Abstracts


This interesting and important paper describes the osteological, and particularly the peri-oral and dental changes found during the examination of about 1000 skeletons from 4 mediaeval Danish leprosy cemeteries. In addition to confirming the now accepted criteria for bony damage attributable to advanced low-resistant leprosy (atrophy of the anterior nasal spine; atrophy and recession of the maxillary alveolar margin, with perhaps loss of the upper central incisors; inflammatory changes on the upper surface of the hard plate), the author found specific changes in the teeth. Thus, in children developing low-resistant leprosy during the first decade of life, characteristic malformations of the permanent maxillary incisors were noted, the tooth diameters being suddenly and concentrically reduced and the pulp cavities showing a similar constriction. Less pronounced changes were also present in the mandibular incisors, and other teeth.

The changes observed are thought to be developmental disturbances occurring during the rapid progress of multibacillary disease in children who subsequently died young. The paper is excellently illustrated with photographs and X-ray pictures of the teeth and affected bones. Clinicians will henceforth be on the lookout for similar changes in young living subjects affected by severe lepromatous leprosy.

S. G. Browne


The authors draw attention to a type of nerve damage in leprosy that appears to be different from the 2 main kinds that have long been recognized, these being destruction of the nerve either by epithelioid infiltrate or by lepromatous granuloma. In one of their 2 patients, in whom clinical and surgical studies were supplemented by arteriographic and histological investigations, the evidence suggested some kind of antigen-antibody reaction. Two alternative mechanisms appear to be possible: either the unusual liberation of normal antigenic constituents from the body cells, or the liberation of extraneous antigens (derived from dead Myco. leprae), which stimulate the host to produce antibodies not only against the micro-organisms themselves, but also against the host’s own tissues—a suggestion earlier made by Browne (Int. J. Lepr., 1965, 33, 881).

S. G. Browne


The author gives a brief summary of the leprosy situation in Ceylon, based on official reports and his own observations. The number of patients under treatment in the population of 12 million is about 4300, of whom 850 (including 150 females) are in the Hendala Leprosy Hospital, and 150 in Batticaloa.

Through the Social Service Agency, the government gives an allowance of 20 rupees a month to the families of patients with infectious forms of leprosy, and 50 rupees a month to patients...
after discharge from 1 of the 2 leprosaria, a sum that is insufficient to encourage a desire to leave the sheltered life of the leprosarium. Out-patient treatment is provided at 9 leprosy clinics and at a “Special Skin Clinic” at the Colombo General Hospital.

The author refers to an apparent lack of concern about leprosy in the Health Ministry, and suggests that serious efforts to control the disease have yet to be made. The social stigma against leprosy remains strong, and physicians lack both knowledge of the disease and desire to co-operate in its detection and management.

S. G. Browne


Plastic and reconstructive surgeons will find much to interest and instruct them in this well-illustrated and well-documented account of the author’s experiences in dealing with the diverse combinations of paralysis of the facial muscles as they occur in patients in Korea. Both upper and lower facial palsy, unilateral or bilateral, and even complete bilateral facial palsy, are by no means uncommon in the Far East. The author’s principal surgical attack on these problems is the use of either the temporalis or the masseter muscle, with suitable sling operations for the sagging face.

S. G. Browne


The author reports the incidence and type of ocular lesions among 890 patients in the main leprosaria of Uganda. Examinations were made by direct inspection in sunlight, with visual acuity estimation and the use of an ×10 loupe. The slit-lamp microscope was not employed and fundus examinations were possible in only a proportion of the cases.

Madarosis was the commonest lesion observed in this way (8.2%), while chronic iridocyclitis (3.1%) was the most serious. Exposure keratitis was uncommon (incidence not stated) although lagophthalmos was seen in 5.6% of cases, 4 patients were totally blind, and 12 were blind in 1 eye.

