

Abstracts

1. MICROBIOLOGY

69. FIELDSTEEL, A. H. & LEVY, L. Neonatally thymectomized Lewis rats infected with *Mycobacterium leprae*: response to primary infection, secondary challenge, and large inocula. *Infection & Immunity*, 1976, v. 14, No. 3, 736-741.

Several experiments were carried out to measure the ability of neonatally thymectomized Lewis rats (NTLR) to limit multiplication of *Mycobacterium leprae*. NTLR inoculated in one hind foot-pad with 10^7 viable *M. leprae* and challenged in the other hind foot-pad with 5×10^3 organisms simultaneously or 120 or 180 days later permitted multiplication in both sites. By contrast, immunologically intact rats similarly inoculated did not permit multiplication from either inoculum. NTLR and immunologically normal BALB/c mice were equally susceptible to infection with *M. leprae*, in that multiplication occurred regularly in the foot-pads of both species when inoculated with a bacterial suspension diluted to provide 5 organisms per foot-pad. Finally, multiplication occurred when 5 viable *M. leprae* diluted with 10^7 heat-killed organisms were inoculated into the foot-pads of NTLR. Although there was some evidence that NTLR are not completely immunosuppressed, NTLR appear to be capable of detecting much smaller proportions of viable *M. leprae* than can be detected by immunologically normal mice.

70. BEIGUELMAN, B. & PISANI, R. C. B. Chromosomal aberrations in leukocyte metaphases of leprosy patients under dapsone therapy. *Hansenologia Int.*, 1976, v. 1, No. 1, 53-60.

... Chromosome analyses were made on leukocyte metaphases of 18 leprosy patients who were ingesting daily doses of 50 mg or 100 mg of DDS and of 40 healthy individuals used for control.

These analyses have shown that the proportion of numerical chromosomal aberrations in the leukocyte metaphases of the leprosy patients did not differ significantly from that observed in the cells of the controls. In contrast, the frequency of cells with chromatid or chromosome breaks and gaps was significantly increased in the leukocytes of leprosy patients.

Multiple regression analysis applied to the data recorded has shown that the increase of breaks and gaps in the chromosomes of leprosy patients cannot be attributed to age, years under sulphone-therapy or to concentration of DDS in blood.

71. DESIKAN, K. V. Correlation of morphology with viability of *Mycobacterium leprae*. *Lepr. India*, 1976, v. 48, No. 4, 391-397.

A concept has been developed in the recent years that the evenly stained "solid" bacilli are living and the "non-solid" forms are degenerate and dead. This communication presents the findings in experimental mice inoculated with material containing 1-10% solid evenly stained *M. leprae* and also with material containing 0% solid organisms. There was multiplication of the bacilli in both the groups. Quantitatively, the yield also was not significantly different. These findings do not support the belief that the non-solid bacilli are necessarily dead. The non-solid bacilli were further classified on the basis of their morphology to the following forms: (a) short

but evenly stained, (b) indented, (c) beaded, (d) dumb-bell shaped, (e) coccoid, and (f) fragmented. Material without solid bacilli, but containing different proportions of the above types of bacilli also gave similar results, making it difficult to say which types of morphological forms are non-living. It appears, therefore, that the recognition of the living status of *M. leprae* by its morphology is highly equivocal and subject to error.

72. CHATTERJEE, B. R. A non-acid-fast coccoid precursor—possible cultivable phase of *Mycobacterium leprae*. *Lepr. India*, 1976, v. 48, No. 4, 398-405.

A non-acid-fast coccoid organism isolated from human leproma, and skin and nasal smears of leprosy patients shows tendency to revert to an acid-fast mycobacterial form during test-tube passages. One of these coccoid isolates gave strong DOPA oxidase activity. There is also preliminary evidence of mycobacterial conversion from these coccoids in intraperitoneally inoculated mice. The possibility that these non-acid-fast coccoids could be a cultivable precursor phase of *M. leprae* has been raised and discussed.

