Abstracts

Leprosy and Genetics. A Review of Past Research with Remarks concerning Future Investigations, by BERNARDO BEIGUELMAN. *Bull. Wld. Hlth. Org.*, 1967, **37**, 461-476.

The few geneticists who are interested in leprosy have been working in this field only since 1962, and have made little progress in solving the problems presented by susceptibility to this disease.

This paper reviews the research that has been conducted, with particular reference to the search for associations between leprosy and certain genetic markers. In each area, the advantages and limitations of different techniques are described, and attention is drawn to sources of bias that may invalidate many of the results that have been published. Of particular interest is the discussion of a new technique for evaluating resistance to leprosy. The proposed technique is based upon the *in vitro* transformation of blood monocytes into macrophages, and the observation of their behaviour against *M. leprae*.

From author's summary.

The Role of General Practioners in Leprosy Control, by BHOLA NATH. *J. Indian Med. Ass.*, 1967, **49**, 10, 470-472.

The author appeals to all general practitioners to become leprosy conscious and to know enough of the diagnosis and treatment of the disease to recognise signs of leprosy during examination for any other disease so that treatment can be undertaken at once and the chance of complete cure made more certain. He points out that the general practitioner has the most vital role to perform in the control of leprosy today. Society's ignorance of the facts of the disease and the age-old beliefs and prejudices prevent the seeking of medical opinion early enough for complete cure. Leprosy is a disease like any other and should be treated as such in the ordinary clinics and only the the small percentage of patients who have gross deformities should be sent to the leprosy clinics. A united effort on the part of the 40,000 doctors doing general work in the endemic areas, each one treating 10 patients, could immediately bring one-fifth of the estimated number of leprosy sufferers in India under treatment.

It is an encouraging sign that doctors in India should realise that early diagnosis of the disease will mean cure before the patient becomes a menace to himself and others and the author makes many helpful suggestions. This is a valuable paper and it summarises comprehensively the ways in which general practitioners can assist the campaign to stamp out leprosy.

3. **Chemotherapeutic Trials in Leprosy. 5. A Study of Methods Used in Clinical Trials in Lepromatous Leprosy,** by M. F. R. WATERS, R. J. W. REES and IAN SUTHERLAND. *Int. J. Lepr.*, 1967, **35**, 3, 311-335.

Although controlled clinical trials were used from the first introduction of successful chemotherapy of tuberculosis, such methods have been frequently neglected in study of the treatment of leprosy. From experience gained in 2 controlled trials at Sungei Buloh Leprosarium and in the light of the recent advances in experimental leprosy, a re-appraisal of trial methods in lepromatous leprosy is presented. It is considered that untreated L2 and L3 lepromatous leprosy patients remain the most suitable for such trials, and that accurate classification is essential. Methods of clinical, histological and bacteriological assessment are evaluated. The importance of recording morphological changes in *M. leprae* is emphasised and it is considered that only those patients with a pre-treatment morphological index (MI) of 25 or more should be included. The general design of controlled trials is discussed, including the advantages and disadvantages of the method of matched pairs and the difficulties resulting from reactions, especially erythema nodosum leprosum (ENL). The design of pilot trials is also considered and similar careful patient selection is advocated. Furthermore, it is suggested that evidence or otherwise of chemotherapeutic activity may be obtained within 4½ to 6 months by studying the effect of the trial drug on the MI. Finally, the different methods available for evaluating the effect of drugs on the intiation and treatment of ENL are presented.

From the authors' summary.

The following 9 abstracts are reprinted, with permission, from *Trop. Drs. Bull.*, 1967, **64**, 11:—

4. **Epidemiologia de la lepra en el centro Oriente** (The epidemiology of leprosy in the Eastern Central Region of Peru), by E. JUSTO *Revta Sanid. Polic.*, 1965, **25**, 1-3, 40-44.

The author reports on the incidence of leprosy in Peru with special reference to the Eastern Central Region. According to the facts obtained by the Statistics Service the population of Peru increases annually by 2% while leprosy increases by 6.53%, so that leprosy increases 3 times more rapidly than the population in general. In Pucallpa in the Eastern Central Region, leprosy in the last 3 years has shown an increase of 13% annually, while it has decreased by 14% in the country generally. These figures cause the author to conclude that it is necessary to create new anti-leprosy centres. The whole country should become interested in leprosy control and the Army, Navy and Air Force should mobilize personnel to help in the anti-leprosy campaign.

J. R. Innes.

5. **Observations sur l'allergie tuberculinique et léprominique des enfants cliniquement sains vivant au contact de lépreux en Guadeloupe** (Observations on tuberculin and lepromin allergy in Guadeloupe), by A. ESCUDIÉ and E. COURMES. *Bull. Soc. Path. Exot.*, 1966, **59**, 3, 289-96.

In Guadeloupe 465 house contacts of patients with leprosy received simultaneously in different arms an intradermal injection of 10 units of tuberculin and 0.1ml. '*brute classique*' lepromin. The Fernandez, early, lepromin reaction, was considered to be more reliable than the Mitsuda, late, lepromin reaction because the authors consider that the latter may be affected by the injection of tuberculin. Of 14 children aged less than one year 21% were lepromin positive and 0% tuberculin positive. Two tables and a graph illustrate the changes in lepromin and tuberculin positivity rates up to the age of 20 years. In 46 people aged 15-20 years 65% were both lepromin positive and tuberculin positive, a further 22% were tuberculin positive alone, and 4% were lepromin positive alone. In 147 people, aged 15-20 years, who lived in the same district but were not close contacts of leprosy, the tuberculin positive rate was 52.3%. The relative value of the Fernandez and Mitsuda reactions is discussed briefly. A BCG vaccination campaign for the prophylaxis of leprosy was started in Guadeloupe in May, 1965. It is suggested that vaccination of schoolchildren should be supplemented by vaccination of newborn infants because the lepromin positive rate is appreciable in children below school age. (The details of the Fernandez reaction that were considered to indicate a positive lepromin reaction are not delineated, and it would be valuable to record how frequently a negative Mitsuda reaction was observed in Fernandez-positive children.)

