Essentials of Leprosy

ALL AFRICA
LEPROSY
AND
REHABILITATION
TRAINING
CENTRE,
ADDIS ABABA,
ETHIOPIA.

ESSENTIALS OF LEPROSY

(3rd Edition)

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and
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Foreword

This booklet is designed for doctors, medical students, and senior leprosy workers. The first edition was published 6 years ago; the fact that this second edition has required rewriting to the extent of becoming effectively a new publication is an indication of rapid progress in the understanding of leprosy.

In a work such as this, which attempts in a small compass to cover the whole field of leprosy, it is hard to maintain a due sense of proportion. This booklet attempts to do so, but with one exception. Disproportionate space has been allotted to the treatment of leprosy and its complications. There is sufficient information for the doctor who is inexpereinced in leprosy to manage the disease and most of its complications with reasonable confidence: we hope this will encourage leprosy treatment in general hospitals.

No small book on a large subject can avoid dogmatism, and this one is no exception. Where statements in this booklet contradict generally accepted teaching, they have been made with careful consideration: and, particularly in the sections dealing with therapy, the treatments advised are those in normal use in ALERT. They have been proved safe and effective, and are also in agreement with current World Health Organisation recommendations.

We are most grateful to the staff members and others working in the Addis Ababa Leprosy Hospital, who over the years have continued our education in leprosy, and have contributed to and reviewed this booklet. But, as editors, we must accept responsibility for the final text.

J. M. H. Pearson
H. W. Wheate

1. INTRODUCTION

1.1. Definition

Leprosy is a chronic infectious disease of man, caused by **Mycobacterium leprae.** It affects chiefly skin and peripheral nerves: but in some forms of the disease **M.leprae** can be found in large numbers elsewhere, particularly in the nasal mucous membrance, smooth and striated muscle, liver, spleen, lymph nodes, eyes, testes, and blood vessel walls. Leprosy can occasionally cause glomerulo-nephritis and polyarthritis, probably due to immune complex deposition.

1.2 History

It is probable that the disease called leprosy in the Old Testament was not leprosy as we know it today. Leprosy has been described in skeletons of Egyptian mummies from the 5th Century A.D.

Moller-Christensen has demonstrated the occurence of leprosy in skeletons unearthed from church burying-grounds associated with leprosy hospitals in Denmark, from as early as the 12th century. Leprosy is thought to have reached its peak in Europe during the 16th century. Endemic leprosy disappeared from Northern Europe at the end of the 19th century, but it is still not uncommon in Southern Spain, Southern Italy, Sicily and Malta.

Little is known of the history of leprosy in Africa. It is probable that it spread from the Middle East along the great trade routes during the Middle Ages. It is possible that its penetration into tropical and Southern Africa is of relatively recent occurrence. There is some evidence, for example, that an epidemic of leprosy occurred in the Eastern Provinces of Nigeria from the 1920's onwards. It is possible that we are at present seeing a similar phenomenon in Ethiopia. Leprosy is well established in the Central Highlands, but there is evidence, both clinical and historical, that cases have only been present in significant numbers in other parts of Ethiopia for a relatively short period.

Armauer Hansen discovered that **Mycobacterium leprae** was the causal organism in 1873. In appearance the Mycobacterium is similar to **Mycobacterium tuberculosis.** It has, however, not been cultured in vitro, and Koch's postulates have yet to be fulfilled.

2. EPIDEMIOLOGY

2.1. Distribution

Leprosy is distributed world-wide. It is estimated that there are a total of 15 million cases in the world, of whom 3½ million are in Africa. Only about 25% of the total cases are being treated. In some areas the figure is certainly much lower than this.

2.2. Influence of Sex

All forms of leprosy are rather more frequent in males than in females, the sex ratio being about 2:1. In adults this difference is less marked in the form of leprosy with few bacilli (tuberculoid leprosy); and it is absent prior to puberty. The reason for these facts is not known, but they are generally attributed to differences in susceptibility rather than exposure.

2.3. Influence of Age

The idea that children are more susceptible to leprosy than adults is not supported by the facts. The peak of the age curve for diagnosis of leprosy is between 15 and 25 years of age. New cases are often seen in old age. It seems probable that all ages are more or less equally susceptible, and that opportunities for contact, coupled with the incubation period, are the most important factors giving rise to patterns of age at onset.

2.4. Source of Infection

The only known source of infection is the human case. It is probable that the more bacilliferous type of leprosy (lepromatous leprosy) is the principal source of the disease, though it must be admitted that contact with such patients often cannot be traced.

2.5. Mode of Transmission

For transmission of leprosy to occur viable bacilli must leave the body of the patient and enter that of the contact. Three factors therefore must be considered : the route of exit, the route of entry, and the "bridge" between them.

2.5.1 The route of exit It is now well established that the usual route is the nasal mucous secretion. It is very unusual to find leprosy bacilli on the surface of the skin, whereas a patient with active lepromatous leprosy will excrete each day in nasal secretions about the same number of bacilli as a patient with open pulmonary tuberculosis will cough up in sputum.

2.5.2 The route of entry. It likely that the usual mode of transmission is via droplets or dust, and the respiratory tract is the normal portal of entry. Penetration through normal skin seems inctrinsically unlikely, though there are a few well documented reports of leprosy lesions at the site of needle pricks or cuts. Inoculation by mosquitoes, scabies mites, or other insects is also possible.

2.5.3.The "bridge". It has been shown that, (at normal laboratory temperature and humidity), **M. leprae** remain viable for at least 24 hours, and sometimes longer. This finding makes droplet or dust-borne transmission a reasonable hypothesis. All the known facts about the spread of leprosy can be explained on this basis.

2.6 Susceptibility

Two separate issues must be considered here; firstly, factors that make an individual more likely to contract leprosy; and secondly, factors that influence the type of disease that develops.

2.6.1 Factors influencing susceptibility

There is some epidemiological evidence suggesting that certain families are more susceptible to leprosy than average. There seems to be no evidence that any particular race is more susceptible than another nor has leprosy been linked to known genetic characteristics. It is probable that susceptibility is little affected by age or nutritional status. It is possible, however, that prior infection by some strains of non-pathogenic mycobacteria (many of which are present in the environment) may affect susceptibility to subsequent infection with **M. leprae**.

2.6.2 Factors influencing the type of leprosy

There is good evidence that more deeply pigmented races tend to develop tuberculoid leprosy, whereas those with paler skins have a higher proportion of lepromatous cases. Moreover, in most races males have a higher lepromatous/tuberculoid ratio than females.

3. BACTERIOLOGY AND EXPERIMENTAL LEPROSY

3.1 Definitions

M. leprae can be obtained from skin lesions by the "slit and scrape" method (see Appendix 1). The material so obtained is spread on a microscope slide, stained, and examined using an oil immersion lens. Two findings are recorded:

3.1.1 The Bacterial Index (BI)

This represents the average number of bacilli per oil immersion field, expressed as 0 to 6 + on a logarithmic scale. It is a very approximate indication of the total bacillary load of the patient. The BI falls during treatment as dead bacilli undergo lysis and are absorbed.

3.1.2 The Morphological Index (MI)

Even in untreated patients a considerable proportion of bacilli show irregular staining and appear fragmented. The MI is the percentage of uniformly stained, solid looking ("morphologically normal") bacilli that are present. The MI is usually between 5 and 50 in untreated patients; it falls close to 0 after about 6 months of effective chemotherapy, the fall indicating that the bacilli have been rendered non-viable. Bacilli appearing fragmented by light microscopy have been shown by electron microscopy to have lost their normal appearance and become masses of structureless cytoplasm.

3.2. Experimental leprosy in mice

In 1960 it was shown that **M.leprae**, when inoculated into the foot pads of mice, produced a limited, microscopic infection. This model has been used for a number of purposes:-

3.2.1 The Multiplication Time has been shown to be 10 - 14 days, a figure which agrees satisfactorily with clinical evidence that the disease has an incubation period of 2 or more years.

3.2.2 The Viability of M.leprae can be tested in this way. It has been shown that when bacilli appear fragmented by light microscopy they fail to multiply on mouse foot pad inoculation.

3.2.3 New drugs, particularly those active against other mycobacteria, can be screened for anti-leprosy activity. This is now a necessary preliminary investigation which must precede clinical trials.

3.2.4 Strains of bacilli obtained from patients failing to respond satisfactorily to treatment can be tested for drug resistance.

3.3. Other animal models

Since 1960 a number of other animal models have been developed, of which two groups are of particular importance.

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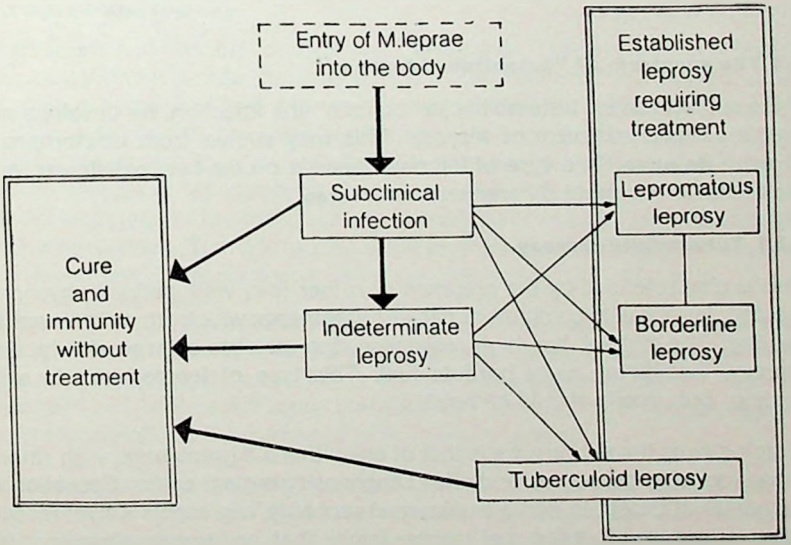

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3.3.2 Armadillos

A number of different species of armadillo have been shown to develop leprosy as a severe systemic disease, which is ultimately lethal, and may be analogous to kala azar rather than leprosy. These animals can be a source of very large numbers of **M.leprae,** and are chiefly of value for this reason. They also offer potential for determining bacillary mutation rates for resistance to different anti-leprosy drugs.