H. E. Hobbs


By subjecting cultured leucocytes containing ingested living Listeria to various concentrations of oxygen and of clofazimine (B 663, Lamprene (Geigy)), the author shows that in aerobic conditions clofazimine potentiates bacterial killing by the macrophages. The potentiation observed corresponds to concentrations of the drug that are obtained in man when therapeutic doses are given. Even serum concentrations that are not high enough to be directly injurious to the organism used, are somehow rendered bactericidal when the macrophages take up the drug. Clofazimine increased the oxygen consumption of the leucocytes; this increased utilization was not infiltrated by potassium cyanide, an observation that suggests that the mechanism is independent of the mitochondrial system.

S. G. Browne


The intriguing observation that Australia antigen (Au (1)) is associated with the occurrence of lepromatous leprosy, is further investigated in the studies reported in this paper from Cebu (Philippines).
ABSTRACTS

The serum findings in a larger group of patients confirm the initial conclusions that Au (1) is found in a significantly higher proportion of patients with lepromatous leprosy than in those with tuberculoid leprosy or in the general population; that males have a higher proportion than females; and that the age-group showing the highest frequency is 6 to 9 years.

The significance of these observations is discussed, and the hypothesis advanced that the postulated gene (which in double dose confers increased susceptibility to hepatic virus infections) may also confer susceptibility to other chronic infections, including leprosy. If this is the case, lepromatous leprosy would follow a pattern of autosomal recessive inheritance in areas of high leprosy prevalence. Individuals carrying this gene would, if exposed to leprosy infection, be more likely to develop the lepromatous type of the disease than those not carrying the gene. Susceptibility is not on these grounds absolute, but such factors as age and sex and possibly other genes are also involved.

S. C. Browne


The authors report 2 cases of severe peripheral neuropathy apparently induced by dapsone, and followed by complete clinical recovery after discontinuance of dapsone treatment. In the first case, the 20-year-old male patient was suffering from pyoderma gangrenosum, and the daily dose of dapsone reached 400 mg (given for 10 days): a total of 26 g of dapsone in 2 months. The other patient, a 17-year-old boy, had widespread and long-standing acne conglobata, and he received dapsone in a dosage of up to 350 mg daily (given for 5 weeks)—a total of 48 g over 5 months.

Both patients experienced signs of distal motor weakness about 3 months after the beginning of dapsone treatment. The first patient had signs of ulnar nerve damage and severe symmetrical foot-drop; in the second patient, the damage was confined to the lower limbs.

The mechanism of toxic peripheral neuritis in these instances probably differs from that of the neuritis of leprosy, whether occurring spontaneously or apparently induced by dapsone.

S. G. Browne


The author reports 16 cases of agranulocytosis with 8 deaths (mainly from Pseudomonas septicemia) occurring in perhaps 200,000 American servicemen taking dapsone as a malarial prophylactic in Vietnam. Apparently no soldiers had developed agranulocytosis while taking chloroquine-primaquine once weekly, or during standard treatment of falciparum malaria with quinine, pyrimethamine and dapsone.

All the 16 patients had been taking 25 mg of dapsone daily, for periods ranging from 3 weeks to 3 months before the onset of signs of agranulocytosis, and 1 of them had taken no antimalarial medication apart from dapsone. Leucopenia is said to be common during dapsone prophylaxis for malaria (and, in fact, its appearance has been taken as an indication for stopping dapsone), but these are the first cases of agranulocytosis to be reported in association with dapsone prophylaxis.

On the evidence submitted in the paper, it is not possible definitely to incriminate dapsone as the sole and sufficient cause of the observed signs: other drugs, including antimalarials, may have played a determining role. Furthermore, the diagnosis in some of the cases would not appear to be convincingly established; for example, 2 patients had a “marked leucocytosis” on the third day, 1 of them with 28,000 white blood cells per mm³. Another patient also suffered from anaemia due to glucose-6-phosphate dehydrogenase deficiency, possibly precipitated by dapsone.

While most leprosy-control schemes, in which many thousands of patients take the equivalent of at least 25 mg of dapsone daily, do not have the kind of medical supervision
available to the American armed forces in Vietnam, it is arguable that if agranulocytosis were a real hazard of dapsone treatment, some few cases at least would have been reported from one of these control schemes.

