosy, all the skin lesions and thickened nerves including cutaneous nerves were counted. Patients were classified as pau-cibacillary (PB) if they had ≤5 skin patches with or without 1 to 2 thickened major cutaneous nerves \( (2, 3, 4) \). Patients were labeled as single skin lesion (SSL) cases if they had only one skin lesion with no detectable nerve thickening. Patients with ≥6 patches and/or ≥2 thickened nerves and those with infiltrations with or without papules or nodules were classified as multibacillary (MB) \( (2, 3) \) cases. Only visible deformity (grade ≥2) was recorded. All the newly detected patients were put on World Health Organization (W.H.O.) recommended M.D.T. according to the type of disease. A new case was defined as one “who had not been diagnosed earlier and had no history of treatment for leprosy in the past.” Patients with active disease found during the survey, with a history of having received some anti-leprosy treatment but had not completed the entire course (defaulters) were recorded as prevalent cases. Period prevalence and New Case Detection Rate (NCDR) were computed per 10,000 population examined. \( \chi^2 \) test of significance \( (5) \) was used for comparison.

**RESULTS**

**Period prevalence.** Examination of the 361,321 population across the district over a 2 year survey period (2001 to 2003) revealed 592 patients with active leprosy, giving an overall prevalence of 16.4/10,000 population. Of the 26 selected Panchayat in the district, the prevalence rate (PR) varied from zero in Naya Bans and Kachura in Ki-raoli Tahsil located in the western part of the district (see the Figure), to 46.9 in Nagla...
At block level in rural areas, a high prevalence (per 10,000) was found in Shamshabad (41.4), and Jetpur Kalan (40.7), and low (1.5) in Fatehpur Sikri, and (2.1) in Jagner blocks. In the urban areas, a high prevalence of 67.5 was recorded in Jetpur town of Bah Tahsil, and zero prevalence was recorded in Kiraoli town (Table 2).

At Tahsil level (rural and urban combined), a prevalence of 31.4/10,000 was noted in Fatehabad, followed by 28.5 in Bah. Kiraoli Tahsil, situated on the western side of Agra, had the lowest PR of 7.2. Among the rural areas, the highest prevalence was recorded in rural parts of Fatehabad (31.8), and the urban area Bah Town had the highest prevalence (39.9). Similarly, the lowest prevalence was recorded in the rural areas of Kiraoli (3.4) and the urban areas if Kheragar (9.7) (Table 3).

Prevalence of leprosy by age gradually increased from 4.6/10,000 in 5 to 14 years age group, to 53.8/10,000 in the age group 45 to 54 years. Age-related prevalence (patients detected in the age group/10,000 population examined) in both rural and urban areas showed similar trends (Table 4). Prevalence was higher among rural males (17.8 vs. 14.9, $\chi^2_1 = 9.9$, p <0.002), and in the urban females (18.0 vs. 14.9, $\chi^2_1 = 10.6$, p <.001) in comparison to their counterparts. However, in the total population, males and females were equally afflicted with leprosy (16.8/10,000 in females and 15.9/10,000 in males).

**New case detection rate (NCDR).** Of the 592 active leprosy cases detected, 523 (88.3%) patients were detected for the first time, and had never taken any treatment for leprosy, giving a NCDR of 14.5/10,000 population in the district (Table 5). The proportion of new cases to total cases found ranged from 79.5% in Bah to 92.3% in Kiraoli Tahsil, indicating a high percentage of cases having remained undetected.

**Duration of disease and deformity grade**

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**Table 1. Leprosy prevalence in selected panchayats in Agra district.**

<table>
<thead>
<tr>
<th>Tahsil (location in the district)</th>
<th>Blocks</th>
<th>Panchayats</th>
<th>Prevalence/10,000 (cases/population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Kiraoli (West)</td>
<td>1. Fatehpur</td>
<td>1. Samra</td>
<td>2.6 (1/3923)</td>
</tr>
<tr>
<td></td>
<td>2. Siktara</td>
<td>2. Naya Bans</td>
<td>0 (0/2875)</td>
</tr>
<tr>
<td></td>
<td>2. Achhnera</td>
<td>2. Raibha</td>
<td>8.7 (4/4576)</td>
</tr>
<tr>
<td>2. Agra (Central)</td>
<td>1. Akola</td>
<td>1. Malpura</td>
<td>0.9 (1/10,595)</td>
</tr>
<tr>
<td></td>
<td>2. Dhauria</td>
<td>2. Dhauria</td>
<td>13.6 (13/9569)</td>
</tr>
<tr>
<td></td>
<td>2. Etmadpur</td>
<td>1. Chamraula</td>
<td>3.4 (2/5948)</td>
</tr>
<tr>
<td>4. Kheragar (South west)</td>
<td>1. Jagn</td>
<td>1. BasajJagn</td>
<td>0 (0/3147)</td>
</tr>
<tr>
<td></td>
<td>2. Kheragar</td>
<td>2. Richhauha</td>
<td>6.3 (1/1589)</td>
</tr>
<tr>
<td></td>
<td>2. Kheragar</td>
<td>1. Digrauta</td>
<td>4.5 (1/2218)</td>
</tr>
<tr>
<td></td>
<td>3. Saiyan</td>
<td>2. Kheragar</td>
<td>5.3 (1/1885)</td>
</tr>
<tr>
<td></td>
<td>2. Fatehabad</td>
<td>2. Iradatnagar</td>
<td>7.0 (2/2848)</td>
</tr>
<tr>
<td></td>
<td>2. Bah</td>
<td>2. Baraura</td>
<td>15.9 (4/2518)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>16.1 (207/128,819)</td>
</tr>
</tbody>
</table>
Table 2. Leprosy prevalence in selected rural and urban blocks of Agra district.

<table>
<thead>
<tr>
<th>Tahsil</th>
<th>Rural Agra</th>
<th>Urban Agra</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blocks (No. of Panchayats)</td>
<td>Prevalence* (Cases/Population)</td>
</tr>
<tr>
<td>1. Kiraoli</td>
<td>1. Fatehpur Sikri (7)</td>
<td>1.5 (1/6798)</td>
</tr>
<tr>
<td></td>
<td>2. Achhnera (7)</td>
<td>5.2 (4/7717)</td>
</tr>
<tr>
<td></td>
<td>2. Etmadpur (8)</td>
<td>10.4 (11/10,626)</td>
</tr>
<tr>
<td></td>
<td>1. Shamsabad (8)</td>
<td>41.4 (50/12,065)</td>
</tr>
<tr>
<td></td>
<td>2. Fatehabad (10)</td>
<td>19.7 (19/9626)</td>
</tr>
<tr>
<td></td>
<td>2. Kheragar (7)</td>
<td>4.9 (2/4103)</td>
</tr>
<tr>
<td></td>
<td>2. Shah Ganj</td>
<td>23.9 (153/63,910)</td>
</tr>
<tr>
<td>5. Fatehabad</td>
<td>1. Shamsabad (8)</td>
<td>41.4 (50/12,065)</td>
</tr>
<tr>
<td></td>
<td>2. Fatehabad (10)</td>
<td>19.7 (19/9626)</td>
</tr>
<tr>
<td></td>
<td>2. Bah (8)</td>
<td>22.6 (31/13,732)</td>
</tr>
<tr>
<td></td>
<td>3. Jetpur Kalan (8)</td>
<td>40.7 (38/9328)</td>
</tr>
<tr>
<td>Total</td>
<td>(92)</td>
<td>16.1 (207/128,819)</td>
</tr>
</tbody>
</table>

≥2. About a third of the patients had the disease of recent origin (<1 year), while in 25%, the initial symptoms had been noticed more than 4 years earlier. Although the median duration of disease, both in rural and urban areas, was 24 months; the mean was slightly higher in rural areas. The duration of disease in newly detected cases was 32.3 months, significantly lower that 48.1 months in prevalent cases (p <0.05). The difference in median duration of disease for the two groups was 12 months (Table 6).

Among newly detected cases, the deformity rate of Grade ≥2 was found to be 1.8% (8/436) in paucibacillary (PB) leprosy, and 19.5% (17/87)—significantly higher—in the multibacillary (MB) leprosy (p <0.05). In the district as a whole, it was also found to be significantly higher in rural populations, 8% (14/175) against 3.2% (11/348) among the urban population (χ² = 5.9, p <0.05). As expected, the deformity rate was 4.8% (25/523) among new cases, significantly less than 17.4% in prevalent cases or defaulters (p <0.05).

DISCUSSION

The findings reveal that the prevalence of leprosy in the Agra district is 16.4/10,000 (592/361,321), and is nearly equal in the rural and urban areas (16.1 and 16.6/10,000, respectively). More than 88% (523/592) of
leprosy cases had not received any leprosy treatment, as they had never been detected and diagnosed as having the disease earlier. The observed prevalence in this study is significantly higher than the state figure (0.9/10,000), which is based on the leprosy elimination campaign (LEC) (6) conducted in the year 2000. The official prevalence of leprosy in Agra during 2002 has been reported to be even lower (0.5/10,000) (unpublished report, 2002, District Leprosy Officer, Agra). The higher prevalence in the present study is possibly a result of more intensive and supervised work undertaken by a team, which has resulted in the detection of large numbers of hidden cases.

As in the case elsewhere in the country, the distribution of leprosy patients is not uniform; some areas and tahsils of the district have a much higher prevalence than the others (Table 3). Geographically, Fatehabad and Bah Tahsil, which have the highest leprosy prevalence of almost 30/10,000, border with Firozabad and Etawa district in which high endemicity is officially acknowledged (6). Within these tahsils, there were also pockets (panchayats and villages) with prevalence as high as 40/10,000 in rural and 67/10,000 in urban areas, while some of their adjoining areas had a fairly low case load. Though age-specific prevalence revealed that cases have been detected at all ages and the prevalence increased with age (Table 4), it is significant that over 8.0% of patients were children (age ≤ 15). This indicates that active transmission of disease is still occurring. This correlates well with the observation that most of the active cases had remained undetected for almost 3 years (mean duration of disease) and may have been the source of infection. In the present study, more female patients were detected. This could be due to examination of larger female populations. As the survey was done during the daytime, large number of male members had gone out to work leaving females at home. On the whole, there was not much difference in the prevalence between male and female (15.9 vs. 16.8, respectively).

Overall, 78% (460/592) of cases had PB leprosy, with SSL accounting for 24.5% (145/592), and significant proportion (22%) of cases had MB leprosy. As the survey was done during the daytime, large number of male members had gone out to work leaving females at home. On the whole, there was not much difference in the prevalence between male and female (15.9 vs. 16.8, respectively).

### Table 4. Leprosy prevalence by age, sex and clinical type.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Prevalence*</td>
<td>Cases</td>
</tr>
<tr>
<td>Age: 0–4</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5–14</td>
<td>17</td>
<td>5.0</td>
<td>32</td>
</tr>
<tr>
<td>15–24</td>
<td>20</td>
<td>9.2</td>
<td>57</td>
</tr>
<tr>
<td>25–34</td>
<td>31</td>
<td>18.7</td>
<td>80</td>
</tr>
<tr>
<td>35–44</td>
<td>41</td>
<td>36.0</td>
<td>67</td>
</tr>
<tr>
<td>45–54</td>
<td>43</td>
<td>56.0</td>
<td>66</td>
</tr>
<tr>
<td>55–64</td>
<td>30</td>
<td>54.4</td>
<td>43</td>
</tr>
<tr>
<td>&gt;64</td>
<td>25</td>
<td>41.3</td>
<td>39</td>
</tr>
<tr>
<td>Gender: Male</td>
<td>96</td>
<td>17.8</td>
<td>164</td>
</tr>
<tr>
<td>Female</td>
<td>111</td>
<td>14.9</td>
<td>221</td>
</tr>
<tr>
<td>Type: PB</td>
<td>153</td>
<td>11.9</td>
<td>307</td>
</tr>
<tr>
<td>(SSL)</td>
<td>(56)</td>
<td>(4.3)</td>
<td>(89)</td>
</tr>
<tr>
<td>MB</td>
<td>54</td>
<td>4.2</td>
<td>78</td>
</tr>
<tr>
<td>ALL</td>
<td>207</td>
<td>16.1</td>
<td>385</td>
</tr>
</tbody>
</table>

*Per 10,000 population examined.

### Table 5. New case detection rate (NCDR) by tahsil in Agra district; 2001–2003.

<table>
<thead>
<tr>
<th>Tahsil</th>
<th>Leprosy cases</th>
<th>New case detection rate (NCDR)/10,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>New</td>
</tr>
<tr>
<td>Kiraoli</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Agra</td>
<td>308</td>
<td>282</td>
</tr>
<tr>
<td>Ermadpur</td>
<td>53</td>
<td>46</td>
</tr>
<tr>
<td>Kheragar</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Fatehabad</td>
<td>83</td>
<td>74</td>
</tr>
<tr>
<td>Bah</td>
<td>117</td>
<td>93</td>
</tr>
<tr>
<td>Total</td>
<td>592</td>
<td>523</td>
</tr>
</tbody>
</table>
### Table 6. Duration of disease by case status.

<table>
<thead>
<tr>
<th>Duration of disease (months)</th>
<th>New cases (523)</th>
<th>Prevalent cases (69)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Percent</td>
</tr>
<tr>
<td>0–6</td>
<td>99</td>
<td>18.9</td>
</tr>
<tr>
<td>7–12</td>
<td>93</td>
<td>17.8</td>
</tr>
<tr>
<td>13–24</td>
<td>119</td>
<td>22.8</td>
</tr>
<tr>
<td>25–48</td>
<td>89</td>
<td>17.0</td>
</tr>
<tr>
<td>49–72</td>
<td>76</td>
<td>14.5</td>
</tr>
<tr>
<td>&gt;72</td>
<td>47</td>
<td>9.0</td>
</tr>
<tr>
<td>Mean</td>
<td>32.3</td>
<td>–</td>
</tr>
<tr>
<td>Median</td>
<td>24.0</td>
<td>–</td>
</tr>
</tbody>
</table>

had MB disease. Among the newly detected patients, a relatively low prevalence of deformities of grade ≥2 was noted [4.8% (25/523), 1.8% among PB and 19.5% in MB patients]. A higher prevalence of deformities was observed among prevalent patients (17.4%). The difference appears to be due to a relatively longer mean duration of disease in prevalent cases (48.1 vs. 32.3 months) than in new cases. Of all the patients with deformities of grade ≥2, about 76% had paralytic problems in hands and/or feet (figures not shown). Since none of the patients complained of any initial symptoms related to these deformities, the frequency of silent nerve damage appears to be high.

