Abstracts

The following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1970, **67**, 4:

1. **La lutte contre la lèpre en Afrique centrale** (Leprosy control in central Africa), by R. Labusquière. *Acta Leprol.*, 1969, No. 36, 5-18.

The thesis developed by the author in this paper is that, in the ex-French colonies of central and west Africa, experience during the past 15 years demonstrates conclusively that leprosy can be controlled and that the numbers of new infections show a progressive reduction. He supports this contention with sober statistics drawn from the 5 countries comprising the French-orientated Union, in which high prevalence rates (above 10% in some districts, and 45% in some villages) and dispersal of the population presented a challenge to the public health administrator and the mobile leprosy teams.

The total population covered in the report is about 10 millions; 165,576 patients were under treatment for leprosy at the end of 1968, 41,335 having been discharged "disease arrested" since the beginning of the campaign. For the last 2 years, the number of new infections registered is about a third of those discharged. Attention is drawn to the 2 countries (Cameroun and Gabon) whose progress lags far behind that of the other 3, and the valid explanation is offered that these 2 have failed to adopt modern methods of mass control.

[This paper is both salutary and reassuring. It provides evidence to support the thesis that leprosy can be controlled in the environment of central and west Africa, where, despite inherent difficulties of communications and scattered populations, mass treatment measures can be applied persistently by supervised teams of medical auxiliaries. It is salutary in the sense that these results can be paralleled by extremely few leprosy control projects in those populous countries where the prevalence of leprosy is high, where the lepromatous/tuberculoid ratio is also high, and where prejudice against leprosy is greater. The local success registered in populations totalling 10 millions does not unfortunately invalidate the far from optimistic conclusions based on much larger figures from countries where only 1 in 5 of those with leprosy are at present able to get treatment.]

S. G. Browne.

2. **Investigations de sept gynécomasties chez le lépreux africain** (A study of 7 cases of gynaecomastia in African patients with leprosy, by A. Carayon, L. Maydat, P. Bobin and F. Blin. *Bull. Soc. Méd. Afr. Noire Lang. Fr.*, 1969, **14** (3), 498-506.

By means of the lymphographic technique that they have developed, the authors visualized the testiculo-funicular lymphatic vessels in 7 patients who had gynaecomastia and long-standing lepromatous leprosy. They were able to demonstrate some degree of lymphatic stasis in these vessels in all the patients. The associated non-inflammatory oedema of the Leydig cells, accompanied by the specific leprosy lesions in the testis itself, is held to provide an adequate pathological explanation of the hormonal imbalance that results in gynaecomastia in leprosy.

S. G. Browne.

3. **An open trial of indomethacin therapy in exacerbated phases of lepromatous leprosy,** by G. Thomas, A. B. A. Karat, S. Karat and P. S. S. Rao. *Indian J. Med. Sci.*, 1969, **23**, 68.

Indomethacin, a non-steroidal drug with anti-inflammatory and antipyretic properties, was given to 19 patients suffering from lepra reaction and to 1 patient who had previously had a reaction. Eighteen patients received 50 mg thrice daily with food, and 2 received half this dose. The all-round effect was only slightly better than could have been expected from parenteral antimony. Side-effects included abdominal pain, headache, vertigo, nausea and vomiting. The drug was discontinued in 8 patients, either because of side-effects or ineffectiveness.

W. H. Jopling.

The following 8 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1970, **67**, 5:

4. **Caractères épidémiologiques et cliniques de la lèpre dans la région de Manga, en Haute-Volta. Confrontation avec d'autres observations dans ce pays** (Epidemiological and clinical characteristics of leprosy in the Manga region, Upper Volta, compared with other observations in the same country, by H. Sansarricq, E. Steen and M. Sauvaget *Méd. Trop.*, 1969, **29** (2), 208-28.

This article presents detailed findings in a selected district in which the leprosy prevalence was studied in depth. The total population comprised 25,443 inhabitants in 28 villages scattered over a circumscribed savannah-type plateau. For 20 years regular annual medical examinations of the people had been carried out for leprosy and other endemic diseases, and treatment for leprosy had been available throughout that period.

The prevalence rate of leprosy at the last survey was almost 25 per 1000 inhabitants, and the highest rates were found in both men and women aged between 35 and 45 years. Since the prevalence thereafter showed a sharp decline, it is suggested that perhaps leprosy shortened the life-span. [This suggestion is

highly debatable, in view of the further facts adduced concerning the slight severity of the disease.]

