**Dissociation between allergy and immunity in mycobacterial infections**

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Received for publication 30 April 1982

**Summary** The relationship between delayed hypersensitivity and granulomatous hypersensitivity to host resistance in mycobacterial infections has been discussed. The grounds for a dissociation between allergic reactions and resistance to infections is reviewed firstly in tuberculosis and then in leprosy. Evidence from clinical observations is compared with data from animal experiments, particularly in mice infected with *Mycobacterium leprae*. Further comparison is made of the use of sonicated bacterial extracts versus autoclaved whole organisms. The relevance of this discussion to the assessment of the efficacy of the various ‘leprosy vaccines’, now being tested, is considered.

**Introduction**

Since the development of tuberculin and its introduction as a skin testing reagent, there has been considerable controversy as to the role of allergic or hypersensitivity reactions in acquired resistance in mycobacterial infections. Thirty years ago this was reviewed extensively by Rich, who identified the earliest work on this subject. In this study it was shown that hypersensitivity produced markedly destructive effects in the tissues and this was related to the level of organisms present. The hypothesis was therefore put forward that acquired resistance in tuberculosis is effected by the accelerated inflammatory reaction caused by local hypersensitivity. The basis of this view was that inflammation is a known protective mechanism in bacterial infections. Inflammation can wall off and prevent the spread of bacteria. In addition, inflammatory exudates are usually strongly bactericidal. Hypersensitivity reactions are among the strongest causes of local inflammation. This view was strengthened by the statement that hypersensitivity as shown by the tuberculin reaction parallels immunity so closely that they must represent...
manifestations of the same phenomenon. Experimentally, guinea-pigs infected with *M. tuberculosis* develop acquired resistance and tuberculin sensitivity in parallel. Neither can be transferred passively with serum, but both can be transferred with lymphoid cell suspensions. Both are therefore manifestations of cell-mediated immunity produced by T-lymphocyte-antigen interaction resulting in the release of lymphokines and macrophage activation. This mechanism of resistance is important as mycobacteria are facultative intracellular parasites capable of multiplying within macrophages, as are other bacteria such as *Listeria* and *Brucella* and ce

This view was questioned, re-ennunciated and questioned again in the case of tuberculosis. However, it is now important to question the subject again as this view has arisen once more in connection with current work on the production of a leprosy vaccine. It is important that the evidence for parallelism between skin hypersensitivity and host resistance be studied as closely in this infection as in tuberculosis.

Delayed hypersensitivity and cell-mediated immunity in tuberculosis

Delayed hypersensitivity reactions in the skin are erythematous indurated reactions reaching maximum intensity 24–72 h after contact with antigenic material. Two types of delayed hypersensitivity reactions may be observed; the tuberculin-type reaction and the Jones–Mote type of reaction. In the tuberculin reaction the skin reaction persists for up to 96 h, and is highly indurated. The Jones–Mote reaction may be observed maximally only 24 h after skin test. Jones–Mote reactions are highly regulated by suppressor cells and are characterized by large numbers of basophils in a subepidermal position as a result of which they are often referred to as cutaneous basophil hypersensitivity (CBH) reactions. Both these reactions have been shown to be T-lymphocyte mediated reactions. A number of other phenomena have been shown to be similarly T-cell mediated. These include contact sensitivity, skin allograft rejection, organ specific autoimmune processes, tumour immunity, granuloma formation and cellular immunity. Two *in vitro* tests for cell-mediated immunity were introduced. These are the lymphocyte transformation test (LTT) and the leucocyte migration inhibition test (LMIT). All these phenomena have been grouped under the heading cell-mediated immunity (CMI). It therefore appeared natural to consider that they measure the same biological reaction. Numerous attempts have been made to correlate delayed hypersensitivity reactions, LTT and LMIT, both with each other and resistance to infection. One such study in the field of tuberculosis defines three types of skin test reactions to tuberculin: (a) typical Mantoux reaction; (b) Jones–Mote hypersensitivity; (c) mixed reaction.

Patients with localized lesions and a prompt response to chemotherapy
showed typical Mantoux reactions and consistently positive results in the LMIT. Patients with chronic disease with surrounding fibrosis showed Jones–Mote or mixed reactions and negative LMIT. Patients with rapidly disseminating lesions showed absent skin reactions and LMIT.

However it is stated\textsuperscript{2} that a high degree of hypersensitivity may be associated either with rapidly progressive tuberculosis or with lesions that are being successfully resisted: and a low degree of hypersensitivity is compatible either with lesions that are being well resisted or with devastating ones.

The dissociation between allergy and immunity in tuberculosis in man has also been highlighted in the results of the Medical Research Council trial of tuberculosis vaccine.\textsuperscript{7} In this study there was no correlation between tuberculin sensitivity and protection from tuberculosis in subjects immunized with BCG vaccine. Moreover, one of the sub-strains of the vole bacillus \textit{M. microti} conferred good protection against tuberculosis and poor levels of post-vaccination tuberculin sensitivity.

In a classical study in the guinea-pig, Rothschild \textit{et al.}\textsuperscript{8} in Rich's laboratory, showed that immunized hypersensitive guinea-pigs could be desensitized with tuberculin so that they no longer reacted hypersensitively with accelerated and exaggerated inflammation and necrosis to the local injection of large amounts of virulent tubercle bacilli or tuberculin. These desensitized guinea-pigs remained as highly resistant to the proliferation and invasion of the bacilli as were the normal immunized hypersensitive controls. These studies were confirmed in a large number of centres in subsequent years.\textsuperscript{2} The converse was shown\textsuperscript{9} by injecting guinea-pigs with tuberculoprotein and Wax D, so that they became highly tuberculin sensitive but showed no increased resistance to infection. Similar experiments were performed\textsuperscript{10} which produced tuberculin sensitivity in guinea-pigs with an extract of BCG. This hypersensitivity was not accompanied by any increase in resistance when the animals were challenged aerogenically with small numbers of virulent tubercle bacilli. A further dissociation between resistance to infection and hypersensitivity in tuberculosis\textsuperscript{11} was demonstrated in inbred guinea-pigs. It was shown that the strain which showed the most marked hypersensitivity reactions following infection was that which showed the least resistance. In a study\textsuperscript{12} of the resistance of inbred rabbits the conclusion that tuberculin reactivity bore no relation to resistance was reached.

Despite the demonstration, in man, that allergic reactions may not result in immunity, there is the observation that immunity and delayed hypersensitivity develop at the same time in experimental animals. This was shown convincingly for tuberculosis in rabbits\textsuperscript{13} and for \textit{Listeria} infections in mice,\textsuperscript{14} and led to the view that immunity to tuberculosis was just another manifestation of tuberculin hypersensitivity in which one stable immunogen was involved that was present in killed as well as viable attenuated mycobacteria. It was implied, moreover, that viable mycobacteria immunized better than
dead organisms because of their ability to multiply in vivo. This produced more antigen and a more sustained immune response. This view, which held considerable attention, was challenged in a series of studies by Youmans and Youmans. These workers were able to prepare a highly immunogenic fraction from attenuated *M. tuberculosis* H37Ra by disrupting the cells carefully in the cold. Fractionation of the material revealed that the antigen which would confer protection to mice was in a preparation that contained RNA precipitated by ethanol from a ribosomal fraction. No DNA or polysaccharide could be detected but there were significant amounts of protein. Despite producing immunity, neither the bacterial ribosomal fraction nor the RNA produced tuberculin hypersensitivity. Thus immunity to tuberculous infection and tuberculin hypersensitivity would appear to be separate responses of the host to different components of the bacterial cell. Both are mediated by a specific T-lymphocyte response and probably involve macrophage activation. However, as different antigens are involved, the responses can be dissociated although more frequently they run in parallel. It is likely that the granulomatous response is a manifestation of the response to the antigen which produces the allergic reaction, rather than being associated with the basic mechanism involved in host resistance to infection.

**Leprosy and Related Animal Models**

Various preparations have been used to assess skin reactivity in man to *M. leprae*. The most frequently used is a preparation of autoclaved whole organism – Mitsuda lepromin. Another reagent commonly used is Dharmendra lepromin in which the organisms are treated with chloroform and ether to remove lipids. A third is a sonicated preparation known as leprosin. Lepromin reactions occur in two phases; there is an early delayed hypersensitivity reaction read at 24 and 48 h and a later nodular reaction read at 3 weeks. Leprosin reactions are generally read at 48 h. All these reagents may be derived from human skin containing *M. leprae* or from infected armadillo tissue. Reagents are best standardized by a bacillary count of the starting material and reagents containing material from $10^7$ organisms/ml give the best results for the Dharmendra antigen. The presence of intact bacilli in the reagent, whether Mitsuda or Dharmendra, is necessary for the development of the late nodular component. Soluble or ultrasonicated reagents produced enhanced 24–48 h reactions and poor late 3-week Mitsuda reactions. It has been found that the late 3-week nodular reaction was the best correlate of the clinical status of the individual tested. Patients with lepromatous leprosy (LL) in which there is a specific defect in host resistance to *M. leprae* are inevitably Mitsuda negative, that is they are unable to manifest 3-week nodular reactions, whereas patients at the tuberculoid pole (TT-polar tuberculoid or BT borderline
tuberculoid) who show a high host resistance to the organism are usually Mitsuda positive. The histology of the 3-week Mitsuda reaction is that of a typical epithelioid cell granuloma, very similar to the lesions in the skin found in TT and BT leprosy. In addition to the lepromin test, cell-mediated immunity may be assessed by the lymphocyte transformation test (LTT) and the leucocyte migration inhibition test (LMIT). Impaired host resistance to *M. leprae* at the lepromatous pole is associated with a failure of cell-mediated immune response in the LTT and LMIT to specific *M. leprae* antigens as well as a negative Mitsuda reaction.

It has been found\(^{18}\) that circulating lymphocytes from patients with lepromatous leprosy failed to be transformed *in vitro* by whole *M. leprae* in the LTT. There was a similar failure of *M. leprae* to produce a positive LMIT. This defect decreased across the leprosy spectrum. Patients at the tuberculoid end showed strong reactivity in both these tests. Although LL lymphocytes could not be transformed by *M. leprae* in many cases they could be transformed by BCG. Although this indicated a strong correlation between the LTT with specific antigen and host resistance, it has been suggested\(^{19}\) that the correlation was not necessarily with the ability of the host to eliminate the infecting organism, but with the strength of the allergic reaction shown by the patient. LTT tests were frequently stronger in actively inflamed BT than in TT. In patients with BT leprosy with silent skin lesions there were fairly low LTT responses. Similarly, BL patients with inflamed lesions will react quite strongly in the LTT, and the response may be stronger than in BT patients in whom there is no evidence of inflammation. These observations indicated that the LTT response was related to the state of hypersensitivity of the patient rather than to his resistance to infection. Moreover, the response in the lymphocyte transformation test may vary depending on the nature of the antigenic preparation.\(^{20}\) Borderline patients with active nerve damage may show a stronger response using sonicated antigen rather than whole bacilli. Patients with predominantly cutaneous lesions, however, react better with whole bacilli than with sonicated preparations.

It is extremely difficult to compare allergic reactions with host resistance to *M. leprae* in experimental models. The limited growth of *M. leprae* in conventional experimental animals precludes such an approach despite the fact that *M. leprae* induces a strong state of delayed hypersensitivity in guinea-pigs. However, comparison of infection with *M. lepraemurium* in high resistance and low resistance strains of mice provides a useful model for comparing such reactions.\(^{21}\) In these studies C57Bl and BALB/c mice were infected subcutaneously with *M. lepraemurium*. C57Bl mice are a high resistance in that they are able to limit local multiplication of the organism, whereas BALB/c mice are a low resistance strain in which there is rapid multiplication of the organism and centrifugal spread to the draining lymph node. In spite of this difference in local immunity the delayed allergic response induced in
the contralateral footpad and the *in vitro* proliferative response of draining lymph node cells to sonicated organisms, were similar in the two strains of mice.

The footpad injection of autoclaved whole *M. leprae*um*urium* into infected C57Bl mice gave a prolonged footpad reaction lasting for 4 weeks. This reaction, which could not be elicited in infected BALB/c mice, was considered to be analogous to the Mitsuda reaction in man and showed infiltration with cells of the mononuclear-phagocyte series as well as lymphocytes.

C57Bl and BALB/c mice were also infected with BCG vaccine. Both strains were equally resistant to the organisms. Footpad testing with sonicated BCG produced a Jones–Mote type of reaction (transient at 24 h) in BALB/c mice and a tuberculin type of reaction (persisting up to 72 h and beyond) in C57Bl mice during the first 21 days after infection. There was no relationship between the antigen specific lymphocyte transformation test using draining lymph node cells and the footpad reaction. It would also appear that the nature of the delayed hypersensitivity test bore little relation to host resistance in this model.

Certain conclusions can therefore be drawn from these studies. Firstly, that delayed hypersensitivity reactions to sonicated mycobacterial preparations may bear little relation to the lymphocyte response to specific antigen *in vitro*. Secondly, these reactions do not appear to be a good monitor of host resistance to mycobacteria during the development of infection in inbred strains of mice. A Mitsuda-type of reaction to autoclaved whole mycobacteria would appear to be a better test and shows strong parallelism with host resistance. However, even this is only a true measure of granulomatous hypersensitivity and there is no evidence that it is a real reflection of host resistance.

**Skin reactions and in vitro Tests to Assess the Efficacy of Leprosy Vaccines**

There are a number of preparations that have been or are about to be tested for use as a leprosy vaccine. These include the use of Cobalt irradiated or autoclaved *M. leprae* with or without the addition of BCG vaccine (and in IMMLEP trials), the ICRC bacillus from Bombay and Mycobacterium W from Delhi (P. Talwar, personal communication). A full trial of a vaccine for increasing host resistance against *M. leprae* in a particular population takes many years to perform. There is therefore pressure to use these vaccines for immunotherapy in lepromatous patients, particularly those with DDS resistance. It is tempting to look for a simple skin test or an *in vitro* test that would indicate that an individual has regained host resistance. One should therefore ask whether the development of a positive allergic skin test reaction is a true monitor of increased host resistance. There is no doubt that positive delayed hypersensitivity or lymphocyte transformation tests with sonicated
mycobacteria are no more than reflections of allergic reactivity and need bear no relation to host resistance as has been shown in the mouse models. The main question is what is the significance of a positive granulomatous reaction of the Mitsuda type. There is no doubt again that this is a true allergic reaction, no different from the type of epithelioid cell granuloma produced by metals such as beryllium and zirconium, where there is no question of a relation to host resistance. The animal model shows a strong link with high host resistance, but can a positive granulomatous hypersensitivity response exist in the absence of an increase in host resistance? In the clinical situation can one find cases of a movement across the hypersensitivity spectrum of leprosy towards the tuberculoid pole while the patient remains highly bacilliferous? Can one have a reversal reaction without an increase in host resistance? A rare clinical picture of Lazarine leprosy is described in which borderline patients develop a tuberculoid clinical picture, but remain a pronounced bacillary population. In this reaction the prognosis as far as nerve involvement is concerned, is poor, as many nerve trunks may be involved and pronounced paralysis may supervene. Thus, there is a risk that the development of a positive Mitsuda reaction in vaccinated leprosy patients might herald the onset of a far more severe neuritis than that seen in the reversal reactions following sulphone therapy.

References

1 Koch R. Weitere Mittheilungen über ein Heilmittel gegen Tuberkulose. Deutsch med Wschr, 1890; 16: 1029–32.


The demonstration of two types of suppressor mechanism in leprosy patients and their contacts by quadruple skin-testing with mycobacterial reagent mixtures

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Received for publication 22 June 1982

Summary A previous study in Nepal involving skin-testing simultaneously with four different mycobacterial reagents (three of them mixtures) revealed that the addition, in the same skin-test site, of pooled reagents from fast-growing mycobacteria locally suppressed the response to pooled slow-growers. This finding has been confirmed in Bombay. It has also been shown that the addition of reagents prepared from certain fast-growing species to that prepared from slow-growers in one skin-test site will suppress the response to the same slow-grower reagent injected alone in the other arm. This type of suppression probably requires recognition of species-specific antigens of the fast-growing species concerned. The importance of the observations in relation to leprosy and possible mechanisms underlying them are discussed.