In conclusion, this survey, representing all the areas in Agra, indicates that leprosy continues to be a significant problem in both rural and urban areas with a larger patient load in tahsils located on the eastern side of the district. The undetected pool of infection has possibly continued to spread infection in the community as suggested by the observation of a child leprosy rate of 8.4%. In view of these findings, there is a need for reappraisal of leprosy elimination campaign activities to make these more effective, so that in the future new patients themselves report at treatment centers on suspicion of the disease. In addition, continued case detection activities, throughout the district, need to be undertaken to detect and treat hidden cases as this is important for achieving the goal of eliminating leprosy as a public health problem.

**Acknowledgement.** The work has supported by a internal grant from the institute. Authors like to thank Dr. V. M. Katoch, Director of the Institute for his support. Data entry help of Mr. Rajendra Kumar, Mr. V. S. Yadav for computer assistance, and the help rendered by 6 PMW and 20 Case searches are also thankfully acknowledged.

**REFERENCES**

Leprosy is a major health problem in India with a prevalence of 3.22/10,000, affecting all age groups from infancy to old age (3). Children below 15 years of age constitute about 15% of total cases of leprosy (2). However, it has generally been observed that in childhood, indeterminate leprosy is the most common type, followed by tuberculoid variant; borderline lepromatous and lepromatous leprosy are only occasionally encountered (18). Various published studies have consistently described reactions especially type 2 to be less common in children than in adults (4, 5, 8, 9, 12, 13, 21).

We describe a 9-year-old boy who presented primarily with erythema nodosum leprosum necroticans (ENL) and was subsequently diagnosed as having lepromatous leprosy.

Case report. A 9-year-old boy presented to dermatology outpatients with the complaint of multiple red, raised, painful lesions over the face and limbs of 4 months duration. These grouped lesions started from the chin, followed by similar eruptions over his upper and lower limbs, and subsided with scaling and bruise-like pigmentation over the next 2 to 3 weeks. However, few lesions had ruptured to discharge pus. He also had episodic fever with each crop of lesions. There was no evidence of any systemic focus of infection on history.

There was no history of light colored or
numb lesions, spontaneous blistering or weakness in any limb. He did not have ocular, nasal, testicular, joint, or any other systemic complaints. None of the family member had leprosy, tuberculosis, or any chronic ailment.

The patient weighed 22 kg and was febrile (101°F), with multiple discrete and large sub-mandibular lymph nodes about 0.5 to 1 cm in size, non-tender and not attached to the overlying skin. On cutaneous examination there was evidence of facial infiltration along with multiple erythematous tender nodules and plaques varying from 0.7 cm to 2 cm were seen over the cheeks, chin, and right earlobe, extensor aspect of upper and lower limbs, lower back, and buttocks (Figs. 1 and 2). Few lesions had overlying irregular ulcers with necrotic base (Fig. 2). Multiple hyperpigmented bluish macules with well to ill-defined margins were also noted on the bilateral upper and lower limbs. Bilateral ulnar, lateral popliteal, and posterior tibial nerves were symmetrically thickened and non-tender.

Hemogram revealed mild anemia (Hb = 10.5 gm%), neutrophilic leukocytosis (TLC = 16,000, DLC = P70 L25 M3 E2), and raised erythrocyte sedimentation rate (ESR = 81 mm in the first hour). The antistreptolysin titer was less than 200 and the reports of throat swab and mantoux test were negative. Other laboratory investigations including liver and kidney function test, blood sugar, urine examination, and chest x-ray were within normal limits. Slit skin smear revealed a bacteriological index of 5+ along with a morphological index of 10%. Routine histopathology section stained with hematoxylin and eosin from the nodule on the left arm demonstrated neutrophilic abscesses superimposed on a diffuse infiltrate of foamy macrophages and plasma cells, along with the evidence of leucocytoclastic vasculitis, which validated the diagnosis of lepromatous leprosy with ENL (Figs. 3 and 4). Fite’s stain showed clumps of acid-fast bacilli (AFB) in the perineural cells and macrophages.

He was started on World Health Organization (W.H.O.) recommended multibacillary (MB) multi-drug therapy (M.D.T.), which included 50 mg of dapsone daily and 300 mg of rifampicin monthly along with 50 mg of clofazimine daily. The patient was

There was no evidence of specific glove and stocking type of sensory loss, or any motor deficit. Systemic examination did not reveal any abnormality.
also started on diclofenac sodium 25 mg thrice daily along with 30 mg of prednisolone. The lesions subsided in 6 to 8 weeks time, with no evidence of recurrence or subsequent neural deficit on follow-up. Prednisolone was gradually tapered over a period of 6 months and diclofenac sodium was continued for another 2 months. Currently, he has received MB M.D.T. for 11 months and there is no significant reduction in the nerve enlargement.

**DISCUSSION**

Children in leprosy endemic areas are exposed to infection by *Mycobacterium leprae*. The youngest age reported for the occurrence of leprosy is about 3 weeks (15). A 1978, a survey among school children in Hyderabad showed the prevalence rate to be 10 to 17 per 1000 (8).

Majority of the pre-pubertal children tend to have indeterminate or tuberculoid type of leprosy (18). The children present with asymptomatic or hypoaesthetic cutaneous lesions and, less often, with neural manifestations. A single lesion present on exposed areas of the body was reported to be more common than multiple lesions of the body. Leprosy workers have been conservative in making a diagnosis of multibacilliary or borderline leprosy in children, despite the fact that all types of leprosy can occur in any age group (18). The reported rate of smear positive leprosy is less than 10% in pediatric age group (16). This appears to be a paradoxical situation and runs counter to the concept that immune responses are poorly developed in the very young children, due to the inability of the immature lymphoid system to deal with and react with foreign antigens (6, 19).

Despite the high prevalence of leprosy in children, the occurrence of both type 1 and type 2 reaction especially ENL is rare as revealed by an extensive MEDLINE search. ENL has been reported in 0 to 3.1% of all the cases of childhood leprosy, which is much less than the reported incidence of 35% among all the age groups (21) (The Table). The largest study comprising 1028 leprosy patients has reported 25 cases of pediatric ENL, out of which only 7 patients were below 10 years of age (7). ENL necroticans, however, has not been reported in pediatric age group to date.

**THE TABLE.** Studies showing incidence of erythema nodosum leprosum in pediatric age group.

<table>
<thead>
<tr>
<th>S No.</th>
<th>Author</th>
<th>Year</th>
<th>No. of patients</th>
<th>ENL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I. Kaur, <em>et al.</em> (12)</td>
<td>1991</td>
<td>132</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>V. N. Sehgal, <em>et al.</em> (19)</td>
<td>1993</td>
<td>161</td>
<td>Not specified</td>
</tr>
<tr>
<td>3</td>
<td>P. V. Prasad (17)</td>
<td>1998</td>
<td>66</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>A. Selvesekar, <em>et al.</em> (1)</td>
<td>1999</td>
<td>794</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>X. S. Chen, <em>et al.</em> (5)</td>
<td>2000</td>
<td>1028</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>H. C. Leu, <em>et al.</em> (13)</td>
<td>2000</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>S. Jain (8)</td>
<td>2002</td>
<td>306</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>K. D. Burman, <em>et al.</em> (4)</td>
<td>2003</td>
<td>20</td>
<td>Not specified</td>
</tr>
</tbody>
</table>
Hypersensitivity responses are known to play an important role in the occurrence of reactions. Reational episodes and disability are less frequently seen in the younger children, due to the poorly developed immunological mechanisms in early childhood (6). Therefore, development of disabilities as a consequence of reactions is, more often encountered in adults and in older children (5, 19).

Jain, et al. reported the incidence of neuritis to be 24.2% in the cohort of pediatric leprosy patients, and emphasized the importance of appropriate use of steroids to prevent deformities (6). Surprisingly, none of these studies on childhood leprosy have described the use of systemic steroids in reactions, with the exception of the study conducted by Thirugananam, et al., who reported one child who developed primary focus of tuberculosis after having received one and a half years steroid therapy (5, 22, 23).

Digeorge, et al. have described numerous side effects of systemic corticosteroids in pediatric conditions, with a special mention of HPA axis suppression, growth failure and retarded bone formation, especially when they are used over a longer period of time (6). Thus, though we should be aggressive in using steroids in reactions to prevent sequelae, the potential serious adverse effects should be screened for.

Lucio’s phenomena is characterized by the development of painful, tender, and purpuric macules, particularly on the extremities, with necrotic center which finally develop a black eschar which heals in a few days to leave superficial atrophic scars (10). This phenomena is typically seen in patients with Lucio’s leprosy, which usually manifests as shiny thickened skin with loss of body hair (but not scalp hair) and widespread sensory loss. Unlike polar lepromatous (LL) there are no skin or ocular lesions, motor palsies, and finger contractions (11). Though this phenomena is characterized histopathologically by leucocytoclastic vasculitis, as seen in the present case, the usual clinical presentation of Lucio’s leprosy was not observed and thus, the possibility was not considered.

Family contacts with leprosy in the pediatric age group are documented to be a significant factor in contracting the disease (5). Though no such history was found in the present case, the importance of contact screening strategies cannot be undermined.

(i) The various factors associated with the prevalence of ENL include older age group, bacillary index of more than 4, multiple enlarged nerves (>5), the presence of nodules and infiltration, more than 1 year of untreated disease and the presence of the anti-PGL-1 antibodies (14). Our patient had facial infiltration, high bacillary index, and multiple thickened nerves though duration of the disease could not be ascertained.

(ii) In the present case, history of fever with the eruption of ENL necroticans lesions along with thickened nerves pointed towards a diagnosis of lepromatous leprosy. Characteristic histopathology, demonstration of acid-fast bacilli and response to therapy further confirmed the diagnosis and excluded other possible causes of erythema nodosum.

(iii) To the best of our knowledge, this report of a nine-year-old boy describes the first case of necrotic ENL along with lepromatous leprosy in a child.

REFERENCES
Leprosy or Hansen’s disease (HD) is often complicated by immune-mediated reactions. Reversal reaction (RR), a delayed type hypersensitivity response, can occur in borderline tuberculoid (BT), borderline borderline (BB) and borderline lepromatous (BL) patients. Erythema nodosum leprosum (ENL) is an antibody immune complex reaction that occurs in BL and lepromatous (LL) patients. The standard treatment for RR is systemic corticosteroids, whereas thalidomide is the most effective drug for ENL (2, 5, 10). While steroids provide rapid control of ENL symptoms, long term use often results in the associated adverse effects (11). Three patients with leprosy reactions and thalidomide or steroid toxicities were treated with mycophenolate mofetil (MMF) as a steroid sparing agent and their outcomes described below.

**Case 1.** A 29-year-old Hispanic male was diagnosed with BL (slit smear average of 4.5) and started on daily rifampin 600 mg, dapsone 100 mg, and clofazimine 100 mg. He developed ENL and RR with a significant neuritis 4 months after treatment was initiated. Daily thalidomide 100 mg and prednisone 60 mg (1 mg/kg) were started and rifampin was changed to minocycline 100 mg daily with moderate improvement of symptoms. Prednisone was slowly tapered to doses ranging from 35 mg to 15 mg daily, and 18 months after the first episode of ENL the patient developed an ENL flare. Thalidomide was increased to 200 mg daily for 1 week and then to 300 mg daily. Symptoms improved. After 2 months of being on high doses of thalidomide and prednisone (30 mg to 40 mg daily), MMF was added as a steroid sparing agent initially at 50 mg twice daily and then at 1000 mg twice daily.

Thalidomide was lowered to 250 mg nightly and several attempts to taper the dose below 40 mg were unsuccessful. Three months later, the patient complained of persistent burning pain in his hands and feet, mostly at night. Due to this burning pain, thalidomide was stopped. Nerve conduction studies demonstrated slowing of ulnar and median motor conduction and a sensory peripheral neuropathy consistent with thalidomide neuropathy. The patient was referred to the U.S. National HD Program where he was diagnosed with a probable thalidomide neuropathy. The recommendation was to restart thalidomide in order to lower the prednisone dose. While on thalidomide 200 mg and prednisone 40 mg, his ENL recurred and the patient developed acute orchitis requiring prednisone 80 mg daily for adequate ENL control. Despite 10 months of MMF 2 grams daily, in addition thalidomide 200 mg and clofazimine 100 mg daily, his prednisone could not be lowered due to flares of lesions and symptoms.

**Case 2.** A 29-year-old Burmese man with BL HD (slit smear average of 4.3) on October 2001 presented with bilaterally enlarged tender greater auricular and ulnar nerves and pink annular plaques on elbows, knees, and the periorbital region. His RR was treated
with prednisone (1 mg/kg/day) with minimal improvement noted after 2 months. MMF 500 mg twice daily was started at 500 mg twice daily and later increased to 1000 mg twice daily. During the 7 months he was on MMF, several attempts were made to lower the prednisone dose. Each taper resulted in an exacerbation of symptoms. The MMF was discontinued.

**Case 3.** A 51-year-old Hispanic female on treatment for BL (slit smear average of 1.1) for 5 months developed a severe RR which was treated with prednisone 40 mg daily and had a good response. After several months, when prednisone was tapered to 5 mg daily, she developed a new RR. Prednisone was increased to 80 mg daily with a subsequent worsening of her diabetes mellitus. MMF 500 mg twice daily was started and then increased to 1000 mg twice daily. The patient had improved signs and symptoms. However, she developed severe gastrointestinal distress which resolved when MMF was discontinued 3 months later.

**DISCUSSION**

Several drugs are available for the treatment of HD reactions, most are used in combination. Prednisone, which remains the gold standard therapy for the acute symptoms of both reactions, is fraught with numerous side effects since these leprosy reactions require many months to years of immunosuppressive therapy. Thalidomide, which is the most effective drug in the treatment of ENL, is also related to toxicities including peripheral neuropathy. Other effective drugs for ENL include high dose clofazimine, which has an anti-inflammatory effect, and pentoxifylline, which like thalidomide inhibits tumor necrosis factor-alpha (TNF-α) production.

Mycofenolate mofetil (MMF), an immunosuppressant agent, has been used in transplanted patients (5, 6), and also as a steroid sparing immunosuppressive in inflammatory skin diseases such as pemphigus vulgaris (6). MMF is a reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH), an enzyme that is critical in the de novo synthesis of purines. Lymphocytes, in contrast to most other cells, depend more on the de novo pathway for purine synthesis than the salvage pathway. Therefore, MMF affects both B and T lymphocyte synthesis. RR is thought to be caused by increased T-cell reactivity to *Mycobacterium leprae* (4) although recent data suggests that humoral immunity may also be involved (5). ENL pathogenesis has been attributed to an increase of TNF-α synthesis which is induced by T cells (1, 5). These mechanisms suggested that MMF would be useful in treating RR and ENL; however, this was not observed during MMF treatment in these patients.