The sensitization of the bone marrow to the effect of toxic drugs, or the summation of potentiation of their effects, is however always a possibility. Leprosy workers should maintain a watching brief for suggestive signs and symptoms, and investigate and report any occurrence of unusual toxic phenomena associated with, and possibly attributable to, dapsone.

S. G. Browne


The authors report the case of a patient with agranulocytosis in whom the blood- and bone-marrow pictures were indicative of a leukaemic condition, but in whom complete recovery ensued. The patient, a 40-year-old woman, was given dapsone, 50 mg 4 times daily, for a resistant type of psoriasis. The blood dyscrasia was considered to be directly due to dapsone (since no other drugs had been given), the time lag was consistent, and a challenge with self-administered dapsone provoked the symptoms described by early leprologists as "dapsone fever".

(A similar case was reported by McKenna and Chalmers in 1958 (*Br. med. J.*, 1958, i, 324)).

S. G. Browne


The author gave dapsone at a dose of 100 mg daily, together with 18 mg of paramethasone, to 4 patients suffering from "pyoderma gangrenosum" seen in Mexico City. All 4 had been previously treated for long periods with various combinations of antibiotics, tuberculostatics and corticosteroids, but it was not until dapsone was given (with paramethasone) that definite clinical improvement, leading to complete cure, was achieved.

Although the author is understandably hesitant in attributing this result to dapsone in a disease that often tends to be self-limiting, he suggests that further work should be done along these lines.

S. G. Browne


In a letter to the *British Medical Journal*, the authors (working as a team, The Uganda Buruli Group) give advance notice of the contents of an article that will appear later. They claim that organisms, resembling *Mycobacterium ulcerans* in several respects, have been isolated from various grasses growing in districts where Buruli ulcer occurs, and that 24 other cultures of mycobacteria, differing in certain cultural characteristics, have been also obtained from the grasses in question.

The publication in full of these important observations is awaited with interest. If *Mycob. ulcerans* can be found on grasses, and positively identified, the way may be open for *Mycob. leprae* to be traced to some similar nidus, just as various fungi pathogenic to human skin have been isolated from soil.

S. G. Browne

A very full biochemical study of nerves in a disease characterized by the clinical features of peripheral neuropathy and gross enlargement of peripheral nerve trunks is of interest to leprosy workers. The following is the authors' summary:

"Analysis of fascicular portions of sural nerves from patients with hypertrophic neuropathy of the Dejerine-Sottas type (HN-DS) has shown a great decrease in cerebrosides in the presence of at least normal amounts of sphingomyelin and possibly increased amounts of sulfatides. The decreased amounts of cerebrosides may parallel the great decrease in amount of myelin but, in view of this great decrease, the normal sulfatide value actually may represent an abnormally large amount of sulfatides. Analysis of a liver specimen from a patient with HN-DS revealed an abnormal lipid profile—a sevenfold increase in ceramide monohexoside sulfates with very low levels of ceramide dihexoside sulfates and of other unidentified lipid sulfates. These findings suggest the existence of a systemic defect in the metabolism of ceramide hexosides and ceramide hexoside sulfates.

Quantitative histologic studies of sural nerves from patients with hypertrophic neuropathy of the Charcot-Marie- Tooth type (HN-CMT) and with HN-DS demonstrated generalized abnormalities of myelinated fibres, but not of unmyelinated fibres. In the sural nerve of the most severe case of HN-DS, myelinated fibres were demyelinated for most of their length, leaving only occasional, short internodes. In sural nerves from persons with typical HN-CMT, approximately 7.5 to 10% of the length of myelinated fibres was demyelinated, but the remainder of the fibre studied also showed evidence of previous demyelination and remyelination. In both disorders, the diameter of the largest axis cylinders of demyelinated regions was less than the diameter of the axis cylinders of largest myelinated fibres of healthy nerves. An actual decrease in the number of myelinated fibres is inferred from the observation of onion-bulb formations without central fibres, from the known decrease in number of Meissner's corpuscles in skin of persons with these disorders, and from the known presence of fibrillations and increases in amplitude of motor unit potentials in these disorders. The present histologic evidence suggests an abnormality of myelination. The changes in axis cylinders may represent the loss of trophic influences from demyelination or a coincident metabolic abnormality in axis cylinders."


