

BIBLIOTECA
CURRENT LITERATURE

This department carries selected abstracts of articles published in current medical journals dealing with leprosy and other mycobacterial diseases.

General and Historical

Basset, A. Quand penser à la lèpre? (When to think of leprosy?) *La Revue du Praticien* **28** (1978) 3625–3640. (in French)

Leprosy should be suspected in subjects coming from or having lived in endemic regions and presenting with very diverse symptoms: disorders of skin pigmentation, skin nodules and infiltrates, nervous system involvement, trophic disorders, and systemic disease. Diagnosis rests on the discovery of Hansen's bacilli in lepromatous leprosy, and on demonstration of neural disorders in tuberculoid and borderline leprosy.—Author's Summary

Browne, S. G. La lèpre—une vue d'ensemble. (Leprosy: an overview.) *Ann. Soc. Belg. Med. Trop.* **59** (1979) 5–9. (in French)

This review article summarizes the information available to leprosy researchers as of the XI International Leprosy Congress in November 1978, in Mexico City. Under epidemiology, it is pointed out that incomplete knowledge exists about the prevalence of leprosy worldwide as well as of the number of persons suffering from each type of the disease; much is known about the source of the infection and its portals of entry though far less is known about how to identify those persons in the population who are more likely to contract the disease because of a specific immune deficit. Under immunology, the author discusses the role of T lymphocytes in determining the degree of resistance to leprosy and, if contracted, the type of leprosy a person will get; he further briefly summarizes research dealing with nonspecific and specific antigens as well as attempts to discover a biochemical substance capable of stimulating lymphocyte recognition of *M. leprae*. Under mi-

crobiology, recent attempts to cultivate *M. leprae* in the armadillo, mouse footpad, thymectomized rat, nude mouse, hedgehog, and Korean chipmunk are mentioned as well as the possible existence of a leprosy-like disease in wild armadillos and the possibility of the transmission of the bacillus through insect bites. Under peripheral nerves, the growing interest of physicians and researchers in the pathogenesis of peripheral nerve lesions and in the use of immunofluorescence studies of immune complexes is cited as well as the beneficial effects obtained through the use of surgery and corticosteroids. Under therapy, the author cites the increasing evidence of dapsone resistance and the dangers of monotherapy.—(Summarized from article)

Northern Territory Department of Health (Australia). Leprosy Policy. Darwin, 1979. 25 pp.

This work serves the dual purpose of detailing the leprosy control objectives of the Northern Territory Department of Health as well as providing an excellent general introduction for the nonspecialist to the basic areas of leprosy identification and control. It begins by tracing the origins of leprosy in the Northern Territory, particularly among the Aboriginal peoples, and states that the three present public health goals of the Department of Health are: 1) to control the spread of leprosy; 2) to treat new cases; and 3) to provide long-term orthopedic care and rehabilitation for patients with disability and deformity. In its discussion of clinical leprosy, the work presents basic information concerning signs and symptoms, types of leprosy, peripheral neuropathy, treatment (dapsone, acedapsone, thiambutazone, clofazimine, and rifampin are dis-

cussed), prevention, and care and repair of disability and deformity. The document continues by discussing the management and control of the disease, dealing with the proper administration of drugs to inpatients and outpatients, rehabilitation, the administrative structure of staff, and delineation of rural areas and their responsibilities. The document stresses the importance of using Aboriginal health workers for screening and basic care of leprosy in rural areas, the need for integrating leprosy screening into other basic public health services, and the "stated aim to cover the population in screening once in every five years, the final date for the present five yearly period being the end of 1980."—G. Gordon

Pelletier, P. L'Institut Marchoux: centre de recherches et de soins pour lepreux (The Marchoux Institute: center for research and care for persons with leprosy). *L'Infirmière Canadienne* **20** (1978) 16–19. (in French)

The author summarizes the principal activities that occur at the Marchoux Institute in Bamako, Mali. Research activities deal with activities such as epidemiology, prevention of complication through proper treatment, and providing human and biological leprosy material to other leprosy research centers to aid in their investigations. The article describes the routine clinical examinations and tests performed on a patient entering for treatment as well as elements involved in the continuing care of patients such as treatment of reactions. It is stressed that for persons living at the center that every attempt is made to preserve for them as much as possible the basic elements of village life to which they have been accustomed. Emphasis is also laid on the idea that the center is committed to providing care and assistance to persons afflicted with leprosy in all the French-speaking countries of Western Africa.—G. Gordon

Research in leprosy (A report of a committee set up by the Medical Research Council to study future prospects). *Clin. Exp. Immunol.* **36** (1979) 1–7.

