Abstracts

following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 5:

1. **Effect of BCG-vaccination upon the multiplication of *Mycobacterium leprae* in the footpads of mice,** by M. MALDA, K. NAKAMURA, and H. KATAYAMA. *Lepro*, 1968, **37**, 2. (In Japanese, English summary.)

In a series of experiments in which groups of 2 to 4 mice were used, vaccination with BCG delayed the multiplication of *Mycobacterium leprae*, injected into the footpad 24 to 51 days before to one month after vaccination. The method of counting the bacilli in the footpads was described in an earlier paper (this *Bulletin*, 1968, **65**, abstr. (2827)); the BCG was administered as a suspension either in saline or in Drackeol No. 6, as an adjuvant.

The results show that the vaccine was more effective if injected subcutaneously into the footpad, or intravenously, than if injected intramuscularly or intraperitoneally. Although in some of the experiments, the live vaccine appeared to afford more protection than the killed one and in other experiments this appeared to be reversed, the highest degree of protection was obtained with the live BCG in the adjuvant.

(As this abstract is based on the English summary and tabulated results, it is difficult to assess the value of the authors' conclusions, especially as the sizes of groups of mice were small.)

S. R. M. Bushby.

Pathological study of nasal deformity in lepromatous leprosy, by C. K. JOB, S. KARAT and A. B. A. KARAT. *Lepr. India*, 1968, **40**, 2.

This study is based on nasal biopsies of 26 patients with perforated septum or other nasal deformity, both in the active stage of lepromatous leprosy and after healing.

The subepithelial tissue, the septal and lateral cartilages and the bony part of the septum were infiltrated by lepromatous granulation tissue with some lymphocytes and plasma cells. In one case a necrotic septum was infiltrated by polymorphs. After healing the cartilage was hyalinized and the eroded area replaced by fibrous tissue. It was concluded that collapse of the nose is due mostly to destruction of cartilage which is brought about by infiltration of lepromatous granulation tissue and not by secondary

D. S. Ridley.

3. **Studies in mice of the action of DDS against *Mycobacterium leprae*,** by C. C. SHEPARD. United States—Japan Co-operative Medical Science Program. Proceedings of a symposium on sulfones. San Francisco, California, 11 May, 1967.

Nine strains of *Myco. leprae* from untreated patients were tested in mice against a diet containing 0.0001% of DDS and all were sensitive. Only 1 out of 6 was sensitive to a diet containing 0.00001% DDS. Apparently the minimal inhibitory concentration of DDS is about 0.02 μg/ml, which 1/100 of the blood concentration in men taking 50 to 100 mg/day. This action is partially antagonized by *p*-aminobenzoic acid. Probably leprosy might be treated effectively by spaced administration of DDS or by injection of repository sulphones, but certain precautions are desirable.

following 5 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 6:

4. **A controlled study of polymorphisms in serum globulin and glucose-6-phosphate dehydrogenase deficiency in leprosy,** by M. F. LECHAT *et al. Int. J. Lepr.*, 1968, **36**, 179.

As a part of a study of genetic polymorphism and leprosy, 5 genetic markers were investigated in patients with leprosy and in control subjects from Cebu, Philippines. There were 557 patients, of whom 256 were affected with lepromatous leprosy, 224 with tuberculoid leprosy, and 77 with other types of the disease or unclassified disease. There were 434 control subjects without manifestations of leprosy, comprised of medical students and skin clinic patients. The markers investigated were haptoglobins, transferrins, serum group-specific components (Gc) and β-lipoprotein (Ag), and glucose-6-phosphate dehydrogenase (G6PD). The phenotypic distributions were analyzed in relation to leprosy, type of leprosy, and lepra reaction. Age, sex, duration of disease, and province of birth in the Philippines were also considered. Gene frequencies were derived.

An association between haptoglobin polymorphism and leprosy is suggested by an excess of Hp 1 : 1 phenotypes and/or the Hp 1 gene, observed particularly in lepromatous but also in tuberculoid or total cases when compared with control subjects. No differences, however, were observed for transferrins, Ag, and G6PD. Because of technical problems, no conclusions were drawn concerning Gc types.

G. R. F. Hilson.

5 **Liver function tests in leprosy,** by A. DHOPLE and S. BALAKRISHNAN. *Indian J. Med. Res.*, 1968, **56**, 10.

In an attempt to determine the degree of functional damage sustained by the liver in patients suffering from various forms of leprosy, the authors employed a battery of tests rather than relying on a single test which in the past has been the basis of most published reports. Morphological changes in the liver cells, and the presence of typical granulomata, have been well documented. The following tests were done on sera from 74 patients with lepromatous leprosy, 36 with

tuberculoid leprosy and 16 healthy controls: serum bilirubin, proteins, turbity (zinc sulphate), cholesterol, alkaline phosphatase and transaminases.