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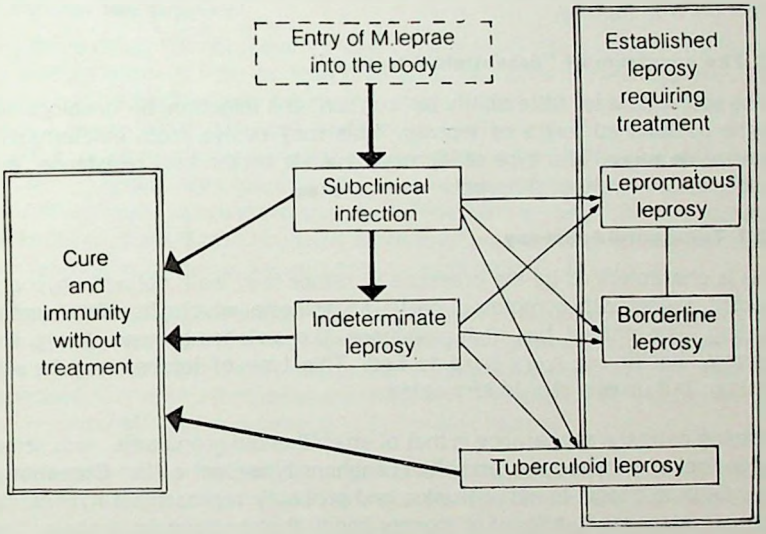


4 CLINICAL FEATURES AND CLASSIFICATION

The natural history of untreated leprosy is shown in outline in Fig. 1

4.1 Subclinical infection

This may be comparable to the "Ghon focus" in tuberculosis: the site of the infection has not been identified. Exposure to leprosy in the absence of clinical manifestation of disease can, however, be demonstrated by immunological tests, which are positive in a high proportion of workers who have close contact with patients. This is the normal response to exposure to **Myco.Leprae** — the development of immunity.

4.2 Indeterminate leprosy

This consists of one or a few vague hypopigmented macules of the skin, which may be slightly dry in texture and sweat less readily than normal. It is very hard to find leprosy bacilli in the lesions, and well overhalf of them resolve without treatment, leaving the contact free of disease and immune to further infection with leprosy.

4.3 The spectrum of "Established leprosy"

If the subject has too little ability to "contain" the infection, he develops one of the established forms of leprosy. This may evolve from indeterminate or arise **de novo.** The type of leprosy depends on the host resistance, and is not related to strain differences in **M.leprae**.

4.3.1 Tuberculoid leprosy

This is characterised by the presence of rather few, well defined, hypopigmented, lesions with complete or partial anaesthesia, which often show central healing. The patient has high resistance, the patches enlarge slowly, and leprosy, bacilli are very hard to find. This type of leprosy may be self-healing, but usually should be treated.

Histologically the appearance is that of an epithelioid granuloma, with rather dense foci of lymphocytes, and often Langhans-type giant cells. Caseation is very unusual except in nerve trunks, and probably represents a hyperactive immune response to a focus of leprosy bacilli that had previously been "immunologically concealed" within the Schwann cells of the nerve.

4.3.2 Lepromatous leprosy

This represents the other extreme of the spectrum of host resistance, where the patient is unable to resist the infection, and the bacilli multiply almost unchecked. They are found in highest concentration in skin and nerves, but are not confined to these sites. There is a bacteraemia of 10^5 - 10^7 bacilli per ml, (in spite of which the patient seldom feels ill,) and bacilli are found in large numbers in nasal mucous membranes, liver, spleen, lymph nodes, testes, eyes, smooth and striated muscle, and blood vessel walls. The skin lesions are multiple, vague, slightly hypopigmented macules, often with only slightly impaired sensation. As the disease progresses raised lesions — plaques and nodules — develop, and there is general infiltration of the body skin, usually maximal in the cooler zones of the body. At later stages, extensive anaesthesia can develop.

The histological appearance in these cases is of a rather uniform infiltration of macrophages heavily loaded with leprosy bacilli. Lymphocytes are scanty, though there may be many plasma cells. The "foam cell" is a degenerating macrophage containing destroyed bacilli and lipid material. Its presence indicates regression of the disease, either from natural causes or during treatment.

4.3.3 Borderline leprosy.

Sometimes called "dimorphous leprosy". This classification includes the large group of patients with intermediate grades of resistance to the infection. The appearance of the skin lesions is very variable. When the resistance is higher (subpolar tuberculoid), they look like tuberculoid lesions, but there are too many for the disease to be classified as polar tuberculoid. When the resistance is lower (subpolar lepromatous) they look like lepromatous lesions, but macules and nodules are more sharply defined, with areas of normal looking skin between them. There is usually some asymmetry of the lesions, whereas polar lepromatous leprosy shows complete symmetry.

In the mid range of resistance, the lesions show a mixed appearance, some looking like tuberculoid, some like lepromatous lesions. Usually, however, there are lesions which have very clearly defined areas of central healing ("punched out" areas) and somewhat less well defined outer edges: these are characteristic of the midrange of borderline leprosy.

An important point to remember when considering borderline leprosy is that the host resistance is unstable. As untreated leprosy progresses the resistance may collapse, and the disease drifts towards the lepromatous pole; this process

is called "downgrading". Similarly under treatment resistance can recover, and the leprosy can "upgrade" towards the tuberculoid end of the spectrum. When these processes occur rapidly, they may be accompanied by fever and episodes of increased swelling and erythema of the skin lesions: these are called "reaction".

Histologically the appearance of borderline leprosy is as variable as the macroscopic appearance: but in any one patient the microscopic appearance is rather uniform, even of lesions which differ macroscopically. In the mid-range of borderline leprosy the characteristic appearance is an epithelioid granuloma with scanty lymphocytes but moderate numbers of bacilli.

4.4. Other types of leprosy

Two types of leprosy are sufficiently distinctive to merit separate description though they are varieties of the established groups of leprosy.

4.4.1. "Pure neural" leprosy

The nerve trunks are damaged and usually enlarged, but no skin lesions are visible. Nerve biopsies show that these patients usually belong to the tuberculoid end of the spectrum.

4.4.2. "Histoid" leprosy

In this variety of lepromatous leprosy patients show very sharply demarcated nodules (which are heavily loaded with bacilli) but relatively uninvolved skin between. The nodules are sometimes in unusual places (eye, antecubital or popliteal fossae, abdomen). These patients are most commonly relapsed cases, having either stopped treatment too soon or developed drug resistance; in addition to active nodules, they often show stigmata of old healed lesions. It is as if the nodules had developed by the multiplication of a few surving bacilli in a small number of skin sites.

4.5 Different nomenclatures in classification

Different nomenclatures are used to classify leprosy in different parts of the world. The differences are accounted for by many factors.

4.5.1. The purpose of the classification

A classification for research purposes must be better defined than one used for field work by relatively unskilled staff.

4.5.2 The need for continuity

An outdated classification may continue to be used in a long term programme so that results are comparable over a long period.

4.5.3 Regional variations in leprosy

A good example of this is the use of "maculo-anaesthetic" to include both subpolar tuberculoid and subpolar lepromatous patients in areas where midrange borderline leprosy is uncommon.

4.5.4 The classification of Ridley and Jopling

This is becoming the most generally used classification for patients in hospital, and particularly for research studies. Its use is now mandatory in programmes involving immunological investigations. The definitions of the five groups are both clinical and histopathological, and there is good agreement between the two when clincian and pathologist are reasonably experienced.

Polar tuberculoid and polar lepromatous are called TT and LL respectively, and mid-range borderline is BB. The types of leprosy between them are BT and BL. The relationship of this classification to others is shown in Table 1. The most important point to note is that, compared to the 3 group classification, BB is more narrowly defined than borderline. BT includes some patients who would be tuberculoid and some borderline: similarly BL includes some who would be lepromatous and some borderline.

4.6 The importance of classification

There are number of reasons why it is important to be able to classify patients with leprosy reasonably accurately.

TABLE I

Different Nomenclatures in the classification of leprosy.

<table>
<tr><td colspan="5">TT | BT | BB | BL | LL</td></tr>
<tr><td colspan="2">Tuberculoid</td><td colspan="2">Borderline</td><td>Lepromatous</td></tr>
<tr><td>Polar Tuberculoid</td><td colspan="2">Intermediate forms</td><td colspan="2">Polar Lepromatous</td></tr>
<tr><td colspan="2">Non Bacilliferous</td><td colspan="3">Bacilliferous</td></tr>
</table>

4.6.1 Problem cases can be seen, with atypical lesions. To know the range of different appearances of skin lesions in leprosy can be important for diagnosis, particularly for those who do not frequently see or treat leprosy patients.

4.6.2 The period of treatment depends on the type of disease. Patients with tuberculoid leprosy may be cured in 2 or 3 years, but borderline cases need longer. Lepromatous leprosy requires at least 10 years treatment: and because of the risk of reinfectionmany authorities advocate life-long treatment.

4.6.3 The risk of complications and their nature varies with the type of disease, and can be forecast with reasonable accuracy if the patient is accurately classified. Most of the complications could be described by the patient as "the disease is getting worse"; so accurate warning is important if patient cooperation is to continue. Few patients will return to a clinic if they think that treatment has made their disease worse.

5. NERVE INVOLVEMENT IN LEPROSY

Nerve involvement is always present in leprosy, can and usually be detected clinically. Bacilli can be found in nerves at any level from the most peripheral nerve twigs to the dorsal root ganglia. But the maximum concentration of bacilli, and therefore the greatest damage, are to be found in two "zones", the dermal nerves, and certain sites of nerve trunks.