Recommendations for future research in leprosy include (i) cultivation of *M. leprae*

in vitro; (ii) genetic control of susceptibility, including twin studies and HLA typing; (iii) precise antigenic analysis of *M. leprae*; (iv) mechanisms involved in the macrophage response to mycobacterial infections; (v) more use of experimental models such as normal mice infected with *M. lepraemurium*; (vi) reassessment of the protection afforded by BCG; (vii) assessment of protection afforded by killed (armadillo) *M. leprae* vaccine; (viii) pathogenesis of erythema nodosum leprosum including a study of the effect of thalidomide; and (ix) development of *in vitro* systems for drug sensitivity testing.—Authors' Summary

Ridley, D. S. The pathology of leprosy. *Southeast Asian J. Trop. Med. Public Health* **9** (1979) 205–208.

The article provides a general inquiry into the pathology of leprosy. Comments on the bacteriology of leprosy, the host response, and the early evolution of the disease process are followed by an outline of the classification of leprosy. Reactions and the characteristics of the lepromin reaction are briefly discussed, and the article concludes with an overview of current problems in leprosy research.—RCH

Rotberg, A. A non-stigmatizing Bible. *Hansenologia Internationalis* **3** (1978) 76–82.

The "tsará-ath" of the Hebrew Books, translated as "lepra" in the Greek "Septuaginta" Bible was a ritual defilement based on various skin and scalp lesions and on blemishes, probably mold, on garment, leather, walls and stones. The previous appellation ("lepra") of those lesions changed to "vitiligo," "psoriasis," "tinea," etc. but is still current for Hanseniasis (Hansen's disease), whose signs cannot be found in the Bible.

This historical linguistic confusion is an important cause of serious psycho-social, medical and preventive problems in Christian endemic countries, spreading to non-Christian areas. The last known example is that of the highlands of Papua New Guinea, where Hanseniasis was "a disease like the others," until the arrival of Western influences and religious missions, resulting in stigmatization and ostracization of patients and their families.

To insure that evangelization should neither be accompanied by discrimination nor by misinformation about the disease, some modern Bible translations are no longer using the word "leprosy." This term has also

been abandoned by the Brazilian Ministries of Health and of Social Welfare, as well as by the United States Public Health Service, and by the government of Portugal.—Author's Summary

Chemotherapy

Chaudhuri, S., Ghosh, S., Chakraborty, T., Kundu, S. and Hazra, S. K. Use of a common Indian herb "Mandukaparni" in the treatment of leprosy. *J. Indian Med. Assoc.* **70** (1978) 177-180.

From this short trial for one year, it is observed that "Mandukaparni" (*Thankuni*) seems to be an effective drug in the treatment of leprosy. Clinical improvement is quicker with "Mandukaparni" in comparison with dapsone. Bacteriological improvement is comparable with dapsone. The drug is well tolerated by patients whereas with dapsone there is a possibility of reaction, which appeared in 3 out of 10 cases. Further observations with these drugs will substantiate the findings in this series.—Authors' Summary

Cohen, S. S. Comparative biochemistry and drug design for infectious disease. *Science* **205** (1979) 964-971.

In the past two decades, biochemistry and molecular biology have demonstrated the existence of potentially exploitable biochemical differences between etiologic agents of disease and their hosts. Known differences between organism and host with respect to metabolism and polymer structure point to the detailed characterization of key proteins as the focus for the development of potential inhibitors. In the last decade, the methodology of the isolation, characterization, and inactivation of proteins and enzymes has been advanced. The present scientific and technological base suggests that new efforts toward the development of selective chemotherapeutic agents for infections caused by bacteria, viruses, protozoa, and higher eukaryotes should exploit the known differences in proteins or other specific biopolymers serving crucial structural or metabolic roles in

the economy of the parasite.—Author's Summary

The article contains particularly interesting observations on therapeutic approaches to tropical diseases with remarks on trypanosomiasis, schistosomiasis, and leprosy. Although comparatively little is known about the biochemistry of *M. leprae* itself, the author assumes that the organism has biochemical characteristics of other mycobacteria. The article concentrates on the biosynthesis of a cell wall polysaccharide, about half of which consists of D-arabinose, as a logical metabolic difference between mammalian cells and the genera, *Mycobacterium*, *Corynebacterium*, and *Nocardia*, which could be exploited in designing specific new chemotherapeutic agents.—RCH

Faber, W. R. and Leiker, D. L. Evaluation of treatment of lepromatous leprosy patients in The Netherlands. *Dermatologica* **158** (1979) 46-54.

