Lepr Rev (1980) **51**, 269–284

Abstracts

167. STONER GERALD L. **Importance of the neural predilection of *Mycobacterium leprae* in leprosy.** *Lancet,* 1979, v.2, 994–996.

Dr Stoner's thesis is that continuous leakage of leprosy bacilli into the circulation from a primary intraneural focus may simultaneously initiate bacillary dissemination and the suppression of cell-mediated immunity (CMI), therefore nerve involvement in leprosy, previously thought of as a diagnostic feature of the disease and as a complication of therapy, is an essential phase in the cycle of infection and reinfection by *M. leprae.* His cogent and well-reasoned exposition can be summarized as follows:

The normal way for effective CMI to *M. leprae* to be induced is by leakage of bacillary antigens to the peripheral lymphon compartment (the regional lymph-nodes) via lymphatic vessels. On the other hand, if antigens are first presented to the central lymphon compartment (spleen, thymus, and bone-marrow) via the bloodstream, a humoral immune response results and is accompanied by a suppressed cellular response. Presentation of antigens to the central compartment before their presentation to the peripheral compartment represents a reversal or 'inversion' of the normal order of immune processing, thus suppression of specific CMI replaces the induction of protective CMI. A peripheral nerve is usually the primary focus of infection, and in the earlier stages leprosy bacilli are confined within the funiculus by the perineurium. There are no true lymphatics within the funiculus, and the perineurium is an effective barrier to the movement of bacilli into the epineurial lymphatic channels, thereby barring them from the peripheral compartment. But they have access to the primary compartment via the bloodstream, and their continuous leakage directly into the circulation, with their concomitant exclusion from the draining lymph-nodes, must preferably stimulate the central compartment, leading to a predominantly humoral response with suppression of specific CMI. The localization of the primary focus of infection within funiculi, and the absence of lymphatic recirculation through the infected funiculi, result in a delay in the 'discovery' of the focus of infection by the immune system and an increase in the leakage of bacilli into the circulation, thereby providing additional stimulation to the central compartment and enhancing suppression of CMI. However, the level of suppression achieved is variable, as is the proportion of bacilli reaching the peripheral compartment during the course of the infection, and these variables influence the outcome and give rise to the spectrum of clinical and immunopathological manifestations observed in leprosy. As long as the stimulation of the central compartment maintains adequate suppression to prevent the induction of delayed-type hypersensitivity (DTH) to those bacilli which do eventually reach the peripheral compartment, the infection progresses towards the lepromatous pole. If the suppression becomes inadequate, the induction of DTH to *M. leprae* precipitates clinical leprosy of borderline type, the range from BT to BL depending on the extent of dissemination and multiplication of bacilli at the time DTH erupts. At the two extremes of this process are the two polar types of leprosy. Polar LL represents an infection in which the central stimulation maintains a completely effective

suppression until the bacterial antigenic load of the fully disseminated infection irreversibly destroys any remaining capacity for CMI or DTH to *M. leprae* in the host. Polar TT represents an infection in which the primary focus never generates sufficient suppression to permit it to escape detection long enough to initiate dissemination.

Although this hypothesis provides an alternative to the genetic-defect (Ir gene) theory of lepromatous leprosy pathogenesis, it allows room for certain genetic influences on leprosy susceptibility and its clinical manifestations. Unravelling the pathogenesis of LL is important because it impinges directly on the question of the effectiveness of potential leprosy vaccines, depending on whether the vaccine primes the peripheral compartment or the central one.

W H Jopling

168. ROOK GAW, STANFORD JL. **The relevance of three forms of delayed skin-test response evoked by *M. leprae* and other mycobacteria in mice. Correlation with the classical work in the guinea-pig.** *Parasite Immunol,* 1979, v. 1, 111–123.

'The controversy surrounding the protective role of 'delayed hypersensitivity' in tuberculous guinea-pigs has never been resolved. This controversy has arisen because the term 'delayed hypersensitivity' is used indiscriminately to describe both a type of necrotic skin-test reactivity which does not appear until 4–6 weeks after infection, and also non-necrotic reactions which can be elicited within a few days. Responses closely analogous to both have been characterized in mice immunized with mycobacteria. Simple criteria are described which allow these responses to be distinguished from one another, and from the Jones–Mote phenomenon. The relevance of each type to protection, susceptibility and immunopathology in leprosy, tuberculosis, leishmaniasis and listeriosis is discussed.'

169. BRIEGER WR. **In-service training methods in health education.** *J Trop Med Hyg,* 1979, v; 92. No 7, 145–149.

Health education has for a long time been confused with health propaganda or simply health teaching. The article begins by clearing up the confusion and states that it is concerned basically with behaviour change, using educational methods.

Anyone who has attempted to develop health education courses will welcome the approach to training outlined in the article, with its emphasis on appropriate selection of training methods. The development of training in health education has been relatively slow in spite of the recognition that it forms a vital part of any public health programme. Four years ago the African Regional Health Education Centre was established in Ibadan, Nigeria, where the author of this article is working.

Health education is a team activity and this is clearly shown in tabular form in the article, where the educational functions of each member of the team are suggested. The seven broad functions are: patient education, community health development, human relations and communication skills, training and consultation, use and maintenance of educational media, educational planning, and group process skills. Some health staff carry out all these functions and others only selected ones.

The author reminds us of two main approaches to training, namely, directive (teacher centred) and non-directive, where the trainee defines his own learning needs and assumes responsibility for developing his own learning plans. In reality most training programmes combine these two methods.

The author draws attention to three of the many principles of training design.

1. Training should be relevant to real life situations facing the trainee.
2. Training experience should be active, not passive.
3. Training should provide enough opportunity for new skills to be thoroughly mastered so that they may be applied on the job.

This demands a great deal of the trainer both in planning and carrying out training courses.

Health education is basically about change. It would be reasonable to suppose that it will become more effective as both trainer and trainee become involved in the study of the process and problem of change. Case studies, simulated games, and role play provide many opportunities for active learning and situations where trainees can not only gain knowledge but develop appropriate skills.

The article ends with two case studies, one suitable for role play concerning health education with a patient, and the second deals with community health education. Any staff involved in teaching health education as it applies to leprosy control and patient care should make use of the case study method. If you are not familiar with it, a small booklet, *Using the case study in teaching and training*, by Le Roy Ford, 1969, Broadman Press, Nashville, Tennessee, is a good introduction.