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**REFERENCES**

Leprosy Profile in Isfahan (A Province of Iran)

ABSTRACT

In Iran, there have been a few cases of leprosy in several provinces, however, native physicians believe that leprosy is not present primarily in an Isfahan endemic area. We performed an investigation either to approve or rule out this idea.

We found 25 lepra patients who were registered and followed in Isfahan Leprosy Health Registration Center, all of whom were infected in other regions and migrated to Isfahan city at a later time.

Final analysis proved that there are not any cases of leprosy by itself in Isfahan as an endemic region at the time of this study (1975 to 2002).

TO THE EDITOR:

In Iran, there have been a few well-known cases of leprosy in the provinces such as Azarbayjan, Khorasan, Lorestan, Khousestan, Boushehr, Hormozgan, and Baluchestan in itself (1). In Isfahan, however, there has been a common belief among medical personnel that there are not any endemic cases of leprosy in the native population of this province area. According to this proposed idea, we decided either to attempt to prove or disprove it by an overall survey on this disease.

MATERIALS AND METHODS

In this descriptive retrospective cross-sectional study, we took the registered records of all lepra cases from Isfahan Medical Health Center, between 1975 and 2002, in whom leprosy as a diagnosis was suggested and confirmed through a skin smear and skin biopsy.

We studied the documents and searched for items such as sex, age, nationality, type of the disease, residential area, and the mode of treatment. We found 25 registered patients from the above period.

RESULTS

From the 25 Lepra patients who had been registered between 1975 and 2002 in Isfahan, the youngest patient was 14 and the oldest was 67 (mean age = 40 years). Twenty of them were in the lepromatous spectrum, and 5 were in the tuberculoid spectrum of leprosy.

In respect to the nationality, 19 were Afghani, 4 were Iranian who had migrated to Isfahan after being infected in other provinces, and 2 were Iraqi. According to the patients’ residential area, the highest numbers belonged to Isfahan city and Khomeinishahr city, respectively (Graph 1). The sex distribution of the patients showed 80% males and 20% females.

Finally, we did not find any lepra patients originally from Isfahan.

DISCUSSION

Leprosy is a worldwide disease, particularly prevalent in tropical underdeveloped countries. Leprosy is endemic in 24 countries (2–5).

Mycobacterium leprae bacilli live in colder areas of the body such as skin, mucous membranes, nerves, or scrotum (4–5).

At the beginning of 2004, the number of leprosy patients undergoing treatment in the world was around 460,000. About 515,000 new cases were detected during 2003. Among them, 43% were multibacillary (MB) cases, 12% were children, and 3% were diagnosed with severe disabilities. During the past two years, the global number of new cases de-
ected continued to decrease dramatically (a reduction of about 20% per year) (6, 7).

New cases are reported annually from many provinces in north east, north west, west, and south of the country. It was estimated that the total number of leprosy patients in Iran until 1982 was 16,500. According to the World Health Organization, there are approximately 30,000 to 45,000 leprosy patients in Iran (1, 7). Iran is not considered as an endemic area for leprosy (1).

CONCLUSION

There was an idea that there were not any cases of leprosy among the native population of Isfahan province in Iran, and the results of the study confirmed this. In Iran, no study has been carried out to determine the predominant clinical forms, and further studies and research in this area are required.

Acknowledgment. We are very grateful to health workers in the Leprosy Registration Center in Isfahan who helped us a lot.

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In this issue of the JOURNAL, Hussein and colleagues report data from a long term seroprevalence study to evaluate the association of HIV infection and leprosy among patients seen at their clinic in Agra, India (8). In the period from 1989 to 1993, 5 of 4025 leprosy patients (0.12%) were HIV positive, whereas in the period from 1999 to 2004, 5 of 2125 (0.38%) were HIV positive. This increase is not significant despite the apparent major increase in HIV infections among subjects screened at the same clinic. In 2004, among 387 persons who were “voluntarily” screened at their request, the HIV prevalence was 40.3%, and it was 43.4% among 106 persons referred for screening (8). From this it appears that the prevalence of HIV infection has not increased in patients with leprosy despite evidence of a substantial HIV epidemic among the population served by the clinic.

So why hasn’t the HIV prevalence increased in a comparable fashion among leprosy patients? Are they resistant or immune to HIV infection? In the past few years some individuals have been identified who are immune to HIV infection despite repeated exposure to the virus. One such group are persons who are homozygous for a 32 base pair deletion in the CCR5 gene that renders them completely resistant to infection with HIV-1 viruses that require attachment to the CCR5 co-receptor to enter the target CD4+ lymphocyte and replicate (3,11). Individuals who are heterozygous for the CCR5 deletion are partially resistant to HIV-1 infection and progress more slowly after infection (14). Also persons with genetic mutations in the CCR2 and SDF-1 genes progress more slowly after acquiring an HIV-1 infection (16). These critically important discoveries have had major ramifications in our understanding of the biology of HIV-1 infections in humans.

Another group of individuals who are partially resistant to HIV-1 infection are those who are heterozygous for HLA alleles (9). Also, subjects who are heterozygous for HLA-B or DR alleles when compared to their HIV-1 positive sex partner appear to be less readily infected than persons who are homozygous with their partner for these genetic loci. However, this resistance to transmission is only relative, not absolute like homozygosity for the 32 base pair deletion in the CCR5 receptor (3,6).

In addition, some patients appear to acquire relative resistance to HIV infection or progression of HIV. Persons who are co-infected with GB virus C, a retrovirus that also infects macrophages and lymphocytes, appear to have slower progression of HIV, and lower HIV viral loads during their GB virus viremia, which is often chronic (7,19,20). Whether or not they are resistant to HIV-1 transmission, as well, has not been determined. Other infections, which have been reported to slow or delay the progression of HIV, and decrease the HIV-1 viral load in infected individuals, include scrub typhus (O. tsutsugamushi), Dengue, and measles (13,17,15). The proposed mechanism for the negative interaction between these infections and HIV-1 also involve the CCR5 co-receptor, which is also the receptor for the Beta chemokines, MIP-1 alpha, MIP-1 beta, SDF-1 and RANTES. These chemokines regulate the immune response and attach to receptors on CD4+ lymphocytes blocking the ability of HIV-1 to attach to and enter CD4+ lymphocytes to produce more viral copies.

Could M. leprae infection also interfere with HIV-1 attachment and entry into CD4+ lymphocytes by attaching to the chemokine receptor? This seems very doubtful for a number of reasons. Whereas untreated patients with polar or borderline lepromatous
leprosy may have high levels of bacteremia, mid-borderline or tuberculoid patients do not. Chemokines are often increased as an acute phase reaction to a systemic infection. But this is probably not characteristic of leprosy patients. However, I am not aware that a systematic study of chemokine levels in untreated leprosy patients has been done. If not, it might provide some useful information.

It seems much more likely that the low rates of HIV-1 co-infection in leprosy patients living in HIV-endemic areas in Africa and Asia, which have been reported in several studies (1, 4, 10, 12, 15), can be best explained on the basis of the epidemiology of the two infections. Clearly, tuberculosis and Mycobacterium avium complex infections have increased dramatically in areas having major AIDS epidemics. Indeed, both of these mycobacterial infections can be classified as “AIDS-related opportunistic infections.” In fact, worldwide the major cause of death among AIDS patients is tuberculosis, so it is the most important opportunistic infection in AIDS patients globally.

Why is leprosy so different? Despite the pandemic of AIDS with over 40 million people infected and living with HIV/AIDS and over 30 million deaths, the virus is quite difficult to transmit. It requires sexual contact or parenteral exposure through injection drug use or a transfusion, or perinatal transmission from an infected mother to her infant. Even sexual transmission through unprotected sex is quite inefficient, varying from a transmission rate of 2 to 3/1,000 episodes of unprotected sexual intercourse in the absence of an active STD to as high as 5 to 6/100 such exposures when one or both partners have an active STD. Injection drug use may be somewhat more effective in transmitting HIV-1 but the prevalence rates are seldom above 25% to 50% among daily injectors in a city with an active AIDS epidemic. Why then is there such a major difference between the TB/HIV co-infection rate and the leprosy/HIV co-infection rate in AIDS epidemic areas. Clearly the data suggest that a much higher proportion of the population has a latent tuberculosis infection than has a latent or incubating an infection with M. leprae. Tuberculin skin test surveys suggest that 30% of the world’s population, or about 1 billion persons, have a latent tuberculosis infection. When a major HIV epidemic infects a population, the rates of TB reactivation increase dramatically as cellular immunity is abrogated by the HIV-1 infection. In addition, an HIV-1 infected person who acquires a new M. tuberculosis infection has a 30 to 40% chance of developing clinical tuberculosis within a year or two of infection with M. tuberculosis, compared to a 5% chance of active tuberculosis in an HIV-1 uninfected person.

It seems very likely that latent M. leprae infections are not too common, even in endemic countries. Many such latent M. leprae infections may have been suppressed, or perhaps cured, with exposure to antibiotics like Rifampin, a Macrolide antibiotic or to BCG. So when a person develops an HIV-1 infection in these countries, leprosy does not follow. These ideas are only speculation. It is not possible to reliably measure latent M. leprae as effectively as latent TB can be diagnosed using the tuberculin test. Some investigators have tested for phenolic glycolipid-1 in sera from HIV-1 infected persons and controls to estimate the prevalence of M. leprae infection (5). One intriguing study from Cuba found that 14.9% of 437 HIV infected patients compared to 1.3% of blood donors had antibodies to PGL-1 (6). However, this test may not be completely specific in HIV-1 infected persons. The specificity could be studied by testing sera from HIV positive population in which leprosy is rare or absent. Furthermore, a positive PGL-1
antibody test may not indicate an active *M. leprae* infection compared to a previous infection that has been cured. Clearly, newer methods are needed to detect latent *M. leprae* infections. Such data together with careful epidemiological studies of the rates of exposure to HIV-1 among leprosy patients might clarify why leprosy seems not to be an AIDS-related opportunistic infection or whether leprosy patients are relatively resistant to HIV-1 infection.

—Kenrad E. Nelson, M.D., Professor

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REFERENCES


A recent study conducted in Vietnam and Brazil revealed a significant association of leprosy susceptibility with the Parkinson’s disease (PD) gene PARK2 and PARKG. Variants in the regulatory region shared by these genes turned out to be a major risk factor for leprosy (9). Although the mutation of the PARK2 (Parkin) gene responsible for familial early onset of PD is not identical with the nucleotide polymorphism found in leprosy patients, it is not surprising that malfunction of a central enzyme results in disease or enhanced disease susceptibility. Parkin is a ubiquitin-protein ligase that controls—together with other ubiquitin-conjugating enzymes—the degradation of proteins by proteasomes. In the last years, it became clear that the ubiquitin-proteasome complex is a hot topic in biological science, because a breakdown of this central catabolic system is associated with severe human diseases, including neurological disorders, inflammation, cancer, and susceptibility of infection.

Proteasomes are the enzymatic heart of the cells. Protein synthesis and degradation are metabolic processes equally essential for prokaryotic and eukaryotic cells. As for the catalytic pathway, lysosomes and proteasomes are two major proteolytic machineries that are involved in protein degradation. While extracellular and cell-surface membrane proteins are mainly targeted to lysosomes, the vast majority of cytoplasmic proteins are degraded by proteasomes.

The enzymatic activity of proteasomes is strictly regulated and acts in concert with the ubiquitin pathway, which primarily tags proteins for degradation (1). Proteasomes are found in archaeabacteria, some eubacteria (e.g., Actiomyces) and eukaryotes. While their role in prokaryotes is not fully understood, they perform multiple functions in eukaryotic cells: degradation of damaged and abnormal proteins into small peptides and processing of proteins thereby yielding proteins of different biological activity including cell-cycle regulators, onco gens, tumor suppressors and transcription factors. Finally, MHC class I restricted cytolytic CD8+ T cells recognize peptides from self- and non-self proteins that are generated by proteasomes. This enables CD8+ T cells to control for and eliminate altered and infected cells. All this crucially depends on the precise function of the ubiquitin-proteasome system and thus, it is not surprising that aberrations lead to pathological reactions and disease (2).

The first step in the substrate selection for proteasomal degradation is mediated by the addition of poly-ubiquitin chains. This “kiss of death” is triggered by the successive action of several enzymes including the Ub-activating enzyme (E1), Ub-conjugating or carrier enzyme (E2), and Ub-protein ligase (E3). Ubiquitin tagged proteins are then recognized and digested by the proteasome, a multiprotein complex (10). The catalytic active sites of the eukaryotic proteasome is housed in a barrel shaped 20S core complex, which is composed of 28 subunits arranged in 4 stacked heptameric rings. The outer rings contain the a-subunits which shape the gates of substrate entry and product release. The two inner rings harbor the β subunits (β1–β7) of which the β1, β2, and β5 subunits are catalytically active. In contrast, proteasomes of prokaryotes encode only one type of α-subunit and one type of β-subunit. Despite this difference the overall architecture of these complexes is conserved. It seems that in eubacteria, proteasomes are not necessary for intracellular proteolysis as most bacteria rely on other cytosolic proteases for protein turnover.
Interestingly, the only eubacteria known to contain proteasomes are the family of actinomycetes to which *M. tuberculosis* and *M. leprae* belong. *M. tuberculosis* is unusual for a bacterium because it lacks two proteases of the HslUV and Lon family (3). Both mycobacteria are intracellular pathogens that spend most of their life inside cells, primarily macrophages. A recent study by Darwin, *et al*., provides an explanation of the strategy used by *M. tuberculosis* to avoid killing in the phagosome (4). They could demonstrate that transposon mutants with insertions in proteasome associated genes of *M. tuberculosis* are highly sensitive to reactive nitrogen intermediates which are produced as major defense mechanism by infected host cells. However, the type of damage that would target a protein for proteasomal degradation is not well understood, yet. Perhaps modifications such as nitrosylation are recognized by the eukaryotic ubiquitin-proteasome system as suggested for proteins with oxidative damage (5). Since the gene products of noxR1 and noxR3 have also been implicated in resistance to nitric oxide it is unclear whether proteasome associated mutations directly affect the degradation of modified proteins or whether the proteasome is needed to convert precursors into active forms of noxR proteins. Moreover, the mycobacterial proteasome is essential for the refolding of proteins that have been damaged by reactive nitrogen intermediates (RNIs) as demonstrated in vitro.