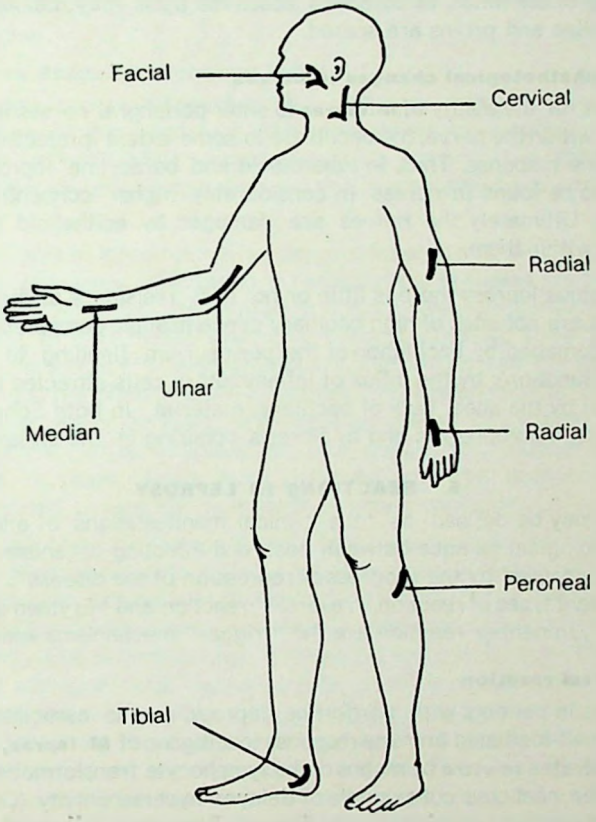
5.1. Nerve Trunk Involvement

The "site of predilection" for nerve enlargement and damage are shown in Fig. 2. Most of them are at positions where the nerve lies close to the skin and passes over a bone structure. The nerve damage leads to sensory, motor or mixed loss according to the nerve affected. Damaged nerves are usally enlarged, and sometimes tender to palpation: but at a late stage in the disease they may be small and fibrotic.

The nerve trunks are damaged at the same sites in all types of leprosy. But in tuberculoid leprosy only one or two trunks, usually near the skin lesion(s) are affected. In lepromatous cases, however, the involvement is symmetrical and affects all the sites of predilection: but damage occurs at a late stage in the disease, the mere presence of bacilli in the nerves not necessarily seriously

impairing their function. Thus in lepromatous cases there can be extensive skin lesions but little muscle weakness. Patients with borderline leprosy have the worst of both worlds; nerve trunks are extensively involved and liable to be rapidly damaged.

FIGURE 2 "Sites of Predilection" for nerve enlargement in leprosy.



5.2 Dermal nerve damage

As with nerve trunks, dermal nerves are damaged most rapidly in tuberculoid leprosy. Tuberculoid patches are usually anaesthetic and always have some degree of sensory impairment; but those in lepromatous leprosy often show almost normal sensation, though there are many bacilli in the nerves. Anaesthesia is varible in borderline leprosy.

In diffuse lepromatous leprosy, the maximal bacillary concentration is usually in the cooler areas of the body, so sensory loss may be more marked in the distal parts of the limbs. In advanced cases the trunk may be, anaesthetic, but the axillae and groins are spared.

5.3 Histophathological changes in nerves

The reason for the ability of **M.leprae** to enter peripheral nerves is unknown. But, once within the nerve, the bacilli are to some extent protected from the host immune response. Thus, in tuberculoid and borderline leprosy, bacilli are often to be found in nerves in considerably higher concentration than elsewhere. Ultimately the nerves are damaged by epithelioid granuloma formation within them.

In lepromatous leprosy there is little or no host resistance to the infection, and nerves are not sites of high bacillary concentration compared with skin. They are damaged by bacillation of the perineurium (leading to loss of its protective function); by the influx of inflammatory cells attracted by intraneural bacilli; by the sheer bulk of bacillary material, in both Schwann cells and invading macrophages; and by fibrosis occuring in the infiamed nerve.

6. REACTIONS IN LEPROSY

Reactions may be defined as "the clinical manifestations of alterations in the immunological balance between host and infecting organism which are not directly caused by the progress or regression of the disease". There are two important types of reaction, "reversal" reaction and "Erythema Nodosum Leprosum", in neither reaction are the "trigger" mechanisms known.

6.1. Reversal reaction

This occurs in patients with borderline leprosy, and is associated with an increased cell-mediated immune response to antigens of **M. leprae,** which can be demonstrated **in vitro** by means of the lymphocyte transformation test. It is probably the most clearcut example of delayed hypersensitivity (Coombs and Gell Type 4 reaction) causing clinical disease. The name "reversal reaction"

was given because it appeard to reverse the drift towards the lepromatous pole that tends to occur in patients with untreated borderline leprosy.

Clinically this reaction is characterised by increased oedema and erythema of previously present lesions. If severe, there is fever and general oedema, and occasionally ulceration of the skin lesions. Histologically there is oedema, epithelioid granuloma formation, and influx of lymphocytes. The reaction can also affect nerves in which **M.leprae** are present: the oedema and granuloma formation are liable to give rise to pain and swelling of nerve trunks, with sudden severe nerve damage. On occasion nerves but not skin can be affected, probably because the concentration of bacillary antigen in the nerve is higher.

6.2 Erythema Nodosum Leprosum (ENL)

This condition is very different to the erythema nodosum that occurs in tuberculosis and other conditions. The name should be considered mainly as descriptive: red (erythema) lumps (nodosum) in lepromatous leprosy (leprosum). It is also an unsatisfactory name, as ENL can affect many other tissues than skin.

ENL occurs only in lepromatous leprosy, and is associated with the deposition of immune complexes, particularly in tissues where **M.leprae** are to be found. It is thus a disorder of humoral immunity, and may be considered as a clinical manifestation of the Arthus phenomenon (Coombs and Gell Type 3 reaction). The skin lesions consist of erythematous nodules which may be intra-or subcutaneous, and are often tender and painful. They disappear after a few days. The condition may be episodic, with crops of nodules developing every few weeks or at even longer intervals: or new nodules may appear day by day for months or years. There may be fever, and the lesions sometimes ulcerate; indeed, severe ENL is a life-threatening condition.

When ENL lesions have subsided the skin usually returns to normal, though a residual mottled hyperpigmentation is not uncommon. In severe recurrent ENL, however, chronic oedema with fibrosis within the skin may develop, causing stiffness and sometimes bizarre contracture deformities of the hands or feet. Histologically, ENL lesions consist of dense polymorph foci in the dermis, sometimes with associated vasculitis. After a few days, before the lesion has fully resolved, the polymorphs are replaced by loose collection of lymphocytes. ENL can affect other tissues where **M.leprae** are to be found, particularly nerves, which however, are damaged more slowly than in reversal reaction, so that a nerve can be tender and painful for some weeks but retain almost normal function. Other tissues which can be affected include lymph nodes,

testes, and eyes, all of which can become inflamed. Hepatosplenomegaly is occasionally seen. More rarely polyarthritis or glomerulonephritis develop. The extent to which the lesions of different tissues are caused by local immune complex formation or deposition of circulating complexes is not known, and it is uncertain what antigens are involved.

7. IMMUNOLOGY IN LEPROSY

7.1 Cell mediated immunity (CMI)

M.leprae is an obligatory intracellular parasite, and, as is the case with other such micro-organisms, resistance to the infection is predominantly a function of CMI. It appears to be well established that there is depression of CMI responses to antigens of **M.leprae**, particularly in lepromatous leprosy, where the defect is complete and probably permanent. In addition, a non.specific depression of the responses to stimulation with phytohaemagglutinin (PHA) and other mitogens has been observed in untreated lepromatous leprosy, but it tends to recover during effective anti-leprosy chemotherapy.

CMI can be assessed **in vitro** by the lymphocyte transformation test (LTT), in which circulating lymphocytes are separated, suspended in cell culture medium, and exposed to the test antigen. Lymphocytes responding by blast transformation indicate their sensitisation to the antigen.

When whole washed **M.leprae** are used as antigen, responses are higher at the tuberculoid end of the spectrum, and usually very low in lepromatous cases. However, the degree of erythema of the patient's skin lesions affects the result; the greater the erythema, the higher the responses in all types of leprosy. The highest responses are found in reversal reactions, where, however, the rise is transient, and the response falls as the reaction subsides. It has not been demonstrated that any of these responses are relevant to resistance to the infection, and the LTT as it can be performed at present is of no value for diagnostic or classification purposes.

7.2 Humoral immunity

The ability of the host to respond to the presence **M.leprae** by producing antibodies to mycobacterial antigens appears to be normal. Such antibodies are present in large amounts in patients with active lepromatous leprosy, the amount decreasing towards the tuberculoid end of the spectrum. The role of

these antibodies in the pathogenesis of leprosy remains unknown. However, by immune complex formation, they are associated with the damaging complication of ENL.

7.3 Macrophage function

Most tissue macrophages are derived from blood monocytes. In response to various stimuli, including products of activated lymphocytes, they migrate into the tissues, where they can adopt a wide variety of forms. In leprosy these forms include epithelioid cells, histiocytes containing globi, foam cells, and a variety of multinucleated cells, according to the type of leprosy and the degree of activity or regression of the disease.

It is clear that in the lesions of lepromatous leprosy macrophages have impaired ability both to kill M.leprae and also, in patients under treatment, to dispose of bacillary lipid degeneration products. There are conflicting reports on the ability of lepromatous macrophages **in vitro** to lyse autoclaved **M.leprae:** it is therefore uncertain whether the **in vivo** deficiency is a defect in the macrophage population **per se** or due to lack of stimulation by other cells.

7.4 The lepromin test

Standard lepromin is prepared from biopsies of nodules from patients with lepromatous leprosy. The biopsy material is homogenised, and some of the skin material removed by centrifugation. The crude preparation, containing both human skin and bacillary components, is autoclaved and standardised according to the bacillary count to a concetration of 1.6×10^8 bacilli per ml.

The preparation is injected intradermally in a dose of 0.1 ml, and the 48-72 hour ("Fernandez") and 3-4 week ("Mitsuda") readings recorded.

The early reading indicates delayed hypersensitivity to the injected antigens. In healthy subjects in non-endemic areas it is usually but not invariably negative. The late reading, on the other hand, is commonly positive even in non-endemic areas, and may indicate ability of the subject to initiate or amplify a response to the injected antigen. Persons who are persistently lepromin negative may therefore be at increased risk of contracting leprosy. In leprosy patients both reactions are strongly positive in tuberculoid, and negative in lepromatous cases.

A positive lepromin test (whether early or late) is not an indication of exposure to **M.leprae;** nor is it a diagnostic test for leprosy. It can, however, be of help in the classification of known cases of leprosy. There is, at present, no serological or skin test available for the diagnosis of leprosy.

8. DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

8.1 Diagnosis of leprosy

There are three cardinal signs of leprosy:-

a) Skin lesions. The presence of localised skin lesions (which are usually hypopigmented and may be erythematous), which show sensory loss, and which do not coincide with the territory of distribution of particular nerves.

b) The presence of acid -fast bacilli in the skin.

c) Nerve enlargement at the sites of predilection.