2. BIOCHEMISTRY, PATHOLOGY, IMMUNOLOGY

73. ABE, M., IZUMI, S., SAITO, T. & MATHUR, S. K. Early serodiagnosis of leprosy by indirect immunofluorescence. *Lepr. India*, 1976, v. 48, No. 3, 272-76.

A fluorescent antibody absorption test for leprosy was found to be highly sensitive. Leprosy bacilli were extracted from a histoid leprosy lesion for use as antigen in the indirect immunofluorescent test using sera which had been absorbed with cardiolipin, lecithin and the polysaccharide of tubercle bacilli (to remove cross-reacting antibodies), and bovine albumin. The screening dilution was 1 in 40.

The test gave the highest titres with sera from lepromatous leprosy patients but, even so, positive results were obtained in 82% of tuberculoid cases, 2 out of 4 indeterminate cases and 3 out of 4 contacts. This compares with a "previous finding" that none of 50 sera from non-contacts was positive. It is acknowledged that further work is needed to establish the specificity of the test. The same technique could be used for the quantitative staining of *Mycobacterium leprae*, and possibly for its identification.

D. S. Ridley

74. SAHA, K., MITTAL, M. M. & MAHESHWARI, H. B. Passive transfer of immunity into leprosy patients by transfusion of lymphocytes and by transfusion of Lawrence's transfer factor. *J. Clin. Microbiol.*, 1975, v. 1, No. 3, 279-288.

About 1200 million viable lymphocytes from normal but lepromin- and tuberculin-positive human beings were transfused in 4 patients with lepromatous and one with tuberculoid leprosy 3 times at monthly intervals. Three lepromatous patients suffered from erythema nodosum leprosum (ENL) whereas the other 2 developed severe reaction whenever put on the smallest doses of dapsone. In one lepromatous patient minimal or no improvement was observed. In the other 4 patients clinical, bacteriological and histological improvement occurred, and 2 patients started to tolerate dapsone. The authors consider that immunotherapy might have a definite role in the management of the disease, especially in cases with ENL.

The repeated transfusion (3 times) of Lawrence's factor into 4 patients intolerant of leprosy drugs produced no discernible improvement.

T. F. Davey

75. MITTAL, M. M., SAHA, K. & MAHESWARI, H. B. **Passive transfer of immunity in lepromatous leprosy patients by Lawrence's transfer factor.** *J. Indian Med. Ass.*, 1976, v. 66, No. 9, 197-199.

Lawrence's transfer factor prepared from leucocytes from healthy donors who were tuberculin and lepromin (Mitsuda) positive was transfused into 4 patients with lepromatous leprosy, each patient receiving transfer factor prepared from 250 ml blood on 3 occasions at monthly intervals. All 4 patients were intolerant to anti-leprosy drugs. After each transfusion reactive symptoms were exaggerated for 3-5 days. Seven and a half months after the first transfusion, while appreciable improvement had occurred in the immunological status of the patients, there was no considerable improvement in clinical histological or bacteriological status. [See also *Trop. Dis. Bull.*, 1977, v. 74, abstr. 357.]

T. F. Davey

76. DE VRIES, R. R. P., FAT, R. F. M. L. A., NIJENHUIS, L. E. & VAN ROOD, J. J. **HLA-linked genetic control of host response to *Mycobacterium leprae*.** *Lancet*, 1976, Dec. 18, 1328-1330.

Non-random parental HLA-haplotype segregation is demonstrated in siblings with leprosy. A test bed for the statistical analysis of non-random segregation among sibships of various sizes. Sibs with the same type of leprosy show a significant excess of identical HLA

This is also true for families in which only tuberculoid leprosy is found, which is by far the commonest type in the population studied. However, sibs affected with different types of leprosy share a haplotype less often than expected. This indicates that both susceptibility to and type of leprosy are controlled by at least 2 HLA-linked genes. Our findings suggest that the equivocal results of previous population studies are due to differences of linkage disequilibrium between HLA-linked genes controlling the host response to *Mycobacterium leprae* and alleles of HLA A and B loci in various populations.