Among the 636 patients with leprosy in the area, only 8 had lepromatous leprosy, giving a lepromatous rate of 3 per 10,000 of the population, or 1.25% of the cases of leprosy diagnosed. No patient was diagnosed as having borderline leprosy [a rather strange observation].

Diagnosis was made on clinical grounds, supported by bacteriological findings from skin smears. The annual incidence of new infections fell from 1.66 per 1000 in 1964 to 0.51 per 1000 in 1967. The initial lesions appeared on parts of the body usually covered by clothing in about 57% of the patients.

Physical disability attributable to leprosy was found in 9.4%. [This is probably an underestimate, since anaesthesia of the extremities was not included.]

The treatment was oral dapsone. Patients with lepromatous leprosy were advised to take treatment for life, and those with tuberculoid or indeterminate leprosy had 3 years of continuous treatment before being placed on observation. After 3 years' observation, and in the absence of clinical signs of relapse, the disease was considered to be arrested.

Comparisons are made between these findings and those (especially leprosy prevalence rates) in neighbouring areas.

S. G. Browne.

5. **Leprosy in Singapore: a survey of this disease between the years 1962-1967,** by K. K. Yew. *Singapore Med. J.*, 1969, **10** (3), 194.

This paper is based on figures derived from statistics of patients with leprosy who have been notified and registered at the Government Skin Clinic. In the 6 years 1962-67, 1358 patients were registered, making a running total since 1951 of 6087 in a population of nearly 2 million, a prevalence rate of 3.08 per 1000. Of the 1358 patients, 510 were classified as positive (lepromatous 287, borderline dimorphous 77, and reactional tuberculoid 146), and 848 as negative (tuberculoid 460, neural 192, and indeterminate 196). According to the histories given by the patients, signs of leprosy had been noted for under a year by 493 patients, and from 1 to 5 years by 309. The majority of patients were aged between 16 and 35 years. Analysis of the prevalence rates according to racial origin indicated that among the Indian and Pakistani community the rate was 1 : 4600, among the Chinese 1 : 8100, while among the Malays it was 1 : 23,300.

[These figures are interesting, but admittedly incomplete. The criteria for separating "positive" from "negative" are not indicated. The meaning of "neural" leprosy is uncertain. Where leprosy prevalence rates depend largely on lay suspicion, and where contact examinations are restricted, the real prevalence of leprosy may be much higher than the figures suggest. Similarly, the higher prevalence of leprosy among the Indian and Pakistani community may reflect many other factors besides a racial "proneness" to infection.]

S. G. Browne.

6. **Erythema nodosum leprosum: a clinical manifestation of the Arthus phenomenon,** by S. N. C. Wemambu, J. L. Turk, M. F. R. Waters and R. J. W. Rees. *Lancet*, 1969, 1 Nov., 933.

Histological features of skin lesions of erythema nodosum leprosum (ENL) include perivascular infiltration with polymorph leucocytes and fibrinoid necrosis of blood vessels. A similar histological picture is seen in laboratory animals in lesions due to the Arthus phenomenon, which is due to the deposition of immune complexes (antigen, antibody and complement) in and around blood vessel walls. Immune complexes are found in the circulation of patients with chronic serum-sickness, some symptoms of which are similar to systemic symptoms of ENL. Frozen sections of ENL skin lesions in 17 patients with lepromatous leprosy, and of lepromatous skin lesions in 6 patients without ENL were examined by fluorescence microscopy for the components of immune complexes. [For details of technical methods the original paper should be consulted.] Immunoglobulin (antibody) and complement "were demonstrated . . . in the areas of perivascular polymorph infiltration in the dermis of ENL lesions in 10 out of 17 patients with this condition", but in none of the 6 patients without ENL. Although *Mycobacterium leprae* failed to stain with fluorescein conjugate prepared with Freund's adjuvant (containing *Myco. tuberculosis*), staining with this conjugate in 7 ENL lesions was interpreted as indicating the presence of a soluble mycobacterial antigen from dead *Myco. leprae* in the immune complexes, because no staining occurred with conjugated sera prepared without *Myco. tuberculosis*. All of the patients with ENL had normal or high serum levels of the C'_3 per ml. High immunoglobulin levels were found both in patients with ENL and those without ENL. [Whether serum levels of the different components of complement are usually increased or decreased in patients with lepromatous leprosy with and without ENL would seem to require further study.]

C. S. Goodwin.

7. **The histoid leproma. Its characteristics and significance,** by J. N. Rodriguez. *Int. J. Lepr.*, 1969, **37** (1), 1-21.