C. S. Goodwin.

6. **Leprosy finger,** by L. KLENERMAN. *Pro. R. Soc. Med.*, 1967, **60**, 6, 547 (Sect. Orthopaed. 25).

A male aged 24 years born in Tanzania and resident in India for 4½ years before coming to England, had been in this country for 18 months when he attended a hand clinic complaining of a right middle finger which had been swollen for 6 months. The finger was not painful, but movement was limited. Radiographs of the hand were normal. A biopsy of the finger revealed that 'the swelling was produced by gross thickening of the digital nerves'. (It would seem unusual that while taking a skin biopsy the digital nerves should be exposed, but an interesting fact came to light. The abstracter has experience of dissection and operation revealing swelling of nerves proximal to the heads of the metacarpals, between which a nerve may become entrapped.) A rash on the right leg, which had been present for 6 months, was found by a dermatologist to be anaesthetic to pin-prick and a diagnosis of leprosy was made. Slight thickening of the right lateral popliteal nerve and the left superficial radial nerve was found. It is stated that the patient had the tuberculoid form of leprosy (although the evidence for this classfication is not delineated). This is an interesting case report.

C. S. Goodwin.

7. **Lupoid features in a case of leprosy,** by L. BONOMO, F. DAMMACCO, A. TURSI and G. BARBIERI. *Int. J. Lepr.*, 1967, **35**, 1, 65-71.

The clinical features and laboratory investigations of an Italian woman who died at the age of 42 with a history of leprosy from the age of 14 years are delineated. Initially, the patient experienced joint pains with remittent fever, and 'later' erythematous skin lesions appeared. Bacteriological sampling when she was 27 led to a diagnosis of leprosy, and the course of her disease was unremarkable until 18 months before her death when she developed continual fever with severe joint and muscle pains. Several features of systemic lupus erythematosus (LE) became noticeable including erythema of the nose and cheeks, and later of the whole of the face and neck and the sternal area. The signs and symptoms responded to high doses of prednisone, greater than 25 mgm. per day. Laboratory examinations revealed anaemia, proteinuria and defective liver function; and tests for rheumatoid and anti-nuclear factors were positive with many typical LE cells. Increases in IgG, IgA, and to a lesser extent IgM immunoglobulins, were detected, with decreased albumin and beta 1A/C globulin values. It is suggested that this last feature has not previously been reported in a leprosy patient. Other studies which have revealed auto-immune features in leprosy patients are discussed, and various suggestions made as to the aetiology of certain aspects of this disease. It is suggested that an immunosuppressive drug such as chloroquine may be beneficial (but this drug has been used by some leprologists for many years).

C. S. Goodwin.

8. **Leprotic nerve abscesses in Northern India,** by V. N. SEHGAL, S. M. TULI and B. DUBE. *Int. J. Lepr.*, 1967, **35**, 1, 60-64.

An examination of 4,000 patients with leprosy revealed 10 with nerve abscesses, 9 patients having tuberculoid leprosy and one patient borderline leprosy. Five patients were subjected to 'nerve decapsulation', and smears from the abscess material and biopsy specimens from the abscess walls revealed no *M. leprae*. The clinical histories of 2 of these patients, and of 5 others, are given. Comparison is made with previous surveys for nerve abscesses. It is stated that if operation is performed early, permanent damage to nerve fibres may be prevented (but no evidence for this statement is presented). The beneficial effect of corticosteroids for one patient is mentioned.

C. S. Goodwin.

9. **Etisul in out-patient treatment of leprosy** (Memoranda), by D. S. CHAUDHURY. *Ghana Med. J.*, 1967, **6**, 1, 8-9.

A report on the use of Etisul in mass mobile out-patient treatment in Northern Ghana is described and compared with the findings in a control area. It is observed that the rate of decline of aggregate infectivity in the area where Etisul was used, expressed in percentage reduction of infectivity, was greater than that in the control area. The use of Etisul in suitable cases is recommended together with dapsone in mass out-patient treatment.

J. R. Innes.

10. **Chemotherapeutic trials in leprosy. 3. Pilot trial of a riminophenazine derivative, B663, in the treatment of lepromatous leprosy,** by J. H. S. Pettit, R. J. W. Rees and D. S. Ridley *Int. J. Lepr.*, 1967, **35**, 1, 25-33.

This trial was the authors' first attempt to design a drug trial with a minimal number of patients. The riminophenazine derivative B663 was given in a dose of 100 mgm. 3 times a day for 6 days a week for 5 months to 4 patients with pure lepromatous leprosy (LL) and to 2 with borderline lepromatous leprosy (BL). The investigations performed and the methods of assessing progress were similar to those in previous trials (see *Trop Dis. Bulletin*, 1964, v. 61, 161; 1966, v. 63, 656), and particular attention was given to the morphological index. Smears were taken after 1½ months', 3 months' and 5 months' treatment, from 6 skin sites including both ear lobes, and biopsy specimens of skin were taken at the beginning and end of the trial. An independent assessor estimated the clinical improvement as 'slight' in all patients. The case history of each patient in the trial is given, and a table contains the details of the bacteriological responses to treatment and the falls in the biopsy index. The average bacteriological index was 4.3 at the start of the trial and 3.9 after 5 months. The morphological index fell on average from 26% to 2.5%, and the biopsy index fell on average to 40%. The results indicate that B663 is an active anti-leprosy drug causing leprosy bacilli to become irregularly stained, presumably killing the bacilli. The fall in the biopsy index is 'almost exactly the figure that would have been expected with DDS in a group comprising one BL patient for every two LL patients, which was the proportion in this trial'. The development of a deep and persistent pigmentation of the skin of 4 Chinese patients is detailed, with the histological picture of an appreciable increase in the melanin content of the basal layer of the epidermis. The drug was thus not acceptable to the pale-skinned patients, and a lower dosage scheme may be worth investigating. The trial method was judged a success, but a more satisfactory protocol would exclude all BL patients and those with a morphological index below 25%.

