Leprosy

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LEPROSY is one of the oldest diseases known to man and yet even today there are many gaps in our knowledge. The causative organism, *Mycobacterium leprae*, was discovered by Hansen in 1874 and it was thus one of the earliest organisms to be associated with a specific disease, at a time when the bacterial causation of disease was very much doubted. However *M. leprae* has not yet been cultivated with certainty and so does not fulfil 'Koch's postulates'. It is a disease which involves many branches of medicine and sugery, and Skinsnes (1969) has remarked that leprosy provides a unique immunopathologic disease model.

Social aspects

The word 'leprosy' evokes fear in the mind of most people through ignorance and prejudice. The recent public reactions to the reporting of the number of cases of leprosy in England and Wales show that this fear is not limited only to the uneducated. Some of the older accounts of leprosy are doubted by many authorities and Andersen (1969) in a recent historical and osteoarchaeological review found no evidence of leprosy in ancient Egypt nor in Biblical writings. It is certainly mentioned in the Graeco-Roman literature but the term used by Hippocrates probably includes a number of other conditions. The extent of leprosy in Europe in the Middle Ages has possibly been exaggerated but there is no doubt that it was widespread, and this may be judged in Britain by the number of old 'lazar houses'. It was not limited to the lower social classes as Robert the Bruce and Henry IV are believed to have had leprosy.

Whether the disease is termed 'leprosy' or 'Hansen's disease' or one of the inumerables names by which it is known in different languages, the pitiable sight of a person with longstanding untreated leprosy will give rise to a feeling of horror in the lay mind. It is paradoxical that this very case of 'burnt-out' leprosy may no longer be a source of infection, whereas the highly active early case with minimal signs may pass unnoticed. There is an increasing awareness in the medical profession that leprosy should be included in the general medical and public health programmes, and not relegated to a specialist service to deal with its particular problems. This more enlightened attitude will help to educate the public and dispel some of the fear. There is however a strong social stigma attached to this disease and as recently as March 1970 the Indian national press reported the alleged burning of a leprosy patient by villagers in the superstitious belief that a village could rid itself of leprosy by burning alive a person suffering from this disease. Such extreme actions are rare but the leprosy patient is still a social outcast in many parts of the world and this leads to concealment in the early stages of the disease and delay in seeking treatment. The greatest need today is for the education of the public and the early detection of the disease, for the early case of leprosy properly treated has the greatest chance of 100 per cent cure.

The extent of the problem

The amount of leprosy in the world is difficult to estimate but is generally taken as about 15 million cases. The majority of these are in the tropical and subtropical regions of Central Africa, India, China, and South America. In these areas the prevalence

rate may be 20 to 40 per 1,000, though there may be wide local differences between one village and another in the same locality.

In Europe there are roughly 50,000 cases of leprosy, while in England and Wales the Secretary of State for Social Services has given the figure of 280 cases of leprosy notified from the beginning of 1964—the great majority of these occurring in Indian or Pakistani immigrants. It is well over a century since the last indigenous case in Britain.

Leprosy follows certain racial patterns and it has been found that the proportion of infectious (lepromatous) cases varies from country to country. Newell (1966) has suggested that the development of lepromatous leprosy in an infected person is a host-determined characteristic that is present in a fixed proportion of the population. The proportion of cases of lepromatous leprosy, and thus a guide to the general infectivity, is approximately 5–10 per cent in Africa, 15–20 per cent in India, 40–50 per cent in China and 70–80 per cent in Western countries. This underlines the importance of being on the lookout for a new case in Britain as it would tend to be an infectious case of lepromatous leprosy rather than the self-healing tuberculoid type.

There are two major difficulties in further research in leprosy. The first has been briefly mentioned—the difficulty of cultivating *M. leprae*. To some extent this has been overcome in the last ten years by the discovery that the organism multiplies in the footpad of mice. A considerable amount of research work has since been carried out by inoculating the footpad of thymectomized, irradiated mice.

The second difficulty is related to the slow rate of multiplication of *M. leprae* and consequently the long incubation period of the disease—which may range from 1 to 5 years. Even when established the disease progresses in a slow and protracted manner. This immediately raises the epidemiological problems of a long-term prospective study. The difficulties of data linkage, quality of data and sophistication of matching in such studies has been well pointed out by Heasman (1968) in relation to Britain, and the comparative difficulties in a developing country are almost insurmountable. When one adds the problems that arise in an attempt to conceal the disease—wrong name, age, address and lack of information about contacts—then the difficulties are multiplied.

Finally there is the economic problem of disability in leprosy. Even if sensory neurological changes are ignored and only disabilities due to motor nerve damage are included, it is estimated that about 25 per cent of all leprosy patients have some degree of disability (WHO 1960). In some countries this may be very much higher and in my own survey work the disability rate is nearer two thirds of all leprosy cases, with about one third being so severely incapacitated that they are incapable of being self-supporting. The personal and national implications of this will be obvious.