Introduction

In a preliminary investigation of responsiveness to shared and species-specific mycobacterial antigens carried out in a Nepalese leprosy hospital it was shown that patients had a markedly reduced response to both groups i and ii antigens as defined previously. It was also demonstrated that a proportion of people exhibited suppression of their responses to the group iv antigens of slowly growing species when injected as a mixture with the antigens of rapidly growing species. This suppression appeared to be specifically triggered by the group iv antigens of some of the rapidly growing species.
The present study employs three of the skin-test reagents used in the preliminary work, together with a variable fourth reagent as described below. The purposes of this study were to determine whether the suppressor phenomenon found in Nepal was present in Bombay and to discover which of the rapidly growing species induced it.

Materials and methods

One hundred and ninety people were studied, including leprosy patients and healthy persons living in Bombay in the Kopri leprosy colony. Thirty-eight of the 190 had received BCG, although this made no appreciable difference to the results.

Each person received 4 simultaneous intradermal tests of 0.1 ml volume containing 0.2 μg protein, two on each forearm. Tests were read at 72 h and recorded as the mean of two diameters of the area of induration. Reactions of 2 mm or more were taken as positive.3

The following reagents were tested on every individual:

1. A pool of equal volumes of sonicate preparations of 12 different slowly growing mycobacteria, each at a concentration of 1 mg protein/ml (reagent SG).
2. A similar pool of 12 preparations of rapidly growing mycobacteria (reagent FG).
3. An equal mixture of the above two reagents (reagent F/S).

These three reagents, which were the same as those used in the preliminary study, were diluted with a tween containing borate buffer (pH 8.0) to 2 μg protein/ml for use.

At the fourth test site, 10 different reagents were tested, each on groups of approximately 20 people. These reagents consisted of equal volumes of reagent SG at 2 μg protein/ml and one of the following reagents also at 2 μg protein/ml.

- Chitin
- Diernhofner
- Duvalin
- Flavescin
- Gilvin
- Neoaurnin
- Nonchromogenicin R507R
- Ranin
- Rhodesin
- Vaccin R887R

These are the constituents of FG, which contained in addition the duplicate preparations of Nonchromogenicin (R812R) and Vaccin (R859R). Reagents SG and FG were administered on the right forearm and F/S and the 4th reagents on the left forearm.
Results

The overall percentage positivity and mean positive reaction size to each reagent are shown in Table 1. They are arranged according to the contents of the 4th reagents. It can be seen from these results that both parameters of response to SG alone are dependent upon the content of the fourth reagent. When this contains Chitin, Dierinhoferin, Rhodesin or Vaccin the mean percentage positivity to SG is 37% and the mean positive reaction size 8.1 ± 5.4 mm. When the fourth reagent includes Duvalin, Flavescin, Gilvin, Neaurumin, Nonchromogenicin or Ranin, the mean percentage positivity to SG is 89% and the mean positive reaction size is 16.6 ± 8.9 mm. In the further analyses, reagents accompanying low responsiveness to SG are called group A and those with high responsiveness group B. The same effect is seen on the response to FG, but to a much lesser extent. Group A accompanies a 47%

Table 1. Percentage positive responders and mean positive reaction sizes for each of the ten different reagents used at the fourth skin-test site

<table>
<thead>
<tr>
<th>Constituents of 4th reagent</th>
<th>4th reagent</th>
<th>SG</th>
<th>FG</th>
<th>F/S</th>
<th>No. in group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1 SG + Chitin</td>
<td>85%</td>
<td>30%</td>
<td>30%</td>
<td>60%</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>10.4 mm</td>
<td>7.6 mm</td>
<td>4.4 mm</td>
<td>11.5 mm</td>
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</tr>
<tr>
<td>2 SG + Dierinhoferin</td>
<td>94%</td>
<td>39%</td>
<td>56%</td>
<td>94%</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>11.6 mm</td>
<td>6.1 mm</td>
<td>8.7 mm</td>
<td>11.0 mm</td>
<td></td>
</tr>
<tr>
<td>3 SG + Rhodesin</td>
<td>100%</td>
<td>21%</td>
<td>47%</td>
<td>84%</td>
<td>19</td>
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<tr>
<td></td>
<td>13.8 mm</td>
<td>5.5 mm</td>
<td>9.8 mm</td>
<td>12.2 mm</td>
<td></td>
</tr>
<tr>
<td>4 SG + Vaccin</td>
<td>89%</td>
<td>58%</td>
<td>53%</td>
<td>63%</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>14.0 mm</td>
<td>10.6 mm</td>
<td>9.8 mm</td>
<td>16.2 mm</td>
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<tr>
<td>Group A mean</td>
<td>94%</td>
<td>37%</td>
<td>47%</td>
<td>75%</td>
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<td></td>
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<tr>
<td><strong>Group B</strong></td>
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<td></td>
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<tr>
<td>5 SG + Duvalin</td>
<td>85%</td>
<td>80%</td>
<td>55%</td>
<td>60%</td>
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<tr>
<td>6 SG + Flavescin</td>
<td>89%</td>
<td>84%</td>
<td>58%</td>
<td>79%</td>
<td>19</td>
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<tr>
<td>7 SG + Gilvin</td>
<td>85%</td>
<td>95%</td>
<td>60%</td>
<td>80%</td>
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<td>8 SG + Neaurumin</td>
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<td>88%</td>
<td>47%</td>
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<tr>
<td>9 SG + Nonchromogenicin</td>
<td>83%</td>
<td>89%</td>
<td>61%</td>
<td>83%</td>
<td>18</td>
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<tr>
<td>10 SG + Ranin</td>
<td>95%</td>
<td>95%</td>
<td>74%</td>
<td>58%</td>
<td>19</td>
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<tr>
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<tr>
<td>Group B mean</td>
<td>87%</td>
<td>89%</td>
<td>60%</td>
<td>72%</td>
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Table 2. The effect of leprosy on the overall results

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<th>Reagent</th>
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<th>TT</th>
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<th>BB/BL</th>
<th>LL</th>
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<td><strong>Group A</strong></td>
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<td></td>
</tr>
<tr>
<td>SG</td>
<td>35%</td>
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<td>38%</td>
<td>36%</td>
<td>14%</td>
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<tr>
<td>FG</td>
<td>60%</td>
<td>32%</td>
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<td>55%</td>
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<tr>
<td>FjS</td>
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<td>59%</td>
<td>88%</td>
<td>91%</td>
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<td><strong>Group B</strong></td>
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<tr>
<td>SG</td>
<td>93%</td>
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<tr>
<td>FG</td>
<td>73%</td>
<td>63%</td>
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</tr>
<tr>
<td>4th</td>
<td>93%</td>
<td>79%</td>
<td>88%</td>
<td>94%</td>
<td>83%</td>
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<td>11.6 mm</td>
<td>14.4 mm</td>
<td>14.0 mm</td>
<td>13.1 mm</td>
</tr>
</tbody>
</table>

positivity to FG and a mean reaction size of $8.6 \pm 4.2$ mm, whereas group B accompanies a 60% positivity to FG and a mean reaction size of $10.0 \pm 5.1$ mm. The inclusion of groups A and B reagents do not seem to have any effect on responsiveness to FjS and only marginally affect the mean positive reaction sizes to the 4th reagents.

Table 2 shows the results obtained with groups A and B reagents according to whether those tested were healthy contacts or had leprosy. Reduced responsiveness to both SG and FG in the presence of group A, as compared with group B, is seen in all classes of persons tested. This is particularly the case amongst lepromatous patients of whom only 1 out of 7 (14%) respond to SG in the presence of group A and 34 out of 41 (88%) respond to SG in the presence of group B. Disease status has little effect in the presence of group B reagents excepting small reductions of responsiveness to FG and FjS in lepromatous patients.

**Discussion**

At first sight the results from Bombay appear to bear little relationship to those from Nepal, due to the different environmental effects of the two places. The system of categorization used for the Nepal data is not readily applicable because the combination of reagents tested does not allow identification of individuals responding to the common antigens, and causes a false
expansion of category 1 (positive to all four reagents). Nevertheless individuals failing to respond to one or more of the reagents can be taken as category 3 responders and for easier comparison with Nepal the individual results for these are shown in Table 3a and b. Table 3a is of persons tested with group A reagents and Table 3b is of persons tested with group B reagents. There is a striking similarity between the results shown in Table 3b and those in Table 3 of the Nepal study. Some of these points of similarity are shown in Table 4, as are points of difference with the results for recipients of group A reagents.

The kind of suppression discovered in Nepal in which the fast grower reagent FG is able to suppress locally the response to the slow grower reagent SG when mixed with it as reagent F/S is equally present in Bombay amongst the recipients of group B reagents (halving the dose of a new tuberculin makes little difference to the response size\(^4\)).

However, amongst the individuals showing suppression of F/S (Table 3b) only a minority show suppression of response to the 4th reagents. Thus it would not be correct to say that the species in the group B reagents, *Mycobacterium duvalii*, *M. flavescens*, *M. fortuitum*, *M. gilvum*, *M. neoaurum* and *M. nonchromogenicum*, are especially associated with the phenomenon. Amongst the results for the 55 persons receiving group B reagents and responding to all four tests 12 showed suppression of response to F/S to half or less of the response to SG and thus also exhibit the phenomenon.

Included in Table 3 of the Nepal data were five individuals, indicated by an asterisk, for whose responses no explanation could be offered. One of these responded only to Burulin\(^4\) and is therefore irrelevant to the Bombay study. Two others were BL patients responding to FG and SG, but not F/S. These individuals and similar ones in the present study marked with asterisks in Table 3b indicate that the addition of FG to SG can be suppressive whether or not there is a positive response to FG alone.

As in the Nepal study, this suppressory phenomenon is shown to a greater extent in leprosy patients than in their healthy contacts and therefore may be associated with disease. However, it must be borne in mind that in neither study was any attempt made to match by age, sex, race, etc., any of the groups studied, although this may become necessary in subsequent investigations.

Also marked with asterisks in Table 3 of the Nepal data were a lepromatous patient and a staff member responding to the F/S mixture alone. Two individuals marked with double asterisks (one BT patient and one LL patient) in Table 3b responded only to F/S and the 4th reagents. However, in Table 3a there are 18 such persons (4/17 contacts, 8/27 TT/BT patients, 3/7 BB/BL patients and 3/6 LL patients). Nevertheless we still have no explanation of this effect.

The most striking feature of Table 3a and shown in Tables 1 and 4 is the dramatic reduction of responsiveness to SG, when the 4th reagents included the group A species, *M. chitae*, *M. diernhoferi*, *M. rhodesiae* or *M. vaccae*. Not shown in Table 3a were the 15 persons receiving group A reagents and respon-
Table 3(a) and (b) opposite. Individual skin test responses expressed as mean diameters of induration (mm) in persons of Category 3 receiving group A reagents (a) and group B reagents (b)

<table>
<thead>
<tr>
<th>Individual No.</th>
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<th>SG</th>
<th>F/S</th>
<th>4th</th>
<th>Individual No.</th>
<th>FG</th>
<th>SG</th>
<th>F/S</th>
<th>4th</th>
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<td>10</td>
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<td>14</td>
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<td>8</td>
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<tr>
<td></td>
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* and **, see text for explanation.
Table (b).

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<td>6**</td>
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</table>

* and **, see text for explanation.
Table 4. Similarities and differences between results for Nepal and Bombay according to the 4th reagent groups.

<table>
<thead>
<tr>
<th></th>
<th>Numbers in category 3 responding to</th>
<th>Numbers in categories 1 and 3 showing suppression of responses to</th>
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<td></td>
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<tr>
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<td>11/12</td>
</tr>
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<td>5/5</td>
</tr>
<tr>
<td>A</td>
<td>9/17</td>
<td>4/17</td>
</tr>
<tr>
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<td>2/5</td>
<td>5/5</td>
</tr>
<tr>
<td>Contacts</td>
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</tr>
<tr>
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<td>5/5</td>
</tr>
<tr>
<td>A</td>
<td>9/17</td>
<td>4/17</td>
</tr>
<tr>
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<td>5/5</td>
</tr>
<tr>
<td>TT/BT</td>
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<td>Nepalese</td>
<td>3/14</td>
<td>14/14</td>
</tr>
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<td>9/11</td>
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<tr>
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<td>8/27</td>
<td>9/27</td>
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<td>14/14</td>
</tr>
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<td>7/7</td>
</tr>
<tr>
<td>Bombay B</td>
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<td>12/13</td>
</tr>
<tr>
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<td>3/7</td>
<td>1/7</td>
</tr>
<tr>
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<td>12/13</td>
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<tr>
<td>BB/BL</td>
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</tr>
<tr>
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<td>12/13</td>
</tr>
<tr>
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<td>3/7</td>
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</tr>
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<td>20/24</td>
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<tr>
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<td>22/57</td>
<td>14/57</td>
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</table>

It is striking, however, that as with group B reagents responses to the 4th reagents themselves are only suppressed in a minority of cases. This use of reagent mixtures has demonstrated two distinct types of suppressor mechanism. The first acts locally, and does not affect other skin-test sites. The second mechanism is associated with group A, but not group B reagents. Thus it seems that when the antigens of slow growers are presented together with antigens of the group A species in one arm, a suppressor mechanism results in failure to respond to the same slow-grower antigens given alone in the other arm. That this mechanism should be operative within 72 h makes it much more probable that an existing system has been triggered than that a new system has been induced. The most likely mechanism would seem to be triggering by the fast grower of some form of suppressor cell perhaps resulting in release of soluble suppressor factors. These could either recognize the antigens of slow growers, or specifically block a particular kind of response. Since the response blocked is exclusively to SG and slightly predominates in BB to LL rather than TT/BT patients, it seems likely that the effect is against Koch-type responses.

On the other hand, the suppression of response to F/S seen in Nepal and in the presence of group B reagents in Bombay, appears to be antigen directed...
Two types of suppressor mechanism in leprosy

rather than response type directed and is greatest in the patient groups (57/128, 45%) rather than staff/contact individuals (7/39, 18%).

The question arises whether these phenomena are consequences of particular types of leprosy or prerequisites for them.

Many other important questions about these suppressor phenomena remain unanswered. Amongst the most pressing is the question of sensitization by the fast growers. One interpretation of the group B results would be that the species concerned do not exert any effect because their species-specific (group iv) antigens are not recognized and therefore the responses to the 4th reagents approximate to those to SG alone. On this basis the response to group A 4th reagents might be to the species-specific antigens of the fast growers themselves and therefore of Listeria type.7,8

If this is true then the effect of each species will depend upon the pattern of sensitization of the persons tested and this would explain why not everyone shows the suppressor phenomena. Similarly, different species will behave as groups A and B in different parts of the world. One species we can be sure of in the presence of active leprosy patients the world over is M. leprae and its effects will be investigated in future studies.

Work in progress in our laboratory and elsewhere (C Brown, I. Brown and M J Shield, unpublished observations) suggests that such suppressor phenomena may be primed by oral intake of mycobacteria. Large numbers of mycobacteria are known to be present in water supplies in Bombay. (J. Kazda, personal communication) just as they were in nineteenth century Norway.10 The implied importance of these phenomena in relation to the development of leprosy requires further investigation.

In conclusion, two types of suppression have been demonstrated in our quadruple skin-testing system in Bombay. One of these is similar to that already demonstrated in Nepal. The second type, which suppresses skin-test responses at distant sites, appears to be associated with recognition of species-specific antigens of 4 of the 10 fast-growing species investigated.

Acknowledgements

We would like to thank Dr R Ganapati, Director of the Bombay Leprosy Project and Dr J K Maniar of the Grant Medical College, Bombay for their support and encouragement of this work. Our thanks are also given to Lepra for the financial support that made this study possible.