C. S. Goodwin.

11. **Occupational therapy in leprosy with particular reference to activities of daily living,** by P. Regis. *Lepr. India*, 1965, **37**, 4, 468-74, 15 figs. on 4 pls.

'It is concluded that methods of occupational therapy can help patients without deformity as well as those with various stages of deformity. In patients without deformity the purpose is to teach them to use their hands and feet in such a way as to prevent deformities by protecting against injury and burns, etc. In patients with various degrees of deformities the purpose is to rectify or reduce the deformities and to enable the patients to utilise even the deformed limbs. The Occupational Therapist can help them (1) in pre- and post-operative treatment of operated hands, (2) in providing aid to daily activities of life, and (3) in earning a livelihood. General principles of activities directed to these ends are described and some specific recommendations are made. It is stated, however, that each patient needs individual attention and special methods of adaptation may have to be used.'

12. **Effect of DDS on established infections with *M. leprae* in mice,** by C. C. Shepard and Y. T. Chang. *Int. J. Lepr.*, 1967, **35**, 1, 52-7.

The effect of chemotherapeutic drugs against *M. leprae* in experimental footpad infections of mice has previously been tested by administration of the drug from the time the animals were infected. This method produces relatively quick and clear cut results. In the present work a situation analogous to that of therapy in a human infection was created by withholding treatment until the bacilli had completed the most active phase of multiplication.

Treatment with DDS (0.1% of the diet) was found to stop further bacillary increase but it produced little change in the numbers of bacilli. It did not appreciably affect the number of solid-staining organisms during the first 57 days, but after 88 days of therapy solid forms disappeared. This is about the same period of time as would be required to bring about a similar result in human leprosy. The viability of the bacilli was not found to be diminished until 88 days, a period which is 7 times the calculated generation time, and viable bacilli persisted in very small numbers even at 318 days despite the high blood level of DDS. The time that DDS takes to kill leprosy bacilli is probably governed by their metabolic activity.

D. S. Ridley.

The following 9 abstracts are reprinted, with permision, from *Trop. Dis. Bull.*, 1967, **64**, 12:—

13. **De ontwikkeling in de lepra-situatie in Nederland tussen 1945 en 1965** (The leprosy situation in the Netherlands, 1945-1965), by D. L. Leiker. *Ned. Tijdschr. Geneesk.*, 1967, **111**, 32, 1401-6.

The English summary appended to the paper is as follows:—

'The total number of leprosy patients residents in the Netherlands during the last 20 years has been estimated at 600. In *c.* 100 cases the diagnosis was never established. About 300 patients still require treatment. An analysis of the data on 450 leprosy patients in the Netherlands showed that the incidence of new patients among immigrants was highest within 4 years of their immigration. After this the rate fell sharply, until after 6 years new patients were only found sporadically. In nearly all patients the infection had been acquired in the country of origin; a few patients were infected by relatives in the Netherlands, although only one such patient has been established beyond doubt. Endemic leprosy among Dutchmen of Eurasian parentage is declining sharply; among the Amboinese it seems to have disappeared almost completely. Immigrants from the West Indies, however, now are a considerable source of new patients, with a leprosy rate of nearly 1%.

'Chemotherapy has probably been the main factor in the reduction of endemic leprosy among immigrants. It has caused a rapid percentage increase of deformed bacteria, which are incapable of trasmitting the disease. They increase more rapidly than the bacteria eliminated from the body.'

14. **Phenoloxidase of** *M. leprae* (Correspondence), by K. Prabhakaran. *Nature*, London, 1967, July 22, **215**, 436-7.

It has already been reported that *M. leprae*, alone among a number of mycobacteria tested, is able to oxidize 3,4-dihydroxyphenylalanine (DOPA) to pigmented products (see below). It is now found that in the range of substrates oxidized the phenoloxidase of *M. leprae* resembles more closely the enzyme of plants than that of mammalian origin. It oxidizes both D and L forms of DOPA and in addition catechol and catecholamines. Taxonomically *M. leprae* belongs to the same class as fungi, which are rich in phenolase. This enzyme might provide an alternative pathway for the utilization of various substrates, which could be used either for cultivation of the organisms or for selective inhibitors.

D. S. Ridley.

15. **Metabolism of** *M. leprae* **separated from human leprosy nodules,** by K. Prabhakaran. *Int. J. Lepr.*, 1967, **35**, 1, 34-41.
Oxidation of 3,4-dihydroxyphenylalanine (DOPA) by *M. leprae*, by K. Prabhakaran. *Ibid.*, 42-51.

In the first of these papers the author reports that suspensions of *M. leprae* obtained from human lepromatous material by the method described earlier (*Nature*, London, 1962, v. 196, 589; *Trop. Dis. Bulletin*, 1963, v. 60, 229) oxidized *p*-phenylenediamine, as as measured by oxygen-uptake in the Warburg apparatus. By measuring the increase in absorbance at 550 mμ. the author detected succinate-cytochrome C reductase activity, and also lactate dehydrogenase activity by the increased absorbance at 340 mμ. in the presence of nicotinamide adenine dinucleotide. The formation of pyruvate from lactate was detected by the carbonyl test, but as the oxygen-uptake in the presence of lactate was inversely related to the pyruvate accumulation, the pyruvate produced was presumably further oxidized.