Of these signs, the first is diagnostic alone. Acid-fast bacilli can occasionally be found in the skin in other conditions than leprosy; and it must be remembered that they are usually not found in tuberculoid leprosy. However, sensory loss is invariably present in tuberculoid skin lesions, though it may not be found in lepromatous macules (which, however, contain acid-fast bacilli).

Enlarged peripheral nerves are very occasionally found in other conditions than leprosy. A more common source of error, however, is failure to recognise that normal sized nerves can be seen and felt.

8.2 Differential diagnosis of leprosy

Leprosy can mimic a wide variety of skin diseases, but if it is always considered as a possible differential diognosis and the cardinal signs searched for, mistakes are unlikely to be made.

8.2.2 From neurological diseases

Neural leprosy with no visible skin lesions is uncommon, but the patient who has been treated for some years can present a problem in diagnosis, as the skin lesions may be all but invisible, and skin smears can often be negative for acid-fast bacilli. Such patients may conceal their past history.

Neurological conditions most commonly confused with leprosy include:-

a) Spinal cord diseases such as syringomyelia, amyotrophic lateral sclerosis, or motor neurone disease.

b) Peripheral nerve diseases, including :-

i) those caused by nerve compression, such as spinal root pressure, carpal tunnel syndrome, and Bell's palsy.

ii) Polyneuritis of any aetiology.

c) Muscle diseases, such as myopathies and myositis.

d) Disease with "trophic" manifestations, such as diabetes mellitus, tabes dorsalis, and congenital indifference to pain.

Important points to remember are that:-

a) Leprosy never causes upper motor neurone lesions, and proximal muscles are very rarely involved.

b) Sensory loss in leprosy may be maximal peripherally, but there are usually islands of preserved sensation on the hands or feet, and the tendon reflexes are preserved and often brisker than usual. Moreover position sense is almost always preserved.

c) Leprosy never damages the brain or spinal cord.

8.2.3 From limb deformities

Many limb deformities, including congenital defects, those due to poliomyelitis, contractures such as Dupuytren's, old injuries, or yaws may, if taken in isolation, be mistaken for leprosy. The diagnosis of leprosy can, however, almost always be excluded by careful inspection of the whole body.

9. CHEMOTHERAPY OF LEPROSY

9.1 Drugs active against leprosy

Sulphones

These include dapsone (4'4 diamino diphenyl sulphone, DDS) and diacetyl sulphone (DADDS). Other sulphones, such as glucosulphone (Promin), sulphoxone sodium (Diasone) and solapsone (Sulphetrone) are now obsolete.

Long-acting Sulphonamides

These have the same mode of action as the sulphones, and many disadvantages compared with them.

Thiureas

Thiacetazone (Amithiazone, TBI) is the only preparation now being manufactured, though thiambutosine (CIBA 1906, DPT) may be available from stocks for a year or two.

Rifampicin

(The only fully bactericidal drug against leprosy).

Notes on these drugs and their uses are given at the end of this section.

9.2 Principles of chemotherapy in leprosy

Whatever drug is used, these are three phases in treatment; they can be most clearly defined in lepromatous leprosy.

Phase 1 — During this period most of the bacilli are killed. With most drugs this stage requires about 6-12 months; but it is much less when rifampicin is used. It is completed when most of the bacilli in skin smears have become fragmented.

Phase 2 — During this period the drugs kill most of the surviving bacilli, and the body mechanisms dispose of the killed ones. This phase is completed in about 5 years, when bacilli are usually not found in skin smears.

Phase 3—At the end of Phase 2 there are still "persisting" bacilli which are drug sensitive but in some way dormant. They appear to survive therapy, and are liable to cause relapse if treatment is discontinued too early. If the disease is to be cured, treatment must continue till these "persisters" have died, whether from drug activity, host resistance, or "old age": this period is probably 5-10 years, but may be longer.

In non-lepromatous leprosy the principles are the same, but the greater the degree of host resistance, the shorter the period required for treatment, as shown in Table 2.

TABLE 2

Different "Phases" in the Chemotherapy of Leprosy

Type of Leprosy	Period of Treatment in Years			
	Phase 1	Phase 2	Phase 3	Total
Indeterminate	0	1	1	2
Tuberculoid	0	1	1	2
Borderline	1	2	3	6
Lepromatous	1	5	10	16

This table requires comments:-

1. The figures assume that the bacilli are fully sensitive, and that treatment is taken regularly and daily in full dosage. Most patients are not fully regular, so these periods are the minimum that should be considered.
2. In borderline cases, longer treatment is needed if they are closer to the lepromatous pole: a shorter period could be risked if they are close to tuberculoid.
3. The question of whether patients with lepromatous leprosy should take lifelong treatment to prevent re-infection is as yet unsettled. In the absence of factual knowledge, the patient's wishes should be the deciding factor.

9.3 Single or multiple therapy

There are two reasons for using multiple drug regimes in other diseases particularly tuberculosis:

1. To cure the disease more quickly. In tuberculosis only regimes including 2 or more bactericidal drugs will shorten the period of treatment. In leprosy only one fully bactericidal drug, rifampicin is available; and, there is as yet no evidence that including it in combined treatment regimes cures the disease more quickly. Moreover, there is no drug which is known to have a specific activity against "persisters" in leprosy, and which can therefore shorten the final phase of treatment.
2. To prevent drug resistance. There is now ample evidence that resistance to dapsone is becoming common, and therefore that all patients with lepromatous leprosy should receive dual therapy for at least the first year of treatment, both drugs being used in maximum dosage throughout. In non-lepromatous leprosy the bacillary load of the patient is small, and the risk of acquired drug resistance therefore less. At present, monotherapy with dapsone in full dosage is advised, but this recommendation may need revision if substantial numbers of patients are found to have developed primary drug-resistant infections.

A further indication for multiple drug therapy is as a period of supplementary treatment for patients with lepromatous leprosy whose treatment was initiated with dapsone in low dosage, and who are therefore at special risk of developing dapsone resistance. The best drug combinations, and the duration of treatment required to kill the population of resistant mutants before they have multiplied sufficiently to give clinical evidence of dapsone resistance, are not yet known.

9.4 Dapsone resistance in leprosy

Resistance to dapsone occurs in patients with lepromatous leprosy, and is acquired during the course of monotherapy, usually with submaximal dosage of sulphones. The history is characteristic — intial improvement, followed by relapse despite continued treatment with dapsone.

As dapsone is well absorbed orally, the only two possibilities in such cases are dapsone resistance, or that the patient is not taking his treatment. Most patients tell the truth on sympathetic questioning. However, the management should include a period of treatment with dapsone in maximal dosage, as fully supervised as possible, and with regular assessments, which must include as a minimum body drawings and skin smears. If possible, dapsone excretion in the urine should be checked. If it is certain both that the treatment is being taken, and that the clinical state is deteriorating, then the diagnosis of dapsone resistance is proved. Independent evidence can be provided by mouse foot pad tests, but they are no more reliable than a well performed clinical trial, and may take as long.

Such a trial is essential to the management of patients suspected of dapsone resistance. In addition to proving the diagnosis, it convinces the patient that dapsone no longer helps his disease. This will make it easier to persist with prolonged treatment with other drugs, which usually have more side effects, and are always more expensive, than dapsone.

9.5 Notes on anti-leprosy drugs

9.5.1 Sulphones

Dapsone (DDS)

Still the drug of choice for treatment because:

1. It has a very high therapeutic ratio.
2. Side effects in normal dosage are uncommon.
3. It is slowly excreted, therefore once daily dosage is possible.
4. It is inexpensive.
5. It is stable, and tablets keep indefinitely.
6. It can be given by injection if necessary.

Dosage:

Use 50-100 mg daily at all times in all adults (for children 1-2 mg/kg body weight).

DO NOT use a "slow build up" at the start of treatment; it does not lessen reactions and does make dapsone resistance more likely.

DO NOT reduce the dosage or stop treatment during reactions — it does not lessen the reaction significantly and will delay the cure of the patient.

Side effects:

Drug allergy (skin rash, fever, jaundice) — always develops within 2 months of starting treatment.

Fixed drug eruption.

Difficulty in sleeping.

Anaemia.

Indications:

For all patients with leprosy except those with:

1. Sulphone or sulphonamide allergy.
2. Dapsone resistance.

A note on "Dapsone Intolerance":
This unsatisfactory phrase is used to cover two conditions:

1. Side effects. Occasional patients develop abdominal discomfort or sleeplessness even on average doses of dapsone. These symptoms can normally be controlled by giving the dapsone in divided dosage with meals, or (in the case of difficulty in sleeping) as a morning dose.
2. The development of reactions in patients receiving dapsone. Reactions are not directly related to dapsone therapy and are not an indication for altering the treatment.

Di-acetyl Sulphone (DADDS)

Advantage:

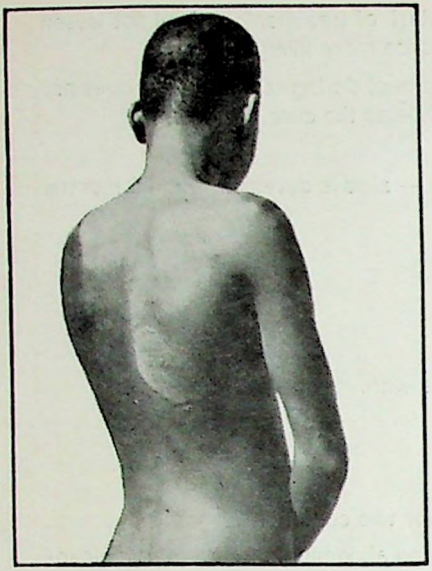
Is given as a very long lasting injection:
Once in 2 months = 2.5 mg dapsone daily;
once in 1 month = 5. mg dapsone daily.

Disadvantages:

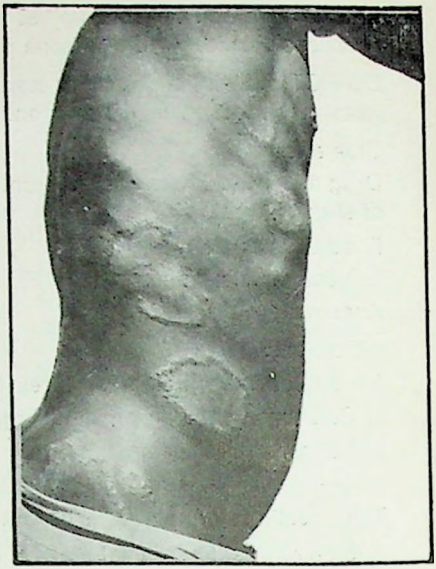
Gives blood dapsone levels that are too low to be satisfactory, and may prolong the period of treatment required to cure the patient.