References

1 Stanford JL, Nye PM, Rook GAW, Samuel N, Fairbank A. A preliminary investigation of
the responsiveness or otherwise of patients and staff of a leprosy hospital to groups of shared or species specific antigens of mycobacteria. *Lepr Rev* 1981; 52: 321–7.


6 Asherson GL, Zembara M. The role of the T-acceptor cell in suppressor systems: antigen specific T-suppressor factor acts via a T-acceptor cell; this releases a non-specific inhibitor of the transfer of contact sensitivity when exposed to antigen in the context of I–J. *Ann NY Acad Sci* (in press).


Further results on dapsone-resistant leprosy in Bamako (Mali)

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Received for publication 6 July 1982

Summary Between 1979 and 1981 a yearly survey of dapsone resistance was performed among two groups of leprosy patients in Bamako. In a first group of patients the yearly incidence was 5.7%, 3% and 4.1%, with a mean of 4.1% per year. In the second group the yearly incidence was 3.4, 0.8 and 2.8% with a mean of 2.3%. Our results confirm research carried out in Addis Ababa (Ethiopia), where a yearly incidence of 3% was found.

The need for the use of combined therapy including bactericidal drugs is emphasized.

Introduction

In a previous publication1 the results were presented on the prevalence of dapsone-resistant leprosy among a population of 105 originally multibacillary patients discharged over the years from the Institut Marchoux and living in a village near the Institute.

In 1980 and 1981 the same population was re-examined and biopsies inoculated into mouse foot pads for detection of dapsone resistance. From 1979 another population of leprosy patients living in and around the city, and treated by the ‘Service des Grandes Endémies’, the traditional diagnostic and treatment service for the endemic diseases, was also investigated. These results allow us to arrive at an estimate of the yearly incidence of dapsone resistance.

Materials and methods

These were as described previously.¹ A yearly bacteriological examination was
performed and from those patients showing a BI \geqslant 2, a biopsy on ice was sent by air to Antwerp.

Results

Thirty-nine biopsies were taken. Bacilli from 10 patients did not multiply in mice, 4 strains were fully sensitive to dapsone, again illustrating that some patients had not been taking their drug recently.

As shown in Table 1 the yearly incidence of dapsone resistance during 1980 and 1981 was 3% and 4.1% respectively among the Institut Marchoux village population and 0.8 and 2.8% among the Grandes Endémies population, leading to a mean of 4.3% per year and 2.3% per year respectively.

Degree of dapsone resistance was generally less important among the latter population, as shown in Table 2. As previously found\textsuperscript{1} there were again cases of mixed populations of sensitive and resistant organisms versus the different concentrations of dapsone tested.

Discussion

Secondary dapsone-resistant leprosy has now been found in all countries where it has been sought\textsuperscript{3} and cases of primary dapsone resistance, multibacillary as well as paucibacillary, are being diagnosed.

Data on the incidence of dapsone resistance are scarce. The first data from Addis Ababa\textsuperscript{2} found an alarming 3% per year leading to an overall prevalence of 30% within a decade.

<table>
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<th>Grandes Endémies</th>
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<td>1981</td>
<td>4/96</td>
<td>7/247</td>
</tr>
<tr>
<td></td>
<td>13/300</td>
<td>18/754</td>
</tr>
</tbody>
</table>

\textsuperscript{(*)as previously published}

Table 2. Degrees of dapsone resistance

<table>
<thead>
<tr>
<th>Resistance Level</th>
<th>Institut Marchoux Village</th>
<th>Grandes Endémies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resists DDS $10^{-2}$ g% in diet</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Resists DDS $10^{-3}$ g% in diet</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>Resists DDS $10^{-4}$ g% in diet</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>
Our results confirm the data, since we found a yearly incidence of 4.3% and 2.3% respectively in two different populations of Bamako, with a mean of 3% per year. The difference in incidence between the two populations studied is statistically significant (0.025 < p < 0.05). What the reasons for this difference are remain unknown.

As shown in Table 2, 7/25 strains are of low-grade and 6/25 of median-grade dapsone resistance, meaning that at least for some time the strains might be inhibited by full dapsone dosage in man. The overall situation, however, clearly points to the necessity for combined antileprosy treatment including potent bactericidal drugs.

Acknowledgements

This study has been partially financed by the Damiaanfonds, Brussels, Belgium. Janssen Pharmaceutica, Beerse, Belgium, generously provided the dapsone-containing mouse food. Technical assistance by A Van Aerde and G Hooft is much appreciated.

References

Reproducibility of sensory testing and voluntary muscle testing in evaluating the treatment of acute neuritis in leprosy patients*

SUSAN LEWIS
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Summary Based on methods discussed at a 'neuritis workshop' held in Karigiri in South India in 1980, this study describes attempts to standardize sensory testing and voluntary muscle testing in a group of 20 patients with tuberculoid leprosy. Patients were assessed by the same observer on two occasions at intervals of 2 weeks. The results confirm that accurate methods for assessing the treatment of neuritis in leprosy remain elusive. In this group of patients however, and under the conditions described, it appears that greater reliance can be placed on sensory testing, particularly fine touch, than on voluntary muscle testing.

Introduction

One of the most controversial problems in leprosy research is the treatment of acute neuritis and how best to evaluate its effectiveness. Sensory testing has been advocated: von Frey hairs of graded sizes were used, exerting pressure of 0.1 g, 0.4 g, 1.0 g, 2 g and 4 g. The thenar and hypothenar areas of the hand were touched four times with each stimulator. They recorded the numbers 'felts' and graded the numbers 'not felt'. They found this to be a sensitive method in the follow-up of nerve involvement.

Voluntary muscle testing was found to be a reliable and reproducible method. The Medical Research Council (MRC) scale of strength was used to give a score for seven muscles supplied by the ulnar nerve and nine muscles supplied by the median nerve. In conjunction with nerve conduction velocity (NCV) studies, both sensory testing and voluntary muscle testing have been used to evaluate the success of treatment.

At the Neuritis Workshop in Karigiri, South India an attempt was made to standardize these tests. The object of this

*Study done at the Schieffelin Leprosy Research and Training Centre, Karigiri, South India, during a student elective period May 1980.
study is to examine the reproducibility of sensory and voluntary muscle testing, using some of the methods recommended at the Workshop.

Methods

Twenty patients with tuberculoid leprosy, as clinically diagnosed, with established nerve lesions were assessed by the author on two occasions, separated by 1 to 3 weeks. Both hands were examined for ulnar and median nerve function using sensory and voluntary muscle testing. Ulnar nerve damage was considerably more common than median nerve damage.

Sensory testing (ST)

Four methods were used: light touch, static two-point discrimination, tuning fork test and pinprick test. Six areas were examined on the palmar surface of each hand (Fig. 1). Ulnar nerve supplied: 1, distal phalanx – little finger; 2, proximal phalanx – little finger; 3, hypothenar eminance. Median nerve supplied: 1, distal phalanx – index finger; 2, proximal phalanx – index finger; 3, distal pulp – thumb.

Light touch

Four stimulators were constructed from nylon hairs which bent at a pressure of 0.5 g, 3.5 g, 5.5 g, 30 g.
The finest hair that was felt in each area was recorded and scored as: 0.5 g = 4; 3.5 g = 3; 5.5 g = 2; 30 g = 1; not felt = 0. Thus the maximum possible score for one nerve was 12 points.

**Static two-point discrimination**

Three paper-clips were used, with the legs bent at 3 mm, 6 mm and 12 mm apart. The six areas were used as before and the shortest distance felt as two separate stimuli was noted and scored for each site as: 3 mm = 3; 6 mm = 2; 12 mm = 1; not felt or felt as one = 0. Thus the maximum score for a single nerve was 9 points.

**Tuning fork test**

The vibrating arm of a 256 Hz tuning fork was touched lightly in each area and a point awarded if the patient could feel the vibration. Thus the maximum score for a single nerve was 3 points.

**Pinprick test**

The patient was asked to state whether the sensation was sharp or blunt. The result was recorded for each test site as: sharp = 3; blunt = 0; not felt = 0. Thus the maximum score for each nerve was 9 points. The sum of the scores for each test gave a score out of 33 for the function of each nerve.

It must be emphasized that even when a nerve is unaffected by leprosy, the score may not reach 33. Tests of two-point discrimination showed performance varied with age and that volar fingertips were twice as discriminating as the thenar and hypothenar areas. Farm labourers with thick skin were often unable to feel the finest hair on the palms of their hands when there was no subjective loss of sensation. Thus a 'normal score' varied between 28 and 33. It is not the absolute score that was of interest in this study but the reproducibility of the scoring methods.

**Voluntary muscle testing (VMT)**

VMT consisted of estimation of muscle power in eight muscles in each hand, four supplied by the ulnar nerve and four supplied by the median nerve. The power was graded according to the MRC scale of strength:
5 Full strength against resistance provided by the assessor's hand or finger.
4 Movement against some resistance is possible. Range of movement is full.
3 There is a full range of movement, not possible against resistance (but can be done against gravity).
2 There is less than full range of movement.
A flicker of movement or muscle contraction can be felt but no actual joint movement.

No movement.

Muscles examined were flexor carpi ulnaris, abductor digiti minimi, first
dorsal interosseus, third palmar interosseus (supplied by the ulnar nerve) and flexor carpi radialis, flexor pollicis longus, abductor pollicis brevis and the first lumbrical (supplied by the median nerve). Thus as each muscle was given a score of up to five points and four muscles were assessed for each nerve the maximum score for an intact ulnar or median nerve was 20 points. This test

Figure 3. Graph showing the reproducibility of the voluntary muscle testing method.
required more positive cooperation from the patients and a greater opportunity for observer error. It is difficult to assign five grades of strength when dealing with small muscles of the hand and requires practice to learn the normal strength in the hand of, for example, an old woman and a young man.

Results

The results consist of a score for ulnar and median nerve function as assessed on VMT and ST. The score achieved on the first visit was compared with that achieved on the second visit using Wilcoxon matched pairs signed ranks test for nonparametric data.\(^7\)

There was found to be no significant difference between the sensory testing scores achieved on the first and second visit in both ulnar and median nerve groups, implying that the method used is reproducible and thus useful. Fine touch score seemed to be most sensitive of the four sensory testing methods used, the scores (out of 12) were compared and also found not to differ significantly. When muscle power was assessed the median nerve group showed no difference in score but the ulnar nerve group showed a significant difference (probability \(< 5\% \ Z = 2.019\)). As the patients had established nerve lesions, tested twice at an interval of only 1 to 3 weeks, this result suggests that this method of assessment is not reliably reproducible. The differences between the first and second scores are illustrated graphically (Figs 2 and 3).

These results confirm the subjective opinion of the author that sensory testing, using a combination of tests described above, is a useful and reproducible method of assessing nerve function in leprosy patients. However, the test does have disadvantages — it is time consuming (each patient requiring up to 20 minutes), requires the full concentration of both patient and assessor and preferably the same assessor on each occasion. However, it is a method valuable in the study of the treatment of neuritis. A strength grade was difficult to assess in the small muscles of the hand and sensory testing was more accurate and useful.

Discussion

In this study, of patients with nerve damage due to leprosy, it was clear that pinprick sensation was present when there was loss of fine touch and that two-point discrimination was lost early. Vibration (as tested with a tuning fork at 256 cps) was often present in the absence of pain sensation. It has been reported\(^8\) when looking at recovery of sensation in the hand following nerve injury due to trauma that pain sensation was the first sensory modality to
Muscle testing and treatment of acute neuritis

recover. However, it was also found that vibration at 30 cps recovered before vibration at 256 cps, that moving touch recovered before constant touch awareness (slowly adapting fibres) and that last to recover was two-point discrimination.

One could speculate that the difference between these findings might be due to an idiosyncratic preservation of one sensory modality in leprosy neuritis or, more probably, the vibrating tuning fork was too diffuse a test, which recruited nerve endings from a larger area of the hand than that being tested. There may be a qualitative difference between sensory loss due to leprosy neuritis and that due to trauma: the 'dying back' phenomenon has been described. It seems that neural and Schwann cell activity is impaired throughout the whole length of a nerve affected by leprosy at any point along its course. Nerve regeneration and neuroma formation does not occur. The qualitative nature of sensory loss in leprosy neuritis warrants further investigation. From the results of this study it seems that VMT is an unreliable method of monitoring nerve damage except in the presence of very gross changes in function. VMT is a difficult test, especially in patients with acute neuritis as they are in pain and reluctant to cooperate.

An accurate method of assessing the treatment of neuritis remains elusive. The most useful parameter seems to be a combination of VMT, NCV, ST and symptoms. However, this type of assessment is cumbersome and hard to standardize between different centres.

I would recommend greater reliance on sensory testing, particularly fine touch and motor conduction studies, rather than voluntary muscle testing.

Acknowledgements

I would like to thank Dr Frank Johnson, Professor J R A Mitchell, Mrs Shirley Tacey, Mr Steve Kolumban and the staff of the Physiotherapy Department at Karigiri, and LEPRA who financed my visit.

References


Functional changes of the ulnar nerve in leprosy patients following neurolysis

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Received for publication 4 May 1982

Summary A functional follow up of ulnar neurolysis is presented. Functional changes have been related to the indication for neurolysis. Motor function of 52% of the nerves was improved in the group in which neurolysis was performed to facilitate nerve recovery. The rate of functional improvement appears also to depend on the duration of the recorded nerve damage and the classification of leprosy. Functional changes in the operated nerve have been compared with the non-operated nerve in cases of bilateral ulnar nerve involvement.

Introduction

Prevention of recurrent neuritis or the relief of intractable nerve pain used to be the main indications for ulnar neurolysis in leprosy. It has been reported\(^1\) that the need for neurolysis for these indications has decreased considerably since the introduction of clofazimine and thalidomide.

Most authors seem to agree that neurolysis is very helpful in the relief of nerve pain and that, whatever surgical technique is employed, neurolysis has no harmful effect on nerve function. Few authors have defined or quantified functional changes of the ulnar nerve following neurolysis. A nerve index\(^2\) has been developed, using voluntary muscle testing, sensory testing and motor nerve conduction velocities, to follow patients with recent nerve damage and to evaluate possible functional benefits of nerve surgery. In one study\(^3\) this nerve index was used to study patients who had ulnar neurolysis, comparing the results with the contralateral affected nerve.

The indications and results of ulnar neurolysis in recent publications are summarized in Table 1. This present study gives the functional changes in
Table 1. Neurolysis in leprosy

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Operated nerves</th>
<th>Classification</th>
<th>Indication</th>
<th>Functional results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ulnar</td>
<td>Median</td>
<td>T</td>
<td>B</td>
</tr>
<tr>
<td>Callaway^4^(1964)</td>
<td>100</td>
<td>X</td>
<td>X</td>
<td>not given</td>
</tr>
<tr>
<td>Parikh^5^(1968)</td>
<td>17</td>
<td>13</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Vaidyanathan^6^(1968)</td>
<td>88</td>
<td>88</td>
<td>0</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Said^7^(1972)</td>
<td>38</td>
<td>32</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palande^8^(1973)</td>
<td>23</td>
<td>23</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carayon^9^(1974)</td>
<td>70</td>
<td>70</td>
<td>0</td>
<td>not given</td>
</tr>
<tr>
<td>Enna^1^(1974)</td>
<td>103</td>
<td>103</td>
<td>0</td>
<td>'lepromatous'</td>
</tr>
<tr>
<td>Oomen^10^(1979)</td>
<td>16</td>
<td>16</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Notes:

a. Indication: prevent progressive paralysis.
b. Functional loss less than 3 months.
c. Functional loss more than 3 months.
d. Recovery related to type and duration of involvement.
e. Duration functional loss less than 6 months.
motor and sensory fibre functions in patients operated upon between 1972 and 1979 at the All Africa Leprosy and Rehabilitation Training Centre (ALER T), Addis Ababa, Ethiopia.

**Method and material**

On 106 patients a total of 129 ulnar neurolyses were performed. The different indications for neurolysis are given in Table 2. The number of indications is higher than the number of nerves operated because of 17 double indications.