P J Neville

170. RAYMOND B ISELY, LARDJA L SANWOGOU, JEAN F MARTIN. **Community organization as an approach to Health Education in rural Africa.** *Int J Health Ed,* Suppl to Vol XXII, No 3, July–September 1979.

Many health education projects implemented with energy and effort have failed to produce any long-term change in attitude or behaviour and such failures have raised honest doubts amongst medical personnel as to the value of health education. This paper describes a successful project in the rural areas of South Central Cameroon, which was initiated by the University of Pittsburgh–OCEAC Project.*

In 1970 a zone was established to facilitate field training of nurses following a short course in Public Health at the capital at OCEAC Headquarters.* The planners asked themselves two questions:

1. What approach should be used to promote health education amongst rural populations, and
2. What steps will be necessary to ensure that health personnel already at work in the area accept the health education approach, and by so doing ensure its continuity?

Out of the many approaches possible the one chosen here was the formation of village health committees in four pilot villages. Auxiliary nurses were trained as visiting health workers in order to assist the village health committees.

The authors then set out in some detail the steps involved in creating a village health committee, 'capable of a minimum of decision making and planning'. This eleven-step process which they call the 'critical pathway to achievement' was taught to the mobile health workers during their training. At monthly meetings the village health committee and the visiting health worker considered community health problems, ranked them in order of priority and selected one problem on which to work. A review of resources was made and finally the committee organized the villages for weekly work sessions in which the health worker took part.

In 1974, one year after the start of the project, eleven committees had been formed and the achievements included latrine construction (eleven committees reported this activity), protection of springs (nine committies), garbage pits (six) and animal enclosure (one). By 1975 the number of health committees had increased to thirty-nine and twenty-seven of them were involved in activities similar to those undertaken in 1974. Equally important was the fact that twenty-five committees were functioning well enough to be able to make plans for future work.

Anyone who has been involved in community development work or community health will be interested, not only in the achievements, but also in the problems encountered and particularly in how they were overcome. Problems include those

*Organisation pour la Coordination de la Lutte contre les Endémies en Afrique centrale (BP 288, Yaoundé, Cameroon).

connected with the rural exodus of people to urban areas, dissension within the village, lack of interest, transportation problems, lack of cooperation from officials and the reluctance of Government to spend scarce funds on village health committees. Project staff involved the Ministry of Health by keeping them well informed and asking them to inspect all the village work as it was completed. In this way disinterest was overcome and eventually gave way to a recognition that the people's participation was vital in any community health project.

In spite of all these problems the achievements after only four years work are impressive, and included: (a) a network of village health committees linked to health centres and to each other, via visiting health workers, (b) a resurgence of self-reliance in some villages, and (c) a concrete example of health education in action for future trainees.

There are also plans to establish a regional health education training centre for French-speaking Africa at the University of Yaoundé.

The visiting health worker was the key person in the project and this cadre of health staff already existed in the area, so health education was added to their function. Their main tasks were to advise established health committees and organize new ones. Additional training was necessary and this consisted of one month's theory and a month of supervised field training. The topics covered during the first month included preventable diseases, techniques of waste disposal, protection of water supplies, methods of health education, particulary emphasizing group work and community organization, the communication process, decision making and planning, basic knowledge about beliefs and practices and simple visual aids. Field work provided an opportunity for the practical application of new knowledge. This is a formidable undertaking in such a short time and unfortunately the article does not describe how the visiting health workers managed to adjust to their new role in the community or how well they were accepted by the village health committees.

This paper is important because it contributes to the debate about Primary Health Care. Active community involvement in Primary Health Care programmes has been endorsed in principle by the major national and international development agencies. It is not always clear however, precisely what the participation includes. A community might participate in policy making and management through health committees, as described in this paper, in evaluation or financial support of the programme, the actual delivery of the services, and as beneficiaries. But whatever form participation takes it does not happen spontaneously. It is a slow, deliberate process.

This paper also helps to clear up some of the doubts about the usefulness of health education. All too often health education is confused with 'health information', and while the latter involves radio talks, giving out pamphlets, pasting up posters and delivering health talks, the former involves modifying human behaviour – no small undertaking as this paper illustrates.

P J Neville

The following are reproduced with our grateful acknowledgement to the Bureau of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT

1. MICROBIOLOGY

171. JARIWALA HJ, KELKAR SS. **Fluorescence microscopy for detection of *M. leprae* in tissue sections.** *Int J Lepr,* 1979, v. 47, No 1, 33–36.

'The fluorescence method was compared with the Fite-Faraco method for detecting acid-fast microorganisms in paraffin sections of cases of leprosy. Biopsies were obtained from 50 cases of leprosy covering all varieties and at varying stages of treatment. The fluorescence method was better than the Fite-Faraco method; 22 biopsies showing acid-fast organisms in fluorescence microscopy and 20 in the Fite-Faraco method. Its superiority was evidenced in two cases in which the organisms were very scanty. Fluorescence

microscopy can also be used to determine the Bacterial Index and the Morphologic Index of organisms. The Morphologic Index, however, was one and a half times higher than that obtained by the Fite-Faraco technic. The ease and speed of fluorescence microscopy appear to be a great advantage.'

172. NGUYEN, HT *et al.* **Comparative ultrastructure of *Mycobacterium leprae* and *Mycobacterium lepraemurium* cell envelopes.** *J Bact,* 1979, v. 138, No 2, 552–558.

173. MORI T, KOHSAKA K. **Isolation culture of 7 strains of *Mycobacterium lepraemurium* and isonicotinic acid hydrazide or rifampicin-resistant Hawaiian strain.** *Jap J Lepr,* 1978, v. 47, No 3, 87–91. [In Japanese.] English summary.

174. CAMARGO EE, KERTCHER JA, LARSON SM, TEPPER, BS, WAGNER HN Jr, 1979 **Radiometric measurement of differential metabolism of fatty acids by *Mycobacterium lepraemurium.* *Int J Lepr* v. 47,** No 2, 126–132

2. IMMUNOPATHOLOGY

175. PRESTON PM. **Serum from infected mice suppresses macrophage-mediated immunity in *Mycobacterium lepraemurium* infection: a model for impaired macrophage immunity in human leprosy.** *Trans R Soc Trop Med Hyg,* 1979, v. 73, No 2, 212–215.