Indication:

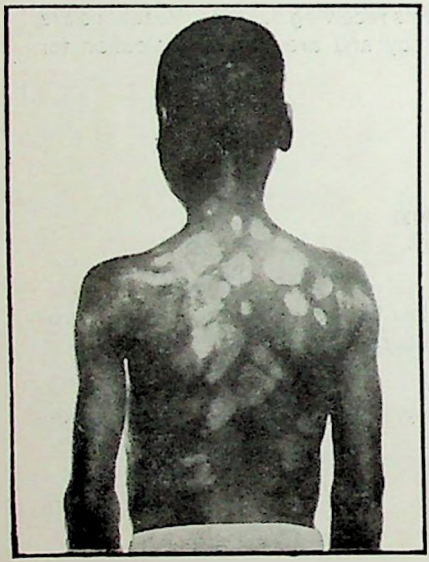
The treatment of non-lepromatous leprosy, if fully supervised treatment administered every 1—2 months is desired.



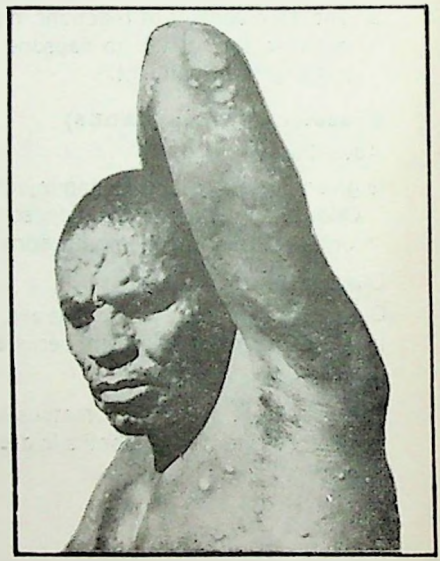
TT leprosy; a single hypopigmented lesion, with two tiny "satellite" lesions.



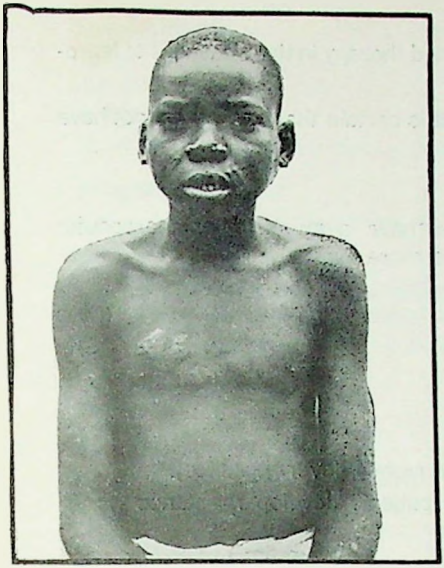
BT leprosy. The lesions have raised edges, and the lowest one shows central healing.



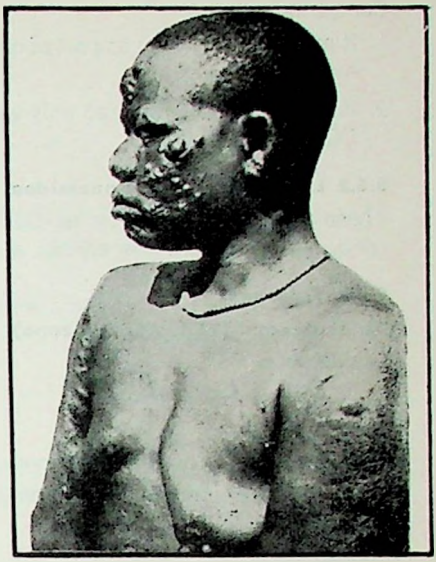
BT leprosy. Multiple hypopigmented macules, some showing a little central healing.



"BB leprosy. Raised lesions of varying sizes, including a large plague with a 'punched out' clear centre"

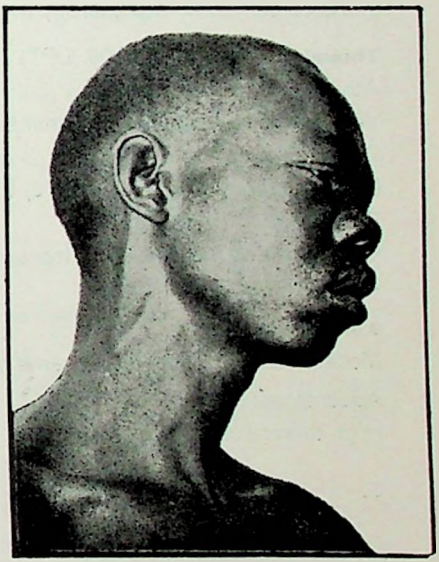


"'BL Leprosy. Mildly asymmetrical lesions of fface, trunk and arms"



"Nodular lepromatous leprosy. The nodules of the face could be described as 'histoid' "

"Diffuse lepromatous leprosy, showing complete symmetry, loss of eyebrows and mild 'leonine face' "



Enlargement of the Auricular nerve.

Photographs : Dr. J.A. Kinnear Brown

Contra-indications:

1. It must be used only as part of combined therapy in the treatment of lepromatous leprosy.
2. It should be administered only when it is certain that patients do not have DDS allergy.

9.5.2 Long-acting Sulphonamides

These act in the same way as DDS, but have a much lower therapeutic ratio, more frequent side effects, and are more expensive.

9.5.3 Thiureas

Thiacetazone (TB1, Amithiazone)

Advantages:

Once daily dosage; cheap.

Disadvantages:

Many side effects except in Africans (skin rashes, fever, jaundice).

When used as monotherapy lepromatous patients develop resistance within 2-3 years.

Indications:

1. As monotherapy in patients with non-lepromatous leprosy who have dapsone allergy.
2. As part of combined therapy in lepromatous leprosy.

Thiambutosine (Ciba 1906, DPT)

Advantages:

Very few side effects (occasional stomach pain)

Disadvantages:

Must be taken 2 (or preferably 3) times daily.

Expensive.

When used as monotherapy, lepromatous patients develop resistance within 2-3 years.

9.5.4 Ethionamide

Mode of action probably the same as the Thiurea drugs.

Advantages:

High therapeutic ratio.

Disadvantages:
Toxic (nausea, malaise).
Rather expensive.
Indications:
For research studies only.

9.5.5 Streptomycin

Different mode of action from other anti-leprosy drugs.

Disadvantages:

Need at least twice weekly injection.
Toxic (vertigo due to 8th cranial nerve damage).
When used as monotherapy, resistance develops in 2-3 years in lepromatous cases.

Not cheap.

Indications:

1. In combination with dapsone in treating lepromatous leprosy with severe ulcerating primary nodules. (Its benefit may be due to its activity against secondary infection).
2. In combination with other drugs in the treatment of dapsone resistant leprosy.

9.5.6 Clofazimine (Lamprene, B.663)

Mode of action different from sulphones, thiurea compounds and streptomycin.

Advantages:

In lepromatous cases – ENL less frequent and severe.
Resistance uncommon (none yet reported).

In non-lepromatous cases – Probably none.

Disadvantages:

Skin discolouration.
Abdominal pain common on high dosage.
Expensive.
Capsules are damaged if stored at high temperatures.

Indications:

Patients with lepromatous leprosy and severe reccurent ENL or neuritis (in combination with dapsone); high dosage (100 mg daily or more) is usually required.

Patients with sulphone resistance (in combination with another non-sulphone drug); minimum dosage should be 100 mg on 3 days per week.

9.5.7 Rifampicin

May be similar to clofazimine in mode of action (cross-resistance has been demonstrated in cultivable mycobacteria).

Advantages:

Kills **M.leprae** more rapidly than other drugs.

Disadvantages:

Serious toxicity, particularly in intermittent use at high dosage (over 900mg). Very expensive.

Indications:

1. When it is important to render a patient with lepromatous leprosy non-infectious as rapidly as possible.
2. In research studies.

10. THERAPY OF REACTIONS AND NEURITIS

Both reversal reactions and ENL can occur in patients who are not receiving anti-leprosy treatment; but both (and more especially ENL) are more commonly seen in treated patients. When patients under treatment develop nerve damage, it is due to a reaction occurring within the nerve. Such nerve damage is usually associated with paraesthesiae (in the case of dermal nerves) or tenderness of nerve trunks at the sites of predilection. Thus reactions and neuritis represent the same process occurring in skin and nerves respectively They may occur singly or together; but the principles of management are identical.

10. 1 Treatment of Reversal Reaction

The most important decision is whether the reaction is mild or severe: the definitions are summarised in Table 3. It is only necessary to add that prolonged (i.e. 6 weeks or more) mild reversal reaction should usually, for treatment purposes, be managed as "severe" reaction, as it tends to cause gradual nerve damage.

TABLE 3

Definitions of mild and severe Reversal Reaction

Site	Mild Reaction	Severe Reaction
Skin	Erythema + mild oedema of previously visible skin lesions.	Marked erythema and oedema of previously visible skin lesions OR Ulceration of lesions OR The appearance of new small lesions OR Oedema of the hands and/ or feet.
Dermal Nerves	Paraesthesiae without increasing anaesthesia.	Increasing anaesthesia of skin lesions OR of hands and/or feet.
Nerve trunks	Even minimal nerve trunk tenderness without loss of function is a danger sign of severe neuritis and needs assessment for loss of function, which can occur very rapidly.	Evidence of loss of loss of function + nerve pain and/or tenderness.
Systemic illness	Mild discomfort and slight fever.	Marked fever, malaise and discomfort.

Whether the reaction is mild or severe, anti-leprosy treatment must be continued, and there is no proved benefit from changing the treatment, either by altering the dosage of dapsone or by changing to any other anti-leprosy drug

10.1.1 Treatment of Mild Reversal Reaction

(a) Give mild analgesics as required.

(b) If available, give fouadin (stibophen) injections.