We were able to assess the results of 100 neurolyses in patients who had at least 1 year of post-operative follow-up. However, if major functional changes had occurred before the first year following surgery and the patient did not have a follow up of a year then the patient was also included. Twenty patients had bilateral ulnar neurolysis.

The assessment technique used in evaluating motor function recovery was the voluntary muscle testing as described \(^{11}\) for leprosy patients.

The same grading system for muscle strength was used as reported by the Medical Research Council.\(^{12}\)

The grades for abduction of the little finger and the abduction of the index finger were totalled. A normal function of the ulnar nerve would thus give a score of 10. When the post-operative muscle score was more than 8 the sensation was reviewed from the record. In our experience sensation is not likely to be present when there is still considerable motor involvement.

**Surgical technique and findings**

All cases for neurolysis in this series were referred from the physicians. There was no bias from the surgeons as to which nerve to operate upon and which to leave under medication alone. The majority of the operations were performed without tourniquet, only towards the end of the series were the operations performed in a bloodless field, thus allowing a detailed recording of the findings.

**Table 2. Indication for surgery related to classification**

<table>
<thead>
<tr>
<th></th>
<th>Pain relief</th>
<th>Functional improvement</th>
<th>Abscess</th>
<th>Not recorded</th>
<th>Number of indications</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>(B)T</td>
<td>11</td>
<td>40</td>
<td>5</td>
<td>2</td>
<td>58</td>
<td>45</td>
</tr>
<tr>
<td>B</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>(B)L</td>
<td>42</td>
<td>32</td>
<td>1</td>
<td>6</td>
<td>18</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>57</td>
<td>75</td>
<td>6</td>
<td>8</td>
<td>146</td>
<td>106</td>
</tr>
</tbody>
</table>

*Note:* Table gives the indications for all operated nerves.
In all cases the nerve was exposed from the exit of the axilla to the entry into the depth of the forearm. In some of the earlier cases a regular anteposition of the nerve was performed, sacrificing the feeder vessels. In the latter part of the series these vessels were carefully preserved. Possible adhesions were freed, and a longitudinal epineurotomy was performed, as far as possible avoiding damage to the epineurial vessels. In the latter part of the series the tissue surrounding the feeder vessels and the nerve was removed. The ulnar intermuscular septum was invariably resected, thus preventing any kinking of the nerve and allowing free play when extending or flexing the elbow.

The epineurium was found to be of varying thickness and the fascicles were typically swollen and yellow. In some cases, notably these of long-standing nerve damage, where functional recovery was not expected, fascicular structure could not be detected.

In most cases the feeder vessels were of normal calibre but, in some, particularly those of long-standing nerve damage, they were engorged, indicating a venous obstruction outside the nerve. The epineurial vessels were in most cases engorged, although in some cases they were thin, even invisible, indicating endoneurial over-pressure.

At the end of operation both the engorged feeder vessels and epineurial vessels assumed normal calibre. Where the epineurial vessels were either thin or invisible, they usually assumed normal calibre. However, in a few cases the nerve became thinner during the operation.

Results

Motor nerve function was considered to have improved or deteriorated when the total muscle grading score had changed two or more points.

Table 3 shows the relationship between the postoperative ulnar motor changes to the pre-operative duration of functional loss. It was not always possible to determine exactly the onset of motor nerve involvement from the records and often the history had to be relied on.

None of the patients with a motor deficit of more than 6 months recovered fully from total paralysis and the average improvement in long-standing palsies was only 3 points.

Table 4 gives the motor function changes per indication and classification. The data in the table suggest that greater improvement is found in (B)T nerves.

Table 5 shows the degree of improvement in muscle strength of the 39 nerves that improved. It will be seen that only 2 nerves recovered their motor function completely from total nerve function loss, whereas 10 nerves recovered completely from partial nerve function loss.

Six patients, 2T, 3BT and 1BL patient had nerve abscesses. Three nerves remained without function postoperatively, 1 deteriorated and 2 improved.
Table 3. Motor function changes related to pre-operative duration of muscle paresis/paralysis

<table>
<thead>
<tr>
<th>Duration (months)</th>
<th>Improved (B)T</th>
<th>Unchanged (B)T</th>
<th>Improved (B)L</th>
<th>Unchanged (B)L</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4–6</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>7–12</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>more than 12</td>
<td>4</td>
<td>8</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>not recorded</td>
<td>4</td>
<td>1</td>
<td>16</td>
<td>36</td>
</tr>
</tbody>
</table>

Notes: The few patients classified 'borderline' have been included in this table under (B)T. Compare with Table 4. Two (B)L patients that remained unchanged have been omitted from this table because there was no functional loss pre-operatively.

Table 4. Changes in motor nerve function

<table>
<thead>
<tr>
<th>Indication—functional recovery</th>
<th>Improved (B)T</th>
<th>Unchanged (B)T</th>
<th>Deteriorated (B)T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional recovery</td>
<td>16 (55%)</td>
<td>12 (41%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>B</td>
<td>3 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(B)L</td>
<td>11 (42%)</td>
<td>14 (54%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>30 (52%)</td>
<td>26 (45%)</td>
<td>2 (3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other indications</th>
<th>Improved (B)T</th>
<th>Unchanged (B)T</th>
<th>Deteriorated (B)T</th>
</tr>
</thead>
<tbody>
<tr>
<td>(B)T</td>
<td>1 (17%)</td>
<td>3 (50%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>(B)L</td>
<td>8 (24%)</td>
<td>24 (70%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (21%)</td>
<td>28 (67%)</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>Overall totals</td>
<td>39</td>
<td>54</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 5. Degree of improvement in motor nerve function

<table>
<thead>
<tr>
<th>Pre-operative Function</th>
<th>Post-operative function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2–3</td>
</tr>
<tr>
<td>0–1</td>
<td>6</td>
</tr>
<tr>
<td>2–3</td>
<td>0</td>
</tr>
<tr>
<td>4–5</td>
<td>0</td>
</tr>
<tr>
<td>6–7</td>
<td>0</td>
</tr>
<tr>
<td>8–9</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
</tr>
</tbody>
</table>

There were 7 nerves that deteriorated but only in one case could the deterioration be attributed to the surgery. In this case there was immediate postoperative functional loss. In the remaining 6 patients other nerves also deteriorated. In these cases chronic erythema nodosum leprosum, DDS resistance and discontinuation of treatment were possible contributing factors.
Table 6. Functional changes in operated and contralateral affected nerves

<table>
<thead>
<tr>
<th></th>
<th>Operated</th>
<th>Non-operated</th>
<th>Operated</th>
<th>Non-operated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>18</td>
<td>13</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Unchanged</td>
<td>23</td>
<td>8</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Deteriorated</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>43</td>
<td>21</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>9</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

*All nerves irrespective of indication for surgery and difference in nerve damage

†Nerves in which functional recovery was expected. Comparable nerve damage: not more than two points difference on totalled VMT score

There were 43 patients who had bilateral ulnar nerve damage and who only had one nerve operated upon. In Table 6 we have compared the results of the operated nerve with the non-operated contralateral affected nerve. The data on sensory changes were reviewed from the record when the post operative muscle score was more than 8. From Table 5 it will be seen that there were 19 nerves which had recovered this muscle strength. Of these only 5 had recovered sensation when tested with bristle no 5.

Pain relief was achieved in an estimated 80–90% of the patients.

Discussion

Motor nerve conduction of both ulnar nerves was assessed regularly in all patients included in this study. We did not analyse these results separately as we soon realized that muscle testing scores alone gave us comparable information. In experienced hands manual muscle testing is a very useful and objective test to evaluate motor nerve function.

Our findings confirm other reports that neurolysis does not harm the nerve. The case notes revealed that prednisolone dependency was a problem in many patients, especially in (B)L patients. We noticed that on occasions prednisolone was given to the patient merely for nerve pain in which the nerve function assessments showed that the nerve was already dead or that decreased nerve function had persisted for many years. This was especially so in the group where neurolysis was performed for pain relief. Progress notes in the patient files also showed that many patients had asked for prednisolone. The problem of steroid dependency in lepromatous leprosy patients has been previously reported.13 It suggests that prednisolone could be reduced and stopped after these patients were given clofazimine. It seems from this observation that the physician should be very cautious in prescribing prednisolone and that he should only prescribe this drug when there are indications of an active neuritis.

Unfortunately it was not possible to relate the results of neurolysis to anti-leprosy and antineuritis treatment. In the early 'seventies patients were still
taken off DDS treatment during neuritis, and when DDS treatment was initiated it was started with a low dose which was gradually increased to 300 mg weekly. As from 1974 patients were given DDS 100 mg daily and DDS treatment was not discontinued when patients developed neuritis. Many patients, in addition to DDS treatment, received clofazimine for varying periods and in differing dosages. In the management of neuritis the picture was the same where different courses with different dosages were given to all patients. As might be expected improvement is greater when neurolysis is undertaken when functional results are anticipated and (B)T nerves do better than (B)L nerves.

More careful studies are needed to determine possible functional benefits of nerve surgery. This study also clearly highlights the importance of careful recording. Future studies in our opinion should include details such as: (a) duration of nerve function loss from history or from record; (b) presence of muscle atrophy as an indication of the duration of loss of muscle function; (c) classification of the disease, type of reaction and bacteriological and morphological index (BI and MI): (d) medication: both antileprosy and immune suppressive drugs; (e) indication for surgery, surgical technique and findings on surgery; and (f) quantification of nerve function changes pre- and post-operatively. From this study it is not possible to determine if neurolysis will give better results than medical treatment alone. However, there do not seem to be important differences between the operated nerve and the contralateral affected nerve. Although the neurolyses reported in this study were not performed in a controlled trial we have attempted to relate the nerve function changes to duration of the nerve damage, indication for neurolysis and classification of the leprosy.

References


The moulded double-rocker plaster shoe in the field treatment of plantar ulcer

B JOSEPH, S JOSHUA & E P FRITSCHI

Received for publication 14 April 1982

Summary The present study has shown that the moulded double rocker plaster shoe offers a very feasible method of treatment of the simple plantar ulcer under field conditions. It is effective, inexpensive, socially acceptable and it can be applied, and the patient sent home, on the same day. There are no significant complications which have been noted either during or subsequent to this trial.

Introduction

A simple plantar ulcer is defined as one that involves only the skin and subcutaneous tissue. A simple plantar ulcer is defined as one that involves only the skin and subcutaneous tissue.1 It has a visible floor, no deep sinus, no local warmth, no oedema or redness and minimal discharge. If very chronic it may show clean punched-out edges.

This study was carried out to determine the usefulness of the moulded double rocker plaster shoe (MDRP shoe), as an outpatient ambulatory treatment of simple plantar ulcers in leprosy patients reporting to the Outpatient Department of the Schieffelin Leprosy Research & Training Centre, Karigiri.

Initially the plan had been to compare this smaller plaster shoe with the standard below knee plaster cast, which has for many years proved its worth in the treatment of these ulcers. However, it was found impossible to implement the predetermined random allocation, because the patients refused to have the standard plaster boot applied unless they were admitted. The present design of the study therefore is based on the fact that, in most village clinics, the normal treatment of simple ulcers is to give the patient some advice, where possible a sandal and some dressing materials for home care.

The following questions were asked:
1. Is the MDRP shoe effective?
2. Is it socially acceptable and economically feasible in the field?
3. Are there any complications?

Materials and methods

Case selection:

Forty-two patients with simple ulcers were selected from the Outpatient Department of the Schieffelin Centre. Those with drop feet were excluded from the trial. Diabetes mellitus was ruled out in all the patients. All the patients were examined clinically and classified. They were fully documented with X-rays, photographs, Harris mat foot prints,\textsuperscript{2,3} full sensory and motor assessment and ulcer measurements.

They were assigned to one of two groups in accordance with a predetermined randomized serial order with 21 patients in each of the two groups. The first group had MDRP shoes applied over the magnesium sulphate glycerine (MSG) dressing. The other group were given MSG dressings for home use, and a pair of standard Y-strap sandals with microcellular sole and an arch support and metatarsal pad. The same type of sandals were issued to the first group to be worn on the good foot initially, and on both after the healing of the ulcer.

All the patients were reviewed after 4 weeks, that being the normal interval between clinic attendances. Where the ulcer did not heal in the first 4 weeks it was re-applied and again reviewed after a 4-week interval.

Both groups were given intensive health education in the care of their feet and were taught the technique of foot soaking, scraping, oil massage and daily foot inspection, and how to deal with pre-ulcerative conditions such as fissures, corns, callouses, blisters and haematomata.

At the first and subsequent visits, all were examined carefully for signs of inflammation such as oedema, warmth, redness, regional lymphadenitis and any change in the ulcer category or size. Repeat X-rays, Harris-mat impressions and photographs were taken. All patients had another session of health education.

Application of the moulded double rocker plaster shoe\textsuperscript{1}

Materials required: one roll of gauze bandage; two rolls of plaster of Paris (POP) bandage (home-made); and one wooden footpiece with two rockers attached.

A sterile mag. sulph. glycerine acriflavine dressing was applied over the ulcer. A gauze bandage was put on over the entire foot up to the ankle joint, care being taken to apply small gauze pads between the toes.
One layer of POP bandage is applied over the whole foot up to the ankle level (below the malleoli), and then the wooden footpiece with rockers is held under the sole. The medial and lateral arches of the foot are filled in with POP bandages. The second roll of POP bandage is then applied over the whole foot including the toes, holding the wooden footpiece in place.

Four hours after application the patient was allowed to walk with full weight bearing on the plaster shoe. This period was possible because the patients selected for this trial had their plaster shoes applied in the Outpatients Department. One hour for drying has been tried in the field and found adequate.
Table 1 shows a comparison of the features of the two groups. It will be seen that the groups were satisfactorily matched in age and sex, and only in classification were there some major differences.

Table 2 shows a comparison of the ulcers in terms of site and size. It can be seen that here also the two groups were well matched.

Table 3 shows the results of the trial at the second visit, and it can be seen that 65% of the ulcers in the trial group had healed in 4 weeks in comparison with 12.5% in the control group.

Figure 3. A pre- and post-treatment foot showing the healing of an ulcer in 4 weeks.

<table>
<thead>
<tr>
<th></th>
<th>MDRP shoe group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Ulcers</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–40</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>41–60</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Over 61</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>N?L</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>L</td>
<td>12</td>
<td>7</td>
</tr>
</tbody>
</table>
### Table 2. Sites and initial size of ulcers

<table>
<thead>
<tr>
<th>Site</th>
<th>MDRP shoe group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of ulcers</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>Base great toe</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Forefoot</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>Lat. border</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Heel</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Size diameter (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 1</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>1-3</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>More than 3</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

### Table 3. Follow up at the first visit – 4 weeks after joining the trial

<table>
<thead>
<tr>
<th></th>
<th>MDRP shoe group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healed</td>
<td>17 (65%)</td>
<td>3 (12.5%)</td>
</tr>
<tr>
<td>Not healed</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>24</td>
</tr>
</tbody>
</table>

**Complications**

The complications that we were specifically looking for were those which are commonly associated with any treatment involving the risk of osteoporosis resulting from plaster immobilization. In our small series this was not seen at all. Also at subsequent visits no case of neuropathic disorganization of the foot was seen. It is possible that the limited immobilization of the foot, below the ankle only, makes this risk negligible compared with the plaster boot.

In the initial experiments there were a few cases which produced ulceration around the open end of the shoe at the ankle. It also happened that some of the patients were able to remove their shoe by just slipping it off! However, with experience, both these difficulties were overcome.

**Discussion**

**Effectiveness.** It is clear from the results that the MDRP shoe is an effective form of treatment even after a minimum period of 4 weeks.

It embodies the three accepted principles of rigidity, immobilization of skin and bones below the ankle, and occlusion.
Social acceptability. The shoe was very well accepted by the patient; in fact, some patients reporting at the Outpatient Department specifically requested the MDRP shoe.

Cost. The cost of a single MDRP shoe is about Rs 5/- (25p or $0.70) using home-made POP bandages.