This paper gives an account of histoid lesions in leprosy and describes investigations on 35 patients with histoid lesions at the Eversley Childs Sanatorium in the Philippines. Twenty-eight were relapsed patients, and the remaining 7 were new and untreated patients. Most were classified as lepromatous but a few were borderline-lepromatous, and the typical histoid nodules were erythematous, round or oval, regular in outline, and shiny. Subcutaneous nodules were rarer and were confined to relapsed patients. Bacilli in the histoid lesions were usually longer than the bacilli in the non-histoid lesions of the same patient, and globi were absent or scanty. Histoid nodules of non-relapsing patients tended to heal on treatment with dapsone (DDS), but the reverse held good in relapsed patients; in fact, in some of these patients new histoid nodules

appeared while under treatment. The view is put forward that the sulphone-resistant bacilli in histoid lesions of relapsed patients are mutant organisms that have merged from a predominantly sulphone-susceptible bacterial population following prolonged treatment with dapsone. Animal footpad studies are to be carried out to verify this assumption.

The paper is illustrated by 12 photographs.

W. H. Jopling.

8. **Chemotherapeutic trials in leprosy. 7. Trial of 50 mgm DDS twice weekly in the treatment of lepromatous leprosy,** by J. M. H. Pearson and J. H. S. Pettit. *Int. J. Lepr.*, 1969, **37** (1), 40-45.

Fifteen patients with lepromatous leprosy in the leprosarium, Sungei Buloh, Selangor, Malaysia, were treated for 12 months with 50 mg dapsone (DDS) twice weekly by mouth. Progress was as satisfactory as would have been expected on a dosage of 300 mg twice weekly, and there was no reduction in the incidence and severity of reactional states. [The results of this trial are not unexpected, and the abstracter would like to see them compared with those obtained from a dosage of 5 mg twice weekly.]

[For Parts 1-6, see *Trop. Dis. Bull.*, 1964, **61**, 161; 1966, **63**, 656; 1967, **64**, 1211; 1968, **65**, abstrs. 584 and 925; 1970, **67**, abstr. 600.]

W. H. Jopling.

9. **A rapid qualitative spot test for the detection of dapsone in urine,** by J. H. Peters, S. C. Lin and L. Levy. *Int. J. Lepr.*, 1969, **37** (1). 46-51.

In California, urine specimens from patients with leprosy receiving oral dapsone and intramuscular DADDS, from healthy volunteers receiving no drugs, and from volunteers taking aspirin, were treated with ammonium sulphate, sodium hydroxide and ethylene dichloride and shaken for 15 minutes. An aliquot of the extract was evaporated to dryness under a stream of nitrogen, the residue dissolved in ethanol and 5 µl (equivalent to 0.5 ml urine) applied to filter paper. After 5 minutes the spot was sprayed sequentially with hydrochloric acid and ethanol, aqueous sodium nitrate, ammonium sulphamate and N-1-naphthylethylenediamine in ethanol. The intensity of the violet colour of the spot was related to the amount of dapsone in the sample. Assay by thin-layer chromatography and spectrophotometry confirmed the accuracy of the spot test, its limit of sensitivity being 0.1 µg dapsone per ml of urine. Urines obtained up to 24 hours after the ingestion of 10 mg dapsone, or up to 6 days after 50 mg dapsone, were routinely positive by the spot test. [The technical skill and equipment needed for this "rapid spot test" place it beyond the reach of most leprosaria, and the effort involved might be equally well spent determining the specific concentration of dapsone in the urine (see Goodwin and Sparell, *Trop. Dis. Bull.* 1970, **67**, abstr. 599).]

C. S. Goodwin.

10. **Human leprosy in normal mice,** by R. J. W. Rees, A. G. M. Weddell, E. Palmer and J. M. H. Pearson. *Br. med. J.*, 1969, 26 July, 216.

Because the number of leprosy bacilli present in the footpads of mice, following injection of lepromatous tissue by the method described by Shepard (*Trop. Dis. Bull.*, 1961, **58**, 214), decreases after 8 to 10 months, it has been generally assumed that the infection is self-limiting, but in the present paper the authors report that multiplication does in fact continue and that the infection spreads to other sites.

In the experiments reported, the number of bacilli present in the inoculation site in the footpad were found to decrease as usual, but histological examination showed that the infection had persisted with small numbers of bacilli present in dermal neurovascular bundles, lying in epineurial histiocytes and sometimes in perineurial and Schwann cells, 2 years after infection. At this time the most striking feature of infection was the presence in the hypodermis and among muscle fibres of an epithelioid-cell granuloma which contained few bacilli and was surrounded in places by lymphocytes; when fully developed, these lesions resembled those of the borderline human disease. At 2 years or later, bacilli were often found in the nose and uninoculated footpads.