In the second paper, the author describes experiments with *M. leprae*, in which DOPA oxidase activity was detected. The activity was determined by measuring in the Warburg apparatus an increase in exogenous respiration when DOPA was added. The possibility of the increase being due to auto-oxidatio was excluded by measuring auto-oxidation at *p*H 6.8 and at *p*H 8.3; a considerable increase occurred at *p*H 8.3 whereas at *p*H 6.8 (the *p*H used in the mycobacterial tests) there was no significant increase. Indole-5, 6-quinone was formed from DOPA by oxidation by the leprosy bacilli but not by *Myco. lepraemurium*, *Myco. tuberculosis* (H37Rv, H37Ra) BCG, *Myco.* 607. *Myco. smegmatis*, *Myco. phlei* or Kedrowsky's bacillus,

The nature of the enzyme that catalyses the oxidation of DOPA is not clear for it failed to oxidize tyrosine to melanin, and the significance of its presence in the leprosy bacillus is discussed. The author concludes that in this organism the oxidase probably provides an alternative mechanism by which different substrates can be oxidized effectively by the organism.

S. R. M. Bushby.

16. **Cryoproteinemia in leprosy,** by L. J. Matthews and J. R. Trautman. *Derm. Int.*, 1965, **4**, 3, 164-8.

Cryoproteinaemia was detected in 40 out of 41 patients with active lepromatous leprosy who were not receiving corticosteroid therapy. Eight of the 41 had acute erythema nodosum leprosum at the time, and in these the cryoprotein level was high: 600-900 mgm.% as against 200-400 mgm.% in those without reaction. However, high blood levels up to 600 mgm.% were also found in 6 out of 6 patients with dimorphous leprosy. No cryoproteinaemia was detected in the following groups (numbers of patients in brackets): active lepromatous leprosy with corticosteroid therapy (4), inactive lepromatous leprosy (5), tuberculoid leprosy (4) and healthy control subjects (19).

D. S. Ridley.

17. **Association between lepromatous leprosy and Australia antigen,** by B. S. Blumberg, L. Melartin, M. Lechat and R. S. Guinto. *Lancet*, 1967, July 22, 173-6.

Australia antigen was found to be more common among patients with lepromatous leprosy than in those with tuberculoid leprosy or in those without leprosy. The frequency was higher in males than in females and in the young than in the old. In the Philippines the incidence among male patients aged less than 20 years was 27% for lepromatous leprosy, 12.5% for borderline and 8% for tuberculoid leprosy; among those without leprosy it was 5.5%. The differences were less striking among females or older patients. These results are analysed statistically. A similar study is being undertaken in India.

Australia antigen was first detected in an aborigine, and has been found to occur mainly in South East Asian populations. Apart from lepromatous leprosy it has been found to be associated also with leukaemia and hepatitis. It is suggested that subjects with Australia antigen have an inadequate immune response and are especially susceptible to these illnesses.

D. S. Ridley.

18. **Morphology of** *M. leprae* **in tissue sections,** by L. Levy, P. Fasal and L. P. Murray. *Arch. Derm.*, 1967, **95**, 5, 451-5.

Estimates of the morphological index (MI) of leprosy bacilli in histological sections were compared with similar estimates made on homogenates of the same pieces of tissue. The results indicated that the differences between the 2 estimates would not be expected to exceed a value of 4 on 19 out of 20 occasions. However,

the highest MI value observed in any of the tissues examined was 14%. The method of estimating the MI on sections was to count only single, isolated bacilli. (It would be interesting to know what the difference between the 2 estimates would have been with more active lesions, in which the solid-staining bacilli sometimes lie preponderately in clumps. The abstracter has noticed also that disproportionate numbers of solid forms are often found in the superficial part of the granuloma.)

D. S. Ridley.

19. **Alopecia mucinosa simulating leprosy,** by J. Fan, Hsin-Shiang Chang and Biao Ma. *Arch. Derm.*, 1967, **95**, 4, 354-6.

In countries where leprosy is endemic and carries a serious social stigma, minor features of the disease may stigmatize a leprosy patient. Two case reports from Taiwan of eyebrow alopecia originally diagnosed as leprosy, but found after histological examination to be alopecia mucinosa are presented. One patient had a slightly elevated hairless plaque in the medial part of the eyebrow (the eyebrow alopecia of leprosy characteristically involves the lateral portion initially). The clinical details of the other patient are not described. No other lesions suggestive of leprosy were found in either patient, although the second patient had been in a leprosarium for 2 years. Histological examination of a skin biopsy specimen in both patients showed 'a marked inflammatory infiltrate in the corium' in association with the hair follicles. In sections stained by the Ziehl-Neelsen method no acid-fast bacilli were found. The sebaceous glands and the hair follicles were degenerate, and PAS and toluidine blue stains revealed the presence of mucin in the degenerate follicles. Treatment with 'topical and oral steroids' resulted in the induration subsiding and regrowth of lanugo hair. In Taiwan there is a 'lay belief that eyebrow alopecia is a sure sign of early leprosy'. The authors point out that this alopecia is usually associated with the advanced form of leprosy disease, and may not be present at all. They rightly emphasize the need, both for medical and social reasons, for an exact diagnosis of leprosy, which in doubtful cases involves histological examination of a skin biopsy specimen.

C. S. Goodwin.

20. **Dislocations du tarse dans la lèpre** (Dislocation of the tarsus in leprosy), by A. Carayon, P. Bourrel, M. Bourges and J. Languillon. *Bull. Soc. Med. Afr. Noire Lang. Fr.*, 1967, **12**, 1, 69-80.