The cost of dressings is very difficult to estimate as it depends on the standard of dressings used. Moreover, the ineffectiveness of dressings, even when supplemented by chappals with an arch support and metatarsal bar is demonstrated.

The cost of a standard below-knee POP boot with a Bohler iron is about Rs 25/- (£1.25 or $3.50) using home-made bandages.

Conclusion

The Moulded Double Rocker Plaster Shoe offers a very feasible method of treatment of the simple plantar ulcer under field conditions. It is effective, inexpensive, socially acceptable and the patient can be sent home on the day of application. There are no significant complications which have been noted either during or subsequent to this trial.

References

Leprosy in Zimbabwe

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Department of Medical Microbiology, Godfrey Huggins School of Medicine, University of Zimbabwe, Salisbury, Zimbabwe

Received for publication 26 April 1982

Summary In Zimbabwe, as in many countries in Africa, leprosy is an endemic disease. The known incidence is approximately 2 cases per 1,000 population and 350 new cases are seen annually.

Many factors have influenced the spread of the disease including the recent bush war but progress in control measures is being made.

Introduction

Zimbabwe covers an area of 390,757km² and is bordered by Zambia, Moçambique, South Africa and Botswana. The country is divided into five provincial areas: Manicaland, Mashonaland, Midlands, Matabeleland and Victoria (Fig. 1).

The last census was taken in 1969, and more recent estimates put the population at 6,625,000, comprising 5,750,000 Blacks, with the remainder Whites, Asians or Coloureds. The Blacks form two predominant groups, each stemming from separate ethnic origins. The numerically superior Shona were the original inhabitants of the area, and the Matebele an off-shoot of the Zulu nation of South Africa.

Situated between the Equator and the Tropic of Capricorn, Zimbabwe experiences a sub-tropical climate owing to the relatively high altitude. A dry season occurs between April and October, and the main rains, delivering a mean annual precipitation of 730.5 mm, fall between November and February.

Politically, the country was administered by the British South Africa Company from 1889 until 1922, when it became a British colony. As Southern Rhodesia it became a member of the ill-fated Federation of Rhodesia and Nyasaland from 1953 until 1963. Assuming the name Rhodesia until 1978, political events saw the change through Zimbabwe-Rhodesia to Zimbabwe, with attainment of legal independence in April 1980.

A bush war engulfed most of the country between 1973 and 1979. During this period, health services were severely disrupted and large numbers of the
Black population migrated to urban areas or were moved to ‘protected villages’. Many fled as refugees to neighbouring countries.

The major health problem is malnutrition and many diseases of microbiological aetiology are present. An expanded vaccination programme is currently being undertaken which hopefully will control, among others, measles and other childhood diseases. Malaria, schistosomiasis and many other parasitic diseases are common. Tuberculosis and typhoid are frequently seen and outbreaks of bubonic plague, cholera and anthrax have occurred.

Leprosy — historical review

Leprosy is endemic in Zimbabwe. The earliest authenticated reference to the disease is found in the report of the Ministry of Health for 1903, where the District Surgeon for Bulawayo reported ‘several cases of leprosy’.

Figure 1. Zimbabwe, showing Provinces and sites of Mtemwa and Ngomahuru Hospitals.
Early statistics of known cases are highly erroneous and reflect the inhumanity of the Leprosy Repression Act of 1919, and the associated regulations. This required that leprosy patients be detained in asylums and also made provision for legal action against any person 'harbouring a leper' and patients who escaped from an asylum. Undoubtedly, many patients remained in hiding being sheltered by their families and friends.

Two 'leper settlements' were established. One of these, at Ngomahuru in the Victoria District, is now a tuberculosis hospital, and the second, at Mtemwa, still houses 70 welfare patients today.

A total of 5,299 patients were admitted to these hospitals during the period 1925–1962. The number of aliens compared to indigenous cases is remarkable (Fig. 2). Many of these people were part of the immigrant labour force employed in mines and on farms and who lost their jobs as a result of the disability caused by the disease. Destitution forced them to seek the protection offered in the settlements. Another contributing factor to the high alien figure is that many were suffering from or incubating the disease when they left their countries of origin (Table 1).

Despite the anathema of the policy of enforced hospitalization, it did permit a statistical evaluation of the geographic distribution of the disease (Table 2),

![Figure 2. Comparison of total and alien cases admitted to Mtemwa and Ngomahuru Hospitals 1925–62.](image-url)
Table 1. Total alien admissions and countries of origin to Mtemwa and Ngomahuru Hospitals, 1925–62

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>3</td>
<td>40</td>
<td>88</td>
<td>119</td>
<td>131</td>
<td>152</td>
<td>313</td>
<td>180</td>
<td>1,026</td>
</tr>
<tr>
<td>Mozambique</td>
<td>18</td>
<td>33</td>
<td>97</td>
<td>189</td>
<td>246</td>
<td>301</td>
<td>182</td>
<td>1,066</td>
<td></td>
</tr>
<tr>
<td>Zambia</td>
<td>21</td>
<td>46</td>
<td>107</td>
<td>159</td>
<td>114</td>
<td>93</td>
<td>48</td>
<td>588</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>3</td>
<td>3</td>
<td>19</td>
<td>37</td>
<td>36</td>
<td>16</td>
<td>114</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3</td>
<td>79</td>
<td>170</td>
<td>326</td>
<td>498</td>
<td>549</td>
<td>743</td>
<td>426</td>
<td>2,794</td>
</tr>
</tbody>
</table>

Table 2. Geographic distribution of cases admitted to Mtemwa and Ngomahuru Hospitals 1925–62

<table>
<thead>
<tr>
<th>Province</th>
<th>1925</th>
<th>1930</th>
<th>1935</th>
<th>1940</th>
<th>1945</th>
<th>1950</th>
<th>1955</th>
<th>1960</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manicaland</td>
<td>8</td>
<td>41</td>
<td>65</td>
<td>50</td>
<td>77</td>
<td>111</td>
<td>117</td>
<td>59</td>
<td>528</td>
</tr>
<tr>
<td>Mashonaland N.</td>
<td>3</td>
<td>26</td>
<td>119</td>
<td>107</td>
<td>86</td>
<td>208</td>
<td>189</td>
<td>126</td>
<td>864</td>
</tr>
<tr>
<td>Mashonaland S.</td>
<td>185</td>
<td>266</td>
<td>185</td>
<td>136</td>
<td>172</td>
<td>195</td>
<td>171</td>
<td>55</td>
<td>1,365</td>
</tr>
<tr>
<td>Midlands</td>
<td>2</td>
<td>71</td>
<td>89</td>
<td>130</td>
<td>161</td>
<td>153</td>
<td>100</td>
<td>78</td>
<td>784</td>
</tr>
<tr>
<td>Matabeleland N.</td>
<td>9</td>
<td>68</td>
<td>50</td>
<td>66</td>
<td>56</td>
<td>99</td>
<td>88</td>
<td></td>
<td>436</td>
</tr>
<tr>
<td>Matabeleland S.</td>
<td>23</td>
<td>44</td>
<td>64</td>
<td>66</td>
<td>60</td>
<td>41</td>
<td>30</td>
<td></td>
<td>328</td>
</tr>
<tr>
<td>Victoria</td>
<td>10</td>
<td>191</td>
<td>106</td>
<td>141</td>
<td>145</td>
<td>186</td>
<td>148</td>
<td>67</td>
<td>994</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>208</td>
<td>627</td>
<td>676</td>
<td>678</td>
<td>773</td>
<td>969</td>
<td>865</td>
<td>503</td>
<td>5,299</td>
</tr>
</tbody>
</table>

Ages of onset and sex (Fig. 3) and types of presentation (Fig. 4). The latter is not necessarily a true picture, as many patients had probably suffered from the disease for long periods before admission and their clinical status had changed.

Numerous forms of treatment were used. Chaulmoogra oil, obtained from *Hydnocarpus kurzii* apparently showed encouraging results and the Forestry Department undertook experimental growth of the trees, a project which did not reach fruition.

Sulphetrone, and later dapsone, were introduced into Zimbabwe in the 1950s, and were spectacular in their success in the management of new and established cases. In the erroneous belief that these drugs would dramatically reduce the numbers of cases and that leprosy was no longer a problem, the Ministry of Health withdrew its support from Mtemwa in 1963. Many patients were discharged with no follow-up treatment. Other patients, many badly crippled and for whom no other home existed, remained at Mtemwa under the care of the Department of Social Welfare and were assisted by the Friends of Mtemwa, which later became the Rhodesia Leprosy Association.

A big step forward occurred in 1966 with the abandonment of compulsory hospitalization for all leprosy patients, and the establishment of out-patient treatment clinics. One such facility was the Tropical Diseases Unit at Harare Hospital in Salisbury, which was subsequently enlarged to accommodate 27 designated beds. Ngomahuru finally closed as a leprosy hospital in 1971, and the Leprosy Repression Act was repealed in 1974.
Figure 3. Type of presentation of patients admitted to Mtemwa and Ngomahuru Hospitals, 1925–62.

Figure 4. Sex and age of onset of symptoms of patients admitted to Mtemwa and Ngomahuru Hospitals, 1925–62.
Leprosy – modern concepts

The numbers of new cases seen since 1962 are shown in Table 3. Undoubtedly, many more cases exist but various factors, including the bush war and failure to recognize symptoms, have contributed to their omission. A review of 1,523 patients shows that in 31.1% the presenting prodromal symptoms were not skin lesions and that in 35.3% of those presenting with lesions diagnosis would be missed without whole-body examination. Known cases are indexed at Provincial Officer of Health level and regular leprosy review clinics are held in the more remote areas.

Now that the disease is more easily managed, and without the insidious methods of control previously used, many new cases come forward for treatment – often encouraged by family and friends. This trend must be actively pursued in view of the social and geographic upheaval experienced by the population during the war. Unnatural overcrowding in refugee camps and protected villages (established to denude large areas of the country of people who would otherwise feed and shelter guerrilla combatants) could lead to an upsurge in cases in future years.

With much of the overseas aid given since independence being used to redevelop rural areas, the Ministry of Health is training large numbers of community health workers who will play a vital role in early recognition of leprosy and channel patients towards treatment.

Leprosy has a wide geographic variation in Zimbabwe, and some areas produce considerably more patients than others. It is hoped that epidemiological studies currently being undertaken will elucidate this problem and provide a basis for future control measures.

References

**Epidemiologic patterns of leprosy in Vallegrande, Bolivia**

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Received for publication 3 August 1982

Summary The Andean province of Vallegrande (6,412 km²; 33,532 inhabitants, of which 99% are mestizos of Indian-Caucasian descent) has been an endemic area of leprosy for centuries. In 1977 the National Center for Tropical Diseases-CENETROP integrated the existing leprosy control activities in a comprehensive basic health service. The clinical status of all known cases was assessed, and an important effort at case finding was carried out by the basic health teams and the mobile leprosy control team. The overall prevalence rate on 31 July 1980 was 9.4 per thousand. The leprosy problem was mainly one of adults, the prevalence rate in males being 60% higher than in females. The proportion of lepromatous and borderline forms was 47%. The epidemiological patterns of leprosy in Vallegrande Province are consistent with those generally found in Latin America.

Introduction

Leprosy is endemic in Bolivia, a landlocked country (1,098,000 km², 5,570,105 inhabitants according to the 1976 census) situated in the heart of South America. The overall estimated prevalence rate is rather low: around one per thousand. In 1976 there were 1705 registered cases but 5,629 estimated;¹ in 1977 1832 registered but 3907 estimated cases.² These differences probably do not reflect changes in endemcity, but accentuate the level of uncertainty in assessing the endemcity. The cases are mainly concentrated in three areas: Chuquisaca Department, Beni Department and Vallegrande Province, Santa Cruz Department (Fig. 1).

*Manager, with Dr B Ribera, of the Medical Team of Vallegrande, CENETROP, which consisted of Drs A Talamas, J Encinas, J Salcedo, F Balderrama, E Valdez, F Zenner, N Siles and P-Y Lambert

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Vallegrande Province (6,414 km², 33,532 inhabitants*) is a dry Andean valley; its altitude ranges from 460 to 2,989 m above sea level, with the main plateau at 2,000 m. Ninety-nine percent of the population is mestizo of triple origin: Caucasian, highland Indian, and Guarani Indian. There are no blacks in this valley, although the name of the former leprosarium ‘Los Negros’ refers to black slaves who lived in this area during the colonial epoch.

The leprosy problem in Vallegrande dates back to the times of the Spanish colonization. A leprosarium was created in colonial times in San Juan del Rosario, 130 km from Vallegrande City, capital of the province.³ The first clinical description of leprosy in this area dates from 1928.⁴ In 1942 the National Leprosy Service was created and the first survey carried out in the province. In 1951 a leprosarium was constructed in Los Negros, situated 70 km from Vallegrande City. This centre was relocated at the beginning of the 1970’s in Jorochito, a locality situated 200 km from Vallegrande City (Fig. 2).

From 1972 to 1975 a programme of active case finding by means of a complete population survey was carried out in the province: 264 old cases

*Estimates are for 1980 and based on the data from the national census of 1976 and on the natural growth of the population.
were rediscovered and 190 new cases diagnosed. A control programme was started, but its efficacy and intensity diminished substantially once the project leader left the area.

In 1977, CENETROP (Centro Nacional de Enfermedades Tropicales) a Belgian–Bolivian project administered jointly by the Ministry of Health from Bolivia and the Tropical Institute from Antwerp, and situated in Santa Cruz de la Sierra, 250 km from Vallegrande, started a comprehensive basic health service in this province. The existing leprosy programme was revitalized and ‘horizontalized’. The first task consisted of the assessment of all known cases, and examination of their contacts. Secondly, the control activities, including case finding, were integrated into the primary health care system, and a mobile team was created to cope with the problem of inaccessibility of 52% of the population. This paper refers to the endemicity and the epidemiologic patterns of leprosy, 31 July 1980.

Materials and Methods

Following the establishment of the integrated health service, the province, for operational reasons, was divided into two zones: Zone A includes the 48% of the population who live no more than one hour's travelling time from a local health centre. In this zone, all the known cases and their contacts have been examined by the leprologist of the Ministry of Health, who works in complete co-ordination with CENETROP. All medical histories and classifications have been checked. Active case finding was carried out in some high risk groups (e.g. all direct family and household contacts, schoolchildren).
All new patients in the OPD of the hospital and in the health centres were routinely screened for leprosy. Zone B includes the remaining 52% of the population living in areas with limited access to curative health care. They were visited twice a year by a team consisting of a physician and a leprosy technician; all registered cases were visited at home, all histories checked, and 'problem cases' (those with an apparent diagnostic, therapeutic or classification problem) referred to the leprologist. During the visits to these remote areas, general consultations were held, simultaneously serving to screen for leprosy. Some cases continued to go for treatment at Jorochito, and even some new cases were detected there. Their registration was checked in order to have a complete centralized record.

With reference to the old cases a critical assessment of the diagnosis was made through the study of their record, the history of the evolution of the lesions and a biopsy if there were still signs of lesion activity. About 90% of the old cases were assessed as still needing treatment.

The diagnostic criteria of new cases were: typical skin lesions, clinical signs of neural involvement (thickening of nerves, loss of sensitivity), a positive smear and a conclusive skin biopsy. The diagnosis was made when two of these criteria were present.

The patients were classified following the Madrid scheme by the leprologist; the classification criteria were mainly clinical, smears and biopsies were done when necessary.

The population data are estimates based on the national census of September 1976, and the population dynamics due to natality, mortality, and migrations.

Statistical procedures: The 95% confidence intervals around the rate ratios were calculated by the 'test based' method, using a computer program. In order to examine differences in prevalence between Zone A and B, while controlling for age and gender as variables, a log linear analysis has been carried out by means of a 'LOGLIN' computer package, available at the Harvard School of Public Health, Boston.

Results

OVERALL PREVALENCE RATE

On 31 July 1980, 316 cases were registered, resulting in an overall prevalence rate of 9.4 per thousand.