77. BJORVATN, B., BARNETSON, R. S., KRONVALL, G., ZUBLER, R. H. & LAMBERT, P. H. **Immune complexes and complement hypercatabolism in patients with leprosy.** *Clin. Exp. Immunol.*, 1976, v. 26, No. 3, 388-396.

The occurrence of immune complexes in the serum and the level of the C3 breakdown product C3d in the plasma from patients with leprosy were studied by quantitative methods and the results were compared in various forms of the disease. These studies were performed on 62 samples from 26 patients. The serum ¹²⁵I-C1q binding activity was found to be increased by more than 2 s.d., as compared to the normal values, in most of the sera from patients with erythema nodosum leprosum (ENL) (80%) and uncomplicated lepromatous leprosy (82%), but also in the sera from patients with tuberculoid leprosy (58%). *In vitro* studies suggested that immune complexes involving mycobacterial antigens were present in leprosy sera. An increased C3d level (>2 s.d.) was also found in most of the plasma from patients with ENL (70%), but rarely in the plasma from patients with uncomplicated lepromatous leprosy (18%) and never in tuberculoid leprosy patients' plasma. The absence of a significant correlation between the ¹²⁵I-C1q binding activity and the C3d level in leprosy patients may suggest that extravascular immune complexes are involved in the complement activation occurring in ENL. The quantitation of C3d in plasma may be of some practical interest in the early diagnosis of ENL complications of leprosy.

78. BJUNE, G. & BARNETSON, R. ST C. **Plasma factors in delayed-type hypersensitivity. Augmentation of lymphocyte responses in borderline leprosy reactions.** *Clin. Exp. Immunol.*, 1976, v. 26, No. 3, 397-402.

The phytohaemagglutinin-induced response of lymphocytes were found to be inhibited by plasma from patients with leprosy when compared with their responses in pooled serum from healthy donors. When patients developed reversal reactions, the initial inhibitory effect of their plasma was replaced by an augmentary effect on the responses to phytohaemagglutinin. The period of augmentation coincided with that of the reversal reaction in patients with borderline tuberculoid leprosy, but was delayed in patients with borderline lepromatous leprosy. The plasma from each leprosy patient was also observed to have the same effect on lymphocytes from unrelated individuals, showing that the inhibition and augmentation were due to factors in the plasma and not to a change in lymphocyte receptors.

It is possible that the normal stable state of leprosy results from the presence of factors in plasma which act as a control mechanism, and that delayed hypersensitivity reactions may be caused by a breakdown of this control.

79. BALAKRISHNAN, S. **Biochemical aspects of reaction states in leprosy.** *Lepr. India*, 1976, v. 48, No. 4, 406-417

Sequential biochemical investigations conducted in cases of leprosy during the reactive as well as subsided phases indicated elevated serum levels of mucoprotein and skin levels of hydroxy-proline and hexosamine in the reactive phase of leprosy. Elevation of the urinary excretion of hydroxy-proline and certain other amino acids was noticed during "lepra reaction". Enhancement of serum levels of aldolase, CPK, LDH and transaminases was observed in the reactive phase of lepromatous leprosy. These findings taken as a whole suggest a generalized tissue breakdown in lepra reaction.

80. PADMA, M. N., PREMANATH, M. & DESIKAN, K. V. **Bacillaemia in reactive states of leprosy.** *Lepr. India*, 1976, v. 48, No. 4, 413-418.

Thirty-five cases of lepromatous and near-lepromatous cases of leprosy in reaction have been investigated for the presence of acid-fast bacilli in blood at the height of the reaction as well as at its subsidence. Only 3 cases exhibited bacillaemia during reaction. It is therefore unlikely that dissemination of the disease is accentuated during reaction as commonly believed. Further, the immune complexes demonstrated to be circulating during reaction are possibly formed by bacillary products and not by whole or fragmented bacilli.