This article, well illustrated with 7 pages of X-ray photographs and diagrams of the disintegrating tarsus in leprosy, summarizes the findings of previous workers and reports briefly on the lesions found and treatment adopted in 19 patients suffering from diverse bony changes in the tarsus associated with leprosy. The causes of the tarsal dislocation (or disintegration) were complex: specific leprotic intramedullary granulomata, neuropathy (*i.e.*, unappreciated traumata to anaesthetic articular surfaces), and infection entering through deep perforating ulcers of the sole. When surgical correction of the drop foot has failed to prevent progressive deterioration of the bones and joints in the tarsal region, the authors advocate early mid-tarsal or subastragaloid arthrodesis. When the metatarsus is destroyed, amputation is the only solution.

S. G. Browne.

21. **Prophylactic value of DDS against leprosy—an interim report,** by P. M. Ali, Dharmendra, S. K. Noordeen and K. Ramanujam. *Lepr. India*, 1965, **37**, 4, 447-67, 3 maps (2 folding) on 3 pls.

In 1960 the Indian Council of Medical Research appointed a Working Group including a statistician to plan a double-blind trial of dapsone used prophylactically against leprosy. The Central Leprosy Teaching and Research Institute, Madras, was selected to carry out the investigation because it is situated in an area where the leprosy prevalence rate is over 2% and because of the facilities of the Institute.

In December, 1961, a house-to-house survey was started of an area including 75,000 people, to diagnose and record leprosy patients. However, because the lepromatous rate was found to be 'a little below 15%, and the average number of child contacts per source was surprisingly low, the survey area was enlarged to include 213,721 people of whom 96% were examined. This survey occupied one year. The survey area of 325 square miles included 381 villages. A detailed map of the area shows the names of villages and where the paramedical workers lived.

All the patients with bacteriologically positive leprosy were listed, with a total of 732 intrafamilial healthy child contacts of 'source cases'. To obtain a statistically sufficient number of child contacts all those below the age of 15 were included. 4,370 persons with leprosy were detected, a prevalence rate of 21 per 1,000, 624 having lepromatous leprosy, a lepromatous rate of 14.3%. 334 of the patients with lepromatous leprosy were bacteriologically negative, 'due to treatment', but they were known to have had 'active' lepromatous leprosy and 52 of the non-lepromatous patients were bacteriologically positive. Of the 676 'source' cases only 362 had healthy intrafamilial child contacts.

Owing to death, emigration and 'refusal' only 585 contacts were studied; and these were divided into 2 comparable groups based only on age and sex, by random allocation.

The dose of dapsone for prophylaxis was 5 mgm. twice a week for children aged 0-2 years; each dose was increased by 5 mgm. at monthly intervals to 20 mgm. twice a week, during the 4th month; from the 10th month onwards the dose was 10 mgm. twice a week. Children aged 3-5 years were started on 10 mgm. twice a week and the dose was increased to 40 mgm.; those aged 6-10 years were given from 25 mgm. to 100 mgm. twice a week, and those aged 11-14 years from 50 mgm. to 150 mgm. twice a week. From the 10th month onwards all received half the maximum dose. 291 children were placed in the dapsone group and 294 in the control group; the latter received a

similar looking tablet of calcium lactate. All tablets were to be swallowed in the presence of a paramedical worker.

A considerable amount of information in this lengthy report defies summary and the original should be consulted. Details are given of the double-blind method, supervision by the paramedical workers, and periodic examination, including examination by a doctor of suspected cases. Ten tables contained details of the source cases and their contacts and many facts concerning the 43 child contacts who developed leprosy during the first 2¼ years of the trial. Fourteen children (4.81%) in the dapsone prophylaxis group and 29 (9.86%) in the control group developed leprosy, this difference being significant at the 2% level, t=2.36. None of the children developed lepromatous leprosy, and all were bacteriologically negative except one child in the control group, whose one lesion regressed spontaneously and 'disappeared'.

During the first 9 months of the trial no difference was observed between the 2 groups in the number of children developing leprosy, but thereafter 17 in the control group and 4 in the dapsone group developed leprosy. By the end of 2¼ years the reduction in leprosy incidence was 'of the order of about 50%'. Dapsone prophylaxis was found to be effective up to the age of 10, but 'there has been practically no protective effect in the contacts above that age'. The conclusion is drawn that dapsone prophylaxis should be started 'as soon as possible after exposure to infection'. Dapsone prophylaxis was found to be more effective in males.

All the 43 contacts developing leprosy were given 'therapeutic' doses of dapsone, and the subsequent clinical response of those in the dapsone prophylaxis group was in some respects more 'favourable' than the control group.

An addendum records the development of leprosy in 7 children during a further 3 months of the trial, giving a rate of 4.90% in the dapsone group and 11.81% in the control group.

Among the child contacts under the age of 10 years, after the first year of the trial only one child in the dapsone prophylaxis group has developed leprosy, while 16 in the control group have developed the disease. (This latter observation is of great importance.)

The trial continues, and details of further studies and their application are discussed. (This trial is a most significant contribution to the study of the prophylaxis of leprosy. If it was possible to know the BCG status of the child contacts this might be a significant area of study.)

C. S. Goodwin.

The following 6 abstracts are reprinted, with permission from *Trop. Dis. Bull.*, 1968, **65**, 1:—

22. **Lucha contra la lepra en la República Dominicana** (The leprosy campaign in the Dominican Republic), by H. Bogaert Díaz. *Revta Dominicana Derm.*, 1967, **1**, 2, 106-10.

The English summary appended to the paper is as follows:—

'Between the 3rd February, 1966 to 1967, 15,903 new patients with skin diseases were seen in the Institute of Dermatology discovering 314 patients of leprosy of which 252 were new patients. 209 came from the Distrito Nacional and San Pedro de Macoris. 88 were lepromatous, 84 indeterminate, 79 tuberculoid and one dimorphous.'

23. **Hepatocyte functional state. Quantitative evaluation with I^{131} rose bengal in lepromatous leprosy patients,** by N. Carvalho, M. P. Azevedo and A. C. R. Marques. *Int. J. Lepr.*, 1967, **35**, 2, Pt. 1, 175-83.

