

## Abstracts

The following abstract is reprinted, with permission, from *Trop. Dis. Bull.*, 1968, 65, 11:

1. **Importância dos focos lepromatosos no controle domiciliar da endemia de lepra—prevenção da lepromatose pela cura da lepra indeterminada** (The importance of lepromatous foci in the domestic control of endemic leprosy—the prevention of leprosy by the cure of indeterminate leprosy), by J. DE. A. PUPO. *Revta Bras. Leprol.*, 1966, 34, 1/4, 19. English summary.

Basing his argument on experience in Sao Paulo the author recommends a prophylactic system for the control of leprosy by the early detection of cases and cure of the patients to prevent the further dissemination of infection. This involves (a) periodic inspection of the homes of known cases, and of their contacts, by mobile units; (b) intensive treatment of patients with infections of the indeterminate type; it is considered that these form 70-80% of early detectable cases (lepromatous 10-17% and tuberculoid 7-17%), and it is important to prevent these indeterminate infections developing further into the lepromatous form; (c) more intensive and more easily available sulphone treatment for patients in the early stage, so as to prevent the development of highly infective open lesions; (d) abandonment of compulsory isolation (which is expensive and which leads to concealment); but existing sanatoria should be maintained on an open door policy to assist advanced cases; (e) preventories (which presumably are homes for children of patients with leprosy) should be converted into general homes for poor children of all types, so as to avoid the stigma of leprosy; (f) the leprosy control service should be integrated into the general public health service, so as to obtain wider facilities and skills and to avoid stigma and popular prejudices.

F. Hawking.

The following 5 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1968, 65, 12:

2. **The modern view of leprosy**, by S. G. BROWNE. *R. Inst. Publ. Hlth Hyg. J.*, 1967, 30, 4/6, 132.

The author gives a clear and concise account of the leprosy situation in England with particular reference to the responsibilities of the Medical Officer of Health. Of nearly 400 patients on the Central Register of the Ministry of Health, about half are quiescent and in the remainder the disease is active although not necessarily contagious. The MOH (Medical Officer of Health) receives notifications of all cases of leprosy diagnosed within his area, maintains a confidential record, sends the list of names to the Ministry of Health annually and, with the assistance of a social health worker, confirms that the patients in his district are receiving treatment. He must inform his opposite number whenever a patient

on his local Register moves into another area. The MOH can help the clinician to obtain the advice of one of the consultants on the Panel of Leprosy Opinion, if this be required, and will arrange for close contacts to have BCG vaccination and periodical medical examination.

W. H. Jopling.

3. **ABO blood groups and leprosy**, by F. VOGEL. *J. Med. Genet.*, 1968, 5, 56.

Many surveys of blood groups in leprosy have been published, and individually each of them has been too small to provide the data for a convincing conclusion. The present report is a statistical analysis of the data compiled from 20 previous investigations, carried out with the aid of a computer.

The conclusion drawn establishes fairly well that there is a slightly higher incidence of groups A and B among patients with lepromatous leprosy and a corresponding increase of group O in those with non-lepromatous (mainly tuberculoid) leprosy. There is little difference between leprosy patients as a whole and healthy control subjects, though the possibility of a somewhat higher incidence of group A in leprosy is not excluded.

D. S. Ridley.

4. **A review of postmortem findings in 37 cases of leprosy**, by K. V. DESIKAN and C. K. JOB. *Int. J. Lepr.*, 1968, 36, 32.

Reports of autopsies in leprosy are relatively scarce, and the present paper is the first to have emanated from India. From 1941 to 1964 autopsies were performed at Vellore on 41 leprosy cases, and of these the tissues were in a reasonable state of preservation in 37; 30 were classified as lepromatous. The disease was of long duration in nearly all cases, being of more than 10 years in 20.