'Differing patterns of *Mycobacterium lepraemurium* infection in inbred strains of mice are of interest as a model system for studying mycobacterial infections of man, e.g. *M. leprae*, which present with a spectrum of clinical disease. *In vitro*, macrophages from both resistant (C57B1) and susceptible (BALB/c) inbred strains of mice can be shown to be equally effective in controlling multiplication of *M. lepraemurium*. Experiments presented here show that *in vivo*, the potential mechanisms of macrophage-mediated immunity are suppressed in the susceptible (BALB/c) strain of mouse by a soluble factor(s) present in the serum and the peritoneal fluid of infected mice.'

176. KIRCHHEIMER, WF, SANCHEZ RM, SHANNON EJ (1978) **Effect of specific vaccine on cell-mediated immunity of armadillos against *M. leprae.* *Int J Lepr*** 353–357.

Six 9-banded armadillos were vaccinated intramuscularly with 3.0×10^8 armadillo-passaged heat-killed leprosy bacilli in Freund's incomplete adjuvant. All were skin-test positive when challenged intradermally at 46 days with 4.0×10^7 *Mycobacterium leprae* (armadillo-derived) and at 8 months with *Myco. leprae*-derived protein. The lymphocytes of the vaccinated armadillos, with 1 exception, underwent significantly increased blast transformation in the presence of intact *Myco. leprae* A. Subsequently, the 6 animals plus 9 non-vaccinated armadillos were challenged by the intradermal inoculation of 10^6 living *Myco. leprae* A. Eight of the 9 non-vaccinated animals developed disseminated leprosy in from 11 months to 3 years. The remaining unvaccinated animal and 4 of the 6 vaccinated armadillos were still alive without signs of leprosy after 6 years' follow-up. 1 vaccinated armadillo died after 3 months from unrelated causes. The sixth was found to have leprosy when killed at 23 months.

M F R Waters

177. MENZEL S, BJUNE G, KRONVALL G. 1979 **Lymphocyte transformation test in healthy contacts of patients with leprosy. I. Influence of exposure to leprosy within a household.** *Int J Lepr,* v. 47, No 2, 138–152. **II. Influence of consanguinity with the patient, sex, and age.** *Ibid.,* 153–160

I. 'Fifty-three household contacts of

lepromatous patients, 37 household contacts of tuberculoid patients, and 91 control persons were examined with the lymphocyte transformation test (LTT) for their responses to whole and sonicated antigen preparations from *M. leprae*, to BCG, *M. avium, M. gordonae*, and phytohemagglutinin (PHA). The study was carried out in the Gurage area of Ethiopia in 15 households with a leprosy patient and 15 matched control households.

'Household contacts of lepromatous patients showed significantly greater LTT responses to antigens from *M. leprae* than the controls, whereas household contacts of tuberculoid patients did not respond differently from controls. Household contacts of lepromatous patients had significantly greater responses to *M. leprae* antigens when the index patients were 'active', i.e., highly bacilliferous, than when they were 'inactive', i.e., having a low bacillary load. The degree of sensitization, as indicated by the LTT response, in different exposure groups paralleled the degree of probable infectivity of the index patient.

'A preparation of antigen from whole *M. leprae* proved to be more sensitive and more specific in the LTT than did a sonicated preparation. A significant degree of cross-reactivity was found among the various mycobacteria in their LTT response.

II. 'The study was carried out in the Gurage area of Ethiopia, where 53 household contacts of lepromatous patients, 37 household contacts of tuberculoid patients, and 91 control persons were examined with the lymphocyte transformation test (LTT) for their responses to whole and sonicated antigen preparation from *M. leprae* to BCG, *M. avium, M. gordonae* and phytohemagglutinin. The potential influence of host factors, namely the state of consanguinity with the leprosy patient, sex and age on the LTT responses was evaluated.

'In the 35 household contacts of 'active', i.e. highly bacilliferous, lepromatous patients, consanguinity with a lepromatous patient was not associated with a significant depression of the LTT responses to *M. leprae* antigens. Male household contacts of active lepromatous patients showed significantly greater LTT responses to *M. leprae* antigens than female household contacts. Possible confounding factors for this finding are discussed. Sensitization of *M. leprae* antigens was present already in a high proportion of the 6- to 14-year-old household contacts of active lepromatous patients, which was the youngest age group examined in our study.

No significant results were found in any of the other patient contact groups with regard to the host factors examined.'

178. SCHEINBERG MA, MASUDA A, BENSON MD, MENDES NF (1979), **Serum amyloid protein SAA, C-reactive protein and lysozyme in leprosy.** *Int J Lepr* v. 47, No 2, 133–137

179. FABER WR, LEIKER DL, NENGERMAN IM, SCHELLEKENS PTA. **A placebo controlled clinical trial of transfer factors in lepromatous leprosy.** *Clin Exp Immunol,* 1979, v. 35, No 1, 45–52.

'The effects of repeated injections of transfer factor over a period of 20 weeks were investigated in fourteen bacteriologically positive patients at the lepromatous side of the leprosy spectrum. All patients showed negative (0 mm induration) skin tests to *M. leprae* antigens (i.e. leprolin and lepromin). Of these patients, seven were treated with transfer factor with a total of 9 units (1 unit being equivalent to 5×10^8 lymphocytes) and seven with a placebo. Maintenance treatment with clofazimine was continued.

'Transfer factor was prepared from the lymphocytes of donors who showed positive skin tests to *M. leprae* antigens (i.e. leprolin $\geqslant$ 12 mm induration, average 15.5 mm or lepromin $\geqslant$ 8 mm induration, average 13.6 mm), as well as a positive lymphocyte transformation *in vitro* to *M. leprae* (the average transformation being higher than the average transformation of lymphocytes of tuberculoid leprosy patients).

'No differences were found between the two groups as regards the clinical course of the disease, the histopathological and

bacteriological evaluation of skin biopsies, changes in skin test reactivity to various antigens (i.e. lepromin, leprolin, PPD, *Mumps, C. albicans, Tr. rubrum* and Varidase), as well as the lymphocyte transformation *in vitro* to various mitogens (i.e. PHA, PWM, Con A) and antigens (i.e. *M. leprae*, leprolin, PPD, BCG, *Mumps, C. albicans, Trichophyton* and Varidase).