Patients with tuberculoid leprosy showed only slight departures from the normal pattern in the protein profile and turbidity tests. Those with lepromatous leprosy showed marked alterations in these tests, and higher serum bilirubin alkaline phosphatase levels. The serum transaminases (glutamic-pyruvic and glutamic-oxalacetic) were normal, in contradistinction to previously reported findings. These results are interpreted as indicating some degree of liver dysfunction (but no active cellular necrosis) in patients suffering from lepromatous leprosy.

(The wide ranges of values obtained in the various tests reflect the severity and duration of leprosy as it affects the structure and activity of a complex organ that has a multiplicity of functions and a considerable reserve capacity.)

S. G. Browne.

Serological tests for treponemal infection in leprosy patients. An evaluation of the fluorescent treponemal antibody absorption (FTA-ABS) test, by M. F. Garner, J. L. Backhouse, C. A. Collins and P. J. Roeder. *Br. J. Vener. Dis.*, 1969, **45**, 1.

Serological tests for treponemal infection were carried out on 270 patients with lepromatous leprosy and 250 normal controls, from the Philippines. All sera were subjected to the Cardiolipin Wassermann reaction, the Venereal Disease Research Laboratory test, the Reiter protein complement-fixation test, the fluorescent treponemal antibody test, the fluorescent treponemal antibody absorption test, and the *Treponema pallidum* immobilization test. A reactive TPI test result was taken as evidence of treponemal infection and all other test results were compared with it.

Sera from 5.6% of the leprosy patients showed evidence of treponemal infection. BFP reactions occurred with 8.1% of leprosy sera, the VDRL slide flocculation test being responsible for the majority of these. Non-specific reactive results to the RPCF and FTA-200 tests are discussed. Special attention was given to evaluating the FTA-ABS test against the TPI test. They were found to be of almost equal specificity and of equal sensitivity.

It is concluded that, where the TPI test is not available, the FTA-ABS test can replace it in detecting BFP and non-specific reactions to serological tests for treponemal infection in sera from patients with the lepromatous form of leprosy.

7. **Studies of sulfone resistance in leprosy. A case of partial resistance,** by J. M. H. Pearson, J. H. S. Pettit and R. J. W. Rees. *Int. J. Lepr.*, 1968, **36**, 2.

Earlier reports (this *Bulletin*, 1965, **62**, 108; 1967, **64**, 633) showed the dapsone (DDS) sensitivities of leprosy bacilli of 4 out of 9 patients who had active lepromatous leprosy, in spite of at least 13 years' treatment with sulphones; one strain was resistant to the drug; the strains were examined after intensive treatment for 6 months with 300 mg DDS twice weekly by injections. This paper describes in greater detail the clinical history of the patient with the resistant strain and the subsequent sensitivity studies. He was admitted in 1937 to Sungei Buloh Settlement, Selangor, Malaysia, at the age of 14, and treated with hydnocarpus oil until 1948 when the treatment was changed to injectable DDS, 400 mg twice weekly. The treatment was continued until 1961 during which time skin smears remained positive, although the clinical response was considered satisfactory. In 1961 multiple small nodules appeared and the treatment was changed to thiambutosine. In January, 1962, a biopsy showed "typical foamy leproma" and in September sulphone therapy was resumed.

In March 1963 he was referred to the Leprosy Research Unit with extensive lepromatous leprosy; positive skin smears showed a morphological index (MI) of 37. With intensive sulphone therapy there appeared to be some clinical improvement and the MI fell to 12. Treatment was continued to March, 1964, when the MI was still 15 and treatment was changed to 500 mg sulphormethoxine (Fanasil) daily, later twice weekly, but because of severe erythema nodosum leprosum treatment was discontinued. The MI had fallen to 4 but in February, 1965, it had risen to 28, treatment during this period having been stopped. In February, 1965, treatment with the rimino-phenazine B 663, 100 mg thrice daily for 6 days a week, was started; the result was excellent.

The sensitivity of the bacilli to DDS was measured by the footpad technique (*ibid.*, 1964, **61**, 929) on biopsies taken in March, 1963, May, 1964, and February, 1965. The final test showed the organism to be resistant to 0.04% sulphormethoxine, and 0.025% DDS in the diet of the mice which gives concentrations of 2.6 to 4.0 μg/mil of DDS in the serum; strains of leprosy bacilli from untreated patients are usually sensitive to 0.0001% or less DDS in the diet.

The degree of DDS resistance of these strains was less than that found in other strains (*ibid.*, 1965, **62**, 108) and the patient is considered to be the first case of reported "partial" sulphone resistance. Other cases presumably exist, and the authors recommend that in the *in vivo* sensitivity test mice be treated with 0.025, 0.01, and 0.001% DDS in the diet, and they conclude that only strains that multiply in mice on the lowest dose can be regarded as fully sensitive and the patient likely to respond to full doses of DDS.