AGE AND SEX PATTERN

Ninety-six percent of the cases were adults (Table 1), the rate ratio for those older than 15 years versus the children being 18.3. There was no difference
Table 1. Distribution of leprosy cases by age and gender

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-14</td>
<td>7 (1.0)</td>
<td>7 (1.0)</td>
<td>14 (1.0)</td>
</tr>
<tr>
<td>15+</td>
<td>187 (19.3)</td>
<td>115 (11.6)</td>
<td>302 (15.4)</td>
</tr>
<tr>
<td>Total</td>
<td>194 (11.6)</td>
<td>122 (7.3)</td>
<td>316 (9.4)</td>
</tr>
</tbody>
</table>

( ) = prevalence rate per thousand population as of 31 July 1980.

Table 2. Distribution of leprosy cases by clinical form, gender and age in Vallegrande province 1980, compared with the endemcity of 1975

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>Age (years)</th>
<th>Vallegrande, 1980</th>
<th>Vallegrande, *1975</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
</tr>
<tr>
<td>Lepromatous</td>
<td>0-14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>15+</td>
<td>64</td>
<td>44</td>
</tr>
<tr>
<td>Tuberculoid</td>
<td>0-14</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>15+</td>
<td>58</td>
<td>31</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>0-14</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>15+</td>
<td>42</td>
<td>23</td>
</tr>
<tr>
<td>Borderline</td>
<td>0-14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>15+</td>
<td>23</td>
<td>17</td>
</tr>
<tr>
<td>Total all ages</td>
<td>194</td>
<td>122</td>
<td>316</td>
</tr>
</tbody>
</table>

*Data.6

in prevalence amongst girls and boys, while the adult male rates were 60% higher than the adult female ones.

CLINICAL PATTERN

Thirty-four percent of the cases were lepromatous, 13% borderline, 29% tuberculoid and 24% indeterminate (Table 2). The multibacillary (lepromatous and borderline) cases were limited to adults, and the rate ratio of males versus females showed a consistent male predominance in nearly all clinical types (Table 3).

HETEROGENEITY OF THE PREVALENCE AT THE LEVEL OF VILLAGES AND ZONES

There were marked differences in the prevalence among the villages, the highest endemcity figures were observed in La Higuera (65.5 per thousand) and El Peñon (36.1 per thousand).

Ninety-eight cases were living in Zone A (prevalence rate 6.1 per thousand) and 218 in Zone B (prevalence rate 12.5 per thousand). The difference between
Table 3. Prevalence rates* of the different clinical forms in the adult male and female population, the rate ratio (male rates versus female ones) and the 95% confidence intervals around the rate ratios

<table>
<thead>
<tr>
<th></th>
<th>Lepromatous</th>
<th>Tuberculoid</th>
<th>Indeterminate</th>
<th>Borderline</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6.6</td>
<td>6.0</td>
<td>4.3</td>
<td>2.4</td>
<td>19.3</td>
</tr>
<tr>
<td>Female</td>
<td>4.4</td>
<td>3.1</td>
<td>2.3</td>
<td>1.7</td>
<td>11.6</td>
</tr>
<tr>
<td>Both sexes</td>
<td>5.5</td>
<td>4.5</td>
<td>3.3</td>
<td>2.0</td>
<td>15.4</td>
</tr>
<tr>
<td>Rate ratio</td>
<td>1.5</td>
<td>1.9</td>
<td>1.9</td>
<td>1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>95% c.i. (l)</td>
<td>1.02</td>
<td>1.25</td>
<td>1.14</td>
<td>0.79</td>
<td>1.34</td>
</tr>
<tr>
<td>95% c.i. (u)</td>
<td>2.21</td>
<td>2.90</td>
<td>3.17</td>
<td>2.15</td>
<td>2.15</td>
</tr>
</tbody>
</table>

*: prevalence rate per thousand (P.R.).

The rates in these two zones is highly significant \(\chi^2_{140} = 37, p \ll 0.001\). The problem of the rate difference, while controlling for age and sex, has been examined by fitting a loglinear model to the lepromatous data. The most parsimonious model that fits the data is the one with the following interaction terms: zone * lepromatous prevalence; gender * lepromatous prevalence; age * lepromatous prevalence. The \(G^2\) with 5 df (degrees of freedom) was 10.61, resulting in a \(p\)-value of 0.060. The contribution of the zone parameter was highly significant: the conditional \(G^2\) (1 df) was 18.6, with a \(p\)-value of \(<0.001\).

Discussion

Leprosy is practically hyperendemic in Vallegrande, with the overall prevalence rate remaining nearly constant since the survey of 1972–1975. Given that for the determination of the 1980 rates all cases were considered, regardless of the activity of the lesions and the duration of the treatment, an increase was expected. Two reasons might explain the lack of an increase of the endemicity. The first is emigration, which is a serious problem in Vallegrande, and results in a slightly negative growth rate for the population. Emigration seems to be non-selective as regards leprosy in general or clinical forms in particular. A second reason could be an under reporting of new cases. Although the principle of ‘horizontalization’ was introduced as a panacea for the case detection and case-holding deficiencies of the existing vertical programme, it seems evident now that case detection has not come up to expectations, despite a reasonable effort by all team members. The magnitude of the under reporting is unknown, although we estimate it to be small.

The leprosy problem in Vallegrande was very small among the children
and not even found in the under-fives. There was no difference in the prevalence rates between boys and girls. This is a common Latin American pattern,\textsuperscript{12} other examples of which were reported in Cuba\textsuperscript{13} and Argentina.\textsuperscript{14} In order to determine whether there was under reporting of cases in children, a school survey was carried out. Of the 3,524 children examined by our leprologist, no single new case was detected although 1 case, previously treated but subsequently lost to follow-up, was observed.

In Latin America, the multibacillary forms are prominent, and are more common in the adult male group.\textsuperscript{15} The sex index for the lepromatous forms is estimated\textsuperscript{12} as 200; in Vallegrande our figure was 145. The overall proportion of the multibacillary forms was 47%, a percentage identical to the other one observed;\textsuperscript{12} similar percentages are reported in Brazil (51\%)\textsuperscript{16} and Argentina (56\%).\textsuperscript{17} This seems to be the order of magnitude generally found in Latin America.\textsuperscript{1,18}

In Vallegrande the distribution of the leprosy endemicity is not homogeneous. But could biases explain the rate differences between zones A and B? Selection bias: if any, should presumably produce an under reporting in the inaccessible area (zone B), thus fortifying the observed association between area and prevalence rate. Observation bias: although the whole team was under the supervision of one and the same leprologist, who herself examined all cases of zone A and checked at least all the records of the patients of zone B, observation bias is possible. Under the assumption that the assessment of the lepromatous cases is less prone to observer subjectivity, the log linear analysis was limited to this group. The difference between zone A and B remained highly significant, consequently serious observation bias is unlikely. Confounding biases: the association between area and prevalence rate is quite strong; it seems therefore unlikely that the observed association could be explained by uncontrolled variables.

The proximity to a health centre (characteristic of zone A) is thus only a 'proxy' for factors that determine the prevalence. Given that the difference in endemicity between zones A and B was the result of the analysis and not the confirmation of a prior hypothesis, a new study is indicated to confirm this difference and to investigate the association between the disease and causal factors like crowding, level of hygiene, skin contact, nutritional status, genetic factors, temperature, poverty, humidity, exposure to tuberculosis.\textsuperscript{19-21} Recently epidemiologists have observed that the case-control methods, largely and successfully applied to chronic diseases, deserve to be used in causal research in leprosy.\textsuperscript{21,24} Therefore this new study should compare the prevalent cases of the moderate (zone A) and high endemic area (zone B) regarding their exposure to those potential causal factors, by case-control techniques. The control of variables and the study of risk factors and of interactions should be carried out by multivariate statistical modelling.

Prevalence rates and patterns are important tools for the description of a
leprosy problem, but for the analysis of the evolution of endemcity in a given community, incidence data are preferable,\textsuperscript{22} (Meade, 1971). The latter type of data has been noted to be sparse in the different endemic areas.\textsuperscript{23} We had hoped that our project would produce incidence data. Our field team found it impossible however to continually update the vital statistics of births, deaths and migrations, without diverting time and effort from the main task.

Acknowledgments

Financial support was given by The Bolivian Ministry of Health, The Tropical Institute of Antwerp, and the Damianfounds from Belgium.

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\end{enumerate}


Leprosy in 18-month-old children, Bichena District, Gojjam Administrative Region, Ethiopia

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National Leprosy Control Programme, POBox 5033 Addis Ababa, Ethiopia

Received for publication 8 June 1982

Summary In a mass survey of leprosy in Bichena District, Ethiopia, where a total of 814 new cases were detected, 2 cases of borderline-tuberculoid (BT) leprosy were discovered in children aged 18 months. Although incubation periods of less than 2 years are generally considered extremely rare, this finding emphasizes that young children under 2 years of age should not be excluded from leprosy surveys in endemic regions.

Introduction

A report on leprosy in children\(^1\) states that the average incubation period (or interval between exposure to infection and the first recognizable symptoms) is 2–5 years, and leprosy cases in children below 2 years are exceedingly rare. In studies\(^2\) on the life history of 462 children born at Kalaupapa Settlement on Molokai and living under a variety of conditions of early exposure to leprosy, it was concluded that living continuously with an untreated lepromatous parent results in leprous infection in about 40\% of such children, with onset of symptoms between 5 and 14 years of age.

Objectives

One of the main objectives of the mass survey which was conducted between 1 February and 14 May 1981 in Bichena District, Gojjam Administrative Region, Ethiopia, was to find leprosy cases as early as possible and put them under regular treatment.
Patients and methods

Leprosy case detection was carried out in 231 localities of Bichena District with a total population estimate of 235,700.

A population count was conducted by focal point survey where all the individuals in the community were gathered at a central place for systematic physical check up. The focal point survey was supplemented by a house-to-house survey.

Results

Eight hundred and fourteen new cases were detected during the survey, 168 (21%) falling in the 5–14 age group and 12 (1.5%) in the 1–4 age group. Among the 12 cases two children of 18 months were found to have borderline-tuberculoid (BT) leprosy.

The first child, a female, had a mother who had been diagnosed 7 months previously as suffering from borderline leprosy and had been treated with dapsone 100mg daily. The child had never visited a clinic before the date of the survey, 20 February 1981. Her father was healthy. The parents stated that the child’s skin lesions had been present for 5 months, and examination revealed a number of hypopigmented macules on the back, arms and buttocks. A biopsy was taken from an active lesion, and the report from ALERT, Addis Ababa, stated: ‘There are multiple small collections of epithelioid cells, lymphocytes, plus a few Langhans type giant cells, throughout the mid-dermis. No AFB seen. Opinion: BT leprosy.’

The second child, a boy, also 18 months old, had a lepromatous father who had been on treatment with dapsone during the previous 10 years, but the mother was healthy. The oldest child in the family, a girl of 10 years, was found at the time of the survey to have tuberculoid (TT) leprosy. The fact that the mother had no leprosy excluded any question of intra-uterine transmission. Examination of the boy revealed hypopigmented macules on both upper arms, buttocks and legs. He was sent to ALERT for further investigation where a diagnosis of borderline-tuberculoid (BT) leprosy was confirmed.

Discussion

In spite of the generally held view that in leprosy an incubation period of less than 2 years is extremely rare, we were able to find two children of 18 months suffering from leprosy out of a total of 814 patients diagnosed in the survey, an incidence of 0.24%. This finding emphasizes that young children under 2 years of age should not be excluded from leprosy surveys in endemic regions.
Acknowledgements

We are indebted to the staff of Armauer Hansen Research Institute Laboratory for preparing the biopsy, and to Dr J Warndorff for reading the result.

References

Domiciliary and Field Work

TEACHING FOOT CARE

E P Fritschi, Schieffelin Leprosy Research & Training Centre, Karigiri, North Arcot District, Tamil Nadu, S India.

Summary. A new approach is being made to the teaching of foot care. The learning of the group is in the context of the team involved. The emphasis is on a practical and participative approach.

Introduction

The care of the foot is not the work of any one person in the leprosy health delivery service. It is essentially a team responsibility. The doctor is required to understand the basic factors which bring about plantar ulceration and to recognize the different types and their treatment. He must be able to prescribe appropriate preventive footwear intelligently and also to operate on feet that require simple surgical intervention. The physiotherapy technician also needs to understand the factors causing ulcers and prevention. He should be able to treat uncomplicated ulcers and is normally the person in the team who gives soaks, makes assessments and applies plaster-of-Paris casts. The third essential member of the team is the shoemaker, often somewhat disparagingly referred to as the 'cobbler'. An intelligent understanding of his role is a very strong motivating factor in his work.

However, the care of the foot is still probably the most neglected aspect in the treatment of the leprosy patient. It has no obvious scientific attraction, it is not important from a public health angle and its aesthetic and cultural appeal is not great.

Nevertheless, the plantar ulcer probably contributes more than any other lesion of neglected leprosy to a patient's mental suffering and social instability.

In the last 2 years we have been involved in teaching the care of feet in several centres throughout the country. This article sets forth the pattern of teaching which has evolved.

The learning teams

It is difficult for a single person to introduce new activities to a programme already established. New ideas meet with resistance on the part of other members of one's institution. The plan was therefore conceived, of training not one member of the team, but all three at the same time.

Thus from the outset participants are invited in teams. Six centres were each asked to send a shoemaker, a physiotherapy technician (or a paramedical worker willing to care for ulcers) and a doctor.
66  Domiciliary and Field Work

As far as possible the aim is for teams to learn together, separating only to study in
greater depth each member’s particular role, for example the doctor to operate, the physio-
therapist to assess, to treat the foot and to apply plasters, and the shoemaker to produce the
prescribed shoes.

The teaching team

The care of the foot is essentially a matter of skills and for a doctor to think that he can
teach a shoemaker to make shoes is the height of presumption. So the logical decision was
to involve a teacher for each topic being taught.

This was easy when the first 2 courses were conducted in our own centre. We then
experimented in other centres to which we were invited, and took to each centre a teaching
team, which consisted of a physiotherapist who was an experienced teacher, a shoemaker
who was skilled and with teaching experience, and a surgeon. The proposed host centre
had been briefed in advance and supplied the necessary materials.

All the members of the course are resident in the host centre and have their meals
together. This serves to increase the team spirit, and to cement a relationship between
members from the same centre.

INTRODUCTION

The first session is introductory, with each member introducing himself and stating his
designation.

The team leaders are asked to report on the activities in the area of foot care in their
own institution. The members of the teams are then asked to state their problems frankly.
This session is conducted bilingually to encourage the shoemakers as they usually do not
understand English. Interesting problems have emerged, problems of role interaction, dif-
ficulties in working arrangements, too many repairs, shortage of supplies, lack of patient
compliance, dissatisfaction with slipper patterns offered. In some cases members of the
same team were not aware of each others difficulties.

SETTING OF OBJECTIVES

Course objectives are then set by the members. The following is a typical set of objectives
compiled from the 5 courses so far conducted.

1 Shoemakers should be able to (a) make 3 pairs of simple ‘Y’ strap chappals per day; (b)
give instruction to patients in shoe maintenance and foot care; and (c) change the pattern
of the uppers.

2 Physiotechnicians should be able to (a) give comprehensive instruction to patients in
routine foot care, soaks, scraping and oil massage and the home treatment of any pre-
ulcerative conditions encountered during inspection of the foot; (b) apply an average of
6 plaster-of-Paris boots or shoes per week; and (c) demonstrate for 6 patients per day the
 technique of foot soaks, scrapes and oil massage.

3 Doctors should be able to (a) diagnose and classify all foot ulcers; (b) be able to perform
the simple operation required for complicated ulcers; (c) correctly prescribe the appropriate
footwear in each case; (d) aim at a target of an average of 45 days for the complete healing
of all ulcers; (e) ensure an adequate and regular supply of materials to the shoemaker; and
(f) maintain statistics of the prevalence of foot ulcers in the field service so as to be able to
evaluate the effect of a greater emphasis on foot care.
CONSTRUCTION OF THE RECOMMENDED FOOTWEAR

In the afternoon of the first day all members of the course watch while the shoemaker of the teaching team demonstrates on a selected patient the full process of the construction of a sandal, from measurement to assembly, fitting and fixing.