'No evidence was found to suggest that transfer factor is a valuable adjuvant in the treatment of lepromatous leprosy patients or that it increases cell-mediated immune reactivity towards *M. leprae*.'

180. WATERS MFR, BAKRI BIN HJ, ISA MD, REES RJW, MCDOUGALL AC. **Experimental lepromatous leprosy in the white-handed gibbon (*Hylobatus lar*): successful inoculation with leprosy bacilli of human origin.** *Br J Exp Path,* 1978, v. 59, No 6, 551–557.

'Leprosy bacilli of human origin were inoculated into a white-handed gibbon by the i.v. and i.p. routes, and also locally into ears, testis and around an ulnar nerve. The animal was observed closely during a period of nearly 15 years and did not exhibit any clinical evidence of cutaneous or neurological disease. At death, a wide range of tissues was taken for bacterial counts and histological examination, and a disseminated and progressive infection was demonstrated. Acid-fast bacilli were found in many sites; their morphological appearance distribution in nerves and pattern of multiplication in mouse footpads, and also the presence of anti-mycobacterial antibody in the serum and the absence of specific lymphocyte transformation were all keeping with an infection by *Mycobacterium leprae*, at an early lepromatous stage. This is probably the first fully documented report of experimental lepromatous infection in a primate. The findings are discussed in relation to the long incubation period of lepromatous leprosy and the difficulties of diagnosing the disease at an early stage in man.'

181. CHAKRABARTY MS, MUKHERJEE KK, CHAKRABARTY SK, GHOSH S, CHOUDHURY S, **Hepatitis B surface antigen (HBsAg) in leprosy patients of Calcutta: its prevalence and subtypes.** *Leprosy in India,* 1979, v. 51, No 2, 182–188.

Sera collected from 234 patients with lepromatous leprosy, 431 patients with tuberculoid leprosy and from 519 other patients attending an out-patient clinic in Calcutta were tested for hepatitis B surface antigen by counter-immunoelectrophoresis. The surface antigen was detected in 3.8% of the patients with lepromatous leprosy, in 2.5% of the patients with tuberculoid leprosy and in 1.7% of the control patients. These differences were not statistically significant.

[These results differ from those of most other reports showing an increased incidence of the surface antigen in patients with lepromatous leprosy. The difference could be due to the insensitivity of the technique used, although similar methods were employed in the earlier studies, or to the fact that the patients were not resident in institutions. The subtyping results are difficult to interpret, but it is noted that antigen with the *ay* determinants was common in Calcutta.]

A J Zuckerman

182. FABER WR, LEIKER D, NENGERMAN IM, ZEIJLEMAKER WP, SCHELLEKENS PTA. **Lymphocyte transformation test in leprosy: decreased lymphocyte reactivity to *Mycobacterium leprae* in lepromatous leprosy, with no evidence for a generalized impairment.** *Infection & Immunity,* 1978, v. 22, No 3, 649–656.

'Untreated leprosy patients were examined with respect of lymphocyte transformation *in vitro* after stimulation with mycobacterial and other microbial antigens, allogeneic lymphocytes, or nonspecific mitogens. Methods were used to circumvent technical variability. The results were compared with those obtained in controls matched for age, sex, race and environment. No evidence was found for a generalized impairment of

lymphocyte transformation *in vitro*, whereas a specific defect towards *Mycobacterium leprae* was demonstrable in lepromatous leprosy patients. The response to *M. leprae*, investigated in untreated and treated leprosy patients, decreased along the leprosy spectrum. Moreover, the results of the one-way mixed lymphocyte cultures showed that lymphocytes from leprosy patients had a normal stimulator and responder capacity, when they were tested against a panel of allogeneic lymphocytes. The influence of serum factors was investigated in untreated leprosy patients in the mixed lymphocyte culture. On average, tuberculoid as well as lepromatous sera showed that a low-level depressive effect of serum factors cannot be considered to be a general feature of leprosy. The correlation between the Mitsuda type of lepromin skin test and the lymphocyte reactivity *in vitro* to *M. leprae* was studied, and a positive correlation was found.'

183. SMELT AHM, LIEW FY, REES RJW. **Lymphocyte response of leprosy patients to human-derived and purified armadillo-derived** *Mycobacterium leprae,* **BCG and PPD.** *Clin Exp Immunol,* 1978, v. 34, No 2, 164–169.

'The lymphocyte transformation test was applied to compare *in vitro* lymphocyte responses of tuberculoid (high resistant) and lepromatous (low resistant) leprosy patients to purified *Mycobacterium leprae* derived from experimentally infected armadillos and crude *M. leprae* derived from man, as well as to bacille Calmette-Guérin (BCG) and purified protein derivative (PPD). It was found that the purification procedure using enzymic digestion did not affect the immunogenicity of armadillo-derived *M. leprae* as compared with the crude human-derived preparation, although 2.5–5-fold higher doses of the purified organisms were required to elicitate equivalent lymphocyte responses. The result indicated the suitability of purified armadillo-derived *M. leprae* as the standard antigen for lymphocytes transformation tests in leprosy. The cross-reactivity studies show a close relationship between PPD and BCG, but not between *M. leprae* and PPD or BCG.'

184. CAUZZI NJ, CORONA CJ, LONDNER MV, MORINI JC. **Immonologic skin titration in leprosy patients and contacts.** *Int J Lepr,* 1979, v. 47, No 1, 13–17.

'A method of studying delayed-type hypersensitivity was developed with specific antigen in leprosy patients and contacts, measuring the dose-response curve at different lepromin concentrations. This 'immunologic titration' is highly efficient for discriminating the degree of hypersensitivity reactions among the groups tested.

'With respect to the Fernandez reaction, the results obtained showed that there was a similar behaviour in all groups studied, except in the tuberculoid group which had a more intense response, four times higher than that yielded by contacts of lepromatous patients.

'In the Mitsuda reaction, a similar behaviour was also found among the different groups, except with respect to the reactivity intensity of contacts of lepromatous patients. Here it was demonstrated that this group had a significant depression in response to *M. leprae* antigen when compared with that from the other groups, independent of the degree of consanguinity or closeness to bacilliferous cases.