S. R. M. Bushby.

A comparison of the effectiveness of two freeze-dried BCG vaccines against *Mycobacterium leprae* **in mice,** by C. C. Shepard. *Bull. Wld Hlth Org.*, 1968, **38**, 1.

In previous publications (this *Bulletin*, 1965, **62**, 880; **63**, 1202), the author reported that vaccination of mice with BCG affords them protection against infections with *Mycobacterium leprae*. The BCG vaccines used in these experiments were mainly fresh liquid pre-

parations grown in the laboratory. The author, in the present paper, now reports results of similar experiments with British (Glaxo) and Japanese (Research Institute for Tuberculosis, Kiyose-Machi) freeze-dried preparations.

The methods used were essentially those described in the earlier publications, but in brief the mice were inoculated intradermally in the flank with 0.01 ml of vaccine. Each vaccine was given in dilutions of 1 : 1, 1 : 10 and 1 : 100 to groups of 20 mice. After 32 days the mice were challenged with 5×10^3 *Myco. leprae* in the right hind footpad. Growth of *Myco. leprae* in unvaccinated control mice was monitored by counts of acid-fast bacilli (AFB) in footpad tissues of pools of 4 mice taken from 4 groups monthly, starting 3 months after challenge. When the harvest of *Myco. leprae* per footpad in the control animals had risen above 1×10^6, counts of AFB were made on pools of footpad tissues of 8 mice from each group; the counts on each group were repeated 3 months later. A liquid vaccine, prepared from a 17-day culture of the Rosenthal strain, was used as a standard.

The results showed that all the vaccines provided distinct protection, but it was not possible to decide which vaccine was most effective because their optimal activities were not manifested at comparable times. At 6 months after challenge, shortly after the growth of *Myco. leprae* in the control mice had reached plateau values, the results were related to dose, and the vaccines appeared to arrange themselves in order of potency. However, in the second harvest, the relative potency of the 2 freeze-dried products had reversed, and the relationship between dose of vaccine and protection was different for each vaccine.

Considerations of results in mice lead to speculation about the ways the vaccine protection might be manifested against *Myco. leprae* in human beings. If the protection were exerted against the potentially infectious inoculum, the result might be simply prevention, or perhaps delay, of clinical disease. If the protection were directed against the new growth of *Myco. leprae* in the subject, the result might be a stabilization of the infection at an early stage, or perhaps a greater tendency for minimal disease to resolve. Based on experience with more acute infections, vaccine prevention is often regarded as a single event in the infectious process, but *Myco. leprae* infections develop extremely slowly in man, and it seems reasonable to assume that a protective effect could be exerted at various times in the infectious process.

S. R. M. Bushby.

The following 5 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1969, **66**, 7:

9. **Is it safe to treat the lepromatous patient at home? A study of home exposure to leprosy in Hong Kong,** by R. M. Worth. *Int. J. Lepr.*, 1968, **36**, 3.

This study provides data for assessing the validity of the assumption, accepted in some circles but not in others, that patients with leprosy who no longer harbour morphologically normal *Mycobacterium leprae* in skin or nasal mucosa, are incapable of spreading the disease. Sixty-six families were identified in which one parent (64) or two (2) were suffering from histologically confirmed lepromatous leprosy, untreated at the time of intake. Of the 109 children exposed to bed contact or close living contact with an untreated parent, in the crowded housing conditions of Hong Kong, 6 out of 63 boys and 4 out of 46 girls developed signs of leprosy. Ninety-five of these 109 children were considered to be at risk, the remaining 14 not having been observed for a minimum period of 7 years.

Further analysis revealed that all the children developing leprosy were among the 70 who had been exposed, while under the age of 7 years, to a parent with untreated leprosy. None of the 30 children born into these homes after the parent had begun taking sulphones, showed signs of leprosy during the minimum period of 7 years of observation, although the skin of the parent continued to harbour *Myco. leprae.*

"A large majority" (unspecified) of the children had been given BCG vaccination, but none received prophylactic sulphones.

It is concluded that sulphone treatment of the patient with bacilliferous leprosy rapidly reduces to zero the risk of his continuing to be the source of contagion. This finding, supported by experimental evidence provided by the mouse footpad technique, indicates that domiciliary treatment of patients with lepromatous leprosy carries no greater risk to the community than prolonged segregation of patients having viable or non-viable *Myco. leprae* in the skin and nasal mucosa.