The thesis advanced by the authors, from their wide reading of the relevant literature and their enquiries in the United States, is that the stigma popularly thought to surround leprosy is not so widespread as some people think, and that therefore the considerable efforts put forward by interested laymen and medical workers are not completely congruent with modern scientific knowledge. In the Western world, the stigma is generally believed to be associated with, or derived from the Old and New Testaments; attempts at "destigmatization" often revolve around efforts to show that this association is without base on historical, medical and exegetical grounds.

The authors suggest that these attempts are of relatively recent origin, and are common in the U.S.A. and in Europe. [The categorical statement that "with the exception of a few small endemic foci, leprosy 'disappeared' from the continent of Europe around the 16th century and has remained absent from that continent since" will be challenged by doctors treating some of the 52,000 leprosy patients still living in European countries]. They view with some concern any extensive public education programme on leprosy in the United States or Western Europe,
which might have undesirable effects in creating or increasing anxiety in vulnerable sections of the population.

In an extended historical section, the authors trace the growing awareness among the colonial powers (Britain in particular) of the existence of leprosy and the threat it posed, and indicate the factors concerned with the development of the stigma that now is held to surround leprosy in the Western world. It is noteworthy that in some countries where leprosy is very prevalent, little or no stigma exists, whereas in Europe and North America—not directly threatened by the disease—the stigma and hence the need to rationalize or to remove it are generally accepted by those most closely concerned with leprosy and its victims. “The myth of leprosy as the disease of the ‘leper’ . . . is still widely disseminated”, and the concept stigmatizes by reason of the implied moral connotation of the words.

The authors conclude that the current destigmatization theory has a mythological foundation: “a rational fear of the disease cannot be attenuated through the myth that it is stigmatized by virtue of a faulty association with Biblical references and images.” They suggest that the necessarily partial and emotional approach of voluntary agencies must be supplemented by the greater resources and dispassionately scientific attitude of Governments facing the medico-social problems of a slightly contagious disease.

S. G. Browne

The following 3 abstracts are reprinted, with permission, from Trop. Dis. Bull., 1971, 68, 1:


Lepromin suspensions for intradermal testing are usually prepared from the skin of patients with lepromatous leprosy, and this may contain varying amounts of tissue debris and clumps of leprosy bacilli. An improved lepromin should have the following properties: (1) it should contain leprosy bacilli that have been subjected to minimal, controlled mechanical trauma; (2) there should be a uniform range of bacterial clump sizes, and (3) freedom from visible, rapidly-settling tissue particles. Thus a standard lepromin containing 160 x 10^6 bacilli/ml can be prepared. An electric blender for initial preparation, and treatment of tissue residues with 7% chloroform to declump the bacilli are recommended. Lyophilized lepromins retain their potency for more than 3 years, while storage at 4°C is less reliable. Dilution of lepromin decreases the frequency of weak reactions, “false-positives”, in patients with lepromatous leprosy. A dilution of 1 in 7.5, producing induration of 3 mm, is equivalent to an induration of 5 mm produced by full-strength lepromin. The Fernandez reaction at 48 hours is not reliably observed with diluted lepromin and is considered unimportant. Further trials of dilutions of lepromin 1 in 4 (40 x 10^6 bacilli/ml) and 1 in 8 are recommended. The diameter of induration at 4 weeks should be recorded in patients and contacts. Four degrees of induration are suggested.

C. S. Goodwin


This eagerly awaited preliminary report, although presented with considerable reservations, will provide useful data for the continuing debate on the protective value against leprosy of BCG vaccination. The purpose of the investigation was to observe, in a densely populated township in a highly endemic area with a high lepromatous/tuberculoid ratio, whether BCG vaccination had any protective effect in children possibly exposed to leprosy infection outside the home.
The authors briefly review a selection of the many publications dealing mainly with the capacity of BCG vaccination to evoke positivity of the lepromin reaction in different populations, different age-groups, exposed or not exposed to leprosy, and exposed or not exposed to tuberculosis and perhaps to anonymous mycobacteria.