'In order to explain this immunosuppression in contacts of lepromatous patients, a hypothesis is proposed. It is suggested that changes could occur in *M. leprae* derived from lepromatous patients, diminishing their capacity to produce an adequate immune response.'

185. BJUNE G. *In vitro* **lymphocyte stimulation in leprosy; simultaneous stimulation with** *Mycobacterium leprae* **antigens and phytohaemagglutinin.** *Clin Exp Immunol,* 1979, v. 36, No 3, 479–487.

'Peripheral blood lymphocytes from 105 subjects with different forms of leprosy and

healthy contacts of leprosy patients were stimulated *in vitro* with different preparations of mycobacterial antigens alone or in combination with a suboptimal dose of phytohaemagglutinin (PHA). In nearly all individuals sonicated leprosy bacilli and PHA together gave a lower ^{3}H-thymidine incorporation than did the same dose of PHA alone. There was no difference in the degree of inhibition seen in the different patient groups or the healthy contacts. High doses of whole, washed *Mycobacterium leprae*, combined with PHA led to an increased thymidine incorporation in borderline tuberculoid leprosy patients who had experienced a reversal reaction, and in healthy contacts with more than 6 months of exposure, while most lepromatous patients and contacts with less than 6 months exposure did not show an augmentation of the PHA-induced thymidine incorporation. The inhibition exerted by sonicated *M. leprae* was dose-dependent, seen even with very low doses of antigen, and was not due to direct cytotoxicity. *M. bovis*, strain BCG, was weakly suppressive in combination with PHA, and sonicated *M. duvalii* had a very marked suppressive effect. There was no correlation between the suppressive effect of *M. leprae* antigens and the other mycobacteria neither was there any correlation with the responses to the mycobacterial antigens alone. Many lepromatous leprosy patients showed significant suppression of background incorporation with addition of *M. leprae* antigens. This paper discusses whether the apparent 'non-responsiveness' in lepromatous leprosy could be due to active suppressor mechanisms operative *in vivo*.'

186. SENGUPTA U, SINHA S, RAMU G. **Immunological assessment of sera of leprosy patients.** *Lepr India*, 1979, v. 51, No 1, 43–48.

'IgG levels were significantly high in sera of all types of leprosy. Household contacts of lepromatous leprosy (LL) cases also showed significantly higher values for IgG when compared to that of control. Except polar tuberculoid (TT) cases and household contacts other types of leprosy revealed a significant rise in IgA levels in their sera. IgM was only raised in borderline tuberculoid (BT) cases.

'C-reactive protein (CRP) was present in the sera of all types of leprosy. Highest positivity (97%) was shown by sera from erythema nodosum leprosum (ENL) cases. Rose-Waaler antibody (RA) was noted in BT, borderline leprosy (BL), LL and ENL cases. Significance of these findings is discussed.'

187. SAHA K, AGARWAL SK. **Immune deficit in patients with lepromatous leprosy: its nature and relation to genetic factors, spectrum, and duration of the illness.** *Int J Lepr*, 1979, v. 47, No 1, 1–6.

'Cell-mediated immunity or hypersensitivity to *M. leprae* and other unrelated antigens, such as tuberculin and dinitrochlorobenzene, was studied in 73 leprosy patients of different histopathologic types. It was found that specific as well as non-specific anergy intensified as the disease spectrum shifted from the tuberculoid toward the lepromatous immunologic pole. Within the lepromatous group, the impairment of cellular immunity became more pronounced as the bacillary load increased. It was found that the impairment of the cell-mediated immunity towards antigens other than *M. leprae* became more severe as the duration of the illness increased.

'Late lepromin responsiveness, which is the hallmark of resistance of an individual to *M. leprae*, may be absent even before the onset of clinical illness. Its deficit seems to be primary and has a genetic predisposition.'

188. BHARADWAJ VP, VENKATESAN K, RAMU G, DESIKAN KV. **Glucose tolerance and serum free fatty acid levels in leprosy.** *Indian J Med Res* v. 69 (April), 567–570.

189. KELKAR SS, MONDKAR AD, WARAWDEKAR W. **Serum immunoglobulins in leprosy.** *Lepr India,* 1979, v. 51, No 2, 189–193.

'Serum immunoglobulins were quantitated by radial immunodiffusion in 25 cases each of tuberculoid and lepromatous leprosy. Immunoglobulins estimated from 50 normal healthy adults were the control. Serum IgG was markedly raised in both tuberculoid (mean 2420 mg/dl) and lepromatous leprosy (mean 2493 mg/dl) when compared with the controls (mean 1288 mg/dl) and the difference was significant ($p < 0.01$). However the difference in serum IgM and IgA levels in cases as compared to controls were not statistically significant. Serum IgM was slightly raised, the mean values obtained being 222 mg/dl in tuberculoid leprosy, 221 mg/dl in lepromatous leprosy and 202 mg/dl in control. Serum IgA was reduced in lepromatous leprosy (mean 129 mg/dl) as compared to the controls (mean 168 mg/dl) and the cases of tuberculoid leprosy (mean 165 mg/dl). The range of values obtained in both groups of patients showed greater scatter than the controls and a few cases of both forms of leprosy showed very low values of both serum IgA and IgM.'

190. MARKS SC Jr. **The cellular basis for extremity bone loss in leprosy.** *Int J Lepr,* 1979, v. 47, No 1, 26–32.

Skeletal lesions in leprosy consist of distal absorption of digits, osteoarthritis, osteomyelitis and osteoporosis. Previous work had suggested that anaesthesia and paralysis were not always major factors. The present study consisted of a histological examination of 60 samples of bone from 5 patients, lepromatous and tuberculoid, for acid-phosphatase activity. Functional osteoclasts and osteolytic osteocytes were demonstrated in areas of resorption in both forms of leprosy. It is suggested that this bone resorption is an acceleration of a normal process which might be caused by release of factors from *Mycobacterium leprae* or stimulated host cells.

D S Ridley

191. BIRDI TJ, SALGAME PR, ANTIA NH. **The role of macrophages in leprosy as studied by protein synthesis of macrophages from resistant and susceptible hosts – a mouse and human study.** *Lepr India,* 1979, v. 51, No 1, 23–42.