During this time, informal conversation is held on the properties of the materials, recommending their costs and availability and possible alternatives. The attention of the group is drawn to technical points, and the principles of ulcer preventive footwear, reasons for recommending the particular pattern chosen, and the essential and non-essential features. Many of the doctors had never seen a slipper being made and were very interested.

DAYS 2, 3 AND 4

These follow a standard pattern, differing slightly in timing according to the convenience of the host centre.

THE FOOT CLINIC

Here a selection of about 15–20 patients are examined by the doctor of the teaching team with the whole group in attendance. (The shoemakers are only asked to attend the first clinic, so that they can see the procedure. Thereafter they concentrate on making shoes.)

The emphasis is on method of examination, diagnosis of ulcer type and the treatment recommended, and examination of the other foot to reveal possible pre-ulcerative conditions such as cracks, callouses, blisters, 'hot spots' etc.

From these clinics cases are selected for demonstration of foot care techniques and for operations later in the day.

LECTURES

After the clinic the physiotherapy technicians and doctors meet together. The subjects dealt with during the course are:

2. Types of ulcer and their treatment. The features of the full plaster-of-Paris boot, and the below ankle plaster-of-Paris double-rocker shoe, and the indications and contra-indications of both.
3. Health education, i.e. teaching the patient how to care for his feet at home.
4. Principles and features of ulcer preventive footwear, and indications for the various types.

DEMONSTRATION

Each day one aspect of foot care is demonstrated to the group. The first demonstration is the taking of a Harris Mat footprint. The shoemakers are included in this since it is primarily a test to monitor the effectiveness of the footwear.

Other demonstrations on the following days include: technique of foot soaks, scraping and foot inspection; applications of the moulded double-rocker shoe; and motor and sensory assessment of the foot.

On each day, in the afternoon, the physiotherapy technicians practise the particular technique that has been demonstrated in the morning. The doctors participate in the operations on the septic feet that have been seen in the morning clinic. The shoemakers complete a pair of slippers for each of the two patients that have been allotted to each of them.
The operations demonstrated are minor, common procedures requiring a minimum of surgical skill and ritual. They include: Excision of ulcer and dorsal drainage, with or without metatarsal joint excision; skin grafting of ulcers; and exploration and laying open of sinus and curettage.

During the week, as far as possible, each doctor is asked to do 2 operations.

EVALUATION AND PLANNING

On the last day the group reassembles. The shoemakers show the patients the slippers that have been made for them and the doctor and physiotherapy technician of his team inspect and check them. If alterations are to be made, such as corrections to straps or checking of the position of the arch support (by Harris Mat footprint technique) this is done on the spot.

The final session is the planning for implementation. Each team spends 1 h together discussing their plan, which is then recorded and reported to the plenary session by the doctor in charge.

FOLLOW-UP

A full report of the course is prepared and sent to each participant and includes the plans which have been made at the final session.

COMMENT

The course is always enjoyed by the participants, many of whom have never considered the wide range of interest and therapeutic activity involved in foot care.

I personally have reservations about the participation of doctors in the operating session. Many young doctors have had a minimum of exposure to surgical technology and some could not even put on sterile gloves confidently and correctly. It would appear that 4 operating sessions is not adequate. The question arises 'Is it better to give a little training than none at all?'.

Suggested reading


ILEP; Guidelines for the Campaign against Leprosy (2nd edition)

The XIVth General Assembly of ILEP in Amsterdam adopted the English version of the final text of the Guidelines. The French version will be submitted to the Working Session in December 1982. These guidelines have been drawn up by the ILEP Medical Commission, in agreement with Member-Associations and various Ad Hoc Working Groups. They are for the use of ILEP Member-Associations, both for the assistance of their own staff and for distribution, if Associations so wish, to those with whom they are working in the field – whether governments, other voluntary agencies or project managers – in order to facilitate mutual understanding. (Source: ILEP Co-ordinating Bureau, 234 Blythe Road, London W14 OHJ.)

Leprosy Relief Work Emmaus-Suisse and PAHO; project in 11 Caribbean countries

Leprosy Relief Work Emmaus-Suisse and the Pan American Health Organization recently signed an agreement totalling US$275,489 to assist 11 Caribbean countries to organize a leprosy control program. Those involved in the 3-year project include Anguilla, Antigua and Barbuda, Bahamas, Barbados, Dominica, Grenada, Montserrat, St Kitts/Nevis, St Lucia, St Vincent and the Grenadines, and Turks and Caicos Islands.

The long-term objectives of the project are:
1. To achieve control of leprosy so as to protect the healthy population and reduce the prejudices against the disease in the general population and in those affected.
2. To prevent or reduce deformities, and to detect early at least 90% of non-infectious cases.
3. To ensure that 100% of the registered infectious cases receive regular treatment, under supervision.
4. To ensure that no less than 80% of the registered noninfectious cases receive regular treatment.
5. To review patients regularly and to ‘release from control’ (discharge) all those who qualify, excluding infectious cases.
6. To provide each year services and facilities for rehabilitation of approximately 50% of the cases found in that year.
7. To provide short-term hospital care for patients with the acute complications of leprosy, who may represent about 10% of registered cases annually, and facilities for reconstructive surgery as necessary and feasible.
8. To ensure the provision of appropriate instruction in leprosy control for all trainees in health-teaching institutions.
Reports, News and Notes

Plans for 1982 include visits to each of the participating countries to assess and review the leprosy control programs with the national designated Leprosy Control Officer. Standard patient record forms (approved by the Standing Committee on Leprosy Control in the Caribbean) recently printed at CAREC* are being distributed to countries in order to facilitate both individual patient supervision and the collection of data for national programme assessment.

OMSLEP; recording and reporting system for leprosy patients

This system has now been published in English and French from the Epidemiology unit of the Catholic University of Louvain, Brussels, with the sponsorship of the World Health Organization. The authors are MF Lechat, CB Misson and J Walter. The summary reads as follows:

1. The OMSLEP system involves recording leprosy patients on an individual patient form. The information recorded summarizes the patient’s condition on detection and following each year of treatment.
2. Two statistics forms summarize the data for all the patients detected or registered each year and can be used to evaluate a leprosy control programme. It is possible to use only the statistics forms if an individual patient form containing the required information is already in use.
3. By this system it is a simple matter to calculate operational indices at the time of detection and after detection, together with epidemiological indices, in order to evaluate the performance and effectiveness of leprosy control programmes. The meaning of the various indices is explained. It is possible to process the data by computer if so desired.

Carville; International Seminar on Hansen’s Diseases, September 1982

The programme for this 7-day seminar covered clinical aspects, treatment, history and development of the Center at Carville, reactions and their treatment, pathology, microbiology, rehabilitation, psycho-social aspects, skin smear techniques, vocational rehabilitation in the field, occupational therapy, orthotics, recent progress in biomedical research, training and education and prospects for the next decade. Thirty-five participants were listed from India, Brazil, Mexico, Africa, Haiti, Nepal, Pakistan, Trinidad, Virgin Islands, Taiwan, Egypt, England and China.

Brazil; College of Hansenology founded

Dr Celio Paula Motta has kindly drawn our attention to the founding of this College which is open to workers in the fields of medicine, biology, chemistry, psychology, anthropology, history, social sciences, nursing, health education, communication – and others who wish to cooperate. Apply to Rua Nascimento Silva, 16/201–IPANEMA–Rio de Janeiro/RJ, Brazil, CEP 22.421.

Resignation of Dr Gordon Ellard from the Editorial Board of Leprosy Review

We record with regret Dr Ellard’s resignation from the Editorial Board of this journal. His numerous contributions not only to Leprosy Review, but also to a wide range of other

journals, are well known to all who work in leprosy and for many years this Board has benefited from his immense experience, particularly in the field of chemotherapy and compliance to prescribed drugs. We record our sincere thanks for his many years of service, not only as a contributor, but also in the expert assessment of articles submitted for publication.

EDITOR

Bureau of Hygiene and Tropical Diseases, photocopy service

The Bureau is introducing for a trial period a photocopy service for its readers. Photocopies of most items abstracted in the two journals, Tropical Diseases Bulletin and Abstracts on Hygiene and Communicable Diseases, except entire publications (e.g. complete books), can be supplied, provided that a copyright declaration form is completed and signed. The charges for photocopies are 20 pence per page for delivery in the UK and 25 pence (US$0.60 cents) per page elsewhere (inclusive of delivery by air mail). The minimum charge is £2.00 (US$5.00) per order. Orders should be prepaid to avoid delay.

For the necessary form please write to: Bureau of Hygiene and Tropical Diseases, Keppel Street, London WC1E 7HT, England.

Correction

We are grateful to Drs Titia Warndorff and Wilhelm Beaumont of ALERT in Addis Ababa for drawing our attention to errors in the figures of the Editorial on ‘Drug compliance in the treatment of leprosy’ and the article by Ellard et al. on ‘The self-administration of dapsone by leprosy patients in Ethiopia’ in Lepr Rev 52, Number 3, 1981. The correct number of outpatients studied was 358 and the numbers quoted in the Editorial (368) and in the summary of the paper (295) are unfortunate errors. Editor.
Letters to the Editor

LEPROSY SURVEYS IN URBAN SLUMS — POSSIBILITIES FOR EPIDEMIOLOGICAL INVESTIGATIONS

Sir,

The problems and difficulties of undertaking effective surveys in densely populated urban areas have always intrigued me. Whilst working in Ghana the low number of leprosy cases registered for treatment at the Accra (capital city) clinic caused concern to the Ghana Leprosy Service and considerable thought was given to the possibility of undertaking an urban survey in that city. Unfortunately at the time there was neither the money or trained staff to mount an effective survey where a near 100% coverage could be assured.

It was with interest, therefore, that I read the article on the leprosy survey undertaken in part of Bombay and published under the above title. Unfortunately the authors did not elaborate on how they obtained the 81% coverage. Materials and methods were given only a few short lines; whilst the whole project is summed up in the sentence ‘This study also shows that the slums could be surveyed, with minimum coverage of 80%, with proper planning and employing trained paramedical teams.’

What would be of great interest to all engaged in leprosy work is a detailed account of how the teams set about their work. The planning of such a complex operation would take considerable time and answers to the following questions would be most useful:

How many medical and paramedical staff were employed surveying the 8 areas?
What census data was available to the teams? areas, districts, streets, houses?
What precautions were taken to ensure that there was no duplication of examinations and how many examinations were undertaken by 1 team in a day?
Was the clinical examination of those seen a full examination, i.e. the whole body and, if so, how was this arranged? Were they examined in their own homes or at a central point?
Was any attempt made to examine the missing 19%?
Was treatment already available to the leprosy patients in the 8 areas and how were the new cases channelled to the treatment points?
Were other diseases noted?

I am sure that a paper on this subject in the ‘Domiciliary and Field Work’ section of Leprosy Review would provide a good deal of interest to many of the readers.

J H ELDON

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0305–7518/83/054072 + 06 $1.00 © British Leprosy Relief Association
Sir,

Greater Bombay (district place) is a very heterogenous complex urban area (deserving to be called super urban) housing a population of 8.2 million (1981 Indian Census). About 40% of population is believed to be living in 840 officially known slum pockets, spread in different municipal wards. The 8 slums included in this study are situated in 2 different municipal wards. No statistical sampling technique was employed. One of the wards (part of H ward) has been adopted by this project for intensive leprosy control programme. The accurate data on population living in these 8 slums were not available from any census source. The approximate size of the population was judged by contacting local leaders or social organizations of each slum. Each slum was surveyed in the quickest time possible so as to obtain fairly valid data. Four to 5 teams were deployed, consisting of at least 1 male and female trained paramedical worker, for house-to-house surveys. The clinical examination was carried out on the doorstep. Children were stripped completely, adults to the maximum extent possible. Satisfactory examination of female population could be done as female workers were employed. Such surveys were always preceded by discussing the importance of case detection with local leaders and by health education programmes, like film and slide shows on leprosy. And even during survey coloured folders on leprosy were shown and facts about leprosy were explained to them. This approach induces awareness about the disease and encourages community participation leading to good co-operation for examination. On average each worker could examine about 40 subjects thoroughly in about 4 h of actual survey period in the field.

In spite of good co-operation from the community only about 60% of the population could be examined during the first visit as the male adult population were at work. However a minimum of 80% examination is aimed at and always could be achieved by undertaking absentee visits (examination of missing population) starting at a different time and even on holidays; in spite of such an approach the remaining 20% of the population, mostly adults, cannot be examined. As soon as a person was examined the date was recorded against his/her name and entered in a family survey form which avoids duplicate examination.

It is interesting to observe that even during and after the survey, suspected cases reported voluntarily to the clinics. Medical teams were posted for case confirmation but not for initial survey programmes. Such surveys have to be planned exclusively with trained paramedical workers as there is acute shortage of medical manpower for leprosy work and medical personnel may not be required for routine survey.

Once the survey was started, the detected leprosy cases were called to the nearest skin clinic established by this project right in the midst of groups of slums or a single slum. About 20% of cases were under treatment in different leprosy centres or at private doctors in Bombay prior to their detection. The common skin conditions like scabies, pyoderma and tinea etc. which were detected during population surveys were also referred to our clinics for simple treatment. In survey forms common skin diseases were alone noted, other complicated medical as well as dermatological conditions were referred to nearby general hospitals where we run our clinics.

With proper planning and approach with a sufficient health education programme, paramedical workers, including untrained workers with sufficient knowledge of leprosy, one can easily survey an urban slum population though certain difficulties are encountered. This study was undertaken only to find out leprosy endemicity in different slum pockets.
Similarly the population living in high income flats also could be surveyed satisfactorily and data on this will form a future communication.

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ERYTHEMA NODOSUM LEPROSUM

Sir,

We were interested to read the hypothesis by Dr Mshana, but his contention that ENL is due to an imbalance of lymphocyte subsets is based on some statements which appear not to be well founded.

1. ‘The hallmark of the lesions is perivasculitis’. The authors whom he quotes make it clear that the hallmark of an ENL lesion is polymorph infiltration of a lepromatous macrophage granuloma. Vasculitis is conspicuous in only half the lesions (minor involvement of blood vessels is a universal feature of inflammatory lesions).

2. ‘Three patients with tuberculoid leprosy ... developed the Lucio phenomenon’. This occurrence is quite exceptional and in need of confirmation.

3. ‘Uveitis as a complication of leprosy ... occurs only during ENL’. Yes, but bacilli, sometimes clinically silent, are a frequent finding. It is just such small masses of bacilli, or their antigenic remnant, whether in skin, nerve, muscle, testis, iris or elsewhere, that are almost certainly present at the site of ENL lesions. However, there is a need for further biopsy reports on this point.

4. ‘ENL-like lesions do not develop in leishmaniasis’. In cutaneous leishmaniasis necrotizing reactions with polymorph infiltration are a common event, and as in ENL perhaps, their initiation is dependent on a moderate parasite load, neither too high or too low.

Evidence of the regular presence of extravascular immune complexes at the site of ENL lesions awaits publication. But why do many immunologists pay so little attention to histology? And why do they often appear to neglect the over-riding importance of antigenic load and antigen–antibody ratios? The significance of the latter in the determination of necrosis in mycobacterial immune complex granulomas is the subject in another recent study.

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References


REPLY. ERYTHEMA NODOSUM LEPROSUM

Sir,

The points raised by Drs DS Ridley, Marian J Ridley are important, they are not in my view sufficient to disqualify the hypothesis.

Perivasculitis may or may not be conspicuous in ENL lesions, but the argument is centred on the presence of polymorph infiltration in an otherwise chronic inflammation. So far the theories for this have been based on immune complexes and Arthus reaction. Immunologically, however, the ENL syndrome does not seem to be precipitated by an Arthus phenomenon and this is the hypothesis.