'The authors studied the hepatocyte functional state in 29 lepromatous leprosy patients, through the radioiodine-labeled rose bengal test as described by Loewenstein. The procedure for quantitative analysis of the uptake-excretion curve is determined by 3 constants:

'1. Uptake half time or interval of time in which a half part of the dye circulating in the blood is absorbed by the liver.

'2. Excretion half time or interval of time in which a half part of the dye absorbed by the liver is excreted by the biliary ducts.

'3. Liver blood volume in percentage relation with the total blood volume.

'The 29 patients were subdivided into 2 groups: (1) those showing functional lesions of the liver cells, and (2) those without such lesions. Other subdivisions were made according to the presence or absence of excretory dynamic disturbances, to hepatomegaly, to reduction or increase of the liver blood volume, to the evolutive phase of the disease and to response to treatment.

'Of those patients presenting evidence of lesions or disturbances of the cellular function or excretory dynamics, 58.6% showed functional deficit of the polygonal cells; 45% showed excretory functional deficit of the biliary ducts; 44.8% showed reduction in the liver blood volume; and 51.7% showed increase in the liver blood volume.

'The conditions for reduction or increase of liver blood volume did not parallel the functional conditions of the liver cells. Likewise, the presence of hepatomegaly, the disease's evolutive phase, and the response to treatment, did not correspond to the hepatocyte functional state.

'As hemodynamic factors and the functional state of the liver cells may change independently, it is necessary to perform the test simultaneously with the measurement of minimum liver blood flow in order to achieve an effective result.'

24. **The drug treatment of leprosy,** by S. G. Browne. *Trans. R. Soc. Trop. Med. Hyg.*, 1967, **61**, 2, 265-71.

The author, after emphasizing that clinical findings and bacteriological sampling leading to a definitive diagnosis of leprosy are the essential prerequisites of treatment, gives the warning that 'treatment' (presumably chemotherapy) 'should be temporarily withheld from patients whose lesions are in a state of acute

exacerbation when they present themselves, and from those whose peripheral nerves at the sites of predilection are very tender'. Indications for in-patient treatment as opposed to the usual out-patient methods are mentioned. A simple dosage scheme for oral dapsone is given, starting with 25 mgm. once weekly and increasing to 100 mgm. once weekly. The signs of activity of the disease process are delineated. It is advised that treatment should be continued in tuberculoid and indeterminate leprosy for one year after such signs have ceased; and in lepromatous, borderline and low-resistant tuberculoid leprosy for 2 years after clinical and bacteriological activity has ceased. It is mentioned later in the article that some authorities advise that for patients with lepromatous and borderline leprosy dapsone should be continued at half the therapeutic dose for years, if not for life. Solapsone is mentioned, and thiacetazone, ditophal, B663 (Geigy), and long acting sulphonamides are listed; but pride of second place is given to thiambutosine, with a dosage starting at 0.25 gm. daily and increasing to 2 gm. daily. 'During the second half of the second year, dapsone should be introduced while the dose of thiambutosine is gradully reduced.' 10 ml. of intramuscular thiambutosine may be given weekly or fortnightly in place of oral treatment. Drug combinations are not recommended.

Toxic skin rashes due to dapsone are described, and a scheme outlined for 'desensitizing for dapsone sensitivity'. This scheme starts with 5 ml. of an aqueous solution of solapsone, 0.5 gm. in 200 ml. of water, being given orally twice weekly, increasing by 5 ml. to the equivalent of 250 mgm. of (solid) dapsone. Antihistamines are advised for a recurring rash. Treatment of acute exacerbation may require antimonials or chloroquine, or the continual use of corticosteroids. The dangers of acute iritis and neuritis are emphasized, and the treatment advised for neuritis includes a procaine injection 'under the nerve-sheath'. Clinical examination and bacteriological sampling at regular intervals after discharge is recommended. General hygienic precautions to prevent the spread of leprosy are discussed.

(This paper should be studied in the original to appreciate the extensive clinical advice that defies summary. In such an article there might have been more information on the dosage of dapsone than the simple scheme recommended. The fact that the weekly dose may be better tolerated if given in divided doses might have been mentioned.)

C. S. Goodwin.

25. **Tratamiento de la reacción leprosa con Indometacina. Resultados negativos en 5 pacientes** (Unsuccessful results of the treatment of lepra reaction (erythema nodosum leprosum) with Indomethacin), by O. Cañizares. *Dermatología*, Mexico, 1966, **10**, 3, 265-9.

The English summary appended to the paper is as follows:—

'The administration of Indomethacin, an anti-inflammatory analgesic and anti-pyretic of non-steroid chemical structure, was studied in 5 patients with erythema nodosum leprosum.

'Four patients had already previously received corticosteroids. In one of them this medication could be discontinued and replaced by Indocin. In another the administration of Indocin succeeded in reducing the requirements of prednisone. In the other 2 patients Indocin failed to cause any improvement. In one patient of erythema nodosum leprosum of recent origin, not treated with corticosteroids, Indocin even at high doses (200 mg. daily) failed to control the reaction.

'No toxic reactions to the medication were observed even when administered in high doses. The therapeutic results obtained with the administation of Indomethacin (Indocin) in the reactional stages of lepromatous leprosy, of the erythema nodosum type, were in general very unsatisfactory. This medication can be added to the long list of therapeutic measures which only occasionally may be useful in the management of the patient with lepra reaction of the erythema odosum type.'

26. **Lepra manchado de Lucio—antimalaricos en reacción leprosa** (Lucio's phenomenon in leprosy. Antimalarial drugs in the management of lepra reaction) by H. Corrales Padilla *Derm. Int.*, 1965, **4**, 3, 147-50. English summary.