'^{3}H-leucine uptake by macrophages from swiss white and C57BL mice before and after *M. leprae* infection was studied. A depression in ^{3}H-leucine uptake after infection was observed only in swiss white mice. ^{3}H-leucine uptake was also studied in blood derived macrophages from normals, and LL and TT patients. A depression was obtained in ^{3}H-leucine uptake after *M. leprae* infection in macrophages from LL patients.'

192. SHARMA S, GANGULY NK, KUMAR B, KAUR S, CHAKRAVARTY RN. **T and B lymphocytes and blastogenesis in leprosy.** *Lepr India,* 1979, v. 51 No 2, 194–202.

'T and B cell percentages and their blastogenic response to PPD and lepromin have been studied in 107 patients of various types of leprosy. T cell counts and their blastogenic response were found to be considerably lower in all types of leprosy as compared to the normal. The counts and stimulation were the lowest for lepromatous leprosy. B cell counts were unaltered in all types of leprosy.'

193. MAHRA V, BLOOM BR. **Induction of cell-mediated immunity to *Mycobacterium leprae* in guinea pigs.** *Infection & Immunity,* 1979, v. 23, No 3, 787–794.

194. ALEXANDER J, CURTIS J. **Development of delayed hypersensitivity responses in *Mycobacterium lepraemurium* infection in resistant and susceptible strains of mice.** *Immunology,* 1979, v. 36, No 3, 563–567.

[An abstract of this paper appeared in *Abstr Hyg,* 1979, v. 54, abstr. 1554.]

195. IBRAHIEM AA, AWAD HA, METAWI BA, HAMADA TAY. **Pathologic changes in testis and epididymis of infertile leprotic males.** *Int J Lepr,* 1979, v. 47, No. 1, 44–49.

196. MASALA C, AMENDOLEA, MA, NUTI M, RICCARDUCCI R, TARABINI CGL, TARABINI CG. **Autoantibodies in leprosy.** *Int J Lepr,* 1979, v. 47, No 2, 171–175.

197. SHARDA DP, PARVEZ M, JAIN AK, BHARGAVA NC, MISRA, SN. **A study of serum fibrinolytic activity in leprosy.** *Lepr India,* 1979, v. 51, No 2, 203–208.

198. COLE FS, BRUSCH JL, TALARICO, L. **A circulating anticoagulant in lepromatous leprosy.** *Int J Lepr,* v. 47, No 2, 121–125

3. CLINICAL

199. CARRICA A, FAUXPOINT B, LABAT P, RIVAUD C, VEDY J. Manifestations ophtalmologiques de la lèpre. **[Ocular lesions in leprosy.]** *Méd Trop,* 1979, v. 39, No 3, 301–306.

'Modern authors estimate from 47 p. 100 to 78 p. 100 the frequency of ocular lesions in leprosy. This frequency varies according to the duration and type of the disease.

'These lesions may result from a paralysis of the V or VII cranial nerves or from a bacteremia, but, more probably, from a spreading of the bacilli from the nasal cavity through the lacrymal ducts. The various lesions of each ocular structure are described with reference to the T. or L. type of leprosy.'

200. SMITH WCS. **Screening for diabetes mellitus in leprosy. Patients with complicated ulcers.** *Lepr India,* 1979, v. 51, No. 2, 236–238.

'All patients admitted to an ulcer ward in a leprosy hospital [in India] over the period of one year were screened for glycosuria. Out of 154 patients screened 4 showed glycosuria. These 4 patients had more severely complicated ulcers evidenced by their longer duration of admission. Early diagnosis and treatment of diabetes in leprosy patients with complicated ulcers is important.'

201. NAAFS B, PEARSON JMH, WHEATE HW. **Reversal reaction: the prevention of permanent nerve damage. Comparison of short and long-term steroid treatment.** *Int J Lepr,* 1979, v. 47, No. 1, 7–12.

The authors studied carefully scored, serial voluntary muscle tests (VMT) in borderline (BT, BB and BL) leprosy patients undergoing reversal (upgrading, type 1 or borderline lepra) reactions on dapsone therapy. Patients treated between 1974 and 1978 continued to receive dapsone in full dosage. In addition they were treated with prednisolone, 30–40 mg daily initially and subsequently the dose was only slowly lowered so that in the second month they were still receiving 20–30 mg daily with a further gradual reduction of dosage so that steroids were continued for another 3 to 18 months depending upon the patient's classification and severity of reaction. The VMT results were compared retrospectively with those of patients treated between 1968 and 1974. The latter patients received only short courses of prednisolone either in an initial dosage of 15 mg daily for 1 week reducing to 5 mg daily in the second month and then stopping or else they were treated for the first week with 45–60 mg daily and subsequently the prednisolone was very rapidly reduced so that they too only received 5 mg daily during the second month of therapy. In addition, dapsone was discontinued for the first 1 to 2 weeks and often only restarted in low dosage. The prolonged steroid regimen of the years 1974 to 1978 was shown to be more effective in preventing nerve damage and in aiding recovery than the short-term steroid regimens used in previous years. In addition it was shown to

be without serious side-effects in the population studied [Although this is a retrospective comparison, the results have important implication for the treatment of reversal reactions, and the paper should be studied by all those interested in the treatment of such reactions whether working in hospital or in leprosy control programmes.]

M F R Waters

202. KOTICHA KK, NAIR PRR. **Treatment defaulters in leprosy: a retrospective study of 42,000 cases.** *Int J Lepr,* 1979, v. 47, No 1, 50–55.

The figure of 42,000 (which refers to the number of defaulters, not the total number of patients in the period studied) is a powerful reminder of the magnitude of the leprosy problem in India; the study is based on cases registered in Bombay only. The authors report findings from a total of nearly 80,000 patients registered at the Acworth Leprosy Hospital during the 25-year period 1950–1974. Deducting those who were not resident in Bombay, together with those who had died, been referred to other centres, or for whom no information was available, they arrive at a final total of 48,345 cases on which this important retrospective study is based.

From this total, only 6,345 (13.12%) were taking treatment regularly on the basis of 'taking treatment for nine months a year for a minimum period of three years'. Thus 42,000 patients (86.9%) had dropped out of treatment. Both regular and 'drop-out' cases are analysed with respect to age, sex, infectivity, degree of deformity, stage of their disease, source of referral and occupation. The conclusions form a pattern which is at times rather complex (for instance '. . . Deformity and regularity, contrary to expectations, are inversely related except in the case of students, industrial workers and the white collar class.') but none of them is as important as the first sentence in the discussion which reads quite simply: 'The drop-out rate in Bombay is alarming.'