(This suggestive study should be repeated on a larger scale, with additional bacterioscopic investigations concerned particularly with the duration of morphologically normal *Myco. leprae* after treatment had been instituted, and the relation of this factor to the occurrence of secondary cases among the child contacts. Data relating to the timing of BCG vaccination, if given, and the appearance or non-appearance of leprosy lesions, should be sought.)

S. G. Browne.

10. **Survival among leprosy patients with special consideration of cancer as a cause of death,** by A. Oleinick. *Int. J. Lepr.*, 1968, **36**, 3.

The author found that the mortality rate among the 953 leprosy patients admitted to the Carville Leprosarium, Louisiana, between 1939 and 1963, was approximately the same as that of the general population. The type of leprosy made no difference. Because of the special circumstances attending the introduction of sulphone therapy during the early 1940's and its application to patients who had been chronically ill with severe leprosy, the mortality rate (among females) was rather higher during the first few years after 1939. During the sulphone era, there was a slight excess in mortality in middle-aged males and older females during the first 5 years after their admission to Carville.

In view of the differences in reported series, and

the theoretical interest of chronic lymphoid stimulation (manifested by hyperglobulinaemia and the presence of numerous auto-antibodies in the serum), a special study was made of the mortality from malignant disease. The risk of leukaemia or lymphoma was not found to be increased in this series.

S. G. Browne.

An electromyographic study of lagophthalmos in leprosy, by J. Chaco, A. Magora, H. Zauberman and Y. Landau. *Int. J. Lepr.*, 1968, **36**, 3.

Clinical and electromyographic (EMG) studies, carried out in Israel on leprosy patients with lagophthalmos, confirmed that the 2 parts of the orbicularis oculi muscle (upper and lower) can be affected independently. Where both parts are affected, the lower is generally the first to be involved and later shows a higher degree of paralysis. Weakness confined to the lower part of the muscle may indicate selective damage to the zygomatic branch of the facial nerve, and trauma apart, is not found in facial palsies of other origins. No EMG evidence of subclinical damage to facial muscles was found, in contrast to findings in hand muscles, and damage to the facial nerve was usually preceded by damage to ulnar and median nerves.

W. H. Jopling.

Pathologic changes and their distribution in peripheral nerves in lepromatous leprosy, by C. K. Job and K. V. Desikan. *Int. J. Lepr.* 1968, **36**, 3.

This is an important study of the clinical and histological appearances of the ulnar, median and radial nerves in lepromatous leprosy. Post-mortem examination of 4 active cases showed that these nerves were normal at their origins but became thickened when they became superficial. Thickening increased gradually in the ulnar nerve, reaching a maximum about 2 cm above the medial epicondyle, then becoming normal in size in the forearm to increase again in thickness at the level of the proximal crease of the wrist. Thickening was abrupt in the median nerve, occurring as it emerged from the cover of flexor digitorum sublimis and reaching a maximum at the level of the transverse carpal ligament. Thickening of the radial nerve commenced in the lower fourth of the forearm where it pierces the deep fascia and divides into medial and lateral branches.

With regard to the histological changes, these were maximal where the nerves were most thickened and consisted of large numbers of foamy macrophages; large concentrations of acid-fast bacilli inside macrophages, perineural cells and Schwann cells; oedema; increased vascularity; thickened perineurium; demyelination; destruction of axons; and diffuse fibrosis. Demyelination was much more prominent than axonal degeneration.

The authors discuss the reasons for these changes being most marked where the nerves are subcutaneous, and suggest that lowered temperature and exposure to trauma are the operative factors.

W. H. Jopling.

Antipyretic and anti-inflammatory action of flufenamic acid in acute reaction of lepromatous leprosy, by C. S. Goodwin. *Lancet*, 1968, Oct. 19, 854.

In 22 cases of lepromatous leprosy with acute reaction, flufenamic acid (Arlef) had a significant antipyretic effect with accompanying fall in the erythrocyte sedimentation rate. Erythema nodosum subsided in 23 out of 25 episodes, and all the signs and symptoms of acute iridocyclitis and neuritis were relieved. High-dosage, short tapered courses, up to 25 mg per kg of body weight per day, were the most effective and were tolerated well. One patient given up to 28 mg per kg per day of flufenamic acid had neutropenia, but 10 days after treatment was stopped his leucocyte count had returned to normal.

W. H. Jopling.

14. **Glucose-6-phosphate dehydrogenase deficiency in leprosy.** Letter from M. Kher and S. Grover. *Lancet*, 1969, *i*, 1318.

The authors found that the prevalence of G-6-PD deficiency was 22% in 120 leprosy in-patients, compared with 9.4% in the general population of Nagpur (Central India) and surrounding areas. They suggest tentatively that this deficiency may predispose patients to infection with *Myco. leprae*. They also remark that sulphones may induce haemolysis in patients with G-6-PD deficiency.

S. G. Browne.