In order that the significance of these observations should be appreciated a brief outline of the present knowledge of leprosy in man is given and it is concluded that the normal mouse provides an accurate model for studying the early stages in pathogenesis of the human disease.

S. R. M. Bushby.

11. **Minimal effective dosages in mice of clofazimine (B 663) and of ethionamide against** *Mycobacterium leprae*, by C. C. Shepard. *Proc. Soc. Exp. Biol. Med.*, 1969, **132** (1), 120.

This article presents important data to justify treating leprosy patients with "spaced ingestion" (e.g. monthly doses) of clofazimine (B 663, Lamprene), or with much smaller doses than are currently used, which may avoid the distressing skin pigmentation sometimes accompanying clofazimine therapy in light-skinned people.

Mice were inoculated in the footpad with 5000 *Mycobacterium leprae* and then given diets containing varying concentrations of clofazimine from 0.01% to 0.000001%, or ethionamide from 0.1% to 0.00001%. Some animals received the drug from the day of inoculation for 183 days, while in the other animals the bacilli were allowed to multiply for 76 days and then the drug was given until 167 days after inoculation. Groups of 4 mice from an inoculated, untreated, control group, and from each of the dosage-schedule groups were sacrificed at 50-day intervals up to 400 days after inoculation, and "the counts of *Myco. leprae* were carried out on pools of the footpad tissues". The minimal effective dose of ethionamide was 0.01% (about 10 mg/kg/day) and its action ceased when the drug was stopped, suggesting a bacteriostatic action alone.

The minimal effective dose of clofazimine was 0.0001%, which is equivalent to 0.1 mg/kg/day, or 7 mg/day in man. After this dosage schedule was completed multiplication of *Myco. leprae* was delayed for at least 80 days. In mice receiving 0.01% clofazimine the characteristic pigment could still be found in the footpad tissues 219 days after the drug was discontinued. [This slow elimination of clofazimine has been detailed by Vischer *et al.*, *Beitr. Klin. Tuberk.*, 1958, **119**, 59.]

[The abstracter has given monthly doses of clofazimine after a loading dose to untreated patients with lepromatous leprosy, with excellent results.]

C. S. Goodwin.

The following 6 abstracts are reprinted, with permission, from Current Literature, *Int. J. Lepr.*, 1969, **37**, 3:

12. **Manifestaciones iniciales de la lepra en la adolescencia y pubertad** (Initial manifestations of leprosy in adolescence and puberty), by D. F. Contreras. *Actas DermoSifiliog.*, 1968, **19**, 459-466.

It is generally recognized that the diagnosis of leprosy in an adult is a late diagnosis. The manifestations in children have been described frequently, but there is a paucity of records on leprosy in adolescence and puberty. The author has seen some 300 initial manifestations in patients less than 16 years old but only 14 among those between 16 and 20 years. The latter were children of patients who had spent their infancy in a leprogenous environment and displayed mild macular skin lesions manifested by hypochromia. For some years the author has emphasized differences between the indeterminate leprosy of infants and adolescents, consisting principally of a greater tendency to hypochromia in children than adults, and anhidrosis and alopecia, which are more clearly evident in adults and adolescents than children. There is reason to believe that lesions first recognized in adolescence had their origin during puberty. All observations point to the importance of search for initial lesions during this period. The disease is generally of indeterminate character at that time. Localization varies greatly; the anterior surface of the thighs is a common site.

E. R. Long.

13. **Sweating under cellulose tape. A test of autonomic function,** by A. B. A. Karat, S. Karat and C. A. Pallis *Lancet,* 1969, **1**, 651-652.

The ability to sweat in a given part of the body is a useful guide to the integrity of its autonomic nerve supply. Leprosy may interfere with sweating in a variety of ways. In areas where the disease is endemic there is widespread need for a simple and reliable test of sudomotor function. In the test suggested by the authors sweat evaporation is prevented by covering the quinizarin indicator, previously lightly sprinkled on the area to be investigated, by a broad layer of adhesive cellulose tape. Exposure to the sun was sufficient, making it possible to dispense with heat cradles. Although the sweating response must have been diffuse, areas of skin under the cellotape invariably showed early evidence of sweating, while adjacent areas of skin, similarly sprinkled with the indicator, failed to change colour (presumably because of simultaneous evaporation of any sweat produced). Three photographs illustrate the results of this procedure.