A course is **either** 2-3 ml daily for 4-7 days

or 5 ml every 2-3 days for 3 or 4 injections

(c) For out-patients, warn them to return at once if the reaction becomes more severe, or persists despite treatment.

10.1.2 Treatment of Severe Reversal Reaction

Only corticosteroid drugs are of any value. For most patients Prednisolone 30 mg daily is enough; occasionally if there is no improvement in a few days, double or treble dosage should be given for a week or two till symptoms are controlled. Most patients will need 20-30 mg daily for about 3 months and then gradual reduction of dosage. BT cases seldom need steroids for more than 6-8 months, but in BL patients, the reaction often persists for a year or more; the dosage and duration of treatment must therefore be adjusted for individual cases, the most important factor being the prevention of permanent nerve damage.

10.2 Treatment of ENL

The treatment of ENL is less straightforward than that of reversal reaction, for two important reasons:-

a) The course of ENL is more variable, ranging from a single crop of lesions, through episodic ENL persisting for some months, to, in very severe cases, a systemic illness with constantly present lesions for up to 5 years or so.

b) More drugs are available for effective treatment. In particular the need for steroids has been lessened since the advent of clofazimine and thalidomide.

10.2.1 Clinical patterns of ENL

In general, ENL can be considered as either episodic or continuous. In Africa most patients develop episodic ENL, but in paler skinned races there is a tendency for ENL to be more continuous, prolonged, and severe.

As is the case in reversal reaction, it is important to decide whether the ENL is severe or mild. This decision, however, is easier to make. Severe ENL is present if any of the following criteria are met:-

a) Skin lesions that ulcerate.

b) Serious nerve pain or evidence of nerve damage.

c) Involvement of the eyes or testes.

d) High fever and systemic illness.

10.2.2 The treatment of episodic ENL

Mild attacks of ENL require the same management as mild reversal reaction, that is:-

a) Analgesics as required.

b) A course of fouadin injections, if available.

c) Warning to outpatients to return to the clinic if the reaction persists or recurs.

In addition

d) Chloroquine 250 mg 3 times daily for 2 weeks is sometimes helpful.

An attack of mild ENL is self limiting, seldom persisting for longer than 2 weeks. Repeated attacks respond to repeated treatment, though courses of fouadin should normally not be given more often than monthly.

A severe attack of self limiting ENL seldom persists for longer than 2-3 weeks, so the initial treatment should be with a course of a steroid (usually prednisolone) for about the same period. Most patients respond well if given

Prednisolone 30 mg daily for 1 week.
then 15 mg daily for 1-2 weeks.

The dosage should then be stopped; it should not be gradually tapered off.

Repeated attacks of severe ENL need repeated courses of steroid treatment. However, if patients develop 3 or 4 such attacks in a period of 2 months or so, experience indicates that the ENL is likely to persist for many months. Such patients should be treated with clofazimine. The initial dose is 100 mg 3 times daily, for about a month: at the end of this time severe attacks of ENL will usually have been suppressed into mild attacks. Clofazimine takes 2-3 weeks to develop its full action; after about a month the dose can usually be reduced to 100 mg daily or twice daily, which should be continued for a year or so, or longer if ENL still persists. Episodes of ENL during clofazimine therapy should be treated with fouadin or steroids according to their severity.

If thalidomide is available it is the drug of choice for treatment of ENL except in women of child bearing-years, for whom it should never be prescribed. It acts rapidly, and should be used in the same way as steroids. 100-300 mg daily is usually effective; because of its sedative action it is best given at night. Polyneuritis has never been observed as a complication in leprosy patients:indeed nerve function often shows rapid and permanent improvement. If supplies of thalidomide are restricted, the drug is best reserved for patients who, despite clofazimine, need repeated courses of steroids. In this way the steroid dosage can be reduced and the dangers of steroid toxicity much lessened.

10.2.3 The treatment of continuous ENL

The principles are the same as in the management of episodic ENL, but because treatment must be continuous and uninterrupted, the risks of steroid toxicity are much greater, and the need to employ the steroid-sparing drugs, clofazimine and thalidomide, correspondingly greater. Treatment should not be in such high dosage that the ENL is fully suppressed; patients should show occasional attacks of ENL, though not so severe as to damage nerves, eyes, or testes.

10.2.4 Anti-leprosy treatment and ENL

It is essential to continue anti-leprosy treatment in full dosage during ENL, and it has been shown that dapsone in full dosage has very little effect on the severity of ENL. If anti-leprosy treatment is discontinued for periods of months, a mixture of ENL and active leprosy known as "progressive lepra reaction", which can be fatal, is liable to develop. In theory, dapsone can be discontinued if patients are receiving clofazimine; but in practice, if this is done, patients attribute the reaction to dapsone, and are unwilling thereafter to take it regularly. Clofazimine is therefore best prescribed as additional therapy to dapsone, and it may have the incidental benefit of lessening the risk of subsequent dapsone resitance.

11. THE EYE IN LEPROSY

11.1 Non-lepromatous leprosy

In non-lepromatous leprosy only the "outside" of the eye is affected by anaesthesia, 7th cranial nerve weakness, or both.

11.1.1 Lagophthalmos can cause exposure of the cornea. Possible sequelae include conjunctivitis, exposure keratitis, and corneal ulceration - the results of failure of eyelid function, which is to clean the cornea and maintain its moisture.

11.1.2 Corneal anaesthesia blocks the afferent arm of the blink reflex, and is therefore liable to cause keratitis and ulceration. When combined with lagophthalmos the eye is in serious danger, as inflammation can reach the point of perforating corneal ulceration without the patient being aware of anything grossly amiss.

11.2 Lepromatous leprosy

In lepromatous leprosy nodules or plaques can form on the eyeball itself, particularly in the upper outer quadrant and at the corneoscleral junction. The treatment is as for the systemic disease; it should be remembered, however that lepromas of the eye are most commonly seen in drug-resistant cases. Lagophthalmos and anaesthesia are less common than in non-lepromatous leprosy. However, **M .leprae** are present in the iris and ciliary body, and can cause iridocyclitis which can lead to blindness by several mechanisms:-

a) Inflammatory cells and exudate form in the anterior chamber, and in the space behind the cornea (where they can deposit as keratitic precipitates): they obstruct the canals of Schlemm and can cause glaucoma, with resul tant optitrophy and blindness.

b) Another cause of glaucoma is adhesion of the inflamed iris to the lens. These synechiae, if extensive, can obstruct the flow of aqueous fluid from the posterior chamber to the anterior chamber. The increased pressure in the posterior chamber then pushes the iris forward causing mechanical obstruction of the canals of Schlemm. Both these processes cause glaucoma.

c) Synechiae can distort the shape of the pupil, pull it off centre, and so interfere with vision. They can also lead to cataract formation and blindness.

d) Prolonged inflammation of the ciliary body can impair its function of aqueous production, and so the eye becomes soft, collapses, and "dies". ("Phthisical Eyeball").

Sclertitis may be associated with iridocyclitis. It takes the form of a red triangular zone in the inter-palpegral area of the sclera, which is tender to touch. Treatment is as for iridocylitis.

11. 3 Management of the eye in leprosy.

11.3.1 Permanent lagopathathalmos

If mild (4 mm or less), eye shutting exercises can sometimes reduce it. But this degree of lagophthaloms often causes very little harm. This is because whenever the eye is shut, including during sleep, the eyeball rolls upwards and outwards ("Bell's phenomenon") so placing the cornea under the upper eyelid.

If there is more than 5 mm of lagophthalmos, a tarsorrhaphy is usually required. Mechanical aids, such as artifical tears and eyeshades to protect the exposed eye at night, can also help to reduce the risk of inflammation of the eye. If anaesthesia is not present, various surgical procedures (such as temporalis muscle transfer) to restore the blink, will help. But if there is impaired sensation, and therefore the stimulus for blinking is not present, the patient seldom makes good use of the operation

11.3.2. Iridocyclitis. There are two varieties: an acute type, lasting a few days, often associated with ENL;and a chronic variety which may continue for many months. The principles of management are the same, and can be expressed alphabetically:

A. Atropine — this dilates the pupil, prevents synechiae, and reduces the risk of glaucoma.

B. Blindness is the likely result of untreated uveitis.

C. Corticosteroids, given locally as eyedrops or ointment, systemically, or most effectively of all by subconjunctival injection.

D. Diamox (acetazeolamide) if there is raised intra-ocular pressure

11.3.3 Other eye complications

Both lagophthalmos and trachoma (which is often common in areas where

leprosy is found) can cause distortion of the eyelids with consequent ectropion or entropion. Correction of these deformities by minor surgery will often be valuable, particularly if keratitis is being caused by eyelashes rubbing on the cornea.

12. PHSYICAL THERAPY IN LEPROSY

12.1 Exercises

In leprosy a motor nerve is often only partially destroyed, leaving the muscles it supplies weak but still functioning. Active exercises in such cases encourage hypertrophy of the remaining muscle fibres and recovery of strength. Even if a muscle is completely paralysed, passive exercises which put the joints through their full range of movement several times a day will prevent contractures. Simple exercises, particularly for the hands, take only a minute or two a day—patients should be taught how to do them at home.

12.2 Skin Care

Skin that is anaesthetic has also usually lost the sweat and sebaceous glands. It tends to be dry, and to crack and become infected more readily than normal skin. Most of these problems can be prevented. The skin, particularly of the hands and feet, is too dry; this can be remedied by soaking them in water for 15-30 minutes and the absorbed moisture retained by applying any ointment or oil and rubbing it into the skin.

13. THE FOOT IN LEPROSY

13.1 The Aetiology of "Trophic Ulcers"

The foot in leprosy can be damaged and deformed as the end result of anaesthesia, paralysis of the intrinsic or extrinsic muscles, or bone damage.

13.1.1 Paralysis of the instrinsic muscle leads to the development of claw toes and undue prominence of the metatarsal heads. Peroneal nerve damage causes "foot drop", and so abnormal stress on the lateral part of the fore-foot when walking.

13.1.2. Bone damage can be due either to osteomyelitis secondary to a penetrating ulcer, or to a little understood process of softening and absorption of the bones of the tarsus, and sometimes also of the phalanges.

13.1.3 When the foot is anaesthetic, the patient can continue to walk on it long after pain would have stopped a normal person and enforced rest. Thus trauma leads on to inflammation and ulcer formation. The ulcers tend to develop in the positions of maximal trauma, which vary according to the deformity that is present.