The results of treatment of the group of leprosy patients at the lepromatous side of the leprosy spectrum registered at the Department of Dermatology of the University of Amsterdam in the years 1950-1976 were studied. The average duration of treatment to obtain bacteriologically negative skin biopsies in patients who were untreated at the time of registration was 5 years. A substantial number of patients suffered a relapse; the main reasons for these relapses were discontinuation of treatment and DDS treatment in low dosage.—Authors' Summary

Faber, W. R., Leiker, D. L., Nengerman, I. M. and Schellekens, P. T. A. A placebo controlled clinical trial of transfer factor in lepromatous leprosy. *Clin. Exp. Immunol.* **35** (1979) 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 ≥ 12 mm induration, average 15.5 mm or lepromin ≥ 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*.—Authors' Summary

Hagan, K. J. and Smith, S. E. Variability of urinary dapsone/creatinine concentration ratios in leprosy patients fully compliant with dapsone therapy. *Lepr. Rev.* **50** (1979) 129–134.

A highly sensitive and reproducible assay procedure for the determination of dapsone (DDS) and hydrolyzable metabolites in urine is described. DDS/creatinine (D/C) concentration ratios, which are used to monitor compliance with DDS therapy, have been

determined on samples of all urine voided throughout a 24 hr period by 7 leprosy in-patients fully compliant with their therapy. The D/C concentration ratios varied both within and between patients over the 24 hr and the time-course of variation showed no closely predictable pattern. Urinary excretion of DDS over the 24 hr was found to be $74.8\% \pm 5.7\%$ (S.E.M.) uncorrected or $90.2\% \pm 6.8\%$ corrected for recovery. Our results indicate an unreliability in the use of single urine samples to determine D/C ratios and hence compliance by individual patients with their DDS therapy.—Authors' Summary

Hagan, K. J., Smith, S. E., Gyi, K. M., Lwin, M. M., Myaing, Y. Y., Oo, K. M., Shwe, T., Tin, K. M., Than, K. N., Hla, T. and Kywe, W. W. The reliability of self-administration of dapsone by leprosy patients in Burma. *Lepr. Rev.* **50** (1979) 201–211.

A study of urinary dapsone/creatinine (D/C) concentration ratios has been performed on 852 leprosy patients in the Rangoon and Mandalay regions of Burma. The results show that, by comparison with in-patients who are assumed to be compliant with their therapy, hospital out-patients and urban and rural clinic patients had overall compliance rates of only 74% and 24% respectively. In each group, substantial numbers of patients were identified who had taken no dapsone (DDS) tablets whatsoever.

The findings are in line with similar studies performed in other countries, and they indicate an urgent need to reassess the existing program of treatment supervision particularly in the urban and rural clinic environments.—Authors' Summary

Kingham, J. G. C., Swain, P., Swarbrick, E. T., Walker, J. G. and Dawson, A. M. Dapsone and severe hypoalbuminaemia. *Lancet* **2** (1979) 662–664.

Severe hypoalbuminaemia developed in two patients on long-term dapsone treatment for dermatitis herpetiformis. The patients had been treated with dapsone for 3 and 11 years before the syndrome developed, and both recovered completely when dapsone was withdrawn. Albumin-turnover studies revealed a great increase in intra-

vascular albumin catabolism and a modest decrease in synthesis.—Authors' Summary

Nigam, P., Dayal, S. G. and Goyal, B. M.

Erythema multiforme bullosum due to rifampicin. *Lepr. India* **51** (1979) 249–251.

A case of erythema multiforme bullosum in a patient with lepromatous leprosy with pulmonary tuberculosis, due to rifampicin, is described. It is stressed that ethambutol may act as a trigger to the toxic effects of rifampicin.—Authors' Summary

Pattyn, S. R., Bourland, J., Warnsdorff, J.,

Cap, A. and Saerens, E. J. Short course two months treatment of paucibacillary leprosy with rifampicin—preliminary results. *Ann. Soc. Belge Méd. Trop.* **59** (1979) 79–85.

The possibility of treating paucibacillary leprosy by a short course rifampicin regimen was investigated in a pilot trial in Bujumbura and a controlled trial in Addis Ababa. Rifampicin was administered once weekly in a dose of 900 mg during 8 weeks.

Clinical improvement continued after the administration of RMP was stopped and no systemic adverse effects associated with the intermittent RMP administration were observed.

The follow-up period was one year. The clinical observations and examination of biopsies give the impression that this short course RMP treatment is not as good as standard dapsone therapy.