The coevolution of host cells and pathogens involves also the ubiquitin-proteasome system. Many viruses need the ubiquitin-proteasome in order to form correct virus particles (Ros), express components of this system as virulence factor (ubiquitin ligase) (6), or modulate the proteasomal activity by directly interacting with defined proteasome subunits (6). On the other hand the ubiquitin-proteasome system is also crucial for infected host cells to fight against invaders by processing and presenting their antigens to cytolytic T cells (6).

At first glance this seems to be paradoxical but taking into account that the ubiquitin-proteasome pathway acts on proteins, a central component of life, it adds up that this system evolved and is used beyond the barrier of species and even different phyli.

**CONCLUSION**

The ubiquitin-proteasome system plays a key role in a broad array of basic cellular processes with protein quality control as central function. Loss or impairment of this function is associated with many different types of diseases. Although we currently do not understand the molecular mechanisms of mutated PARK2 and PACRG and enhanced susceptibility to leprosy, it is interesting to note that PD and leprosy are diseases that both affect the nervous system which seems to be extremely sensitive to aberrations in the ubiquitin-proteasome system. Although accumulation of ubiquitin conjugates and/or inclusion bodies is characteristic for many neurodegenerative diseases, a firm and direct pathogenetic linkage to aberrations in the ubiquitin-proteasome system has not been established yet. So far, we can only speculate how mutations in PARK genes relate to leprosy susceptibility. Controlled degradation of proteins derived either from the pathogen *M. leprae* or infected host cells might be fundamental for the integrity of infected cells as well as induction of immunity against leprosy. As consequence, the failure of ubiquitination may result in accumulation of toxic proteins in highly sensitive nerve cells which, once damaged, cause paralysis and disfiguration typical for leprosy patients.

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Prof. Diltor V. A. Opromolla passed away last December, 2004 at age 70. He studied medicine at the Pontifical Catholic University of São Paulo where he graduated in 1957, and took his Ph.D. in dermatology in 1973 at the University of São Paulo (USP). Soon after, he started his studies on leprosy at the State Department of Leprosy Prophylaxis where he met two other important names in Brazilian leprology, Dr. Abraham Rotberg and Luiz Marino Bechelli. In 1958, Prof. Opromolla moved to Bauru where he joined government health services as a leprologist in the local leprosarium, which later become the Instituto Lauro de Souza Lima. He soon started to approach patients with a wide view, including, at that time, prevention of disabilities. Apart from the standard treatment, Prof. Opromolla had a particular concern for disabilities, and he inaugurated a special clinic named “The Healthy Foot Room” where patients could have full examination of feet, treatment of foot ulcers and talks on prevention of ulcers and self-care. It was a tremendous success and the “room” was further expanded in the late 1970s with the visit of Prof. Arvello, from Venezuela, who was introducing the concept of prevention of disabilities by simple techniques in the Americas. The visit of Dr. Arvello and the commitment of Prof. Opromolla was the beginning of a deep modification in the institution and how it regards P.O.D. and rehabilitation for leprosy-affected persons. In the clinical side, Prof. Opromolla was introducing new drug treatments and led the studies on the use of rifampicin in the treatment of leprosy. At that period, compulsory internation was discontinued in Brazil and the old leprosarium was becoming an unstable institution. One of the outstanding contributions of Prof. Opromolla was to make a clear diagnosis of this situation and to lead a group of doctors and scientist to transform the old leprosarium of Bauru in to a modern and solid research and training institution. He succeeded in this regard. Today Instituto Lauro de Souza Lima is a leading institution in leprosy in Brazil and is acknowledged in the international community. The scientific production and the massive number of trainees each year earned the Institute the position of Leprosy National Referral Center for the Ministry of Health and for the World Health Organization—and this is a concrete result of the continuous and dedicated work of Prof. Opromolla and his abilities to gather people of different areas to form a real multidisciplinary institution to serve leprosy-affected persons. He served also as consultant leprologist for the Ministry of Health and was a leading member of the W.H.O. Leprosy Expert Committee for several years. Prof. Opromolla took as his responsibility the renovation and up-dating of Hansenologia Internationalis, the only regular leprosy periodical published in the Americas, serving as editor from 1989 until his death. He fought hard to improve the quality of the published articles, to produce bilingual issues and to obtain funds to publish and distribute the journal. His personal scientific production was remarkable, with more than 200 articles published and several chapters in books, apart from his own book on clinical leprosy. One of his personal prides in this field was the invitation to write the preface to the 2nd edition of Hastings’ Leprosy.
In April 2004, he was compulsorily retired as he reached 70 years of age, but he kept the same routine at the Institute, participating in the clinical rounds, lecturing, and actively attending scientific meetings. Although fragile due to the illness that took him, he continued to accept engagements on behalf of leprosy and leprosy-affected persons. A few days before his death he was visiting Rio Branco, in the State of Acre, to discuss further research on Lobos’s Disease. It was also opportune that, just one month before his death, the Ministry of Health awarded him one of the top prizes in the field of public health in Brazil.

One week after his death, a ceremony was held in the Saint Judas Thadeu Church in Bauru, which was packed with those who had known or worked with Prof. Oromolla. It was an opportunity to remember again past experiences. It was also a moving occasion and a celebration of his work and life in the cause of science and the leprosy-affected person.

—Marcos Virmond, M.D., Ph.D.
# AFRICAN LEPROSY CONGRESS

## Scientific Program

**Eskom Convention Center, Johannesburg (Midrand), South Africa**

31 January to 3 February 2005

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## Opening Ceremony.

Dignitaries participating in the Opening Ceremonies included:

- Dr. Manto Tshabalala-Msimang, Minister of Health, Republic of South Africa
- Dr. Asomou Baah, Assistant Secretary General, W.H.O

Mr. Yohei Sasakawa, W.H.O. Goodwill Ambassador for the Elimination of Leprosy

Dr. Antoine Kaboré, Director of Communicable Diseases, W.H.O, AFRO

Dr. Bide Landry, Regional Advisor, Africa, W.H.O Leprosy Elimination Program

Dr. Gopal, President, IDEA

Dr. Deepack, President of ILEP

Dr. Noordeen, President of ILA

1The list of Congress attendees will be posted on the ILA web-site, and keynote presentations will be published in subsequent issues of the JOURNAL.
Remarks on the opening of the Congress.
Dr. Manto Tshabalala-Msimang.
Minister of Health, Republic of South Africa

It is a great pleasure for me to welcome you to South Africa for this second conference of the International Leprosy Association to be held on the African continent.

This Congress coincides with the celebration of the World Leprosy Day. The World Leprosy Day was founded by Count Raoul Follereau, who was deeply involved in the fight against leprosy, particularly in Africa. Count Follereau campaigned to reverse the negative images associated with leprosy, as did Mahatma Gandhi. The ideals of Gandhi and his willingness to personally care for people affected by leprosy did much to change public perceptions of this disease.

One cannot think of leprosy without being reminded of banishment and exile. Of course in the South African context, the prison of Robben Island comes to mind. Robben Island was for about 80 years a home to leprosy patients before it was made a prison that is now synonymous with the triumph of human rights and freedom. I am delighted that many of you will be visiting Robben Island after this congress and that you will have the opportunity to see this place that is of historical significant to the ideals of freedom and democracy in this country and across the world.

Great strides have been made against leprosy in Africa and the rest of the world since the first meeting of the International Leprosy Association was held on the African soil in Cairo in 1938.

Leprosy treatment has developed significantly during the past decades. We are especially proud that African researchers have played a leading role in developing new interventions against this disease. We in Africa can also boast of our own leprosy research facility, namely ALERT based in Addis Ababa. We can mention Davey’s trials with oral Dapsone in 1948 in Nigeria, Browne’s introduction of clofazamine in 1960 in Nigeria and the vaccine trials of Karonga in Malawi in the 1980s as just three of the many significant investigations into leprosy that have taken place in Africa. These studies have made a global contribution to the armory against leprosy.

We have seen many successes in the fight against leprosy in Africa. These have been due to developments such as the introduction of multi-drug therapy and the very high success rates associated with it. The simplification of various procedures has enabled workers with limited skills to undertake leprosy work successfully and civil society participation in the efforts against leprosy has improved significantly.

African countries have demonstrated determination to work towards the elimination of leprosy as defined in the resolution of the World Health Assembly of 1991 and significant progress is being made towards the realization of this goal.

In South Africa we are proud of the contribution made by our specialists who have published their findings in the International Journal of Leprosy and Other Mycobacterial Diseases and Leprosy Review. Their work should contribute in enhancing the knowledge of the international health community charged with the treatment of leprosy. I am pleased that at this Congress you will be hearing a presentation by one of our dermatologists on South Africa’s experience in providing leprosy treatment at a general hospital following the closure of the last of our specialized leprosy facilities.

Until 1977, hospitalization for leprosy treatment was compulsory in South Africa.
Specialized leprosy institutions began to close during the 1980s and in 1997, the remaining institution, Westfort Hospital, was closed.

We are pleased that leprosy has been reduced to very low levels in South Africa. About 50 new patients are detected each year. However, 40% of our newly diagnosed patients suffer from Grade 2 (W.H.O.) disabilities. This indicates that a large percentage of our patients are only being diagnosed after having suffered from the disease for some time. There are about 160 patients that are registered for treatment. At least 3000 people have disabilities related to leprosy amongst the economically active age groups in the country.

Despite the fact that new patient detection levels have reached very low numbers as both a percentage of the population and in absolute numbers, we are intensifying the implementation of our leprosy control policy.

The goal of the leprosy program is to decrease the current prevalence of leprosy in order to work toward the eradication of leprosy. The objectives of the program are to:

- Develop standard guidelines for the early diagnosis and management of patients
- Prevent disability and rehabilitate disabled patients
- Establish a central register and measure treatment outcomes
- Ensure that there is at least one medical doctor with leprosy expertise in each teaching hospital to which leprosy patients can be referred
- Ensure that early diagnosis of leprosy is included in the PHC training material of health professionals.

Our aims are to:

- Increase awareness of the continuing existence of leprosy
- Promote the early treatment of patients with multi-drug therapy
- Promote community involvement in case detection
- Ensure that that multi-drug blister packs are made available at the treatment points used by leprosy patients
- Improve the knowledge of health staff supervising leprosy treatment to enable them to help patients and avoid disabilities.

In South Africa, leprosy treatment has come a long way, from the darkness and isolation of Robben Island to the bustle of PHC clinics in our modern facilities. However, we acknowledge that much needs to be done to ensure that leprosy patients benefit fully from the advances in treatment seen in recent years.

This conference provides us with an opportunity to celebrate the progress that has already been made on our continent towards providing treatment for all patients. It also reminds us of many patients who have not yet received treatment and the many people who have had leprosy and who suffer from disabilities. All these people need our help. We have an excellent opportunity here of learning from each other. I am particularly pleased to see that the conference program has sessions dealing with “reaching the Unreached” and “Community Based Rehabilitation” which should facilitate the sharing of best practices.
Most of you have had first hand experience of the harsh attitudes towards this illness. We all have an important role to play in changing perceptions of leprosy and promoting the rights of leprosy patients. I am glad that this congress will also discuss the factors that impact on our interventions against this disease.

Many of you work in difficult conditions, providing care for your patients in innovative ways and for that I salute you. I wish you well during this congress and trust that you will be able to return to your work-areas refreshed with a deeper understanding of leprosy and better equipped to serve those whose health depend on you.

It is my pleasure to declare the African Leprosy Congress of 2005 open.

Docteur Antoine B. Kaboré,
Directeur Régional de l’OMS pour l’Afrique

Le Docteur Luís Gomes Sambo, le nouveau Directeur régional de l’OMS pour l’Afrique, aurait souhaité être en personne parmi vous à ce congrès qu’il qualifie lui-même d’historique parce que:

(i) c’est le premier congrès de l’Association Internationale de la lèpre (ILA) dans un pays de la Région africaine de l’OMS,

(ii) le congrès a lieu en 2005, terme fixé pour l’élimination de la lèpre en tant que problème de santé publique au niveau national dans tous les pays,

Malheureusement, ce congrès coïncide avec sa prise de fonction. Il a dû se résigner à nous désigner pour le représenter et vous transmettre son message.

En son nom, je voudrais tout d’abord remercier le Gouvernement de l’Afrique du Sud et en particulier le Président de la République et La Ministre de la Santé pour toutes les facilités qu’ils ont offertes pour que ce congrès soit une réussite. Nous connaissons l’hospitalité légendaire de l’Afrique du Sud et nous sommes émerveillés par la qualité de l’organisation et la disponibilité de nos frères sud-africains chaque fois que nous avons l’occasion de participer à une réunion dans ce beau et grand pays.

Je voudrais remercier tous les responsables de l’Association Internationale de la Lèpre pour les efforts qu’ils ont consenti pour organiser ce congrès en Afrique car, de mémoire, il s’agit des premières assises sur le continent.

Je voudrais aussi remercier toutes les organisations non gouvernementales regroupées ou non au sein de la Fédération Internationale des Associations contre la Lèpre (ILEP) pour leur dévouement à la cause des malades de la lèpre et pour tous les efforts qu’ils ne cessent de déployer pour faire de l’élimination de la lèpre une réalité visible en Afrique.

Enfin, je voudrais remercier tous les participants à ce congrès pour leur implication dans les programmes d’élimination de la lèpre et leur contribution à l’organisation de la lutte contre la lèpre dans la Région africaine de l’OMS.

(Résultat des programmes d’élimination de la lèpre). Grâce à vous tous, le programme d’élimination de la lèpre est un des programmes les plus réussis de la Région. La détermination des pays à combattre la lèpre a été la clé de tous les succès que nous avons eus. Grâce à l’engagement politique au plus haut niveau des Etats membres, et grâce au dynamisme des responsables nationaux, la lèpre a été considérée comme une priorité nationale et les services de santé se sont focalisés sur les activités d’élimination. Ainsi, plus d’un million et demi de cas de lèpre ont été détectés et guéris dans la Région au cours des dix dernières années. L’importance de la maladie a été considérablement réduite. La prévalence est passée de 1,500,000 malades en 1990 à 45,000 en 2003. L’élimination de la lèpre a été réalisée au niveau régional où le taux de prévalence est actuellement à 0,80 cas pour 10 000 habitants. Dans les pays, la
situation s’est inversée. En 1990, nous avions 42 pays très endémiques dans la Région. Aujourd’hui seuls trois pays présentent la lèpre comme un problème de santé publique majeur et je peux vous assurer que ces pays sont à pied d’œuvre pour atteindre le seuil de l’élimination de la lèpre.

(Résumé de l’histoire de l’élimination de la lèpre). Qui pouvait croire en un tel succès?