They then give a very fair summary of the results reported to date in the other two large-scale and adequately planned trials of BCG vaccination currently in progress, that is, in Uganda and in New Guinea. It would seem that BCG vaccination in Uganda has conferred protection against early forms of leprosy for a period of 3 years or more in about four-fifths of children exposed to intra-familial risk. These findings are not necessarily applicable to communities with different total prevalence rates or with different proportions of lepromatous cases. In New Guinea, BCG vaccination has provided no unequivocal protection of exposed individuals, though preliminary findings were encouraging and suggested that some protection was afforded in persons in the 10-29 years age-group.

In the WHO trial in Burma, the potency of the BCG vaccine used was determined, and considered to be satisfactory from the standpoints of both viability and antigenicity. No distinction was made between household contacts and other children, since attack rates were similar in both groups.

The incidence of leprosy in the 2 comparable groups of children, vaccinated with BCG and unvaccinated, is analysed in a series of useful tables, taking into consideration the degree of tuberculin sensitivity, age, and so on. The findings at each of the 3 annual re-examinations showed no significant differences in the pattern of leprosy incidence in the 2 groups, although inconsistent fluctuations were observed from year to year. Nor did BCG have any appreciable effect on the forms of leprosy that did develop in both groups, which were mainly tuberculoid or indeterminate. The Mitsuda reaction was in general more highly positive in children who had received BCG vaccination, and in the children in this group who developed leprosy. Other interesting facts emerged. In addition to the lack of protection afforded by BCG vaccination to children exposed to leprosy in the home, was the grossly similar risk arising from index patients suffering from lepromatous or from tuberculoid leprosy. Again, naturally occurring tuberculosis infection did not confer any significant protection against the subsequent development of leprosy. In the first annual follow-up, the incidence of leprosy was rather higher in the BCG vaccinated group, suggesting that the vaccination may have had an enhancing or accelerating effect on the appearance of incipient leprosy lesions.

A comparison of the results obtained is made, the methodology and some of the epidemiological aspects of the 3 trials are discussed, and suggestions are offered to explain the considerable apparent discrepancies in their results. [The whole paper deserves detailed study.]

S. G. Browne
The following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1971, 68, 3:


Thenar muscle biopsy specimens from patients with lepromatous leprosy, with no history of myopathy or neuropathy, showed the presence of leprosy bacilli in 13 out of 13 cases. The great majority were in macrophages or Virchow cells but a few were seen lying free in relatively intact muscle fibres.

Histologically there were varying degrees of lepromatous infiltration, forming a granuloma in some cases. The muscle fibres showed reactional changes secondary to the infiltration. When severe this involved destruction of the muscle fibres together with perimysium and endomysium.

[It is very interesting that muscle lesions were found in all 13 cases though nasal smears were positive in only 6. These lesions, however, are not strictly comparable to the multiplication of bacilli in mouse muscle; nor is it safe to assume a similar involvement of deep muscles.]

*D. S. Ridley*


Sera from 552 patients with lepromatous and 384 with tuberculoid leprosy, and from 251 people without leprosy, were collected at Chingleput and in the surrounding district in South India. Two tables give details of the incidence of Australia antigen in the various age-groups and types of leprosy, together with results of comparable studies in Cebu in the Philippines [see this Bulletin, 1970, v. 67, abstr. 1548]. In South Indian patients 6.2% of those with lepromatous and 2.1% of those with tuberculoid leprosy had Australia antigen, the highest incidence being in those under the age of 20 years. Among people without leprosy the incidence was 2%, but below the age of 20 the incidence was 7.9%. The difference in the incidence of Australia antigen between the lepromatous leprosy group and the tuberculoid group is significant. Frequency was higher in males, and in younger males than in older males. These age, sex and classification differences are the same as those previously reported for the larger Cebu study. The authors discuss the "inadequacies" in the sample selection in India, namely, that no attempt was made to match the patients and those without leprosy as to caste and location. Patients with lepromatous leprosy were "mostly" living in an institution, and this may have influenced the incidence of Australia antigen in this group. However, in Cebu, institutionalization did not appear to be a factor determining the frequency of this antigen in leprosy patients. The authors postulate that people who are homozygous for a gene which indicates susceptibility to chronic infection with serum-hepatitis virus are also susceptible to chronic infection with other organisms, and may be more likely to develop lepromatous leprosy when infected with *Mycobacterium leprae*.