Visceral lesions were not found in any of the non-lepromatous cases, but they were found in all the lepromatous cases that were regarded as active and in some that were inactive. The distribution of the microscopic infiltrations of foamy macrophages and of acid-fast bacilli is described; they did not differ significantly from the findings given in previous reports. Of the associated diseases that were found the commonest was chronic inflammation of the kidneys of one sort or another, which was present in 24 of the 30 lepromatous cases; and the most important was tuberculosis, present in 10 cases. Tuberculosis was the commonest cause of death, but 5 patients died of tetanus and in 8 there was no other explanation than leprosy itself. Surprisingly, amyloidosis was found in only 4 cases and atheroma also was rare.

D. S. Ridley.

5. **Immunological basis for depression of cellular immunity and the delayed allergic response in patients with lepromatous leprosy**, by J. L. TURK and M. F. R. WATERS. *Lancet*, 1968, Aug. 24, 436.

Resistance during infections with mycobacteria is due to cellular immunity mediated by lymphocytes rather than to serum antibodies. Biopsies of supratrochlear or axillary lymph nodes of 9 patients with lepromatous leprosy showed that the lymphocytes in the paracortical area of the nodes were almost completely replaced by pale-staining phagocytic reticulohistiocytes (the stain was methyl-green pyronin). Germinal centres were normal and their marginal zone of lymphocytes was not decreased. This pattern was similar to that of lymph nodes of guinea pigs treated with antilymphocyte serum, which depresses cell-mediated immunity. In one patient whose immunity was on the increase after 7 months of therapy, as indicated by a shift in his classification towards borderline, there was evidence of the beginning of a repopulation of the paracortical area with small lymphocytes. In tuberculoid leprosy the paracortical areas were well populated with small lymphocytes and immunoblasts.

It is suggested that in adults the paracortical areas take over the control of cell-mediated immunity from the thymus.

D. S. Ridley.

6. **The therapeutic effect of 4,4'-diacetyldiaminodiphenylsulfone (DADDs) in leprosy**, by C. C. SHEPARD, J. G. TOLENTINO and D. H. McRAE. *Am. J. Trop. Med. Hyg.*, 1968, 17, 192

4,4'-diacetyldiaminodiphenylsulphone (DADDs) is a repository sulphone which slowly releases dapsone (DDS) or the monoacetylated derivative, and this trial, carried out in the Philippines, was designed to decide if the rate of release of active drug from acceptable doses in man was great enough to be therapeutically active in lepromatous leprosy. DADDs was given intramuscularly in a dosage of 225 mgm every 77 days to 10 patients who were matched with 10 other patients with lepromatous leprosy given oral dapsone in a dosage of about 100 mgm daily.

During the period of the trial (48 weeks) nasal washings were performed every 4 weeks, and clinical assessment and skin smears every 8 weeks; a skin biopsy was carried out at the beginning and at the end of the trial. Regular observations were made on blood levels and urinary output of sulphone. The two chief criteria of response to treatment were the decrease in numbers of *Mycobacterium leprae* in the nasal washings, and the decrease in the ratio of solid staining *Mycobacterium leprae* in skin smears. By both these measurements DADDs was as active as DDS.

Nine of the 10 patients receiving DDS and 8 of the 10 receiving DADDs, experienced erythema nodosum leprosum in some degree. Two patients receiving DADDs died during the trial; one developed miliary tuberculosis, and the other suffered severe lepra reaction through the trial and died in the last week. The authors do not say what methods (if any)

were adopted to control lepra reactions, but in the case of the reacting patient who died they state that "several cortisone preparations were administered, but the dosage did not exceed 3 mg per day".

W. H. Jopling.

The following 10 abstracts are reprinted, with permission, from *Int. J. Lepr.*, 1968, 36, 3:

7. **Primary diffuse lepromatous leprosy with erythema necroticans (Lucio phenomenon)**, by S. L. MOSCHELLA. *Arch. Dermat.*, 1968, 97, 593.

Case report of 46 year old white man, born in Cuba, who lived there 29 years before migrating to the United States. Medical examination disclosed lepromatous leprosy. Microscopic study disclosed intense vasculitis of vessels of all types, with numerous bacteria with the characteristics of *Mycobacterium leprae*.