La découverte de la Dapsone dans les années 40 avait suscité un vif espoir de vaincre la maladie, mais l’apparition des résistances dans les années 60 avait vite fait de transformer cet espoir en rêve.

Avec l’adoption de la polychimiothérapie dans les années 80, l’espoir renaissait de nouveau mais les doutes persistaient dans les esprits face à l’expérience de la Dapsone. En 1991, lorsque l’Assemblée mondiale prenait la résolution d’éliminer la lèpre (Résolution WHA44.9), nombres de partnaires n’y croyaient pas vraiment. Aujourd’hui, grâce aux efforts déployés par tous les pays et l’enthousiasme que l’élimination de la lèpre a suscité dans le monde, cette résolution s’est traduite en réalité.

Dans la Région africaine de l’OMS, la couverture géographique des services de santé par la poly chimiothérapie anti-lèpre (PCT) est à plus de 90% au niveau des districts sanitaires et dans tous les pays. La qualité de la prise en charge des cas de lèpre a été nettement améliorée et les taux de guérison sont supérieurs à 85%. L’intégration du dépistage et du traitement de la lèpre dans les soins de santé primaires a conduit à une augmentation significative des taux de guérison.

Au-delà de la souplesse dans la délivrance des traitements, c’est surtout à la mise en œuvre de la stratégie d’élimination de la lèpre que nous devons tous les succès enregistrés. Ses principaux éléments tels :

- le renforcement de l’accessibilité géographique, financière et culturelle des services de diagnostic et de traitement de la lèpre,
- la disponibilité des médicaments et la gratuité des traitements pour les malades,
- la mobilisation sociale en faveur de l’élimination de la lèpre,
- la prise en charge précoce et correcte des malades,
- le suivi régulier des programmes et la mise en œuvre rapide des interventions correctrices,
- l’organisation des activités de soutien telles la formation, la supervision régulière et la sensibilisation des populations.

ont été extrêmement utiles pour l’atteinte des résultats.

Je voudrais ici remercier les responsables des programmes nationaux d’élimination de la lèpre, les membres du groupe de l’Alliance mondiale pour l’élimination de la lèpre et tous les partenaires qui ont contribué à ce succès, plus particulièrement la Nippon Fondation et Sasakawa Memorial Health foundation, la fondation Novartis pour un développement durable, l’Agence internationale danoise de développement (DANIDA), la Banque mondiale et toutes les Organisations Non Gouvernementales membres de la Fédération internationale des associations contre la lèpre (l’ILEP).

(Défis actuels). Malgré les efforts déployés et en dépit des bons résultats obtenus, l’élimination de la lèpre est encore fragile et beaucoup de choses restent à faire pour la consolider à tous les niveaux: régional, national, intermédiaire et district dans les pays.

- Plusieurs pays vacillent encore autour du seuil de l’élimination et d’une année à une autre, se retrouvent tantôt en dessous, tantôt au-delà du seuil d’un cas pour 10.000 habitants.
- Plusieurs pays ont des districts encore très endémiques à cause du stigmate de la maladie, du manque d’information et...
de l’absence des services de prise en charge des cas.
• La détection est encore élevée. Plus de 40.000 nouveaux cas sont dépistés chaque année. Cette détection témoigne du succès des campagnes et des projets d’action spéciale. Elle constitue aussi un indicateur de la persistance de la transmission de la maladie dans les communautés.
• Le stigmate social de la lèpre est encore présent. La maladie continue de faire peur et les malades sont toujours victimes de rejet que seule l’ignorance justifie. C’est dire que dans le domaine de l’information et de la sensibilisation sur la lèpre, nous avons encore beaucoup à faire. La réhabilitation sociale des malades et leur intégration dans les communautés doivent se poursuivre en collaboration avec les autres secteurs.

Nous savons tous que la Région africaine est à un tournant critique de son histoire. Les défis qu’elle doit relever sont nombreux. La pauvreté et la misère persistantes dans les populations nous préoccupent. Les maladies émergentes et ré-émergentes s’ajoutent aux épidémies et ne facilitent pas le développement harmonieux des programmes de santé. En dépit de ces conditions difficiles et de la précarité des services de santé, les États africains ont engagé des efforts pour éliminer la lèpre. Nous devons les encourager à poursuivre cet engagement et à maintenir la lèpre dans la liste des priorités nationales des services de santé.
Face aux défis actuels, la responsabilité des pays et surtout des programmes nationaux est grande. Sans une volonté nationale, rien ne peut se faire. La responsabilité du bureau régional de l’OMS pour l’Afrique est aussi importante mais elle est conditionnée par la détermination des pays. Toutefois, l’OMS poursuivra ses efforts pour aider les pays à s’approprier les programmes, assurer la pérennisation des activités et obtenir plus de résultats en espérant que nous réaliserons un monde sans lèpre. Pour y parvenir, les partenaires doivent aussi tout mettre en œuvre pour poursuivre leurs appuis financiers et logistiques aux programmes.

(Orientations futures et perspectives). Tous, ici présents à ce congrès, nous savons que la mise en œuvre de la stratégie d’élimination de la lèpre a été faite dans un climat difficile où l’absence de définition claire des rôles et des responsabilités entre les partenaires ainsi que l’absence d’un mécanisme efficace de coordination n’ont pas facilité la collaboration. Cette situation n’a pas permis aux pays de bénéficier pleinement de l’appui que nous devions leur apporter.
Dans l’intérêt des nations et au regard de nos engagements, nous invitons toutes les structures et les organismes (scientifiques, responsables de programmes, partenaires publics et privés, Organisations non gouvernementales nationale et internationale passionnées par la cause des malades de la lèpre) à tourner la page et regarder vers l’horizon sous un angle d’espérance et avec une volonté d’ouverture pour une amélioration de la collaboration et de la coordination des interventions dans les pays. Nous pensons qu’il s’agit là d’une condition essentielle pour réaliser un monde sans lèpre.
L’OMS poursuivra ses efforts. Une nouvelle stratégie qui prendra en compte la situation épidémiologique actuelle dans laquelle la lèpre devient de plus en plus rare sera proposée. La contribution de tous les partenaires à l’élaboration de cette stratégie permettra de mettre en place le cadre et les conditions d’une meilleure collaboration. Dans cette nouvelle stratégie qui sera essentiellement orientée vers la consolidation des acquis des programmes nationaux, la priorité au niveau inter-pays et régional sera le renforcement de la coordination et de la collaboration entre les partenaires. La création d’un cadre de concertation pour retrouver l’harmonie tant nécessaire au bon déroulement des programmes nationaux occupera une place prépondérante. J’ai la ferme conviction que nous aurons l’adhésion de tous.
Je finirai mon propos en vous rassurant une fois encore que dans le cadre du rôle que les États membres ont confié au Bureau régional l’OMS, l’Organisation s’engage à poursuivre son appui aux pays pour l’élimination de la lèpre.
Je souhaite beaucoup de succès à votre congrès et vous remercie pour votre attention.
Mr. Yohei Sasakawa,
W.H.O. Goodwill Ambassador for the Elimination of Leprosy.

I would like to begin by expressing my sincere gratitude to Her Excellency Dr. Mantombazana Tshabalala-Msimang, Minister of Health of the Republic of South Africa, for opening this Congress with such a wonderful song. I also had the opportunity to speak with her before the meeting. I was highly encouraged to hear from her that, although the issue of leprosy has not been addressed extensively so far during her term, she realized that there is a need to do more to inform the media and general public about the disease, and that she would do her best to adjust her schedule so that she can attend the upcoming workshop on Robben Island.

This Congress has been organized by ILA under the leadership of Dr. Noordeen, who has always been at the forefront of the medical battle against leprosy. The results he has achieved to date have been outstanding. I would like to express my deepest admiration for Dr. Noordeen for bringing together here today a diverse group of people from ILA, ILEP, IDEA and other organizations dedicated to the battle against leprosy, as well as program managers and field workers from many of Africa’s English-, French- and Portuguese-speaking countries. I firmly believe that we are all gathered for a common purpose: to create a world free of leprosy and a world free of discrimination.

As you know, W.H.O. has been working toward the goal of reducing the prevalence rate of leprosy to less than one case in 10,000 people in every country in the world by the end of 2005. Drugs have been made available free of charge everywhere in the world in hopes of achieving this. While the achievement of this goal will by no means mark the end of the battle against leprosy, there is no doubt that it is a very important milestone, and one that I hope we will all work for together.

Before arriving in South Africa, I visited India, where I was heartened by the steady progress being made toward elimination, which has seen the prevalence rate come down to 1.98. I am confident that India will achieve elimination by the end of 2005. Following India’s example, I believe that it is important to set specific goals, and set them high.

Fortunately, thanks to the concerted efforts of individuals and organizations around the world, we have come a long way in the medical battle against leprosy. Since the 1980s, 14 million people have been liberated from the disease. As W.H.O. Goodwill Ambassador for Leprosy Elimination, I have been traveling the world to spread correct knowledge about the disease, repeating our three simple but important messages tens of thousands of times: Leprosy is curable. Free treatment is available. Social discrimination has no place.

Unfortunately, these messages have yet to reach many people. We need to do more.

Although the medical battle against leprosy is progressing smoothly, there is another important question that we must face. That is the question whether the 14 million people who have been cured of leprosy have been able to assimilate back into society in the way that people cured of other diseases such as tuberculosis or malaria have. I am afraid that this has not been the case.

The medical advances that have been made to date in the treatment of leprosy are truly remarkable. On the other hand, determined efforts to root out discrimination and stigma are only just beginning. Faced with this issue, I visited the Office of United Nations High Commissioner for Human Rights for the first time two years ago. I was truly surprised to find that such a serious human rights issue as discrimination against people affected by leprosy had never before been brought before the UN Commission on Human Rights. Together with the members of IDEA, who are also here today, I convinced its Sub Commission on Promotion and Protection of Human Rights to investigate the issue, and subsequently the Sub Commission unanimously adopted to further study the state of discrimination against leprosy affected people and their families. As a result, we are very fortunate to have with us today, Prof. Yozo Yokota, the Japanese member of the UN Sub Commission on Human Rights. Prof. Yokota is here to listen to all you have to say, so that he can go back and share your thoughts with the other members of the Sub Commission.

“Leprosy is curable. Free treatment is available. Social Discrimination has no place.”
I believe that this meeting is a truly historic occasion in the long history of leprosy. It has brought together people from around the world who have personally experienced and overcome the disease. They have come to share their stories, voice their opinions and serve as partners in leprosy elimination. Their stories are more powerful and revealing than anything I can say here at this podium. I cannot stress enough the important role they have to play.

I have already remarked already on the diversity of those present. I believe it is the intention of Dr. Noordeen and his team that we debate the issues more widely, more deeply and more vigorously than ever. This diversity also represents the best way for the three messages — Leprosy is curable. Free treatment is available. Social Discrimination has no place — to reach as many people as possible. I hope you will join me in this effort.

**Dr. Bidé Landry,**
Coordonnateur régional du programme d’élimination de la lèpre pour la Région Africaine de l’OMS

First, I wish to thank the organizers for the privilege of being part of this historic meeting, and for the opportunity to be here to listen and to learn from men and women who have been working in leprosy for many years.

I have always been intrigued by the devotion and dedication of people working in leprosy and I am hoping that by being associated with you, I will also be affected with your passion and compassion.

An uncle of mine, a Roman catholic Bishop, many years ago educated me that to be involved in leprosy, one must have at least one of the three Ms. You must either be a Missionary, a Mercenary or Mad. In my short life, I have seen a few people who have been able to combine all the three qualities.

Distinguished Ladies and gentlemen, we have a lot to be proud of. Within the last 20 years; the number of countries, where leprosy is a major public health problem has fallen from 122 to 9.

Over 14 million people have been cured of leprosy. In place of despair, there is now hope that future generations will not have to deal with leprosy that way our generation has had to struggle with leprosy.

This historic congress, therefore represent a period of celebration. We are here to celebrate not only our achievements. But also the lives of those who have sacrificed their lives to ensure that leprosy does not destroy lives. We are also here to celebrate the lives of all those who have and continue to suffer the disease in silence.

But the congress is also an opportunity for reflection. Our top priority should remain to support the 9 remaining countries to reach the elimination target.

It is worth remembering that our ultimate aim is not elimination but a world free of leprosy. We talk about 14 million of people cured from leprosy. This is not completely true. People might have been cured physically but not emotionally, mentally and spiritually. This is because the biggest society is still not cured from the stigma of the disease. And as long as the society is not cured, no one will be completely cured. Curing the society of the stigma of leprosy is a very big and long-term agenda.

I have no doubt that the post elimination era will be as challenging as the pre elimination agenda. We will need even more support and resources. We need to be more creative, so that leprosy control moves from the margins to the mainstream of health policy, health strategies, health service delivery and health budget.

“We have no option but to work together.”

We have been successful so far because of the collective action of national governments, NGOs (both local and international) foundations, the private sector, (especially the pharmaceutical sectors, researches and scientific community) and through the vision foresight, leadership efforts of a number of special individuals. Some of whom are here with us.

The key of our future success is partnership. We have no option but to work together. I know that W.H.O. has not always been a good partner and occasionally we have been part of problem rather than being part of the solution. We have not always adequately recognized the special role NGOs play. We are keen to learn from our past mistakes and not to repeat our old mistakes. We ask the same from our partners. We will not always agree. Occasionally one may disagree but we should always reach a consensus.
If ever there was a just war, the war against leprosy is one such war.
On behalf of the millions who have benefited and will benefit from your work, I salute you and wish you a very fruitful congress.

Working Together For A World Without Leprosy
Dr. Sunil Deepak
President International Anti-Leprosy Federation (ILEP)

Honorable Minister, distinguished guests, dear friends and colleagues,

ILEP is honored to be associated with this historic Africa congress of ILA. ILEP has chosen its mission as “Working together for a world without leprosy”.

When we say “working together”, we mean 15 autonomous members of ILEP that are together since 1966 and that support activities in 94 countries of the world. As ILEP members, we recognize that the combined efforts of ILEP members as a federation is greater than the sum of their individual efforts. “Working together” also means the high quality technical expertise from the ILEP’s Technical Commission and its support for research, scientific journals and teaching materials. Finally, it also means our national and local partners including Governments and national programmes at different levels, national and local non-governmental organizations and families and associations of persons affected with leprosy.

For reaching the goal of a world without leprosy, the support provided by ILEP member associations has an operational dimension that includes financial support, technical advice, training and human resources, teaching materials, equipment, drugs, etc. This support from ILEP members is based on a holistic view of leprosy that means attention towards diagnosis and treatment of the disease, prevention of disabilities, community education, care and rehabilitation and the human rights approach.