Three patients in the RMP group developed neuritis; this was not significantly different when compared with the dapsone group and the neuritis developed after the RMP treatment had been stopped. Continuing observation of the patients is necessary.—Authors' Summary

Pearson, J. M. H., Haile, G. S., Barnetson,

R. St. C. and Rees, R. J. W. Dapsone-resistant leprosy in Ethiopia. *Lepr. Rev.* **50** (1979) 183–199.

During the 5 years between 1973 and 1977, 254 patients suspected of developing dapsone-resistant leprosy were seen in the Addis Ababa area. They were drawn from a pool of about 1,500 registered patients with

lepromatous leprosy, giving an incidence of about 3% per annum (among patients at risk). Fifty-one were proved resistant by mouse footpad tests, and 57 more by clinical trial. The remainder, who continued in trial treatment, conformed to the clinical pattern of those proved to be dapsone resistant. Only 2 patients were proved to be sensitive to dapsone.

In addition, among 106 suspected cases from elsewhere in Ethiopia giving a "classical" history, 28 were proved resistant by mouse footpad tests, and only one was dapsone sensitive. Eleven out of 17 patients who relapsed having discontinued dapsone treatment were also found to have developed dapsone-resistant leprosy (7 by mouse footpad tests, and 4 more by clinical trial): 2 were sensitive to dapsone.

Mouse footpad testing for primary dapsone-resistant leprosy was performed in 29 patients. Fourteen lived in the Addis Ababa area; 5 of them were resistant. Fifteen came from elsewhere in Ethiopia; 11 were resistant. Dapsone-resistant leprosy has become so widespread in Ethiopia as to threaten the practical possibility of leprosy control by chemotherapy alone.—Authors' Summary

Sahoo, S. K., Tripathy, N. and Debi, B. P.

Acute fatal DDS poisoning. *Lepr. India* **51** (1979) 244–248.

Acute dapsone (DDS) poisoning is rare, and such cases are either accidental or suicidal. Though accidental DDS poisoning is reported in children, the same is fairly uncommon in adults. Only two such cases are reported in Indian literature. We here report four cases of fatal suicidal DDS poisoning in adults, resulting in death in three cases. The reported acute symptoms include nausea, vomiting, hyperexcitability followed by depression, and carpopedal spasm or convulsions. The most marked signs are dyspnea and cyanosis. The symptoms are due to methemoglobinemia and or sulfhemoglobinemia. Normally, dapsone induces red cell hemolysis, even with small therapeutic doses of 25–100 mg per day, and in toxic doses it reduces the oxygen carrying capacity of blood and damages the red cells, making them more vulnerable for hemolysis. The peculiarities of the presentations in this series are the manifestation

of a severe hemorrhagic episode in one case and progressive jaundice in another, besides cyanosis. None of the cases had carpopedal spasm or convulsion. Out of four cases, three died in spite of intensive care, intravenous vitamin C, exchange transfusion (2 cases), and other supportive measures. Intravenous methylene blue could not be used in these cases due to nonavailability.—(Adapted from authors' abstract)

Sharma, G. S., Gupta, P. K., Jain, N. K., Shanker, A. and Nanwati, V. Toxic psychosis to isoniazid and ethionamide in a patient with pulmonary tuberculosis. *Tubercle* **60** (1979) 171–172.

The case is reported of a patient who developed a psychotic reaction firstly to isoniazid and secondly to ethionamide. Recovery was complete following withdrawal of each drug.—Authors' Summary

Shwe, T., Lwin, K. and Thwe, K. The efficacy and tolerability of rifampicin in Burmese patients with lepromatous leprosy. *Hansenologia Internationalis* **3** (1978) 30–41.

Seventy-one Burmese adult patients with lepromatous leprosy were treated with various regimens of rifampicin monotherapy,

450 mg daily for 60 days or 900 mg once weekly for 12 weeks or 450 mg daily for six months. Of the patients, 18 had relapsed after stopping DDS therapy, 20 were intolerant of DDS, 18 were DDS resistant and 15 had received no previous treatment.

Rifampicin produced a 75% reduction in the size of skin nodules in two thirds of the patients and a complete disappearance of nodules in the others. After one month drug treatment the MI fell to zero but the BI remained unchanged. The once weekly regimen was as effective as the daily treatment. Four patients had to be withdrawn due to ENL reactions.—Authors' Summary

Yawalkar, S. J. and Vischer, W. Lamprene (clofazimine) in leprosy. *Lepr. Rev.* **50** (1979) 135–144.