E. R. Long.

8. **Syndromes paraplégiques en milieu lépreux. A propos de 12 cas observés en Nouvelle-Calédonie** (Paraplegic syndromes in a leprosy environment in the light of 12 cases observed in New Caledonia), by G. DESMOULINS and G. ZELDINE. *Bull. Soc. Path. exot.*, 1968, 60, 482.

From New Caledonia, the authors report 12 observations of paraplegic syndromes, spasmodic at the very first, in a leprosy population belonging to the Melanesian race. A certain relationship seems to exist between these pathologic observations and the neurologic syndrome "kuru" described in the highlands of eastern New Guinea. The hypothesis of a genetic factor in the appearance of these accidents is put forward, because the genetic patrimony of Melanesians seems to be similar to that of New Guinea Papuans.

9. **Indométhacin dans les états réactionnels lépreux** (Indomethacin in leprosy reactional states), by H. THIERS, J. ROUSSET, J. COUDERT, M. R. BATTESTI and M. LU HUNH THAN. *Lyon Med.*, 1967, 12, 899.

In severe reactional states in leprosy requiring corticoids in high dosage for prolonged periods, indomethacin is of great interest in that it leads to weaning from the corticoid or reduction to very small doses. The dose of indomethacin seems to be of the order of 150-200 mgm. In early or moderately severe reactional states indomethacin permits reduction of corticoid dosage, with sufficient rapidity without interruption of specific treatment. Treatment by indomethacin should, nevertheless, be carried out long enough to avoid evolutive relapses. In inflammatory neuritic states in the course of reactional episodes, the action of indomethacin seems limited and only relatively effective. In the case of patients not receiving antileprosy treatment, modification of the reaction of the human organism toward the leprosy bacillus seems to thwart the effect of the treatment. Ultimately the effectiveness of the treatment by sulfones reappears after the suppression by indomethacin.

**10. Preliminary test using DMSO as a vehicle for drugs in leprosy,** by R. O. YEATS. *Ann. N. Y. Acad. Sci.*, 1967, **141**, 668.

Dimethyl sulfoxide as a skin wash in 70% strength was used as a vehicle to test the effect of dapsone (8 patients), isoniazid (7 patients), and para-amino-salicylic acid (8 patients) in dosage of 10 mgm/ml applied in solution with cotton applicators to the skin of leprosy patients with tuberculoid markings. All patients were on dapsone orally. Improvement noted in the amelioration or disappearance of tuberculoid markings, in all 3 groups, was rapid and marked, but about equal. No control with DMSO alone was tested, but it was believed that improvement in each group was due to the DMSO rather than the drug in solution.

*E. R. Long.*

**11. Editorial. Transfer factor and leprosy.** *New England J. Med.* 1968, **278**, 333.

There is increasing interest in granulomatous disease characterized by suppression or abolition of delayed hypersensitivity. Boeck's sarcoid and Hodgkin's disease are notable examples. If normal persons are injected with transfer factor, i.e. a dialyzable moiety prepared from extracts of blood leucocytes from sensitive donors, the systemic delayed sensitivity displayed by the donor, i.e. tuberculin type sensitivity, develops in the recipient. This induced hypersensitivity persists as long as 2 years. Patients with sarcoidosis or Hodgkin's disease, however, when injected with transfer factor, prove incapable of developing tuberculin type delayed hypersensitivity. This lack of response suggests the existence of a central immunologic deficit due to a still not understood aberration of immuno-competent cells that may either cause or result from the disease itself. Thus patients with depressed delayed hypersensitivity are expressing an impairment of the cell populations normally engaged in the synthesis, replication or transport of transfer factor. Bullock's study (see abstract IJL 36 (1968) 246) furnished evidence of the extent of impoverished delayed hypersensitivity in leprosy in terms of a loss of established immunologic memories and a diminished capacity for active sensitization, and raises the query if the aberrant processing of transfer factor in the granulomatous diseases named above has relevance to the immunologic predicament of patients with lepromatous leprosy. In the latter disease intracellular infection, resulting in reticuloendothelial blockade, may lead to failure of transfer factor production, with general impairment of the mechanism for delayed hypersensitivity. The loss of delayed hypersensitivity to lepromin may result from such infection. The lepromatous type of disease goes virtually unchecked by the host whose macrophages are laden with *M. leprae*, in contrast with the conditions holding for the tuberculoid type. In other diseases, including tuberculosis, acquisition of specific hypersensitivity is associated with good prognosis and ultimate recovery. It is possible that preparations of transfer factor from lepromin-sensitive human donors would also function as a rapidly acting therapeutic immunizing agent, and