For achieving this goal of a world without leprosy, ILEP members promote integrated and sustainable approaches to the fight against leprosy that include combined programmes and general health services, strengthening of referral services, training of personnel in general health services and promotion of community-based rehabilitation and socio-economic rehabilitation programmes.

In this scenario, we see many challenges for continuing the fight against leprosy including:

- Ensuring adequate attention towards leprosy in primary health care settings and in combined programmes
- Networking with organisations involved in non-leprosy related activities and promoting their attention towards needs of leprosy affected persons.
- Strengthening the coverage of general health services.
- Sustainable and effective strategies for the fight against leprosy in the post 2005 period.

In conclusion I would like to reaffirm that ILEP members are committed to work together with Governments and all stakeholders and partners in Africa to ensure the provision of sustainable, quality services for treatment and care of persons affected with leprosy for as long as these are needed. I also wish the participants of the African congress of ILA for fruitful discussions that will contribute to the realisation of our goal for a world without leprosy one day. Thank you.
Introduction. Dr. J. P. Bréchet and Dr. Alexandre Tiendrebeogo

The elimination strategy is based on 2 key elements: Early diagnosis of leprosy and effective treatment with a standard M.D.T. treatment.

However, the implementation of these key elements is fraught with many difficulties such as:

- Problems in training and communication due in part to the low level of skills at the periphery where health centers constitute the front line in contact with the population, and also where there exists low awareness of leprosy about symptoms, access to treatment and gratuity of M.D.T.

- Problems of organizing activities at the Health Unit level where detection and treatment are often part of a vertical program, and where treatment is either prolonged or cases recycled due to deformity or reaction.

- Problems of access to detection and treatment centers due to low geographical coverage, financial constraints (transport cost and loss of salary while going to Health center) and social stigma.

This symposium looks at operational aspects of detection and treatment through the shared experience of different approaches in Africa, which is the continent with the greatest number of countries having a high prevalence of leprosy.

Detection of Leprosy.

a) Active and passive detection by Dr. Alexandre Tiendrebeogo

Passive detection is examination of suspected cases presenting themselves spontaneously; it needs to be supported by health education campaigns and availability of free M.D.T. The advantage is that it facilitates integration of leprosy into general health services, is cheap and is appropriate in areas with good health coverage.

In Active detection, suspected cases are gathered in a village and examined during a visit in the village, it needs to be accompanied by flexible distribution of M.D.T. and a repeated visit after 2-3 months. The advantage is that hidden cases are more easily found and community participation helps to reduce stigma of leprosy in isolated areas or those with poor health coverage.

Treatment likewise can be adapted to monthly supervised M.D.T. distribution, flexible M.D.T. distribution for 2 to 3 months and accompanied M.D.T. distribution of the whole course of treatment.

A good combination of all these strategies will ensure a high success rate of detection and treatment adapted to the prevalence, health coverage and context of leprosy in the area.

b) Active and passive detection in Mali by Dr. Samba O. Sow

Comparing 2 strategies of leprosy cases finding it was found that active case finding is more efficient but expensive, allows early detection, treatment and prevention of disabilities, should be repeated for 2 to 3 years in remote areas according to the prevalence, while Passive case finding should be accompanied by education sessions in order to be more efficient.

The 2 strategies need to be combined in most endemic countries for leprosy elimination.

c) Urban leprosy and detection in Madagascar by Dr. Claude Rattrimoarivony

The case of Antananarivo, capital of...
Madagascar with a rapidly growing population coming from the rural areas. Although the Prevalence rate is low (0.14/10,000) the number of new cases detected is constant and is mainly constituted by MB cases (94%). Reaction appears in 20% of cases. This may be due to having only one Dermatology reference center for Confirmation of Diagnosis. To improve detection staff need to be trained in active case finding and follow-up in the suburbs as well as to raise awareness of the indifferent population. The case for social assistance in the urban context is made so as to look for defaulters and improve the cure rate.

Quality of Diagnosis.

a) Results of ULR in Cameroon – Dr. Charles Nsom Mba

Updating of Leprosy Registers was performed in 10 Provinces over 2 years and resulted in a marked reduction of the Rate of Prevalence from 0.82 to 0.46 per 10,000. The main lessons learned were that detection depended on the information about leprosy and the level of awareness of the community. The health workers required updating about leprosy and improvement in M.D.T. coverage in order to achieve the reduction in Prevalence. Hence the recommendation to pursue this activity as a routine supervision activity.

b) Validation of diagnosis in Angola – Dr. J. P. Brechet

With an increase in case detection and Prevalence, justification to validate the diagnosis of leprosy became obvious. First high endemic Provinces were visited, registers updated, patients examined and staff assessed in their skill to diagnose Leprosy. The impact of previous training was poor and a new strategy of in service training during supervision visits was introduced. The validation included 3 elements: Patient examination, validation of information support (charts and Register) and validation of statistical reports.

Thus the main elements to confirm diagnosis include: patient examination by 2 trained technicians, systematic review of nerve assessment (sensitivity, muscle strength testing, deformity grade) and clinical diagnosis. In Angola only 60% of cases were confirmed, 6% were wrong diagnosis and 34% were non leprosy cases disappeared due to migration of population and poor follow-up. It is recommended to expand the confirmation of diagnosis by involving dermatologists and medical doctors as well as to strengthen formative supervision visits.

Strategy in Leprosy Treatment.

a) Accompanied M.D.T. in Madagascar.

Assessment by Dr. A. Tiendrebeogo

Due to a low cure rate (55%) in Madagascar and in an effort to improve the treatment completion rate, accompanied M.D.T. was introduced in 2000. Over a 3 year period up to 21,000 new cases of leprosy were treated. An assessment of this strategy was performed by taking a sample of 962 cases treated in 2001 in 32 districts and examining them in 2003, after completing treatment. The results showed a high cure rate (98%) against a lower cure rate for supervised M.D.T. distribution (86%). Patients living more than 10 km from the health center showed lower cure rate with supervised M.D.T. It is therefore recommended to pursue Accompanied M.D.T. distribution for people living more than 10 km from the health centers and to continue supervised M.D.T. distribution to those living near the Health Unit.

b) Comments about Leprosy Treatment by Dr. V. Pannikar

The current M.D.T. blister packs is still the main form of treatment and W.H.O. will continue to provide free M.D.T. to all countries treating leprosy patients up to the year 2010. Other treatment schedules are being studied and the results will not be published until 2010. (ROM and Uniform M.D.T., 5 year prospective study to assess relapse rate)

The key points are Flexibility in M.D.T. distribution (how and when to adapt distribution to where patients are living), elaborating joint guidelines for finding defaulters, developing tools to diagnose relapse and to be aware of the risk of Rifampicine drug resistance.

c) Strategy for Leprosy Control in a low endemic country – case of Sudan by Dr. E. Tanyons

In Sudan Master clinics were developed in each Province according to population
density and accessibility. These clinics confirm diagnosis of suspected cases and start M.D.T. treatment. This is a method to facilitating supervision and makes good use of scarce medicines and Human resources. The Seminars for increasing awareness of leprosy are undertaken for health staff and community leaders. The expected result is reliable and valid reports.

These topics raised some very practical issues such as active versus passive detection, financial aspects involved in these strategies, despite the fact that pockets of leprosy exist and require to be detected, in any case and by any means available.

Diagnosis of leprosy can be improved by careful examination and confirming the diagnosis by 2 examiners, including where possible dermatologists and performing formative supervision visits of Health workers.

Treatment schedules need to be flexible and adapted to the patients taking into account distance, follow-up and community participation, so as to minimize defaulters and obtain a high cure rate.

Dr. J. P. Bréchet
Dr. A. Tienderébéogo

Symposium on
REACHING THE UNREACHED

Preamble. As an introduction to the symposium, the moderator made the following remarks:

- The current strategy for Leprosy Elimination centres on early detection and prompt treatment with M.D.T.
- For many years it was recognized that in some countries and regions, there were pockets of patients that could not be easily accessed through the conventional leprosy elimination programs.
- This situation continued to persist in spite of claims of high geographical coverage and the integration of leprosy services into the Primary Health care package.
- Innovative approaches spearheaded by W.H.O. namely Special Action Projects for Elimination of Leprosy (SAPEL) and Leprosy Elimination Campaigns (LEC) were implemented by several countries leading to significant successes in reaching underserved and detecting and treating hitherto hidden leprosy cases.
- In spite of the efforts, new leprosy cases continue to be detected in numbers and with established deformities. This suggests that leprosy cases continue to occur in the community but are not detected in time.
- The possible explanations include factors that prevent the cases from accessing the health services, e.g. long distances, cost and stigma.
- Some patients with suspect symptoms do present to health facilities but are not detected due to the lack of relevant knowledge and skills among the health workers.
- This symposium was meant to review the achievements made through the previous innovative approaches, to decide if some aspects are still relevant. Country presentations, especially from high prevalence countries, would highlight the problem of unreached patients and the measures taken to reach them. The overall output would be a collection of recommendations and possible approaches to reaching the unreached.

Presenters. The symposium was moderated by Dr. H. Joseph Kawuma (Uganda), and the country presentations chaired by Dr. J. Chwuku (Nigeria).

There were brief presentations by: Dr. L. Bide (W.H.O./AFRO); Dr. B. Njako (Tanzania); Mr. Mitiku Ensermu (Ethiopia); Dr. J. Mputu (DRC); Dr. Samuel Hermas (Madagascar); Dr. Ndeve A. (Mozambique).

Synopsis of presentations. The World Health Organization (W.H.O.) Medical Officer reiterated the contribution of Africa to the global leprosy burden referring back to his key note address on Leprosy Elimination in African Region of W.H.O.

Describing the successes achieved with
LEC and SAPEL projects in the past, he indicated how these were no longer appropriate in the form used then but that innovative approaches could still be used to address the yet unreached patients.

The presentation from Tanzania described factors behind the uneven distribution of leprosy cases in the country. While some areas were simply high prevalence pockets, the distribution was also influenced by: geographical coverage by the National Elimination Programme due to, among others, bad terrain and lack of training of health workers. Dr. Njako listed the measures taken to overcome some of the problems with particular emphasis on the gains made through increasing the skills of health workers in over 80% of health units and promoting functional integration.

A presentation from Ethiopia described the current leprosy elimination status. There are no apparent high endemic pockets or hard to reach areas. This leads to the optimism that, if the present strategy is sustained, the leprosy burden will continue to show a downward trend. The current PHC strategy in the country is focusing on improving health in the home or household. The challenge to the NLEP is to ensure that aspects relevant to early detection and treatment of leprosy will be integrated in this strategy.

The Leprosy Programme Manager of DRC justified the thinking that there are still many unreached cases. There is an increasing number of newly detected cases in spite of poor geographical coverage as a result of war and a poor road communication network. Attempts to use community volunteers especially in the underserved areas were frustrated by unforeseen demands for remuneration (for would be volunteers). The strategy will continue to be pursued but engaging volunteers identified by the community.

Madagascar has, perhaps, the most severe leprosy burden in the region. The country presentation reported that the strategy to reach yet unreached cases was based on intensified community mobilization and education.

Mozambique’s health services in general were affected by the protracted war. The brief country presentation described a gradual improvement of the elimination programme between 1994 and 2003. Prevalence rate at the end of 2003 was 2.2 per 10,000. To reach unreached cases, they invested mostly in training of staff in government and private health services, social mobilization and health education. Coupled with a systematic updating of registers, they are optimistic that the leprosy burden will continue to go down.

Comments, conclusions and recommendations. The contents, recommendations and discussion points arising from the various presentations can be summarized as follows:

(i) Deliberate efforts should be made by National Programmes and their partners to continue the search for underserved areas and populations in order to reach the yet unreached leprosy cases and to provide them with M.D.T. services.

(ii) “Reaching the unreached” is a Primary Health Care strategy aimed at ensuring equity in health care. Leprosy control strategies should aim at improving access of underserved populations to general health services including M.D.T. services and should target equal not greater access.

(iii) Particular attention should be paid to strategies to increase access of women to health services, and ensure coverage of urban and peri-urban areas including slums in view of increasing urbanization in the different countries.

(iv) Efforts to increase geographical coverage should be sustained. This could be by using volunteers in areas in which basic health infrastructure does not exist. Experience shows that it is essential that the volunteers are identified by the communities served and that, as a prerequisite, adequate training is carried out, logistics ensured and a referral system put in place.

(v) Existing organized groups should be used for sensitization and mobilization. Examples: School Children to identify suspects and direct them to volunteers; Religious Groups that are active in the hard to reach areas for communication, advocacy and social mobilization; and Ex-Patients for mobilization.

(vi) The following general measures may be taken to ensure that leprosy related priorities remain in the correct places.

• To ensure that leprosy continues to be
given deserving emphasis in country health strategies e.g. the focus on families and households in Ethiopia.

- Services for diagnosis and treatment, training and re-training of existing staff must be sustained.
- Intensify use of dermatological services as an entry point to identify leprosy suspects.
- Ensuring inclusion of leprosy in the curricula of medical schools and other health training institutions.
- Organizing operational research in the suspect pockets.
- While LECs and SAPELs are no longer appropriate in their original design, it is possible to apply selected, sustainable elements of LECs in the known pocket areas.

- Community Rehabilitation and Social Economic Rehabilitation Programmes should be maintained on the agenda for their primary purposes but also because they present good opportunities for community mobilization.
- It is important for leprosy related bilateral and multi-lateral agencies (referring to the particular case of W.H.O. and the ILEP Organizations) to improve their internal coordination in order to avoid sending conflicting messages to countries.

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Symposium on
COMMUNITY-BASED REHABILITATION (CBR) FOR PEOPLE AFFECTED BY LEPROSY

Introduction. Many people affected by leprosy live with the long-term physical and psychosocial consequences of the disease. In 1998, the number of people living with leprosy-related visible impairments was estimated to be 2 million. Social problems resulting from stigma are often not restricted to the person who has had leprosy him or herself, but affect whole families. Therefore the number of people indirectly affected by leprosy will be much larger than this. The physical impairments may lead to continued risk of further disability and to limitations in activities of daily living. Visible impairments (deformities), activity limitations and/or stigma may lead restrictions in social participation, such as problems in family relations, marriage, education or employment. A substantial proportion of people who suffer such adverse circumstances will learn to cope and overcome their disadvantages. Yet others may require assistance to restore or optimize their functioning and social integration. Services offering a wide variety of rehabilitation interventions to meet such needs have traditionally been offered in and through institutions. Elsewhere, specialized socio-economic rehabilitation outreach programmes have attempted to improve the social participation of people affected by leprosy. However, the coverage of both institutes and outreach programmes is small compared to the global need for such services.