*C. S. Goodwin*


Sixty leprosy patients suffering from reaction phases received short, high-dosage, tapered courses of flufenamic acid (FFA), and the drug appeared to be effective in relieving the manifestations of reaction in lepromatous leprosy, such as fever, erythema nodosum leprosum (ENL), neuritis and iridocyclitis. Reaction in borderline and tuberculoid leprosy was not so well relieved. These high doses were well tolerated, gastrointestinal symptoms being the commonest side-effect. Temporary neutropenia occurred in 1 of 4 patients who received 28 mg/kg daily,
but the leucocyte count returned to normal 10 days after the drug was stopped. Levels of serum glutamic oxalacetic transaminase (SGOT) and of glutamic pyruvic transaminase (SGPT) were raised in a number of patients when treatment with FFA was commenced, and in some there was a significant fall during the time when the largest doses were being given.

W. H. Jopling


At Carville, Louisiana, U.S.A., the authors compared thermographs depicting skin temperature patterns of normal subjects with the configuration of sensory loss to pinprick in a series of patients with lepromatous leprosy, and found that the pattern of sensory loss tends to involve the cooler skin surfaces earliest and then progresses on the basis of relative skin temperature. Thus the limbs are affected first—the dorsa of feet, the lateral aspects of legs, and the dorsal aspects of hands and forearms—whereas the scalp, axillae, intergluteal fold and the inguinal areas are all warm regions that tend to show normal sensation even in far advanced cases.

W. H. Jopling


A double-blind controlled trial in 24 patients with lepromatous leprosy in reaction showed that clofazimine (B 663, Lamprene) successfully controlled erythema nodosum leprosum and had a useful effect in preventing recurrence once the reaction had been controlled. The dosage of clofazimine was 100 mg 3 times a day, and the authors consider the drug to be safer and more effective than prednisolone. The only side-effect observed was red/black skin pigmentation, and the patients were willing to accept this in return for relief of symptoms.

W. H. Jopling


A Nigerian man, aged 35 years, suffering from advanced lepromatous leprosy, was treated at the Oji River Leprosy Settlement. The patient's Morphological Index (MI) was 35% initially and the Bacterial Index (BI) 3.3 (maximum 4). Dapsone 50 mg was given twice weekly for 52 months, each dose of the drug being swallowed in the presence of a doctor or a leprosy worker. After 6 months treatment, the MI was 0% and after 35 months “even fragmented bacilli and acid-fast dust were no longer to be seen” in skin smears. After 52 months, small fleshy papules appeared on the skin of the arms and the lumbar region. The histological picture was granulomatous tissue crammed with *Mycobacterium leprae*, 80% of which were morphologically normal. “There was no suggestion of any defect in intestinal absorption” (of dapsone). Apparently normal skin, earlobes and nasal mucosa “remained free from bacilli”. Tissue from one of the papules was injected into the footpads of mice receiving dapsone in their diet. Multiplication of *Mycobacterium leprae* was found in 10 out of 12 footpads of mice receiving dapsone 0.006% in their diet, and 6 out of 12 footpads of mice receiving 0.025% dapsone.

The significance of this case history is discussed, including its relevance to field work by medical auxiliaries. Dapsone given in a “low-dose regimen facilitates treatment. . . . On balance, then, the risk of the emergence of resistant strains is most probably outweighed by the undoubted advantage of a reduced rate of complications” (of low dose dapsone).
The rate of excretion of dapsone varies widely and may be very rapid. Now that the minimum inhibitory concentration of dapsone for *Myco. leprae* is known approximately, a rational discussion of dapsone dosage and treatment intervals in relation to maintaining satisfactory anti-bacterial blood levels would have added to the value of this paper. That alternative low dosage regimens are rational, such as 10 mg or 25 mg daily, 50 mg thrice weekly or 75 mg or 100 mg twice weekly, should be more widely known.

*C. S. Goodwin*