Medical aspects

The skin clinic of a general hospital is probably the most likely place to see a patient with the earliest signs of leprosy, as it is only later in the disease that neurological signs become obvious.

The diagnosis of leprosy rests on three findings:

1. Clinical evidence of nerve involvement
2. Demonstration of *M. leprae* in a skin smear
3. Histological examination of a biopsy specimen.

Although at least one of these three conditions must be fulfilled before the diagnosis of leprosy is made it is generally the appearance of the skin that is first observed.

The clinical picture of leprosy should be considered as a spectrum with two well-defined polar forms of leprosy and an intermediate mixture of the characteristics of these two forms. At the one pole the patient with virtually no resistance will develop lepromatous leprosy—this is characterized by multiple, small, vague hypopigmented

macules scattered all over the trunk and limbs. These are often difficult to see and it is essential to examine the patient in good light. Later in the course of the disease the patient will develop a diffuse, often erythematous infiltration, particularly of face and ears, and this may finally go on to the nodular appearance of the 'leonine' facies of leprosy. Lepromatous leprosy is characterized by the unrestrained multiplication of *M. leprae* and by the late development of neurological signs—the sensory loss when it does occur is of the 'glove and stocking' distribution in the limbs.

At the opposite pole the patient with a high resistance will develop tuberculoid leprosy. The skin lesion is large, clearly defined and often single. The edges of the lesion are raised, there is marked hypopigmentation or erythema, sweating is impaired and there is sensory loss. Due to the high resistance there is an absence of *M. leprae*, these having been eliminated by the macrophages. The brisk response of the body results in a short history and also early nerve damage—often presenting as thickened cutaneous nerves adjacent to the skin lesion or as a single nerve motor paralysis.

Between these two polar types there is a group, either termed dimorphous or borderline, which exhibit features of both forms of leprosy. The skin lesions are more clearly defined than in lepromatous leprosy and appear in greater number than tuberculoid leprosy. There is usually some sensory loss, especially in the larger macules. *M. leprae* are found in varying numbers and nerve damage develops later than in tuberculoid leprosy but is much more extensive.

Having briefly outlined the main characteristics of the developed case of leprosy it is most important to emphasize the appearances of the early indeterminate form of leprosy. This is often a single, small hypopigmented macule which may occur anywhere on the body but in a large number of cases appears on the buttocks or trunk. There is no sensory loss and *M. leprae* are not detected by ordinary methods, and the only means of positive diagnosis is histopathological examination of a biopsy specimen. Many of these lesions disappear without treatment and some authorities regard them as analogous to the 'Ghon complex' of tuberculosis. However, many of these early indeterminate lesions later develop into one of the characteristic forms of leprosy. It is vitally important not to overlook such a lesion because treatment at this stage will lead to complete cure in most cases—whereas ignoring such a lesion may commit the patient to fully developed leprosy. It should be added that this indeterminate lesion is more often seen only during leprosy survey programmes as the patient is frequently unaware of the lesion, however it is quite possible in Britain that a person may consult their doctor at this stage.

The range of differential diagnosis to be considered is wide and ranges from the macules of nutritional dyschromia, leucoderma, pityriasis rosea etc.; through the raised lesions of psoriasis, scleroderma and the fungus infections; the nodular conditions such as neurofibroma and Kaposi's sarcoidosis; and finally the destructive nasal lesions caused by syphilis or lupus vulgaris. The possibilities of mis-diagnosis operate in both directions and it is not unknown for a case of lupus vulgaris to be admitted to a leprosy hospital, and on the other hand two conditions may co-exist as I well remember one patient with nodular lepromatous lesions and neurofibromatosis.

The neurological manifestations of leprosy tend to follow a definite pattern. As has already been mentioned the sensory loss is seen early in the skin lesions of tuberculoid leprosy, whereas the sensory loss in lepromatous leprosy appears late and is of a generalized 'glove and stocking' distribution. It must be emphasized that by the time anaesthesia has developed the disease is well established, and therefore sensory testing must be carried out with a fine wisp of cotton wool to determine the early stages of sensory loss. This is time consuming and requires a certain amount of intelligence on the part of the patient, but it is a vital part of the establishment of a firm diagnosis.