The same is true for people with other disability. An estimated 600 million people worldwide live with one or more disabilities. Only a fraction of these have access to rehabilitation services. The reasons include poor geographical coverage of existing services and the high cost involved in specialised, particularly institution-based services. Community-based rehabilitation (CBR) has been devised as a strategy to make basic rehabilitation services widely available to all people with disability. CBR is defined as “A strategy within community development for the rehabilitation, equalization of opportunities, and social integration of all people with disabilities. CBR is implemented through the combined efforts of disabled people themselves, their families and communities, and the appropriate health, education, vocational and social
services.” (UN, W.H.O., and ILO. Joint position paper, 1994)

It is important to realize that CBR and institution-based rehabilitation are complementary. For many people, CBR services may be sufficient to meet their needs. However, an estimated one third of people with disability will require specialist services (e.g. reconstructive surgery) at one point or other during their rehabilitation. Another important point to realise is that there is no one “method of doing CBR.” Essential characteristics of CBR are that programs or services are participatory, involving the client and his or her family as key stakeholders, and that the services empower the people concerned to take control of their own lives and optimize their abilities. Often, CBR programs are multi-disciplinary and multi-sectoral, including staff, services and/or skills from medical, paramedical, social, educational and vocational disciplines. Since CBR is a community-based service, often people with many types of disability are included. However, traditionally, this has not included people affected by leprosy, either because separate rehabilitation services catered for their needs or because stigma against leprosy was and is still present within CBR programs also.

Because the needs of people affected by leprosy are very varied, ranging from physical prevention of disability activities to education and vocational training, these can be addressed well within the context of a general CBR program. Leprosy programs should therefore aim at integration of the rehabilitation needs of people affected by leprosy into general CBR programmes. This is also called “mainstreaming” of leprosy rehabilitation.

Stigma and discrimination by Dr. Wim van Brakel. A major factor leading to social exclusion of people affected by leprosy is the stigma against leprosy found in most societies around the world. Stigma has major impact on psychosocial life of individuals, families and communities, it leads to violation of human rights, has strong negative consequences for public health programmes. Currently, there is no widely accepted intervention model or even a standard definition of stigma and a comprehensive, strategic approach to interventions is missing. In principle, many of the negative consequences of stigma can be addressed through CBR. There is also an indication that the empowerment that results from client-participation in CBR activities reduces stigma. However, the impact of such activities is often not measured and, as a consequence, the effectiveness of CBR in reducing stigma is not known.

Stigma measurement is usually fragmented and often condition-specific, e.g., only community attitudes to leprosy are assessed. This is partly because there is no generic set of instruments available for a comprehensive assessment of stigma.

In November 2004, the Royal Tropical Institute Leprosy Unit in the Netherlands organised an international research workshop on health-related stigma. Seventy researchers, experts and people affected by stigmatized conditions discussed their concepts, findings and experiences regarding stigma related to leprosy, HIV/AIDS, tuberculosis, Buruli Ulcer, mental illness, epilepsy and physical disability. A striking finding was that, despite marked differences in determinants of stigma, the experiences and consequences of stigma appeared very similar across different health conditions and cultures. Because of this, common conceptual frameworks, strategies for stigma reduction and stigma measurement tools appear feasible. A new consortium, the International Consortium for Research and Action Against health-related Stigma (ICRAAS), was launched to reduce health-related stigma and its harmful consequences, including discrimination and social exclusion.

The role of self help groups in community-based rehabilitation of people affected by leprosy by Ms. Jannine Ebenso.

In Nigeria, the planning cycle is used in the management of CBR programs.

Planning. Needs analysis. SHG can help them to analyse their own problems and brainstorm strategies. SHG can have an important role in identifying the real needs in a community. In Nigeria, we have been involved with groups in various communities. We have seen the value of sharing the local knowledge and personal experience of groups of people with disabilities (not all as a result of leprosy) in the planning process of our projects.
Implementation. Groups can decide the duration, standard, quality, and quantity etc of all aspects of the CBR project. Group members should be the prime movers, not outside “experts.”

Monitoring progress. Are we on track? Will we achieve this year’s objectives? Any minor amendments needed? Are resources sufficient / allocated wisely? Need re-allocating?

Evaluating impact. Have the aims and objectives been achieved?

The Gwada Community Development Association in Nigeria has built itself up over the last 3 years. Meeting monthly, the groups discuss and plan for their development. Even though most are affected by leprosy, there are also interested members of the community in the group. To date the group have planned prevention of disability activities including a successful eye care screening programs in an onchocerciasis endemic area by the eye team attached to the leprosy program and distribution of protective footwear to people with plantar anaesthesia. They also organized socio-economic rehabilitation activities like micro-credit schemes, where the members are responsible for setting up criteria and limits, deciding on the beneficiaries, monitoring repayments, tracing defaulters and setting interest rates.

Self-help groups can be review using the criteria presented by Cornielje, et al. (2000), which were developed for the evaluation of CBR projects.

(i) Restoration of quality of life. Self-care groups (SCG) in Ethiopia have seen benefits of their activities in terms of reduction of ulcers and improvement in the skin care of the hands and feet. Group members mentioned feelings of “belonging to a group,” improved self-respect and dignity and confidence to participate socially. In Nigeria, SCGs are just coming up, but the initial feedback is very encouraging, with neighbours and friends assisting one another in finding solutions to the problem of recurrent ulcers. Small cooperatives have developed that are concentrating on improving the socio-economic status of the group members. IDEA Nigeria was launched in December 2003. A National Committee has been formed and each state is being encouraged to form their own branches and committees. Already letters of introduction have gone to the Federal Government of Nigeria informing them about the needs of people affected by leprosy.

(ii) Locus of power. Effective empowerment requires that clients participate in all aspects of the process so that ownership is achieved and benefits are sustainable. Equality of access to local resources and services is a common objective. In many instances empowerment is realized through (in-)formal education, (vocational) training and paid employment, but it may equally take place through participation in self-help groups, community-based organizations and through processes of active participation in the development of co-operatives. A successful example of empowerment is the community development group in Kuta Village, Niger State, Nigeria. After they had voiced their needs and started to get organized, they managed to meet several of the main needs by themselves.

(iii) Involvement of others. Integrating previously stigmatized or excluded individuals in the community demands a level of community involvement, though this may vary from acknowledgement or mere tolerance through to active encouragement, participation and ownership. Community participation is seen as indispensable to empowerment since only through such participation social, economic and political changes will take place. These changes are imperative in the process of enabling people with disabilities to become integrated into mainstream society. CBR may be defined as a system that uses existing resources of manpower and material within the community to promote integration of disabled people in all spheres of life.

(iv) Range of activities. Often, the focus of rehabilitation is only on specific disabling conditions that require (specific forms of) rehabilitation, e.g. the improvement of locomotion through physical therapy, or the prevention of disabilities by making appropriate footwear available. In Nigeria, the Joint National Association of Disabled People (JNADP) is a self-help group for people with all manners of disability from many different of causes. People affected by leprosy are represented on the National Committee. At the JNADP annual meeting in May 2004, representa-
tives of the Federal Government of Nigeria were present. A national policy on rehabilitation of the disabled is being put in place. As people affected by leprosy were in attendance, their needs will also be taken into account. In Kebbi State, the people affected by leprosy have joined this group and have brought about an increase in the number of services offered by the rehabilitation services. Partnerships have been developed between government, NGOs and community associations as well as the group members and there is good collaboration and information and resource sharing in the three groups that are members so far.

(v) Benefits of small groups in CBR. They provide an opportunity to share experiences, develop new attitudes and acquire new life skills. They create a public voice for the rehabilitation process and encourage participation. They develop confidence as individuals “go public” about the impact of leprosy. They provide a powerful voice when confronting officialdom.

The Ethiopian National Association of Ex-Leprosy Patients (ENAELP) by Ms. Birke Nigatu.

The ENAELP is an association legally established by leprosy-affected persons to advocate their rights and create awareness in the society about leprosy, which is badly misunderstood and unnecessarily feared. In addition, the ENAELP is committed to socio-economic rehabilitation of its members to enable them to regain dignity and self-esteem. Currently, the association has 20,000 members in 54 local associations in the seven regions of Ethiopia. To achieve its objective, the ENAELP has been implementing awareness, advocacy and socio-economic rehabilitation projects, in partnership with national and international agencies.

The awareness and advocacy work of ENAELP ranges from publishing a bilingual annual magazine called the “Truth” to printing of posters, brochures and caps and radio broadcasting using the government media. Commemoration of World Leprosy Day, which was started by ENAELP in 2000, has been also an important event to advocate the rights of persons affected by leprosy. ENAELP also lobbies the government and all others concerned for equal participation and equal opportunities of persons affected by leprosy. So far the association has protected and averted the displacement of members from their settlements and it is doing its level best in advocating the availability of quality treatment and POD for affected persons. ENAELP is the founder and an active member of the Ethiopian Federation of Persons with Disabilities. ENAELP has a good relationship with the Ministries of Labour, Social Affairs and Health, who assist the association through a steering committee established together with the ENAELP.

Parallel to the awareness and advocacy work, ENAELP carries out socio-economic rehabilitation activities for its members. They belong to the most disadvantaged groups because of stigma and poverty. To speed up integration, it is essential to empower persons affected by leprosy socially and economically. This will demonstrate that they have the potential and the skill to be productive like any other citizen. To this end, ENAELP works with revolving fund schemes for members to enable them to engage in dignified income generating activities. The association also provides primary and higher education opportunities for children of members, empowering families to break the cycle of stigma and accompanied poverty. With the same aim, ENAELP organises self-help groups for women affected by leprosy, providing training in handcraft production. So far, these strategies have proved very successful.

A Key to success in CBR: Designing an appropriate program using a participatory approach by Dr. Denis Byomungu.

There are many who are in need of rehabilitation. There are many patterns of CBR conducted in Africa. There is an urgent need to evaluate CBR programs in order to identify the most effective CBR approach. This paper reports lessons learnt by The Leprosy Mission in the DR Congo in designing a CBR program using a participatory approach.

The following questions were asked:
(i) What is the community? People affected by leprosy vs. all community: in DRC rural areas: community in a defined area and in urban areas: members of self-help group.
(ii) How does the community participate? All the community, through representatives or beneficiaries: Rural areas: through rehabilitation committee members and in urban: through members of self-help group.

(iii) Expected level of participation: full community-led vs. provision of services within the community: The programs in DRC was community-led with some guidance.

(iv) Beneficiaries: People physically disabled by leprosy vs. community affected by leprosy, other disabled in or excluded. In DRC, people with leprosy-related disability and their household and people with other disability were considered (up to 15% of the budget).

(v) Depth of outreach: how to deal with the poorest (destitute), ignore there special needs vs. welfare: Targeting the helper (usually family member), breaking the cycle of poverty through scholarship combined with income generating activities, assisting the community to care for their poor through communal projects and using services from other organizations caring for the poor.

(vi) Meaning of rehabilitation: welfare vs. development: micro-credit schemes, community awareness and advocacy work.

(viii) Program against stigma: community awareness and advocacy.

(ix) End point of rehabilitation: approximately 3 years or 3 loan cycles.

(x) Long term goals: Client: Re-insertion, respected role, self-esteem, earning and supporting the family, personal learning and development. Community: CBR and Community Development and Project: Sustainability through Revolving Loan.

Conclusion. For sustainable transformation to happen, we need to see in our projects the principles described in an old Chinese poem on community development: “Not a showcase, but a pattern; Not odds and ends but a system and Not relief but release.” This starts by designing an appropriate CBR program with full participation of all stakeholders, including beneficiaries and communities where they live.

Issues related to integration of rehabilitation activities related to leprosy in CBR programs by Sunil Deepak, Jayanth Kumar, and M.V. Jose

The progressive integration of vertical leprosy control programs into primary health care services, has been accompanied with calls for integration of rehabilitation activities related to leprosy affected persons in community-based rehabilitation (CBR) programmes. Keeping this in mind, during the last twelve years, AIFO/Italy through its partner organization AIFO/India has organized a series of workshops and training courses in India to promote the conversion of vertical leprosy control programs in CBR programmes and integration of persons with leprosy-related disabilities in these CBR programmes. At the same time, CBR projects targeting all people with disability, including persons with leprosy-related disabilities, were initiated.

Recently a participatory evaluation exercise was carried out in three AIFO-supported CBR projects in Karnataka state of India: SRMAB project in four sub-districts of Mandya district; MOB project in three sub-districts of Mandya district; and AMSK project in Bhalki sub-district of Bidar district. This evaluation, carried out through focus group discussions, looked at two specific aspects.

Integration of persons with leprosy-related disabilities in CBR activities. CBR projects have many components including medical, educational, social, etc. Integration of leprosy-affected persons in CBR was evaluated mainly by looking at their participation in heterogeneous self-help groups (SHG). Implications for change in role from vertical leprosy workers to CBR workers: the feelings of ex-leprosy workers, who were now working as CBR workers, need to be carefully considered.

Regarding inclusion of leprosy affected persons in SHGs, the discussions brought up the following issues:

(i) CBR workers, people with disability and leprosy-affected persons all agree that integration of persons with leprosy disabilities in SHGs is problematic and requires proper planning and follow-up.

(ii) Persons with more visible deformities face more problems.

(iii) Self-stigma or perceived stigma among leprosy-affected persons, their fear that they will not be accepted, is a big obstacle.
(iv) Other disabled persons may express negative feelings about integration of leprosy-affected persons, but usually this obstacle can be overcome through awareness and discussions.

(v) The integration was gradual over a period of many years – examples of leprosy-affected persons active in a SHG stimulate more persons to join.

- Regarding the feelings of ex-leprosy workers, the discussions showed that the change of role from leprosy worker to CBR worker is perceived as a big problem, especially by persons with long-standing experience as leprosy workers. Some of the issues that came out included:
  (i) Higher workload: “before we just distributed drugs and explained a few things, now the work is never over…”
  (ii) Loss of expertise: “before we had clear cut competence, now we have to facilitate but problems are more difficult to solve…”
  (iii) Closer contact with persons and their families by home visits: “earlier, people had to come to the ambulance, now we have to go to homes…”

For these reasons, for contemplating any change in (vertical) leprosy programs to start CBR activities, the ex-leprosy workers made the following recommendations:
- The role-change of the health workers from prescriber to facilitator is a key issue and needs to be tackled by sufficient planning and discussions.
- Workers need support in the transition period through training, dialogue, sharing of experiences and opportunities to talk about problems.
- Change must be planned and gradual.