The geographical distribution of leprosy of Lucio is somewhat restricted and outside Mexico it has only been reported a few times: from Costa Rica by Romero and associates in 1949 (*Trop. Dis. Bulletin*, 1950, v. 47, 371), and Honduras in 1962 when the present author reported the first patient seen with it in that country Lucio's phenomenon (necrotizing angiitis) should be considered to be a particular type of reaction of the form described by Lucio and Alvaredo in 1852, and identified by Latapí in 1938.

The author discusses the results obtained with a triple antimalarial agent consisting of quinacrine hydrochloride, chloroquine phosphate and hydroxychloroquine sulphate, in the management of leprosy reaction.

(See also *Trop. Dis. Bulletin*, 1964, v. 61, 928.)

J. R. Innes.

27. **Reactivation of the dorsiflexors of the foot in leprotic paralysis of the common peroneal nerve. Observations on 26 patients,** by A. Carayon, P. Bourrel and M. Bourges. *Int. J. Lepr.*, 1967, **35**, 2, Pt. 1, 111-18.

'The results of reactivation of the dorsiflexors of the foot by 2 muscles from the posterior compartment of the leg (the tibialis anterior by the tibialis posterior; and the extensor hallucis longus and the extensor digitorum longus by the flexor digitorum longus), tend to demonstrate that this operation is to be preferred to (1) the operation of Lambrinudi, which often meets with delayed healing of bone and soft parts and septic complications, and requires a long period of immobilization, (2) transfer of the tibialis posterior muscle to the tarsus, which often results in non-union due to leprous dystrophy of the bone.

'The reactivation of the dorsiflexors of the foot by the tendons of the tibialis posterior muscle and flexor digitorum longus (26 patients) is performed in the leg, at some distance from the site of trophic disturbances, by a surgical technic that is at once simple and lasting. The period of immobilization is short (16 days), and complications are encountered very rarely.'

The following 8 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1968, **65**, 2:—

28. **Nuevos datos en relación con la composición antigénica de** *M. leprae* (The antigenic composition of *M. leprae*), by S. CALDERON MANES, M. SALAZAR MALLÉN and S. ESTRADA-PARRA *Revta Invest. Salud. Publ.*, 1967, **27**, 2, 117-24.

The English summary appended to the paper is as follows:—

'Two extracts were obtained from leproma rich in *M. leprae*. The crude one consisted in pepsin digested material and the purified contained only polysaccharides.

'Agar precipitation using sera from tuberculous and lepromatous patients as well as from rabbits immunized with *Nocardia brasiliensis* showed that the crude extract gave 5 precipitation bands with the lepromatous serum, one of them being identical with that using *Mycobacterium tuberculosis* var *hominis* as antigen. The purified extracts precipitated with the serum from a tuberculous patient giving a band identical with that produced with PolyINb obtained from *N. brasiliensis* and this precipitation could be inhibited through absorption with PolyINb.

'Two lepromatous sera precipitated with the purified extract and with PolyINb giving a band of identity and also one and 2 extra bands, suggesting the presence in this fraction of other species-specific polysaccharide antigens.

'No precipitation was observed with the sera from other 3 lepromatous patients, from one of the tuberculoid type and from 6 healthy donors.'

29. **Treponemal immobilization tests in leprosy,** by H. G. S. RUGE. *Br. J. Vener. Dis.*, 1967, **43**, 3, 191-6.

Sera from 420 patients with lepromatous leprosy were obtained on 5 occasions, with 24 weeks elapsing between each sampling. (All the patients were not tested on each occasion.) Four lipoidal antigen tests and the pallida reaction with Reiter antigen were performed on all sera and each patient's serum was tested at least once by the TPI test; this was repeated when it or the other tests had been found positive on a previous specimen. TPI tests were performed on 618 out of the total of 1,699 sera tested.

The TPI test gave positive or doubtful results on sera from 50 patients; 7 of these had slinical evidence of burnt-out yaws, 35 had latent yaws and 2 had latent syphilis. In 4 patients the TPI test was thought to be non-specific and in 2 it was inconclusive. Of the other tests, the VDRL showed the closest agreement with the TPI (71.2%), followed by the Reiter test (66.2%). Agreement with the TPI was less with the Wassermann reaction, in which the original or cardiolipin antigens were used, and with the Meinicke test.

The TPI test showed some fluctuations in consecutive examinations of the same patients' sera taken at different times. This occurred more frequently in the more seriously affected patients and may be explained by abnormalities in the serum globulins. The frequency of anticomplementary and false positive results with the other tests was lower after treatment with antileprotic drugs and improvement in the serum protein pattern. It is suggested that it is preferable to defer mass investigations of patients with leprosy for treponemal disease until their leprosy has been treated.

A. E. Wilkinson.

30. **Epidemiological significance of skin reaction to Dharmendra antigen in leprosy survey,** by M. MAEDA. *Lepr. India*, 1967, **39**, 2, 44-61.

This is a detailed and painstaking account of a leprosy survey in Japan in which skin reactions to lepromin, tuberculin and certain other mycobacterial antigens were compared, and the influence of previous BCG vaccination on the skin reactions was noted. The lepromin used was of the Dharmendra type, and the results were read at 48 hours. It was found that BCG was more potent in the positive conversion of the lepromin than the tuberculin reactions. The article should be read in the original by those interested.

D. S. Ridley.

31. **Los casos dimorfos de lepra. Una etapa en la evolución de un caso?** (Dimorphous leprosy. A stage in the evolution of the disease?), by A. SAUL. *Dermatologia*, Mexico, 1966, **10**, 3, 465-84. English summary.