The role of antigenic load and antigen–antibody ratios is difficult to assess but must be seen in the context of all the immunological disturbances seen during ENL. Once this is done deposition of complexes or activation of the complement cascade in situ, secondary to a delayed type hypersensitivity, becomes a real possibility. The complexes can then regulate the local reaction and thus perpetuate a pathology initiated by a different mechanism. Immune complexes, therefore, have a role to play in ENL, but the argument put forward in the hypothesis is that these complexes are not the initiating factor.

Incidentally, while not offering direct evidence for the hypothesis, we have recently found that together with other immunological disturbances, there is an increased level of Natural Killer (NK) cell activity during ENL (Converse P, Humber DP, Mshana RN, Belehu A, in preparation). These NK cells are known to be stimulated by Interferon (IFN). While the role of these cells in the pathogenesis of ENL is not yet clear, it is of interest to note that IFN has recently been reported to abrogate Suppressor T cell response of delayed type hypersensitivity in animals. If this is true also for human beings it is quite possible that the increase in NK cell activity in ENL is mediated by an increase in IFN which at the same time reduces suppressor cell activity. We are in the process of assaying IFN levels in the evolution of ENL.

Taken as a whole, ENL can only be explained in full by evoking an initiation phase which is most likely to be a cell mediated response, and a secondary perpetuation phase which might involve immune complexes.

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Reference

Sir,

During the past 2 years a total of 20 lepromatous cases in relapse have been seen in this Institute. All had received dapsone as monotherapy in the past, the total period of treatment varying from 7 to 30 years with a mean of 18 years. On mouse footpad testing, 6 cases have been confirmed as resistant to dapsone: at levels of 0.01% in 2 cases, at 0.001% in 1 case and at 0.0001% in 3 cases. According to the patients' account no anti-leprosy drug other than dapsone had ever been taken. The other 14 cases await the results of mouse footpad testing.

Figure. Multiple, bilaterally, symmetrical lesions: raised, red or pink, with central 'dimpling' or umbilication. The area photographed includes the upper left buttock together with part of the loin and lumbar region.

In 5 cases (25%) the clinical manifestations on the skin were unusual, not only for relapse cases in this country but for any pattern of leprosy, treated or untreated, as seen here. The skin lesions (Figure) consisted of multiple, bilaterally symmetrical lesions of approximately 1–2cm diameter, raised, red or pink, and with central 'dimpling' or umbilication. Whilst appreciating that some of these resemble lesions with the 'punched-out' centres of mid-borderline (BB) leprosy on the Ridley–Jopling scale, their large number, small size and bilateral symmetrical distribution are unusual and do not correspond to published accounts of patients with lepromatous leprosy who are known to relapse with features of borderline leprosy.

The purpose of this letter is to draw attention to yet another form of leprosy, as seen in Korea, which appears to be associated with dapsone resistance and relapse. Perhaps similar findings will be encountered in other countries and ethnic groups.

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PRIMARY DAPSONE-RESISTANT PAUCIBACILLARY LEPROSY IN ZAIRE

Sir,

Primary dapsone-resistant leprosy has been documented in a case of BT leprosy regressing into a BL form of the disease, when *Mycobacterium leprae* could be isolated in mouse foot pads and dapsone resistance proven. In view of the increasing prevalence of secondary dapsone resistance, more cases of primary dapsone resistance can be expected. Where secondary dapsone-resistant leprosy develops only in multibacillary forms of the disease, primary dapsone-resistant leprosy may be expected to occur in all forms of the clinical spectrum of the disease.

We observed 2 cases of primary resistant paucibacillary leprosy in Zaire.

The first patient is a boy, 8 years old, who had BT leprosy since the age of 5 and was treated with DDS 100 mg/week. New lesions continued to appear under this treatment. In January 1980 supervised treatment was commenced with a single dose of rifampicin 30 mg/kg and clofazimine 200 mg/week, given for 5 months. Later on the patient was given dapsone again by a nurse, without our knowledge. During the following months, the disease progressed. The patient was hospitalized, a skin biopsy confirmed the diagnosis, and then received a supervised course of dapsone, 50 mg/day for 3 months without any regression of the lesions. He was then treated with 8 weekly supervised doses of rifampicin, 22 mg/kg. During the next months there was steady improvement of the lesions. The boy lived with his mother, a known lepromatous patient, clinically suspected of secondary dapsone resistance.

The second case is a girl, now 13 years old. Because her mother had lepromatous leprosy the child was given dapsone prophylaxis, 100 mg/week at age 6. A year later she developed BT lesions on her back and dapsone dosage was increased to 200 mg/week. The disease progressed. Thiambutasine $3 \times 250$ mg/day was added for 18 months with only slight improvement. The girl was hospitalized, a skin biopsy confirmed the diagnosis, while she was given a supervised course of dapsone 50 mg/day for 4 months. No clinical improvement resulted. Eight weekly supervised doses of rifampicin, 17 mg/kg, were administered, resulting in a spectacular change in the lesions which nearly disappeared within 2 months. In this second case, the patient's mother also has clinically secondary dapsone-resistant lepromatous leprosy.

The practical importance of primary dapsone-resistant paucibacillary leprosy is the difficulty of diagnosis. Isolation of the bacilli cannot be performed and only lack of improvement under supervised sulphone treatment and quick regression of the lesions after administration of the bactericidal drug rifampicin allows to make a diagnosis.

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References


The following translation from the original publication in German was made by a medical student from Muenster during a period of clinical training in Oxford, September 1982. Editor

Das Mykobakterium Leprae Und Die Mesenchym-reaktion Des Integumentes Bei Lepra Lepromatosa Und Interpolarer Lepra (Mycobacterium leprae – Mesenchymal Reaction of the Skin in Lepromatous and Dimorphous Leprosy), by M Bierther, EM Lemmel, KF Schaller, D Schranz. Ernst-Rodenwaldt Institute, Koblenz. In cooperation with the German Leprosy Relief Association. 41-page monograph, paperback, illustrated with 72 electron micrographs, 1978.

This study aims to correlate different structural appearances of Mycobacterium leprae with the clearly distinguishable mesenchymal reactions of the skin in lepromatous and dimorphous leprosy by electron microscopy. Additionally, the authors discuss the morphologically distinctive basic mechanisms of the anti-infectious response. The main headings are as follows: 1. Sites and fine structure of leprosy bacilli, and 2. Mesenchymal reaction of the skin: in the exudative phase; in the phase of bacterial phagocytosis and digestion; in the phase of circumscribed granulomatous reaction.

The work is based on the electron microscopical examination of skin biopsies taken from 6 untreated patients with lepromatous leprosy and 3 untreated patients with dimorphous leprosy. Diagnosis was confirmed by clinical examination and histopathology.

The biopsies were pre-fixed for 4–12 h with 5% glutaraldehyde in 0.1 M phosphate or cacodylate buffer (pH 7.2); sent to Koblenz in the buffer; fixed with 2% OsO₄ and 1% K₂C₂O₇ solution; dehydrated in alcohol and then embedded in durecupan after 12–23 days. Because this method renders the nucleus-equivalents of the bacilli invisible, the biopsies of 3 patients were fixed in 1% OsO₄ solution plus 1M CaCl₂ immediately after taking.

During the following dehydration in the increasing alcohol series the uranyl contrast methods of Wohlfarth-Bootermann in 70% alcohol was used. The findings can be summarized as follows:

1. Sites and fine structure of dividing and resting leprosy bacilli

M. leprae was detected on the skin surface in 2 cases, in 1 case it could be found in the orifice of a skin appendage and in all cases it was present in the corium, intra – as well as extracellularly.

In lepromatous leprosy the bacilli were predominantly rod-shaped, whereas in dimorphous leprosy mainly bigger forms with invaginations of the cytoplasmic membrane, vacuoles and membrane bodies in the cytoplasm could be seen. The nucleus equivalents show a reticular pattern of the DNA, which lies in an electron-dense nucleoplasm. The nucleoplasm is connected with the cytoplasmic membrane through the cytoplasm by numerous channels.

2. Mesenchymal reaction of the skin

Morphological changes of capillaries and their involvement in the cellular defense against the leprosy infection. The endothelial cells show an increase in volume, enlargement of their nucleus and disintegration of the cellular association. They can protrude into the vessel and obstruct its lumen. Their cytoplasm contains numerous morphologically different vacuoles containing leprosy bacilli, which appear to be structurally unchanged. Some biopsies show rupture of the cytoplasmic membrane and release of M. leprae into the capillary.

Similar changes can be seen in the adventitial and smooth muscle cells of the vessels. This process leads to destruction of these structures; finally only remains of endothelial and smooth muscle cells are found. In the periphery, fibroblasts produce amorphic base-substance and collagen fibrils which push forward towards the former vessel centre.

Morphology, activity and phagocytic capacity of macrophages and their failure to digest M. leprae in the exudative phase. Big macrophages with the typical morphological signs of increasing activation (increase in number of lysosomes, ergastoplasm profiles) are the predominant cell type. Their caryoplasm shows characteristic spherical inclusions which might reflect the functional changes of the nucleus due to the presence of leprosy bacilli. Precondition for the endocytosis of M. leprae is a close contact between the bacillus and the macrophage which can occur on the whole surface. The mycobacterium gets surrounded by an ingestion vacuole which is subsequently taken into the cytoplasm. The bacilli appear to be completely unaltered, they are even able to multiply themselves and get into the interstitial space after destruction of the macrophage. The digestion of M. leprae is accompanied by a marked change in the cellular picture.

Appearance of lymphoid cells–phase of increased phagocytosis and digestion. Small lymphocytes which were absent during the exudative phase...
can easily be detected. They seem to leave the capillaries trans-endothelially. They take up appo-
sitional contact with the macrophages, indenta-
tions can actually be seen. At this stage the macro-
phages are characterized by intensive digestive
processes. Primarily the cell wall remains intact
whereas the cytoplasm shows marked features of
destruction (osmiophila). Finally, bacterial cell
wall rests can be found in the vacuoles. In the
meantime laminated membrane convolutions indi-
cate macrophage degeneration.

These processes point out a mutual depen-
dence; the direction of flow of information how-
ever, cannot be detected.

Appearance of mast-cells, amyloid deposits and
giant cells. Apart from macrophages, some mast
cells can be detected, especially near vessels close
to the epidermis. Characteristic features are lyso-
some-like inclusions which can be stained with
Pb-citrate and therefore are easily distinguishable
from macrophages. Additionally they do not
contain bacilli. Closely under the epidermis lies a
homogenous hyaline substance, presumably amy-
loid. It may be the product of permanent exposi-
tion of antigen products of leprosy bacilli to
immune competent plasma cells.

Finally, a few giant cells which can be poly-
nuclear and show bacterial inclusions were detected.
Their number seems to correlate with the intensity
of the infection.

Epithelioid- and giant-cells as a feature of the phase
of circumscribed granulomatous formation in
dimorphous leprosy. Macrophages are again the
predominant type of cell. Additionally to the
previously described mesenchymal reactions, how-
ever, areas of macrophages forming a granuloma
can be seen. The granuloma is surrounded by a
macrophagic infiltrate. The macrophages lie along
the collagen fibres of the connective tissue which
is slightly oedematous. They contain leprosy
bacilli and breakdown products and surround nerve
fibres, lymph- and blood-vessels.

In the granuloma no phagocytosis could be

demonstrated. The membranes of adjacent macro-
phages show indentations. Inside the granuloma
lie big epithelioid cells which still show close
relationship to macrophages. On the other hand
they have a differently structured chromatin-
pattern of the nucleus and a remarkably high
number of mitochondriae, which is an obvious sign
of intensive metabolism. Additionally, many
organelles with a secretary function are present
which could be involved in a synthetic process. The

authors suggest that foreign substances, which are
produced by the chronic stimulus, could be taken
up from the interstitial space, metabolized and
detoxified and released as less toxic products
which would imply a protective function.

In summary. The study confirms that the killing of
bacilli depends on cellular defence mechanisms.
However, it does not explain the initial reactions
caused by M. leprae. Although it describes the
mycobacterium in different phases, a coherent
description of the structural changes of M. leprae
is still missing. Nevertheless, this study covers the
morphological changes and reactions of the skin in
lepromatous and dimorphous leprosy at electron
microscope level in detail and it should be of great
value as a work of reference to researchers in this
field.

M W A HENTZE

Tuberculosis in Children by F. J. W. Miller. Published
by Churchill Livingstone 1982. Price £8.00, 294 pp

This is a paperback, 14 by 21 cm, and includes an
extensive index. It is produced in the series
"Medicine in the Tropics": Part I is devoted to
Basic Facts — 1 Evolution of the primary infection
with Mycobacterium tuberculosis, 2 Tuberculin
sensitivity and the tuberculin test, 3 Epidemiology
of tuberculosis, 4 BCG vaccination, and 5 Control
of tuberculosis. Part II describes Clinical Manifesta-
tions under the following headings — 6 The
recognition, diagnosis and treatment of tuberculosis
in children, 7 Intrathoracic tuberculosis and
miliary spread, 8 Oral and alimentary tuberculosis,
9 Tuberculosis of the skin, 10 Tuberculosis of eye
and conjunctiva, 11 Suprafacial tuberculous
lymphadenitis, 12 Tuberculosis of the central
nervous system, 13 Tuberculosis of bones and
joints, 14 Tuberculosis of genital tract and breast,
15 Tuberculosis of the renal tract, 16 Tuberculosis
of liver, spleen, haemopoietic system and adrenals,
17 Congenital tuberculosis and infection early in
infant life, 18 Tuberculosis in immigrant children
in the United Kingdom, 19 Non-tuberculous myco-
bacterial infections, 20 Tuberculosis in animals.
The appendices include information on the
examination of gastric contents for AFB, laryngeal
swabs, staining of M. tuberculosis and another acid-
fast bacilli (Ziehl-Neelsen method), and the exami-
nation of c.s.f. for AFB. There are many pages of
references and a very full index. This book is
superb value and should be on the shelves of all
dealing with tuberculosis in children and adults.
Abstracts


The authors describe 3 major categories of amyloidosis, the first associated with immunocytic dyscrasias, the second complicating chronic infections and certain neoplasms, and the third occurring as a heredofamilial disorder. Renal amyloidosis may occur in all 3. Case histories are given of 3 adult African males presenting with classical features of nephrotic syndrome secondary to renal amyloidosis.

The first patient had been diagnosed as a case of tuberculoid leprosy 7 years previously, and initially had received treatment with dapsone. On admission he had gross signs of neglected leprosy—damaged cranial nerves (5th and 7th), bilateral interstitial keratitis, anaesthesia and severe clawing of all 4 fingers of both hands, and extensive neuropathic ulceration of both feet. Stool examination revealed ova of *S. mansoni*. The second patient had Bence–Jones proteinuria, and bone marrow biopsy confirmed a plasma cell dyscrasia. A rectal snip contained ova of *S. mansoni* and *S. haematobium*. The third patient also had Bence–Jones proteinuria but the cause of the renal amyloidosis was not established. An immunocytic dyscrasia was suspected.

The authors question the view that amyloidosis is a singularly rare disease in Africans, for in their experience it accounts for 3% of adult African patients with nephrotic syndrome compared with a figure of 7% in the UK. They comment that amyloidosis is not known to complicate tuberculoid leprosy but has an incidence of 6–8% in the lepromatous type. Reviewer's Comments. In describing the first patient in this series there is a statement that 'the ravages of tuberculoid leprosy were all too readily apparent'. However, a diagnosis of tuberculoid leprosy cannot be sustained on the evidence, for deposition of leprosy bacilli in both corneae and widespread fibrotic damage to nerves supplying face, hands and feet, are pathognomonic of late-stage lepromatous leprosy. My conclusion is that this patient's leprosy was borderline-tuberculoid (BT) when he was seen 7 years previously, and in the absence of adequate treatment, or because of dapsone resistance, his disease downgraded to subpolar lepromatous (LLs). Hence, contrary to the title of this paper, renal amyloidosis occurred as a complication of lepromatous leprosy.

W H JOPLING
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BOOK REVIEWS

ABSTRACTS

Printed in Great Britain at the Alden Press
Oxford, London and Northampton