The message of this study is that patients do not attend for the treatment periods which have been advised – and even extended in recent years – for the drug treatment of leprosy. Similar analyses from other parts of India, and from other endemic areas are essential if we are to devise realistic programmes of drug treatment for patients with this disease.

A C McDougall

203. NIGAM P, DUBEY AL, DAYAL SG, GOYAL BM, SAXENA HN, SAMUEL KC. **The association of leprosy and pulmonary tuberculosis.** *Lepr India,* 1979, v. 51, No 1, 65–73.

Pulmonary tuberculosis was diagnosed in 20 of 793 patients [? out-patients] under treatment for leprosy in a region of India [not named] during the period January 1972 to October 1977, an incidence rate of 2.5%. These 20 patients are described in respect of age, sex, and leprosy type, together with details of their tuberculosis such as clinical presentation and response to treatment: 11 patients improved; 5 'could not be followed', and 4 died. These fatal cases were elderly with extremely poor general condition and nutrition. However, the authors give no details of the 793 leprosy patients, nor any statistics of the general run of tuberculosis patients in that particular region, so no comparisons can be made.

204. BRYCESON A, PFALTZGRAFF RE. **Leprosy. 2nd edition.** pp. vii + 154. 1979. Churchill Livingstone, 23 Ravelston Terrace, Edinburgh EH4 3TL. [ISBN 0 443 01588 0] [£4.00]

This second edition, thoroughly revised and in part rewritten, emerges as an excellent little manual intended for the practitioner in the tropics who wants to be able to recognize and understand and treat leprosy. Although the (black and white) illustrations are mainly of lesions in the deeply pigmented Bantu skin and some of the text reveals its African orientation, the book will appeal

to medical workers in all countries, particularly those brought up in the stimulating atmosphere of modern immunological ideas and concepts.

The pathological basis for the variety of clinical manifestations as well as for the different types of 'reaction' in leprosy is particularly well covered. The section on treatment takes cognizance of recent findings concerning dapsone resistance and persister organisms, viable but drug sensitive. While most of the recommendations are unquestionable, it should be pointed out that (a) thiambutosine is no longer on the market (pp. 45–46); 4% boric acid lotion to treat or prevent infection of the exposed conjunctiva (p. 95) would not commend itself to many ophthalmologists today; and (c) the strict injunction 'never attempt to operate directly on nerves' (p. 108) would be challenged by many practising and experienced surgeons.

The proof-reading of this edition is much better than that of the first, but 'epithelioid' (p. 5), 'bacteriostatic (pp. 42, 46, 123) and 'bactericidal' (p. 122) appear under various incorrect guises.

The social aspect of the care and management of leprosy sufferers has not been neglected in this edition, nor has the organization of a leprosy programme and ancillary services.

S G Browne

205. KERR JM. **Social factors operating against effective leprosy control in the highlands of Papua New Guinea.** *Hansenologia Internationalis,* 1978, v. 3, No 1, 83–86.

206. KAUR S, MALIK SK, KUMAR B, SINGH MP, CHAKRAVARTY RN. **Respiratory system involvement in leprosy.** *Int J Lepr,* 1979, v. 47, No 1, 18–25.

207. OSAKA R. **[A survey of the social situations of leprosy patients in JALMA Leprosy Centre, Agra, India I. Survey on the medical aspects of in-patients.]** *Jap J Lepr,* 1978, v. 47, No 3, 92–98. [In Japanese.] English summary.

208. DUTTA RK. **A study of patients with erythema nodosum leprosum syndrome.** *Leprosy in India,* 1979, v. 51, No 2, 209–212.

'25 cases of Erythema Nodosum Leprosum (ENL) Syndrome have been clinically evaluated. Majority patients (84%) were males in the middle age group. Fever (56%), arthralgia (100%) and neuritic pains (100%) were common presenting constitutional symptoms. ENL was not related to DDS therapy or to any precipitating factors. Severity of reaction graded by clinical scoring was well correlated with fibrinolytic activity. Fibrinolytic activity was found decreased in all the cases. The decreases in fibrinolytic activity was more so pronounced in patients having higher clinical scorings.'

209. BROWNE SG. **The diagnosis and management of early leprosy for medical practitioners.** Revised edition. 35 pp. 1979. The Leprosy Mission, 50 Portland Place, London W1N 3DG.

This booklet (pocket-sized, 12 by 18 cm) is aimed, as the author says in the introduction, at dispelling '. . . ignorance among medical men, particularly in those countries where leprosy does not constitute a major problem . . . ' It is, however, so well written and comprehensive that it may well have an application to those working, or intending to work, in the main endemic areas – for the early and correct diagnosis of this disease is not invariably easy, even to those with experience. There are 16 colour plates and although the quality is for the most part excellent, the selection in a few instances calls for comment; thus – the lesion at the angle of the mouth in Fig. 1 may be macular, but those shown nearest the camera in Fig. 3 appear to be raised, especially at the edges. Fig. 13 does not reproduce well to show 'Many large ill-defined lesions' and the extent and severvity of the lesion shown on the face, neck and ear in Fig. 16 raises a question as to the definition of 'early' in this context.

These are minor criticisms and in no way

detract from the overall value of this booklet. The section on management includes a description of drug treatment for leprosy, which essentially follows the recent recommendations of WHO. In view of the currently prevailing advice that dapsone should be given in full dosage from the outset in all types of leprosy, it is, however, of particular interest that Dr Browne has added the following paragraph on the treatment of borderline leprosy: 'Because in some countries dapsone given initially at the maximum dose . . . appears to be associated with the appearance of reversal reaction, care should be exercised in treating patients with borderline lerposy. In such patients, a gradual build-up of dosage is advocated by some authorities.'

A C McDougall

210. CHACKO CJG, BHANU T, VICTOR V, ALEXANDER R, TAYLOR PM, JOB CK. **The significance of changes in the nasal mucosa in indeterminate tuberculoid and borderline leprosy**. *Lepr India,* 1979, v. 51, No 1, 8–22.