81. SHEPARD, C. C., VAN LANDRINGHAM, R. & WALKER, L. L. **Immunity to *Mycobacterium leprae* infections in mice stimulated by *M. leprae*, BCG and graft-versus-host reactions.** *Infection & Immunity*, 1976, v. 14, No. 4, 919-928.

Infections of mice with *Mycobacterium leprae* in one rear foot-pad immunized them against a second infection in the other rear foot-pad. Purified bacilli harvested from the first infection also produced immunity when injected into the foot-pads of previously uninfected mice. Injections of BCG afforded similar protection, but had no adjuvant effect on *M. leprae*. *M. duvali*, a cultivable mycobacterium that is reported to be more closely related antigenically to *M. leprae* than BCG is, provided much less protection against *M. leprae* challenge than BCG did. Moreover, when *M. duvali* was mixed with BCG, it was not any more effective than BCG alone. Graft-versus-host reactions, induced by injections of parental spleen cells into F1 hybrids, provided no protection against *M. tuberculosis* and *M. marinum* challenge. They gave moderate protection against *M. leprae* in one experiment but not in another with a different

schedule. Allogenic spleen cells had a protective effect when injected locally into the infected foot-pad. The effect produced by these injections of spleen cells was a delay in the appearance of bacterial growth; however, there was no decrease in the rate of logarithmic growth when it did appear and no reduction in the eventual plateau level.

3. CLINICAL ASPECTS

82. GANAPATI, R., DESHPANDE, D. H. & CHULAWALA, R. G. **Calcification of cutaneous nerves in leprosy—a case report.** *Lepr. India*, 1976, v. 48, No. 3, 309-310.

A boy aged 13 years, attending a leprosy clinic in Bombay, had an anaesthetic tuberculoid lesion on the front of the right forearm. There was thickening of the ulnar nerve and also of the cutaneous nerves in relation to the lesion. Firm nodular swellings along the course of the cutaneous nerves showed evidence of calcification on X-ray (the radiograph is reproduced). Calcification was also demonstrated histologically. The authors comment on the rarity of reports of nerve calcification in leprosy but suggest that if more radiological and histological studies were undertaken more such cases would be revealed.

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83. ISHIHARA, S. [A case report on leproma in the tongue.] *Lepro*, 1975, v. 44, No. 4, 199-201. [In Japanese.]

The English summary appended to the paper is as follows:

“A male patient aged 75 had complained of the paresthesia on the both soles about 10 years ago. He noticed the nodules on bilateral earlobes, and swelling of the face in 1970. He had been not registered as leprosy, and had been treated as a heart disease until October, 1973.

“On that time he had been diagnosed as lepromatous leprosy and admitted to National Suruga Leprosarium. The patient had remarkable lepromatous lesions in the oral cavity, uvula, soft and hard palate and tongue together with skin lesions.

“One of the lepromas of the tongue, sized 3 mm x 4 mm, was taken off surgically and it was observed histopathologically. The mucous membrane is thinner than usual without rete pegs. Submucous tissue is occupied by masses of leprous infiltration, without ‘free zone’. And the leprous infiltration invade into the muscle tissue of the tongue. Many acid-fast bacilli are detected in the leproma.

“Since he had been treated over 1 year with DDS, lepromas of the tongue clinically disappeared, and also the sense of taste has gradually recovered.”

[The appearances of the tongue before and after treatment, and the histological changes, are illustrated in photographs.]

84. FLEURY, R. N., OPROMOLLA, D. V. A., TOLENTINO, M. M. & TONELLO, C. J. S. **Hanseniasis virchowiana do couro cabeludo. [The scalp in lepromatous leprosy.]** *Hansenologia Int.*, 1976, v. 1, No. 1, 25-32.