13.2 Management of the Ulcerated Foot

Almost all ulcers will heal given time and rest without weight-bearing. The larger the ulcer, the greater the tissue distortion on healing; also when large ulcers heal there is little subcutaneous tissue, and the skin, adhering to bone, is more liable to recurrent ulceration. The principles of treatment are the normal principles of surgical treatment of injuries: debridement, including removal of dead bone; rest; and antibiotics for acute infection.

Ulcers will sometimes heal even when walked on, provided the body weight is well distributed by a plaster of paris (POP) cast or by suitable shoes. The application of a POP cast should be delayed till the ulcer is clean and infection controlled. In general dressings should be avoided unless they can be renewed twice daily: a wet, pus-soaked dressing slows healing—it is better for the feet, socks, and shoes to be washed carefully with plain water each day.

13.3 Principles of Prescribing Footwear in Leprosy

Use a miorocellular rubber insole to distribute the weight uniformly. Extra padding to form an arch support will relieve pressure on the metatarsal heads if claw toes are present.

Use sandals if the foot is distorted so that there is a risk of ulcers on the dorsum or side of the foot. The thongs can be placed to avoid bony prominences.

Use moulded shoes designed to give maximal support around the edges as well as on the sole if the foot is reduced in size. "Plastazote" shoes are the most suitable.

If necessary use a less suitable shoe that the patient will wear rather than the "best" which, because of its odd appearance, will only be worn when the patient attends his clinic.

14. THE PLACE OF SURGERY IN LEPROSY

This section makes no attempt to give any details of surgical procedures or their indications. It is merely a list of conditions in which surgical treatment can assist in therapy or rehabilitation. It should be remembered that some of the common and simple procedures (particularly in the management of infection and eye problems) can be undertaken by non specialist doctors or trained paramedical workers.

14.1 Surgery of infection

Drain abscesses, debride ulcers, remove dead bone from infected lesions.

14.2 Surgery of bone

Arthrodesis of claw toes and of tarsal bones in "disorganised feet"; arthrodesis of the wrist when there is complete paralysis (flail wrist).

14.3 Tendon transfer operations

For "drop foot" and mobile claw hand.

14.4 Eye Surgery

Tarsorrhaphy, temporalis transfer, ectropion and entropion operations, iridectomy for certain cases of glaucoma.

14.5 Surgery of nerves

Release of osteoligamental tunnels where nerves are liable to constriction (Ulnar, median, tibial). Incision of the nerve sheath. Nerve grafts (experimental).

14.6 Plastic surgery

Release of contractures, rebuilding the collapsed nose, injection of inert plastic to conceal muscle wasting of the hands, eyebrow grafts.

14.7 Amputation for intractable ulceration

15. PRINCIPLES OF LEPROSY CONTROL

The aim of control of any communicable disease is to reduce its incidence until it no longer remains a public health problem. The principles that can be applied, however, vary greatly with different diseases. In smallpox, for example, the existence of a safe, effective, and long lasting vaccine has made eradication possible, the principle used being whole population vaccination. In malaria, the principle of control is interruption of the chain of infection by mosquito destruction, chemoprophylaxis, and house screens or mosquito nets. In cholera, control measures chiefly consist of preventing cholera vibros contaminating the water, their destruction by water purification, and preventing people ingesting contaminated water.

In leprosy, however, none of these measures is feasible. There is no sufficiently effective vaccine; there are no intermediate hosts, nor does **M.lepare** survive for long outside the body; and chemoprophylaxis is impracticable in most situations. There is at the present time no possibility of primary prevention (i.e., the detection and protection of persons at risk). Leprosy control must be based on secondary prevention; that is, the early detection and regular treatment for a sufficiently long period of all cases existing in an area.

15.1 Early detection (case finding)

This is important in limiting the period of infectivity of the patient, and is probably the easiest part of leprosy control. The simplest methods are examination of known contacts of leprosy patients, and limited surveys (such as schools, factories, army units). In areas where the leprosy prevalence is low, it may be necessary to rely on these methods of case finding. Other patients may be persuaded towards self presentation by suitable publicity: but the most effective encouragement is a reputation for excellence of the leprosy treatment programme.

Mass (whole population) surveys are the only way to ensure that all cases are known, and so are important in evaluating the initial problem(and ongoing results) of a control programme. But they are unpopular with both staff and "the mass", hard to supervise adequately, and in some areas operationally impossible.

15.2 Regular treatment for sufficiently long (case holding)

This is the greatest problem of leprosy control, and the quality of a treatment programme is best judged by its success in this sphere of operation. The duration of treatment which is required necessitates a quite unusual relationship between health worker and patient, so that the patient will attend regularly for treatment, and have confidence in the worker's concern for his welfare. There are so many personality variables that one can wonder why so many patients do actually attend for treatment for periods of many years, often showing remarkable determination to do so.

Integration of leprosy treatment with other treatment services is almost universally accepted as the ideal. Such integration is likely to be of maximal value in areas where the social stigma of leprosy is greatest. If, for instance leprosy is treated in a skin clinic, the patient can obtain treatment without declaring himself a "leper"; this is not possible in clinics where only leprosy is treated.

15.3 The requirements of a successful control programme

Probably a leprosy control programme in which all infectious patients receive treatment for 75% of the time will, if maintained for 20 years or so, "control" leprosy in that area. The sequential aims of a programme can be summarised as follows:-

1. Early detection and regular treatment of large majority of cases.
2. Clinical and bacteriological inactivity of all treated cases.
3. Reduction to negligible figures of new cases.

Such a programme will include in its requirements:-

1. Familiarity with the extent of the problem in the area, with related socio-economic factors, and with general attitudes to leprosy.
2. Evaluation of the reasons for success or failure of already existing programmes, and an outline of priorities and targets for the future.
3. Assessment of resources, including
   Manpower (capabilities, training, responsibilities.)
   Transport and communications
   Facilities for referral on specialist advice
   Drugs
   Money
   Other (Publicity and education material, etc.)

4. Development of relationships with concerned bodies, whether Ministry of Health, area clinics, or village councils.
5. Concern for individual problems including staff working conditions; and provision for treatment of patients with special medical and/or social problems, including continued care of the severely disabled.
6. Continuous supervision of field programmes.
7. Ongoing evaluation of programmes, and application in the field of results of research programmes.

16. PRINCIPLES OF REHABILITATION

Just as medicine may be defined as "the diagnosis, treatment, and prevention of disease," rehabilitation may be defined as "the diagnosis, treatment, and prevention of dehabilitation". In the context of leprosy, dehabilitation chiefly affects three areas of life the disease can cause a patient to lose his family and place in society; his work and means of livelihood; or his self respect.

16.1 Preventive rehabilitation

Regardless of his infectivity, the deformed patient is at greater risk of dehabilitation. Prevention of deformity, by early diagnosis (before deformity has developed), by the correct treatment of neuritis (which is the chief cause of deformity developing during treatment) and by health education (to prevent increase in deformity from contractures, injuries, and infections) is the most important part of this process that can presently be carried out : it has been termed "preventive rehabilitation". The surgical correction of deformity can be a part of this process.

16.2 Active rehabilitation

Active rehabilitation is concerned with providing work for patients, and assumes (possibly correctly) that a patient who has a job can also keep his family and preserve his self respect. It includes two main activities:-

16.2.1 Workshops for the unskilled

These can provide a limited number of permanent jobs, and should be judged in business — economic — terms; i.e, will the workshop make a profit (or at least avoid a loss)! Such workshops can seldom supply more than a fraction of the need, and must be supervised to ensure that work is adjusted

in such a way that it does not cause further damage to patients hands or feet. Decisions on fair salaries for handicapped persons are often hard to reach.

16.2.2 Training programmes

The aim of these is to produce workers with skills that enable them to earn an independent living. They always, by their nature, lose money; but have a turnover of trainees. Ideally no one should enter such a scheme unless a "way out" to a paid job is previously, arranged. It is demoralising to be trained and still have no work at the end.

16.3 Loss of self respect

The diagnosis of the patient with loss of self respect is difficult. One indication is the state of the hands and feet. The patient with recurrent ulcers and progressive deformity, which defy treatment and health education, is probably in this category; he no longer cares about his body (remember, though, that he may need some deformity to earn satisfactory living as a beggar). Treatment is almost impossible. Prevention lies chiefly in the attitudes of friends and relatives, though leprosy clinics which are interested in patients, and treat them as persons rather than "lepers" will help. In the long run education away from fear of the disease is the only prevention or cure of dehabilitation.

17. PRINCIPLES OF HEALTH EDUCATION IN LEPROSY

Health education may be defined as "the process which leads to better understanding of health problems and realistic action to solve them."

It follows that health education is not merely instruction – one way communication. There is little evidence that knowledge—of say the cause of plantar ulcers—leads inevitably to action to prevent them.

Health education is two-way communication. The focus is clarification, for both leprosy worker and patient, of what are the real problems, and what, in a particular situation, is the best action that can be taken to solve them.

The starting point must be the time of diagnosis, and it is hard to overestimate the value of a few minutes of discussion, between patient and doctor (or health worker) at this time. The patient should be given a realistic view of what dapsone can do, and know in particular that it alone will not reverse

deformity, prevent or cure ulceration, or cure anaesthesia. He should also know roughly how long he will need to take dapsone, and (in many cultures) be informed that tablets are better than injections for curing leprosy. Because of the rushed conditions in most clinics, the communication at this initial interview is likely to more one-way than is ideal; but it may have the effect of guiding the patient subsequently towards asking the important questions.

Health education often involves work with groups, and a leader who can listen, summarise, and direct the discussion towards possible action is essential. Health education in a leprosy programme must be evaluated on the results of the actions it starts, not on the efforts (talks, meetings, films, etc.) that go into it. A health education programme must therefore include:-

1. Setting of measurable targets
2. Training of personnel at all levels by appropriate methods in communication skills (the example of one person is worth 20 lectures!) and ensuring that the information communicated is accurate.
3. Regular evaluation of the results of the programme.

It should be remembered that patients should not be the sole target of health education. There are many misconceptions about leprosy among the general public (and also in medical circles) that health education might aim to correct. In this context key groups of individuals, such as medical and nursing training schools, teacher training colleges, community leaders, rotarian groups, and the like, might be selected as specific "targets". Results of such programmes, however, can seldom be quantified.