'A study of nasal biopsies from 137 leprosy patients classified on the basis of clinical, microbiological and skin biopsy as Indeterminate, Tuberculoid, Borderline-tuberculoid and Borderline-leproma was undertaken. Changes suggestive of leprosy viz., nerve and smooth muscle inflammation with a few acid fast bacilli in a proportion of the biopsies were seen in all groups of patients examined. This suggests, that even in Indeterminate and Tuberculoid leprosy the disease becomes generalized by the time clinical manifestations appear in skin. Tuberculoid granuloma was seen in two nasal biopsies from Borderline-tuberculoid leprosy patients, one of which was located in the wall of a vein, suggesting the possibility of intravascular dissemination of the disease even in non-lepromatous leprosy. 33 of the patients were children 15 years and below and they also showed changes such as nerve and smooth muscle inflammation but bacilli were seen only in the Borderline group. These findings suggest involvement of the nasal mucosa early in the course of the disease as 70% of the children had the skin lesion for less than one year . . . '

211. BROWNE SG. **Organizing a leprosy control programme.** *Trop Doctor,* 1979, v. 9, No 2, 93–96.

4. THERAPY

212. LANGUILLON J, YAWALKAR SJ, MCDOUGALL AC. **Therapeutic effects of adding rimactane (rifampicin) 450 milligrams daily or 1200 milligrams once monthly in a single dose to dapsone 50 milligrams daily in patients with lepromatous leprosy.** *Int J Lepr,* 1979, v. 47, No 1, 37–43.

The objective of this 6 months' trial was to compare the effects of adding rifampicin 450 mg daily or 1200 mg once a month to a standard dapsone regimen of 50 mg daily in 30 patients suffering from lepromatous leprosy and previously untreated. Patients were allocated by a randomized code to one or other of the 2 treatment regimens, 15 to group A (daily rifampicin) and 15 to group B (monthly rifampicin). Assessment of progress was based on clinical examination, skin smears, nose-blow smears, and skin biopsies. Results are clearly shown in a series of tables, and from these it can be seen that results were good and practically identical in both groups. Treatment was discontinued in 2 patients in group A because of 'severe ENL and haemolytic anaemia' in one and 'haemolytic anaemia and icterus' in the other, but all 15 patients in group B completed the trial. 2 patients in group B required treatment for severe neuritis, and a third was found to have haemolytic anaemia at the end of the trial. Comparing the 2 treatment regimens the authors favour the addition of rifampicin on a monthly basis because it is better tolerated and the reduction in cost is substantial.

W H Jopling

213. RUSSELL DA, WORTH RM, JANO B, FASAL P, SHEPARD CC. **Acedapsone in the prevention of leprosy: field trial in three high prevalence villages in Micronesia.** *Amer J Trop Med and Hygiene,* 1979, v. 28, No 3, 559–563.

'The 1,659 non-leprous people in a Micronesian population experiencing an. annual leprosy incidence rate of about 7/1,000 were offered 15 acedapsone (DADDS) injections during 1967–1970 for leprosy prevention purposes. Subsequent annual surveillance showed an initial cessation of new cases during the 3-year DADDS campaign, followed by a resumption of cases thereafter at a yearly level of about 2/1,000, with a longer pause and slower rise among those who received the full regimen. A secondary wave of cases that has occurred since 1973 among children born after 1968 shows that post-campaign transmission occurred, probably principally from relapsing multibacillary cases with onset before the campaign. Recommendations are made for a balanced, long-term control program with DADDS preventive treatment limited to contacts of multibacillary cases.'

214. LEIKER DL. De chemotherapie van lepra. I. Sulfonen en sulfonamiden. [**Chemotherapy of leprosy. I. Sulphones and sulphonamides.**] *Ned Tijdschr Geneesk,* 1979, v. 123, No 23, 969–972.

5. MISCELLANEOUS

215. LEPR. REV., 1979, v 50, No 1, 51–58. **XI International Leprosy Congress, Mexico City 1978.** [Binford CH, Chairman]

A useful summary of the seven workshops at the Congress, one of which drew a thousand people, and for which 333 abstracts were printed in three languages.

The workshops were on experimental leprosy, microbiology, immunology, experimental chemotherapy, epidermiology and control including field therapy, human aspects, and on teaching materials for leprosy workers.

It is interesting to note that in experimental leprosy the immunologically deficient mouse has been joined by the armadillo, the nude mouse, the thymectomized rat, the hedgehog, the Korean chipmunk, as Dr Stanley Browne points out in an editorial on the Congress. Large quantities of *Mycobacterium leprae* are now required by, and supplied to, the World Health Organization Immunology in Leprosy Programme. This account of the Congress, and the editorial, provide an invaluable account of the state of play in leprosy work today.

Ralph Schram

216. MATTHEWS CME, JESUDASAN M. **A leprosy health education project.** *Int J Lepr,* 1979, v. 46, No 4, 414–425.

'Results of a survey of knowledge and attitudes of the general public towards leprosy and knowledge, attitudes and practices of leprosy patients are reported. This survey is the base line for a health education project, based on social psychological theories of behaviour, which is described. The results of the survey show that the general public has very little knowledge about leprosy; patients have more knowledge. Attitudes measured with a Likert scale are negative for the general public and only slightly positive for the patients. Allopathic treatment for leprosy is preferred by most, but many do not relate the 'patch' to leprosy and therefore do not seek early treatment. There is much need for health education.'

[A study in the Christian Medical College, Vellore, India.]

217. VOGELSANG TM. **Gerhard Henrik Armauer Hansen, 1841–1912.** *Int J Lepr,* 1979, v. 46, No 3, 257–332.

In the same number of the journal that carries his own obituary, the author, with his wealth of knowlege of the Hansen family and their home town of Bergen, has given us this detailed and beautifully written account

of the life work of Gerhard Henrik Armauer Hansen.

It is well illustrated, with photographs of Hansen, Danielssen, the house of master-shoemaker Andreas Michelsen Schram (Hansen's grandfather), and the Claus Hansen family of 13 children, including Gerhard at the age of 13 years. There are 54 references, 3 pages of important names in the story, and 3 appendices giving lists of 58 publications by Hansen on leprosy and 101 on other topics, 13 of the author's earlier publications on Hansen, and a genealogy.

It would be worth buying this number for this article alone. It was originally published in Norwegian and we are indebted to Anwei Skinsnes for the editing, amendment and improvement of the translation into English started by the author.

Ralph Schram