convert the progressive lepromatous type of leprosy to the more benign tuberculoid type. Transfer factor might prove of benefit in chronic granulomatous disease in which antimicrobial therapy alone is inadequate.

*E. R. Long.*

**12. Inhibition of haemaggregation by lepromin and other mycobacterial substances,** by C. S. GOODWIN, D. A. TYRRELL, B. HEAD and R. J. W. REES. *Nature (London)*, 1967, **216**, 1019.

Human erythrocytes suspended in glucose at pH 5.5.8 may aggregate and precipitate as a deposit in a tube or other container. This hemaggregation can be inhibited by a variety of substances, including viruses, acids and tuberculin in either its old or purified form. The inhibition caused by tuberculin is correlated with skin sensitizing activity, and in turn is inhibited by specific antibody. The authors studied a corresponding phenomenon in the case of *M. leprae* and lepromin. The following materials were tested as inhibitors: (1) integral lepromin from patients with lepromatous leprosy, prepared by Wade's modification of the Hayashi-Mitsuda method, (2) washed *M. lepraemurium* and *M. tuberculosis*, (3) cytoplasmic fractions of *M. leprae*, *M. lepraemurium* and *M. tuberculosis*, prepared by cell rupture procedures, (4) washed cell walls of these 3 strains of mycobacteria, and (5) normal skin. Fresh human Group A erythrocytes were used. Borax-succinic acid buffers with serum albumin in phosphate buffer, were used as suspending media. The results indicated that at the optimum pH of 5.6 the cytoplasmic fraction of *M. leprae* had a high inhibitory titer (1/3,200). The cytoplasmic fraction of *M. tuberculosis* was much more inhibitory to hemaggregation than cell wall preparations; the difference in the case of *M. lepraemurium* was not so great. Lepromin, in several dilutions tested, inhibited hemaggregation; the highest titer was found in preparations with the most alkaline buffer. Because hemaggregation was inhibited by both crude skin extracts and highly purified bacilli and their products, it seems probable that the activity of lepromin preparations is due to a component of the leprosy bacillus.

*E. R. Long.*

**13. Lepromatous leprosy in reaction. A study of the liver and skin lesions,** by B. KRAMARSKY, H. A. EDMONDSON, R. L. PETERS and T. B. REYNOLDS. *Arch. Path.*, 1968, **85**, 516.

The inclusion of leprosy in the differential diagnosis of hepatic granulomas seen on biopsy is often neglected in the United States. In the parts of the world where leprosy is endemic, the possibility is more likely to be considered, although the frequency of hepatic involvement in the early stages of leprosy is not known. It seems reasonable to assume that the Kupffer cells swollen by phagocytic vacuoles represent the foamy lepra cells (Virchow's cells) of light microscopy. The recognition of lepra cells with vesicular cytoplasm, tendency to form syncytial clumps, lack of necrosis, and their frequent location near the central veins all taken together should alert the pathologist to the possibility