APPENDIX 1

Technique of "Slit Skin" smears

Skin smears are normally taken from at least one ear lobe and at least 2 skin lesions; they are best taken from their active edges.

A fold of skin is held between thumb and forefinger tightly enough to prevent bleeding. An incision about 5 mm long is made in the skin; it should be deep enough (about 2 mm) to extend well into the dermis. Any blood is wiped away.

The scalpel blade is then turned so that it is at right angles to the skin slit. Holding the skin fold tightly, the scalpel blade is scraped firmly down the incision, thus removing some of the subcutaneous tissue on the tip of the scalpel. This material is spread as a small thick film on a microscope slide.

When the material has dried, it is fixed by flaming the under surface of the slide, which should be made slightly too hot to be placed on the bare hand.

Staining is according to the normal Ziell Nielsen technique, except that **M.leprae** are decolourised more readily than **M.tuberculosis**; decolourisation must therefore be much briefer, and preferably use less powerful agents, such as 0.5% hydrochloric acid in 70% alcohol.

The Bacterial Index (BI)

Over	1000	bacilli	in	an	average	oil	immersion field	= 6 +
100-	1000	"	"		"	"	"	= 5 +
10-	100	"	"		"	"	"	= 4 +
1-	10	"	"		"	"	"	= 3 +
1-	10	"	"	10	"	"	"	= 2 +
1-	10	"	"	100	"	"	"	= 1 +
	no	"	"	100	"	"	"	= Negative

The Morphological Index (MI)

This is the percentage of bacilli counted which show a uniform solid stained appearance.

APPENDIX 2

Indications and techniques of biopsies

A. Biopsies for Histopathology

1. Indications for skin biopsy

a) **When the diagnosis is uncertain.** In such cases the biopsy should be taken across the edge of the lesion, so as to include normal looking skin.

Remember, however, that when the lesion is a hypopigmented macule, the appearance in leprosy is commonly that of non-specific inflammation. Careful testing for impairment of sensation or deficient sweating will give a positive diagnosis of leprosy more often than will a biopsy.

b) **For accurate classification.** When the diagnosis of leprosy is certain the whole biopsy should be taken from a typical active lesion. Usually it is best taken fairly close to the edge, and from an erythematous area if there is one present.

c) **To diagnose a reaction.** In the case of suspected ENL the best lesion to biopsy is an early one; the histopathological changes may become non-specific in a day or two. If reversal reaction is suspected, the more 'mature' the lesion the better; often, however, the reaction can only be definitely confirmed histologically by serial biopsies at intervals of about 2 months.

d) **To assess the progress of treatment.** Such biopsies should be taken either from the most active looking lesion (particularly if relapse or drug resistance is suspected) or from an adjacent site to a previous biopsy (particularly if assessment of a drug treatment is being undertaken).

2. Method of skin biopsy

Choose the biopsy site; if possible, select an area where the incision can follow the normal skin creases. Infiltrate the area with local anaesthetic.

Using a sharp scalpel, excise an ellipse of skin. It should be at least 1 cm long. The width, however, matters little; 2 mm is usually ample, and the thinner the biopsy, the better the fixation. The incisions should be vertical, and extend right through the dermis to the subcutaneous fat. To avoid tissue distortion always handle the biopsy gently, and apply forceps at the corner, not across the centre.

Do not allow the biopsy to dry; blot gently on gauze to remove blood; straighten it, and immerse in fixative (see below). If the biopsy tends to twist up, straighten it on a small piece of cardboard, and put it with the card into fixative.

Close the skin incision with suitable sutures.

In some circumstances a punch biopsy is more practicable than using a scalpel; but unless punches are kept well sharpened they cause more tissue distortion. Punch biopsies of 5 mm or less heal well without sutures, and require a dressing for only a few days; this is often an advantage. But such biopsies are too small for accurate histological classification; so when such small punches are used take two biopsies close together.

To take a punch biopsy, apply gentle pressure and rotation to the punch till it has penetrated to the subcutaneous fat; then remove the punch, lift the biopsy gently with fine forceps, cut through the fat at the base of the cylinder of tissue. Blot the biopsy gently to remove blood, and immerse in fixative at once. Rinse the punch immediately in water to avoid blood clotting in its lumen.

3. Nerve biopsies

Nerve biopsies are normally only performed for research purposes. However, they can be of value in patients suspected of early replased tuberculoid leprosy, when the nerve may show evidence of active leprosy before new skin lesions or deterioration of nerve function develop. They are also occasionally useful to confirm the diagnosis in patients with enlarged nerves but no visible skin lesions.

Full details of the technique of nerve biopsy are given in:-

"Changes in Sensory Acuity Following Radial Nerve Biopsy in Patients with Leprosy". Brain 1971 **94** 43 (J.M.H. Pearson and A.G.M. Weddell)

4. Fixation of biopsies from leprosy patients

The most suitable fixative for skin biopsies in leprosy (and other granulomatous skin diseases) is Ridley's Zenker-formol, the formula for which is given below.

After about 2 hours fixation in this fluid, the biopsy should be transferred to 70% alcohol, in which it may be kept indefinitely. 10% neutral formalin may be substituted for 70% alcohol; being non flammable, it may be more suitable if the specimen must travel by post.

Ridley's Fixative

Formaldehyde 40%	10 ml
Mercuric Chloride	2 G
Glacial Acetic Acid	3 ml
Distilled Water	to 100 ml

This solution is stable; the fixative need not be made up from two solutions at the time of use. However, if a sediment develops, pour the fixative gently to avoid the sediment entering the bottle and contacting the biopsy; or remove it by filtration.

5. Staining biopsy material from leprosy patients
The "TRIFF" stain has the advantage of demonstrating bacilli and tissues together. Full details are given in:-

> "An Improved Technique for the Histopathological Diagnosis and Classification of Leprosy". Leprosy Review 1965 **36** 1. (E.A. Wheeler, E.G. Hamilton and D.J.Harman).

B. Biopsies for Mouse Foot Pad Inoculation

These biopsies are most commonly taken from patients suspected of developing dapsone resistance.

1. Preliminary Investigations

Chose 4-6 active looking skin lesions which are suitable for biopsy, and take skin smears from them: check the BI and MI of each. Select for biopsy the lesion with the highest MI, provided the BI is 4 + or more.

2. Biopsy technique

1. Clean the skin very thoroughly.
2. Take the biopsy according to the normal procedure; but the biopsy should be larger, about 15 mm long and 5 mm wide.
3. Blot the biopsy free of blood, then rub the cut edge on a clean microscope slide, thus making an "impression smear".
4. Put the biopsy in a clean, dry, sterile bottle, and seal it.

5. Keep the biopsy at 4% C (in a refrigerator or on ice in a vacuum flask) till it is processed. THE BIOPSY MUST NOT BE FROZEN.

6. Before processing the biopsy check the BI and MI of the impression smear. If either is low, the biopsy is unlikely to be suitable for mouse foot pad inoculation.

3. Transportation.

If the biopsy is to be processed elsewhere:-

a) pad the biopsy container with adhesive plaster to avoid a sharp edge breaking the wall of the vacuum flask.

b) pack the vacuum flask in a well padded package, or suspend it on rubber (old inner tube) strands in a small light weight crate.

A biopsy will only keep cool for 36 to 48 hours in a flask well packed with ice. If transportation will take longer, arrangements must be made for it to be re-iced en route. The mice should be inoculated within 5 days of taking the biopsy.

4. Inoculation from skin smears

Mouse foot pad inoculations can also be set up using skin smears from active lesions. This technique has some advantages over the use of biopsies. For details see:-

> "A simplification of the mouse foot pad infection using **Mycobacterium leprae** from skin scrapes" Lepr. Rev. 1975 **46** 105 (J.M.H. Pearson).

APPENDIX 3

Techniques of sensory testing

Sensory tests are performed for different purposes, but the technique is the same though the stimulating object varies. The test stimulus must first be demonstrated to the patient, with his eyes open, in a skin area without anaesthesia. The patient is asked to point to the place touched by the tester. The procedure is repeated, but with the patient's eyes shut. Finally, sensation in the relevant site is tested. In each case the stimulus object is touched gently on the skin, as if sensation to pin prick were being tested.

1. To determine whether there is sensory loss in a skin lesion that may be caused by leprosy, use a piece of cotton wool rolled at one end to a fine point. If the patient fails to feel the stimulus in the lesion, but feels it in adjacent skin, sensory loss is present.

2. To test for anaesthesia of the hands or feet, use, for the hands, a stiff nylon bristle about 2 cm long mounted on wire, for the feet, the point of a ball point pen. Touch firmly enough to bend the bristle slightly, or to indent the skin of the foot slightly. If the patient fails to feel the stimulus, the degree of anaesthesia is sufficient for him to be at risk of inadvertent self injury.

3. To follow the progress of neuritis, use serial tests every few weeks. Test the relevant skin areas with nylon bristles of varying stiffness, and record the softest one felt by the patient. Full details of this test, and precautions needed if it is to give reliable results, can be found in:-
   "Changes in sensory acuity following radial nerve biopsy in patients with leprosy". Brain 1971 **94** 43. (J.M.H.Pearson and A.G.M.Weddell).

GLRA — DEVELOPMENT AND AIMS

German Leprosy Relief Association (GLRA), which financed the printing of this small volume was founded in 1957, a non-governmental, interdenominational organization which is contributing to the anti-leprosy campaign throughout the world.

Since its foundation GLRA made available 203 Million DM for

— 496 leprosy centers, district and national programmes
— construction of hospitals, dispensaries and other accommodations
— research work and equipment
— training

Moreover, printing and propagation of technical literature on leprosy and information about this disease in Europe and the endemic countries were covered by these funds.

185 doctors, nursing staff and other experts worked for GLRA in the field of leprosy; in addition there was/is a number of native doctors and other staff being paid or receiving allowances from GLRA.

GLRA attaches great importance to a cooperation within the International Federation of Anti-Leprosy Associations (ILEP), to the creation of which GLRA made a considerable contribution.

GLRA aims at an integration of leprosy services into the public health service.

In consideration of its statute and according to the will of its benefactors GLRA supports rehabilitation and resocialization projects and thus takes further care of those leprosy sufferers, who as a result of the disease, are blind and crippled and are consequently not accepted from society.

Acknowledgment.
The original photographs were taken by the late Dr. J. A. Kinnear Brown