The English summary appended to the paper is as follows:

“A study was made of the scalp involvement in 30 males suffering from active Virchowian hanseniasis (lepromatous leprosy). Clinical evaluations were made before and after the patients’ heads were shaved and 4 ‘punch’ biopsies were performed in standardized locations. The results showed that shaving increased the possibility of detection of clinical lesions, which are present in the large majority of the patients. These lesions were principally of the macular form. The results also showed the existence of alopecia related to the specific process. Histopathologically,

all patients showed signs of specific involvement either by the presence of infiltration or by the presence of bacilli in the core of infiltrated mononuclears. In spite of this involvement, it could not be compared with that observed in the rest of the skin. The infiltrated areas were always discretely regressive. Bacilli were always few and granular. This finding demonstrates the anatomical peculiarities of the scalp, which is not a suitable locus for the development of bacilli."

4. THERAPY

85. BULL. WLD HLTH ORG., 1976, v. 53, No. 4, 425-433. **Experimental chemotherapy in leprosy.**

The Memorandum reviews the considerable progress that has been made in research on the chemotherapy of leprosy during the last 10-15 years, as a result of which it is now possible to study the same topics in leprosy as are studied in other bacterial diseases. Thus drugs have been screened in mice for their activity against *Mycobacterium leprae*. Those that have been found to have the greatest activity against *M. leprae* at acceptable dosages—dapsonе, rifampicin, and clofazimine—have been characterized in terms of the minimal effective dosage and rate of bacterial kill. Similarly, their pharmacokinetics in man and in certain animals have been defined. The theoretical basis for drug trials in leprosy patients is discussed in terms of the number of viable and the number of dead *M. leprae* that remain at various stages of therapy.

[There are 59 references.]

86. GANAPATI, R., NAIK, S. S., SHAH, M. H., SHIRSAT, L. S. & GAITONDE, B. B. **Clinical trial of DADDS in lepromatous leprosy.** *Lepr. India*, 1976, v. 48, No. 3, 238-243.

Injection of 225 mg acedapsonе (DADDS) every 70 days to 23 patients with lepromatous leprosy produced clinical regression noticeable shortly after the second injection. Three to 7 injections led to a fall in the morphological index from 5.0-0.6. Erythema nodosum leprosum was encountered in 7 patients and it is thought advisable to discontinue dapsone when this complication occurs. Dapsone levels in the blood were found to be more than 10 ng/ml before each fresh administration of acedapsonе. The trial extended to 7 injections.

T. F. Davey

87. BARNETSON, R. ST C., PEARSON, J. M. H. & REES, R. J. W. **Evidence for prevention of borderline leprosy reactions by dapsone.** *Lancet*, 1976, Nov. 27, 1171-1172.

Sixty-eight patients were included in a prospective study of the treatment of borderline leprosy. Thirty-four were treated with dapsone 5 mg daily, and 34 with 50 mg daily. Reversal reactions developed in 11 of those on 5 mg daily and in 3 of those on 50 mg daily. The statistically significant difference between the 2 treatment groups indicates that, contrary to previous teaching, dapsone given in higher dosage does not predispose patients to reversal reactions and indeed may prevent them.

88. CARAYON, A. **Limites actuelles de la chimiothérapie antihansénienne sur la névrite et danger de ses effets secondaires immunologiques. [Current limitations of anti-leprotic chemotherapy for neuritis and danger of secondary immunological effects.]** *Méd. Afr. Noire*, 1976, v. 23, No. 10, 567-577.

From his long and wide field experience in Africa, the author gives timely warnings against generalizations in the treatment of leprosy. Since the pathology of nerve damage is complex

and multifactorial, treatment that is successful in controlling the disease may have little effect, or an adverse effect, on the appearance or worsening of damage to peripheral nerves. The action of anti-leprotics on leprosy bacilli present within the nerves depends on such factors as diffusion of the drug and its relative solubility in lipids, and on such side-effects as rupture of the bacilli and of tissue cells. Another factor that has some bearing on the limitations of drug therapy is the apparent induction of suprarenal insufficiency through some little understood mechanism.

The author reviews the wide range of drugs now available for the treatment of leprosy and attempts to assess their place in the prevention and control of damage to the peripheral nerves. He favours clofazimine in the general treatment of multibacillary leprosy and suggests that, despite the fact that it does not enter the nerves themselves, it appears to exert its bacteriostatic effect by intracellular concentration in the neighbourhood of engulfed and multiplying bacilli.