In leprosy the peripheral nervous tissue is highly susceptible and Brand (1964) has

emphasized that the motor involvement is found in certain typical sites—the ulnar nerve just above the elbow and wrist, the median nerve just above the wrist, the common peroneal at the neck of the fibula, the posterior tibial 3–4 ins above the ankle, the zygomatic branch of the facial nerve in the region of the zygoma or the whole facial nerve in the bony canal. The commonest lesion is an ulnar paralysis with loss of lumbrical action or clawing of 4th and 5th fingers and later clawing of all four fingers; next in order of frequency are foot-drop from a common peroneal paralysis, median nerve paralysis with loss of opposition of thumb to little finger, lagophthalmos and lower facial paralysis. More rarely there may be a radial nerve paralysis with wrist drop. Paralysis of the posterior tibial nerve results in inability to spread the toes which may appear to be a trivial disability, however Price (1965) has shown that in the majority of cases plantar ulceration is associated with paralysis of the posterior tibial nerve. It is important to palpate for thickened nerves at the sites mentioned—in particular the ulnar nerve above the elbow and the lateral popliteal at the neck of the fibula—as thickening may be detectable before there is obvious nerve involvement. If pain is elicited while palpating a nerve this indicates the need for prompt treatment with corticosteroids as untreated neuritis may quickly result in paralysis.

The differential diagnosis of the neurological manifestations of leprosy must include the toxic, nutritional and compression neuropathies. The problem is simplified as in leprosy there are always associated sensory and motor lesions. Traumatic injury is usually obvious though false histories are often a trap, but the unusual histories do occur and I had one Tibetan non-leprosy patient whose ulnar nerve had been permanently damaged when he was bound in chains after the occupation of Tibet. Finally there are the genetically-determined neuropathies. Although these are rare diseases when they do occur they may cause confusion and I have seen one hereditary sensory radicular neuropathy who spent some years in a leprosy hospital.

The disabilities of leprosy and the tragic end result of no fingers and no toes was for a long time thought to be due to the direct action of the *M. leprae* and the misconception that leprosy itself destroyed the tissues. In the majority of cases the damage is due to the sensory loss and subsequent ignoring of trauma to hands or feet. A hot cup or a nail in a shoe is soon appreciated by the normal person, but with loss of sensation the pain is not felt and the damage is done before the patient notices. In the feet motor paralysis alters the mechanics of the foot and this, together with the anaesthesia, soon leads to plantar ulcers and loss of toes. Job (1965) has clearly shown that the small bones of the hand may develop leprous osteomyelitis with resulting necrosis and caries of the bone, and that the cartilagenous and bony framework of the nose may be infiltrated by lepromatous granulation tissue.

Having considered the clinical picture of leprosy the final diagnosis rests, as has already been mentioned, on the clinical evidence of nerve involvement, the demonstration of *M. leprae* or the histopathological findings. The first of these conditions has been dealt with. The demonstration of *M. leprae* is a standard practice in leprosy work and is a relatively simple procedure. Skin smears are taken from certain sites—usually ears, forehead, cheek, chin, chest, back, arm and thigh—by pinching up the skin in a fold and making a small cut with a scalpel blade. The side of the small cut is scraped and the tissue obtained smeared on a slide, the smears from all sites on the same patient being put on the same slide. The smears are then stained either by Ziehl-Neelsen technique or by using acid carbol fuchsin and counterstaining with methylene blue. When *M. leprae* are present they are easily seen as acid-fast, rod-shaped bacilli. The estimation of the acid-fast bacilli in the skin smears of a patient with leprosy is useful in order to classify the leprosy, to assess the degree of severity of infection and to observe the response to treatment. The accuracy of this is open to a number of fallacies, but a rough method of assessment has been devised by Ridley (1964) using a logarithmic index (the Bacterial Index).

This is not the place to discuss the histopathology of leprosy except to re-emphasize that a biopsy specimen is desirable for the diagnosis in some circumstances and is also a great aid to the correct classification of leprosy. Leprosy is essentially a disease of the peripheral nerves and there is often obvious perineural inflammation and involvement of the Schwann cells. The tuberculoid form of leprosy is characterized by the severe inflammatory 'tubercle' reaction, whereas in lepromatous leprosy a diffuse sheet of granuloma is seen and the Schwann cells are often distended with bacilli.

From the clinical picture, together with the results of skin smears and biopsy, it is possible to classify the form of leprosy. This is not of mere academic interest as it has a real bearing on the duration of treatment and the prognosis. The classification may not remain constant as it is dependent on the immunological resistance of the patient which may be altered by treatment, rest, nutrition etc. It is more common for a patient at the lepromatous end of the spectrum of leprosy to move towards the tuberculoid type than for the converse.