In conclusion, integration of leprosy-related rehabilitation services and CBR is feasible and it improves the sustainability of the project activities. The CBR approach has a great deal to offer for integration and rehabilitation of leprosy-affected persons. However, both these aspects require careful planning, preparation, support and training and a gradual implementation process.

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Ms. Birke Nigatu
Dr. Denis Byamungu
Dr. Sunil Deepak

Symposium on
PREVENTION OF BLINDNESS IN LEPROSY
IN AFRICA

The problem of eye involvement as a cause of disability in leprosy is well recognized. Of often, however, the focus is on the unique pathology, rather than the significant impact on the stigma associated with leprosy and on the quality of life of people affected by leprosy. Lagophthalmos, besides being a condition that is potentially blinding, is also disfiguring and disabling, perpetuating the stigma associated with leprosy. Vision loss, whether due to cataract or corneal disease secondary to lagophthalmos, significantly decreases quality of life. As life expectancy is increasing worldwide, the prevalence of visual impairment and blindness, associated with aging, is also increasing. For these reasons we must continue to address the problem of eye disease in leprosy in Africa.

Recently, the primary shift in the discussion of ocular leprosy has been from the clinical conditions found in patients affected by leprosy to a discussion of the best approaches to integrating eye care and leprosy control activities to increase awareness, access to, and acceptance of eye care services by people with leprosy. In Africa it is recognized that there are deficits in the number of eye care professionals; in some countries there are fewer than one ophthalmologist per one million population. Consequently, it should be recognized that access to and the quality of service delivery received by leprosy patients will only be as good as that
which is available to the general population. Nevertheless, with the recent launch of the VISION 2020 Initiative to achieve elimination of avoidable blindness by the year 2020 there have been significant improvements in planning for eye care delivery in Africa. Clearly, blindness cannot be eliminated; the initiative focuses on those causes of blindness that either can be prevented (e.g., trachoma, onchocerciasis) or cured (e.g., cataract). By putting systems into place in Africa it is hoped that utilisation of services such as cataract surgery can be high enough in a defined population that no one becomes blind due to cataract. It is critical that leprosy patients be integrated into these national and district VISION 2020 programmes to ensure that avoidable blindness is eliminated in leprosy patients at the same level as in the general population.

Burden of potentially blinding eye disease in leprosy patients in Africa. Findings from the Longitudinal Study of Ocular Leprosy (LOSOL) has indicated that approximately 11% of newly diagnosed MB patients will have potentially blinding ocular pathology at the time of their disease diagnosis. Findings suggest that there is little difference in the prevalence of ocular pathology between different countries, once age and other demographic factors are controlled for in the analysis. Older patients have a considerably higher risk of having eye disease, probably due to a wide-range of reasons, than younger patients at the time of their disease diagnosis.

Work carried out among Tanzanian patients currently on M.D.T. (n = 371), sampled from regions listed as endemic, suggest that 13.5% have some form of leprosy related ocular disease and that 9.4% have potentially blinding pathology. Blindness (<6/60 in the better eye) was recognized in 6% of the study population. Similar to the LOSOL study, old age was associated with potentially blinding pathology, as was the duration between recognition of clinical signs (by the patient) and enrollment in M.D.T. Cataract was the leading cause of vision loss and few of the patients had sought eye care services. Separately, a study carried out in Nigerian leprosy villages demonstrated a three-fold higher prevalence of potentially blinding pathology and a three-fold higher prevalence of blindness (17.9%). In both settings it was noted that these patients were not part of any routine, integrated eye care service.

Guidelines for the management of eye disease in leprosy and for integrating leprosy patients into general eye care services. In 2001 ILEP sponsored a workshop of leprosy control program managers, ophthalmologists, epidemiologists, and others to develop guidelines for the management of eye disease in leprosy and on integration of leprosy patients into general eye care services. Key components of these guidelines include:

(i) Creating a strong collaborative relationship between the national leprosy control program and the national prevention of blindness committee.

(ii) Establishment of 4 key signs to be detected at the time of leprosy diagnosis to guide eye care management and disability prevention. At the time of leprosy diagnosis all patients should be examined for lagophthalmos (any gap in mild closure), visual acuity, the red eye, and presence of a facial patch. All people with lagophthalmos, decreased vision (<6/18), persistent red eye (2+ weeks in duration), and/or a facial patch in reaction should be referred by the basic health worker to a higher level for clinical evaluation, or as per guidelines in the national leprosy control and prevention of blindness programs. It is estimated that approximately 20% of newly diagnosed leprosy patients will require referral to a supervisor or an eye care professional.

(iii) Steps to be taken at the time of discharge from anti-leprosy treatment At the end of anti-leprosy treatment all patients must be educated regarding the risk of eye disease and informed that they should return for examination if they develop lagophthalmos, diminished vision, a red eye, or a facial patch in reaction. Explicit instructions regarding referral must be given to each discharged patient. All patients with lagophthalmos should receive continued periodic follow-up.

(iv) Suggested revisions to the current W.H.O. disability grading system for eye disabilities (see below).

(v) Strong encouragement to provide cataract surgery with implantation of an intraocular lens, when feasible.

(vi) Adoption of different procedures,
other than simple tarsorrhaphy, for the correction of lagophthalmos.

These guidelines serve as a basis for the integration of leprosy patients into the general eye care infrastructure in leprosy endemic countries. Nevertheless, it is recognized that a failure to operationalize the guidelines will lead to the continued poor access to eye care services and continued stigma, poor quality of life, and blindness in leprosy.

Disability grading of the eye in leprosy. Recent research carried out in Tanzania showed significant discordance in the grading of eye disability when done by an eye care professional compared to an integrated health worker (IHW). IHWs recognized 3 people with grade 2 disability while the eye care professional recognized 13 people; similarly the IHW recognized 8 people with grade 1 disability while the eye care professional recognized 60. Improved training could assist with assessment of lagophthalmos and testing of vision, however, without significant efforts and training and provision of instruments, IHW are not going to be able to assess iridocyclitis and corneal opacities. The current disability grading system for the eyes is impractical for most programmes. Accordingly, it is recommended that visual acuity (either visual impairment [visual acuity <6/18] or blindness [visual acuity <6/60], depending upon the setting) and lagophthalmos should become the primary indicators for monitoring disability (grade 2) and that corneal hypoesthesia, corneal opacities, and uveitis should be removed from the leprosy disability-grading scheme.

Lagophthalmos surgery. Lagophthalmos surgery should be provided to patients who need it. Evaluation of the need for lagophthalmos surgery should be based on one or more of the following conditions: size of lid gap, corneal exposure, corneal hypoesthesia, visual acuity, and/or cosmetic difficulties. Research in Egypt (over 300 surgeries) has shown that the modified lateral tarsal strip procedure had excellent success; over 80% showed a reduction of lid gap of more than 3 millimeters and complete lid closure was achieved in 50% of eyes. Lid closure was associated with lagophthalmos; the longer the duration the less degree of closure. Less closure was also found in patients with severe lagophthalmos and of an older age. The advantages of the modified lateral tarsal strip procedure were that it was simple, could be carried out in one stage (yet, repeated later, if necessary), it does not require long term follow up or physiotherapy, corrects ectropion and entropion, is cost-effective, and has a cosmetically appealing result. The “Prevention of Blindness” manual will have a section on this procedure. Simple tarsorrhaphy should be discontinued, expect in emergency cases. There are many barriers that prevent patients from accepting lagophthalmos surgery, one of which is the poor cosmetic result of tarsorrhaphy. With the adoption of better surgical techniques, programmes need to be developed to increase the uptake of lagophthalmos surgery.

Cataract and cataract surgery. Cataract related vision loss is higher in leprosy patients than in the general (age-matched) population. Cataract is the leading cause of blindness in leprosy affected persons and many do not have access to general eye care services. Experience in Nigeria has shown that the cataract surgical coverage (% of people receiving surgery among those who need surgery) is generally quite low in leprosy patients. Many patients had opted to have couching performed by itinerant traditional healers; outcomes of this procedure (using a thorn to puncture the cornea and dislodge the lens to the back of the eye) are very poor. The barriers to use of service noted in Nigeria, a similar throughout Africa fall under the headings of awareness (of the service, of where to go, of the expected outcome), access (high cost of surgery, inadequate transportation network), and acceptance (fear of poor outcome, fear of discrimination by hospital staff, and social support in the family). Improving uptake of surgery requires that surgical management should be carried out in base hospitals rather than as an outreach activity in order to assure high quality of surgery and to manage any surgical complications. This will also, with time, reduce the stigmatization of leprosy. Similar to the general population, in which “bridging strategies” are successful in increasing access to surgical services leprosy patients need to be brought to the base hos-
Hospital for surgery. Clear policies regarding subsidies for surgery need to be developed and implemented.

Surgical experience from both Asia and Africa has shown that leprosy patients, even with complicated cataract, can generally benefit from implantation of an intracocular lens. There is no evidence to suggest that post-operative inflammation is more common in patients with a history of chronic uveitis. Not implanting an intracocular lens will, in most cases, result in a patient that is still blind.

Integration of leprosy patients into VISION 2020 at the national and district level in Africa. Integration of leprosy patients into general eye care services can best be accomplished through the development and implementation of national and district VISION 2020 plans. There are a number of steps recommended to achieve integration.

(i) Assessment of needs and capacities. Evidence in Africa would suggest that approximately 10% of newly diagnosed leprosy patients and three times this number of leprosy settlement patients have potentially blinding pathology. These figures can be used to calculate the needs in most African settings. Assessment of capacity for eye care should include listing of ophthalmologists and cataract surgeons by region and compilation of information on routinely used referral practices, in particular the use of “bridging strategies” to identify and get patients to hospital. Skills of integrated health workers in the 4 key signs of ocular leprosy and the skills of eye care providers in lateral tarsal strip procedure for lagophthalmos and implantation of IOL for cataract surgery should also be determined.

(ii) Establishing a national strategy and national policies. Most every African country has a national prevention of blindness committee (NPBC), comprising the Ministry of Health, NGOs, service groups, and others. The Leprosy Control programme and the NPBC should meet and review the needs assessment and capacities in the country. Together the two should develop strategies for integrating leprosy patients into general eye care services in the country. Policy decisions regarding such issues as the cost of cataract surgery for leprosy patients and the potential for subsidy and waivers should be determined.

(iii) Clearly defining the training needs required for integrated health workers, supervisory personnel, and the referral eye care providers. It is anticipated that integrated health workers will need to upgrade training. Also, supervisory personnel, and eye care workers (ophthalmic clinical officers, cataract surgeons, and ophthalmologists) will likely require some upgrade training regarding lagophthalmos surgery. Training should also cover procedures for monitoring uptake of eye care services (primarily cataract and lagophthalmos services), and the outcome of services received.

(iv) Implementing integration at the VISION 2020 planning level. VISION 2020 implementation planning occurs at the district level; a district being defined as having a catchment population of between 1 and 2 million people. At this level there is expected to be at least one ophthalmologist or cataract surgeon and a team supporting these individuals. Each district should have a VISION 2020 Task Force. The district leprosy control officer should meet with the Task Force to plan out and implement the integration strategy. The aim is to integrate leprosy patients into the routine system for service delivery, eliminating the need for special structures and personnel for leprosy patients.

(v) Program monitoring. Monitoring should be built into the district VISION 2020 plan whereby the district leprosy control officer can verify eye care coverage and outcome of services.

Strategic planning and implementation are critical tools for leprosy control and prevention of blindness to ensure that persons affected by leprosy are fully integrated into general eye care services in Africa. By doing so it is possible to eliminate avoidable blindness by the year 2020.

Prepared by: Paul Courtright (1), Swapan Samanta (2), Essam el Toukhy (3), Hemed Kilima (4), Caleb Mpyet (5), and Muthiah Arockia Rajan (6)

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References

NEWS and NOTES

Damien-Dutton Award

The 2004 Damien-Dutton Award was presented to Dr. Michael F. R. Waters, OBE, FRC P, by Trevor Durston of the Leprosy Mission International of London and Dr. Wayne Myers of the American Leprosy Mission, at a ceremony held in London, England on Tuesday, November 30, 2004. Dr. Waters has a wide knowledge and experience on leprosy and is well known for his demonstrations and lectures. He served from 1959 to 1976 as the Director of Leprosy Research in Malaysia. He has published numerous papers on leprosy and its treatment. His ability to communicate with enthusiasm and lucidity to non-medical workers has earned him the praise of many throughout the world. He received numerous honors throughout his lifetime.

Dr. Waters wrote, “I am both very honored and humbled by the kindness of the Damien-Dutton Society on being named as the recipient of the Damien-Dutton Award for 2004. Although the leprosy world has changed drastically since I first started my work in 1959, we all continue to pray that the love and compassion of Christ may continue to be shown to all of those suffering from leprosy just as it was shown so remarkably by Father Damien.”

Photo: Dr. Waters (right) and Dr. Meyers
**Notice.** *From Carville, U.S.A.*, Ceremonies were held on Feb. 12, 2005, to mark the departure of the Daughters of Charity from their service to the National Hansen’s Disease Hospital at Carville, L.A. Sr. Marie ThJrPse Sedgwick, Provincial, West Central Province, St. Louis, presided over the ceremonies, describing Carville as “a place of miracles.” Appreciation was also expressed by Bishop Robert Muench, Diocese of Baton Rouge, Capt. Charles Stanley, Director, National Hansen’s Disease Programs, and Colonel Herbert Oliver on behalf of Louisiana Gov. Katherine Blanco. Beginning in 1896, 116 Sisters of the Daughters of Charity have served at Carville in 109 years of continuous service. The NHDP continues to provide care to new and previously diagnosed patients from its facilities in Baton Rouge, and several patients who are retired but able to live independently still reside at Carville.

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<td>28–30 Jul-05</td>
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<td>Sheraton Hotel, Seattle, USA</td>
<td>US-Japan Cooperative Medical Science Program Tuberculosis/Leprosy Panel</td>
<td>Gail G. Jacobs, Program Officer NIAID/NIH</td>
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<td>12–30 Sep-05</td>
<td>ALERT, Addis Abbaba, Ethiopia</td>
<td>Clinical leprosy &amp; tropical dermatology for Physicians</td>
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<td>7–16 Nov–Dec 05</td>
<td>ALERT, Addis Abbaba, Ethiopia</td>
<td>Clinical leprosy and management of combined leprosy, tuberculosis, and HIV/AIDS control programmes for senior field staff</td>
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<td>Joao Pessoa</td>
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*Le Secours aux Lépreux (Canada), 1275 Rue Hodge Bureau 12, Montreal H4N 3H4, Canada

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*Pacific Leprosy Foundation, 115 Sherborne Street, Bag 4730, Christchurch, New Zealand.