The apparent effect of the various drugs on cellular immunity in relation to progressive nerve damage is briefly assessed and the indications for the use of rifampicin, clofazimine and the sulphonamides are reviewed, together with the action of the various anti-inflammatory products now available. He gives a warning against the use of drugs in borderline leprosy that might provoke dangerous degrees of cellular reaction, with resulting irreversible damage to peripheral nerve fibres.

This paper should be consulted in the original for its summary of wide-ranging work.

S. G. Browne

5. SURGERY

89. MILLER, S. H. & WOOD, A. M. **Surgical treatment of facial nerve involvement caused by leprosy.** *Am. J. Trop. Med. Hyg.*, 1976, v. 25, No. 3, 445-448.

Following a discussion of nerve damage underlying facial paralysis in leprosy, muscle transfer procedures are described: temporalis transfer to the eyelid, and masseter transfer to the mouth and nasolabial fold. These were found successful in small minimally equipped hospitals in

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90. NAMASIVAYAM, P. R. **A spiral splint for claw fingers.** *Lepr. India*, 1976, v. 48, No. 3, 258-260.

A simple spiral splint made from galvanized iron wire is described for use in early paralysis of the small muscles of the fingers and in claw fingers. This splint will prevent stretching of the weak or paralysed muscles by keeping the metacarpophalangeal joints of the fingers in slight flexion. It will also help to prevent flexion contractures of the interphalangeal joints by encouraging active extension of these joints.

91. ANTIA, N. H., VANKANI, B. & PANDYA, N. J. **Surgical decompression of the ulnar nerve in leprosy neuritis.** *Lepr. India*, 1976, v. 48, No. 4, 362-370.

and extraneural and intraneural decompression without jeopardizing the vascular supply, in the early cases gave satisfactory results in 41 ulnar nerve decompressions undertaken in this study.

Sensory as well as motor recovery was obtained. However, sensory recovery was more significant in all and also in each patient with motor recovery.

The recovery was better in patients seeking treatment within 6 months of the onset of the symptoms.

The patients with tuberculoid type responded better to the nerve release.

A funicular biopsy is a feasible and practical method not only to confirm the diagnosis but also to histologically classify the disease and provides a guide to the type of damage to the nerve.

6. EPIDEMIOLOGY AND CONTROL

92. NOORDEEN, S. K. **Leprosy in Lakshadweep Islands.** *Lepr. India*, 1976, v. 48, No. 3, 244-257.

This territory, under the administration of India, was surveyed for leprosy in 1961 and again in 1965-67, when a prevalence rate of 24.4 per 1000 was found, its features consistent with an active epidemic situation. A fresh epidemiological survey in 1974 by a very experienced leprologist is reported and indicates a continuing serious situation with a prevalence rate at 25.1 per 1000, and with incidence among non-contacts similar to that among contacts. There are encouraging features, such as very few open cases and most new patients having only minimal disease potentially unlikely to produce deformities.

T. F. Davey

93. WKLY EPIDEM, REC., 1976, v. 51, No. 51, 389. **Leprosy control.** [In English and French.]

In 1971 a Leprosy Control Unit was established in Trinidad and Tobago, with the emphasis on an out-patient approach and on case-finding and case-holding. The intensification of case-finding efforts raised the average number of newly diagnosed cases from 46 per year for the period 1961-70 to 92 per year in 1971-75. At the end of December 1975 a total of 914 patients were on the registry. The prevalence is 0.86 per 1000 population. There are 10 clinics throughout the country. The disability rate fell from 70% in 1968 to 11% for the period 1971-75. This is attributed to the maintenance of regular chemotherapy and to the prompt treatment of relapsing episodes. Sixty per cent of the cases diagnosed in the past 5 years are leucoid type.

F. I. C. ...

Thanks are due to the Director, Bureau of Hygiene and Tropical Medicine for permission to reprint Abstracts from *Tropical Diseases Bulletin*, February, March and April 1977.