Chemotherapy

The treatment of leprosy has been revolutionized by the use of Dapsone B.P.C. (DDS, 4:4-diamino-diphenyl-sulphone) which was first used for this purpose in 1947. It is the most effective of the modern drugs that have been used for leprosy and has the additional advantage of being very cheap—the total drug cost for the treatment of an adult for one year being only 15p.! Views are changing with regard to the most effective dosage. It used to be customary to give 100 mg to 200 mg daily but this was found to give rise to a lot of side effects and the fashion swung to the administration of low doses. The risk of such low doses producing Dapsone-resistant *M. leprae* has always been recognized and Browne (1969) has reported a case where such resistance developed after 52 months on a dose of 50 mg Dapsone twice weekly. The optimum weekly dose, given either as daily or twice weekly divided doses, is probably between 150 mg and 300 mg. It is important that the patient be started on small doses—5 mg or 10 mg thrice weekly—and the dose gradually increased until the maintenance dose is reached in 3 to 4 months.

Treatment should not be started until a definite diagnosis has been made, for the stigma of leprosy is such that grave psychological trauma may be caused by wrongly labelling a person as having leprosy. Once the diagnosis has been made then it is reasonable to treat the patient in his own home and admission to hospital is only required for the complications of leprosy, such as lepra reaction or plantar ulcers. Treatment should be continued for two years in the tuberculoid form of leprosy, and for life in the lepromatous form. The latter is usually not practicable but treatment should be continued for at least two years after all clinical and bacteriological evidence of active leprosy has disappeared. Even then cases occur where there is a reactivation of the leprosy after some years and hence the suggestion that treatment should be continued for an indefinite period in cases of lepromatous leprosy. One word of caution should be added—Dapsone and other sulphones may sometimes give rise to a haemolytic anaemia and therefore treatment should not be started if the haemoglobin level is below 10 gm per 100 ml.

Alternative drugs are sometimes used and these include injectable Dapsone (Sulphetrone), thiambutosine (Ciba 1906), thiacetazone (TB 1), long-acting sulphonamides and B 663 (Lamprene). These are used when there is some indication for discontinuing Dapsone therapy, such as lepra reaction or drug sensitivity.

Lepra reaction is a term used for the acute manifestations of leprosy which may appear as the exacerbation of a lesion or more commonly in lepromatous leprosy may present as pyrexia, rose spot nodules (erythema nodosum leprosum), subcutaneous nodules, iritis, neuritis, orchitis or arthritis. The reactions are debilitating, particu-

larly erythema nodosum leprosum, and may lead to prolonged periods of ill-health. Lepra reaction can occur before any treatment has been given, but the frequency of these complications is increased by the giving of specific antileprosy drugs. The patient with lepra reaction should be in hospital as general nursing care is required. In addition to analgesics and antipyretics certain drugs are used to control the reaction—intravenous potassium antimony tartrate or one per cent mercurochrome, antimalarials and finally corticosteroids. The latter are always used with caution in a chronic disease such as leprosy as indiscriminate use may result in the patient becoming steroid-dependent. The only indication for the immediate use of prednisolone is neuritis when it should be used in large doses to prevent further motor nerve damage, the dose being reduced as soon as possible. Iridocyclitis should also be energetically treated along conventional lines (atropine and hydrocortisone) as it is a major cause of blindness in leprosy.

Surgical aspects

Dr R. G. Cochrane, president emeritus of the International Leprosy Association, refers to surgery as 'The ambulance work of leprosy'. It is quite true that the aim in all leprosy work is to detect the cases early and so prevent a lot of unnecessary deformity. However it is also true that many cases of leprosy are unfortunately only seen when there is already established deformity and it is to these patients that the modern developments in surgery offer hope of rehabilitation. In this sphere Dr Paul Brand is well known for his original work on tendon surgery and operations for replacement of the lumbrical group of muscles, and Dr N. H. Antia for his work on nasal reconstruction and reconstructive surgery of the face in leprosy patients. In addition there are many standard orthopaedic operations that are employed. The emphasis on the place of surgery in correcting the deformities due to leprosy in recent years has underlined the need for preventive care and in particular the importance of physiotherapy in the treatment of deformed hands. Almost all leprosy hospitals have a physiotherapy department with specially-trained technicians to instruct patients in the pre-operative and post-operative care of hands and feet. The importance attached to these departments also helps to impress the leprosy patient with the need for continual examination and care of hands and feet when they are at home.

Conclusion

To many general practitioners leprosy may only bring to mind the small print of medical textbooks and recall the self-sacrificing work of such people as Father Damien and Dr Albert Schweitzer. There is still a need for christian compassion in the care of the severely-deformed patient with leprosy, but at the same time modern medical treatment can prevent many of these deformities. Early detection and diagnosis is vital if effective treatment is to be given, and this is made more difficult by the social stigma and chronic course of leprosy. The co-operation of patients will only be achieved through education and an enlightened approach to the disease. In Britain the average general practitioner may never see a case of leprosy, but the possibility exists, particularly with those who are treating immigrants, and the significance of the hypopigmented macule with sensory loss must not be overlooked.

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