of leprosy. Acute episodes that occur in the course of lepromatous leprosy may bring the patient to the hospital. Fever, malaise, and skin nodules accompanied by hepatomegaly were the chief findings in our 2 patients. Peripheral nerve manifestations when present are helpful in clinical diagnosis, but they may be absent, as in one of our cases. Biopsies of the skin and liver were obtained from one patient with Lucio's type of leprosy and from one with erythema nodosum leprosum. Vasculitis, a dense inflammatory exudate, and necrosis of the skin characterized the Lucio type of leprosy; in erythema nodosum leprosum the vasculitis was not so severe and necrosis did not occur. Large numbers of organisms in the endothelial cells of the vessels in the skin could have given rise to bacteremia and development of the disease in the liver. The liver in the patient with Lucio's phenomenon contained tuberculoid lesions, whereas necrosis of sinusoidal walls and many Virchow's cells were noted in the other patient. Leprosy bacilli in Kupffer cells were easily demonstrated with electron microscopy. The presence of the bacteria within membrane-bound phagocytic vacuoles and the fusion of lysosomes with the vacuoles were seen.

14. **Histobacteriología de la almohadilla plantar del ratón inoculado con *M. leprae*** (Histologic and bacteriologic study of the footpads of mice inoculated with *M. leprae*), by M. BERGEL. *Publ. Cent. Estud. Leprol. (Parana)*, 1966, **6**, 5.

The author made a histologic and bacteriologic study of the footpads of mice which had been inoculated with 0.03 to 0.05 cc of recent leproma suspension taken from patients with untreated lepromatous or borderline leprosy. The animals were divided into 2 groups, one of which had normal food and the other a pro-oxidant diet; it was found that the experimental leprosy developed much better in the footpads of the animals that had been fed on the pro-oxidant diet. Two types of granuloma were found. In one type the granuloma was large and found in a deep part of the skin with damage to vascular and nerve elements and even muscular tissue. The bacilli in these granulomata were either "globi" or isolated and were large and acid-fast, which indicated a state of great vitality. In the other type, the granuloma was found in the dermis and was small and contained only isolated bacilli. This confirms the findings of Palmer *et al.* concerning the presence of bacillary groups in striated muscular tissue in the

footpads of mice with the bacilli showing characteristics which indicated a great degree of vitality. [Abstract by J. R. Innes, *Trop. Dis. Bull.*, 1968, **65**, 268.]

15. **The antimycobacterial activity of Rifampin**, by G. L. HOBBY and T. F. LENERT. *Am. Rev. Resp. Dis.*, 1968, **97**, 713.

A series of experiments were performed to compare the *in vitro* and *in vivo* activity of Rifampin (3-4-methyl-piperazinylinomethyl) rifampin SV) with that of isoniazid against mycobacteria. The data obtained suggest that on a weight basis Rifampin is approximately one-half as active as isoniazid against isoniazid-susceptible stains, both *in vitro* and *in vivo*, but is active at least *in vitro* against isoniazid-resistant strains of *M. tuberculosis*.

16. **Leprosy and genetics. A review of past research with remarks concerning future investigations**, by B. BEIGUELMAN. *Bull. WHO*, 1967, **37**, 461.

It has long been believed that an hereditary factor is concerned in susceptibility to leprosy. Pedigree analysis supports the general concept. In recent years geneticists have approached the problem by studying the association between leprosy and certain genetic markers, such as ABO and Rh blood groups, glucose-6-phosphate dehydrogenase deficiency, haptoglobins, transferins, Australian antigen, and taste sensitivity for phenylthiourea. No firm relation, however, has as yet been established between susceptibility to leprosy and these markers. The relatively low fertility of leprosy patients as compared with that of healthy people has been considered as of possible genetic association, but the frequent pathologic-anatomic genital involvement in the male, which is more frequent than that in the female, may account for the total low fertility of leprosy patients. The author considers a phenomenon brought to attention recently, viz. the lysing capacity of macrophages for *M. leprae*, as of more moment (*see* Beiguelman, B., and Quagliato, R. Nature and familial character of the lepromin reactions. *The Journal*, 1965, **33**, 800-807). He believes that investigation of healthy persons, by the technic of differentiation of blood monocytes into macrophages, should be undertaken to determine if a dimorphism in lysing capacity truly does exist, and if heterogeneity in lysing capacity for *M. leprae* can be related to sex and age.

E. R. Long.