N. D. Fraser.

14. **The sensitivity to dapsone (DDS) of *Mycobacterium leprae* from patients with and without previous treatment,** by C. C. Shepard, L. Levy and P. Fasal. *Amer. J. Trop. Med. and Hyg.*, 1969, **18**, 258-263.

Thirty-two isolates of *Myco. leprae* from 27 patients with leprosy were tested in mice for sensitivity to 0.0001% DDS in the diet. All 11 isolates from previously untreated patients and 6 from patients with some treatment were sensitive to 0.0001% DDS. This dosage in mice is estimated to produce blood and tissue concentrations of about 0.02 μgm/ml, or 1/100 the concentrations produced in man by standard dosages of DDS. Since 0.00001% DDS was usually not effective, the usual minimum inhibitory concentration of DDS for *Myco. leprae* in untreated patients appears to lie between 0.02 and 0.002% μgm/ml. Fifteen isolates from 10 other patients with previous treatment were found resistant to 0.0001% or more DDS in the diet of mice. These patients had begun treatment 11 to 20 years previously. Seven had begun with glucosulfone and 2 with sulfoxone. It seems possible that the irregularity of the DDS supplied by these drugs contributed to the appearance of DDS-resistant *Myco. leprae.*

Authors' summary.

15. **Las formas sub-microscopicas del bacilo de Hansen en la lepra humana. Nota previa** (Submicroscopic forms of Hansen's bacillus in human leprosy. Preliminary note), by J. Gay Prieto and G. G. Gonzalez. *Med. Cutanea,* 1968, **2**, 599-605.

In 1 case of early lepromatous leprosy in the deep layer of the dermis, close to the bacillary remains and in the wax capsule of the bacilli it was possible to see a small body with a dark centre and clear perpheral area wrapped in a thin membrane. In 2 plates degenerated bacilli and large L cells could be seen, inside of which several elementary bodies were observed. In another case of tuberculoid leprosy it was also possible to see, beside the degenerated bacilli, the big L cells. These findings permit the assumption that *Myco. leprae* has a cycle like that of many other germs. In certain circumstances the bacilli lose the acid-fast resistance, becoming granular and adopting forms similar to those described by Convit in the hamster. Afterward, around the bacillary remains, elementary bodies appear which are wrapped in the beginning in the bacillary membrane, like big L cells. Finally, the membrane breaks and the elementary bodies are released.

From authors' summary.

16. **Estudio histológico de la reacción de Mitsuda, en pacientes de lepra lepromatosa y su valor pronóstico en los casos bacteriológicamente negativos** (Histologic study of Mitsuda reaction in lepromatous leprosy patients and its prognostic value in bacteriologically negative cases), by O. Reyes. *Med. Cutanea*, 1968, **3**, 135-139.

The literature reviewed by the author offers conflicting views on the meaning of a positive Mitsuda test in patients with lepromatous leprosy who have received specific treatment for many years and are negative to bacteriologic examinations at the time of the study. In this study, more than 176 patients in such conditions were tested with integral lepromin antigen, and 78 clinically negative responses and 98 positive, with more than 3 mm diameter, were found. Biopsies of the positive reactions gave the following results: 76 showed positivity of varying intensity; 9 were negative; 3 showed an isopathic reaction; 1 gave a picture similar to a fibrohistiocytoma; 1 showed the structure of a rheumatic nodule; and 1 was a reaction of the giant cell type. Eight patients with a histologically positive Mitsuda reaction in whom treatment had been stopped, had relapses with bacteriologically positive lesions. It is concluded that in lepromatous patients without bacilli after many years of treatment, a positive Mitsuda reaction does not permit evaluation of the degree of of resistance of the patient, and has no prognostic value.

Author's abstract.

17. **Enhancing effect of antilymphocytic globulin on human leprosy infection in thymectomized mice,** by J. M. Gaugas. *Nature, Lond.*, 1968, **220**, 1246-1248.

Administration of antilymphocytic serum (ALS) to thymectomized mice enhances the course of infection by *Myco. leprae.* From heterologous rabbit ALS, globulins (ALG) were precipitated by ammonium sulfate, and administered at weekly intervals to thymectomized and normal mice killed 9.5 months after footpad inoculation of *Myco. leprae* from a leproma from an untreated leprosy patient. In normal mice bacillary multiplication was spontaneously arrested when the bacilli reached a little more than a million. Thymectomy plus administration of ALG, however, increased susceptibility to the point of 30-fold multiplication of this figure. The generation time of 14 to 26 days appeared unchanged. Heavily parasitized macrophages were prominent, but the enhanced lesions were almost devoid of lymphocytes. Careful search failed to show spread of infection to adjacent regions of the body.

E. R. Long.