In the present-day classification of leprosy the idea of polarity is still valid in that patients with lepromatous and tuberculoid leprosy show opposing characteristics in accordance with the immunological situation of the host. The author discusses the so-called dimorphous patients and advances the hypothesis, giving examples, that patients with dimorphous leprosy do not represent a group within the classification but a transitory phase in the evolution of a lepromatous or tuberculoid patient more or less stable, or of an interminate patient with a doubtful immunological situation. The patient is dimorphous at the time of examination only. The phase is transitory and should be considered as belonging to the acute stage of the disease. The author illustrates his argument with photographs and photomicrographs.

J. R. Innes.

32. **Les manifestations viscérales dans la lèpre** (Visceral manifestations in leprosy), by J. LANGUILLON. *Méd. Trop.*, 1967, **27**, 3, 283-92.

This article provides a useful and moderately comprehensive summary of knowledge concerning visceral damage in leprosy and adds some original data on the histological changes seen in the liver and on liver

function tests. Although attention is usually directed to the manifestations of leprosy in the skin, the nasal mucosa and the peripheral nerves, the lymphatic nodes, the liver and the testes are consistently involved in lepromatous leprosy. On the other hand, the lungs, the kidney and the digestive tract (apart from the naso-pharynx) are but rarely the seat of leprosy lesions.

Of practical importance are the author's observations on the persistence of *M. leprae* in the Kuppfer cells of the liver after they can no longer be found in the skin and nasal mucosa; the possible occurrence of emboli composed of bacilliferous Virchow (lepra) cells; a subclinical malfunctioning of the suprarenal cortex in lepromatous leprosy.

(Many works and workers are cited in the text, but no references are appended—a regrettable oversight.)

S. G. Browne.

33. **Intérêt de l'éthionamide en thérapeutique antilépreuse** (Value of ethionamide in the treatment of leprosy) by H. Floch, N. Rist and J. C. Jacobi. *Bull. Soc. Path. Exot.*, 1966, **59**, 5, 715-24.

A clinical trial of ethionamide (a thioamide derivative of isonicotinic acid) in 19 patients with leprosy was undertaken to resolve the conflicting reports of the efficacy of the drug. Laviron *et al.* (*Trop. Dis. Bulletin*, 1958, v. 55, 1021) reported favourably; but Languillon *et al.* (*ibid.*, 1962, v. 59, 564) concluded that it had no action and was moreover badly tolerated.

The 19 patients were a heterogenous group composed of 13 patients with lepromatous leprosy (of whom 10 had already received treatment for unspecified periods), one borderline, 4 reactional tuberculoid, and one 'simple' tuberculoid. The daily dose (0.25 gm.) was given for a variable period (4 to 18 months). No toxic side-effects were noted with this dose. The clinical improvement was said to be 'striking' or 'spectacular' in all the groups. The bacteriological results were not less impressive. (No information is given concerning bacterial morphology, and smears were not taken from the nasal mucosa.) In both skin smears and histological sections in patients with lepromatous leprosy, *M. leprae* either disappeared completely or their numbers were very much reduced. This result occurred also in the 10 patients who despite previous treatment had remained bacteriologically positive. The possibility of the development of resistance to the drug after the lapse of several months is suggested, but not followed up.

Since strains of *Myco. tuberculosis* have shown a cross-resistance to ethionamide, a thiosemicarbazone and the diphenyl-thioureas, the authors suggest that ethionamide should be given in combination with other anti-leprosy drugs.

S. G. Browne.

34. **Sur la thérapeutique des réactions lépreuses** (Treatment of lepra reaction (acute exacerbation in lepromatous leprosy)), by H. A. Floch. *Bull. Soc. Path. Exot.*, 1966, **59**, 5, 745-52.

During a clinical trial of ethionamide (Floch *et al.*, above) the author was able to wean 14 patients (10 suffering from lepromatous leprosy and 4 from reactional tuberculoid leprosy) from dependence on corticosteroids (unspecified). Within 10 days of beginning treatment with ethionamide (0.25 gm. daily), and in conjunction with a daily intraveous injection of of 10 ml. of a 20% aqueous solution of sodium hyposulphite, and nicotinic acid and B complex, the author succeeded in suppressing the corticosteroid; signs of acute exacerbation began to disappear. This combined medication was apparently efficacious in the treatment of exacerbation occurring in both lepromatous and tuberculoid leprosy. The bacteriological results were equally gratifying, *M. leprae* disappearing in a few months from the skin smears in a high proportion of the patients treated.

S. G. Browne.

35. **L'insuffisance de la corticosurrénale dans la lèpre lépromateuse—essai de pathogénie de la réaction lépreuse** (Cortico-adrenal insufficiency in lepromatous leprosy. Enquiry into the pathogenesis of lepra reaction), by J. Languillon, H. Plagnol and P. Giraudeau. *Bull. Soc. Path. Exot.*, 1966, **59**, 5, 740-44.

By means of Thorn's test (a fall of 50% in the eosinophil count in the peripheral blood, and a 50% increase in the serum uric acid after an injection of corticotrophin), the authors show that 7 out of 10 patients with lepromatous leprosy, and 7 out of 10 with lepromatous leprosy in a phase of acute exacerbation, had cortico-adrenal insufficiency. These findings are held to be in keeping with the well-known clinical observations that mental or physical stress, the administration of potassium iodide, the puerperium, excessive dosage or over-rapid increments of dapsone (DDS, diaminodiphenyl sulphone) may all apparently provoke an acute exacerbation (lepra reaction).

The authors throw doubt on the vaunted efficacy of the extremely numerous and diverse drugs used in the treatment of lepra reaction, and illustrate this by showing a cure rate of 80% (complete with clinical and biochemical amelioration—*e.g.*, fall in the C-reactive protein) in a series of 15 patients who were given a placebo. They suggest that patients who do not respond to either the placebo, or one or other of the standard drugs generally used, really need corticosteroids, which alone will control the exacerbation.

S. G. Browne.