This article is a reproduction of the basic information booklet on clofazimine from Ciba-Geigy Ltd. The chemistry, preparation, pharmacokinetics, therapeutic effectiveness, indications, dose schedules, toxicity, tolerability, and precautions in the use of clofazimine in leprosy are reviewed. The article contains a great amount of practical information from the company as well as from the literature (45 references) and should be read in the original.—RCH

Clinical Sciences

Alchorne, M. M. A., Rotberg, A., Michalany, J., Vargas, P. de O. and Cassiano, T. P. Prognostic considerations based on a study of 38 hanseniasis patients submitted to Mitsuda tests 23 to 35 years previously. *Hansenologia Internationalis* **3** (1978) 5–11.

Out of 2,775 hanseniasis patients Mitsuda tested by one of the authors (R) from 1933 to 1947, 38 were re-examined in 1970/1971. Twenty-eight had been treated regularly; 6 did not receive sulfones. Improvement or disappearance of dermatological lesions occurred in 31 (81.5%), independently of reactivity. All eleven bacteriologically positive out of 19 Mitsuda negative patients became bacteriologically negative, which is partly attributed to sulfones. One treated bacillary

negative patient became positive. Twenty-eight (76.3%) were neurologically aggravated, independently of reactivity but more evidently among the stronger reactors. As regards classification, all initially "tuberculoid," "Virchowian" and "dimorphous" patients continued in their types or group, but only 7 (41.2%) out of the 17 initially "indetermined" remained so. Four (23.5%), two Mitsuda ++, two +, changed to reactional tuberculoid; 6 (35.3%) (3 Mitsuda -, 2+, and 1++) changed to the Virchowian type. These developments according to reactivity confirm the pathogenetic theory postulated in 1937 by one of the authors (R). Mitsuda reactivity remained generally unchanged, rarely increased or decreased. The good prognostic value of the strong Mitsuda test is generally confirmed, but

only as regards classification, bacillation and dermatological lesions—not from the neurological and social viewpoints.—Authors' Summary

Bharadwaj, V. P., Venkatesan, K., Ramu, G. and Desikan, K. V. Glucose tolerance and serum free fatty acid levels in leprosy. *Indian J. Med. Res.* **69** (1979) 567–570.

An oral glucose tolerance test (GTT) was conducted in 20 patients with lepromatous leprosy and 8 with tuberculoid leprosy. Free fatty acid (FFA) estimations were done in the sera collected at 0 and 2 hr, after the start of GTT. Patients with active lepromatous leprosy and also cases of lepromatous leprosy with erythema nodosum leprosum (ENL) showed a flat type of glucose tolerance, the flatness being remarkable in ENL cases. Fasting serum FFA levels were very high in lepromatous leprosy patients. Serum specimens collected 2 hr after oral glucose administration showed a decline in FFA content.—Authors' Summary

Chakrabarty, M. S., Mukherjee, K. K., Chakrabarty, S. K., Ghosh, S. and Choudhury, S. Hepatitis B surface antigen (HB_sAg) in leprosy patients of Calcutta: its prevalence and subtypes. *Lepr. India* **51** (1979) 182–188.

High incidence of Hepatitis B surface antigen (HB_sAg) in lepromatous leprosy patients has been reported by many workers. This paper reports on a study undertaken over a period of more than two years to determine the prevalence of HB_sAg and its major antigenic subtypes among the various clinical types of leprosy and apparently healthy individuals of the Calcutta population. The overall incidence of HB_sAg in lepromatous leprosy is found to be 3.8% (9 out of 234) in our study. The incidence of HB_sAg in tuberculoid leprosy and non leprosy control cases were almost identical, 2.5% (11 out of 431) and 2.7% (14 out of 519) respectively. The incidence of HB_sAg in lepromatous leprosy in the present study was apparently higher than tuberculoid or non leprosy cases, although statistically not significant. Hence the association between HB_sAg and lepromatous leprosy could not

be established in our study. None of the major antigenic subtypes of HB_sAg could be related to any particular type of leprosy. The subtypes "ad," "ay" and "ar" were present at varying proportions in all the groups tested. The antigenic subtype "ay" was found to be prevalent in the Calcutta population in higher proportions.—Authors' Summary

Chan, S. H., Oon, B. B., Kamarudin, A. and Wee, G. B. HLA and leprosy in Chinese. *Tissue Antigens* **13** (1979) 73–74.

HLA associations in leprosy have been shown in some studies but not in others. We have studied 77 unrelated Chinese leprosy patients; 40 lepromatous (LL) and 37 tuberculoid (TT and BT). The control group consisted of 238 unrelated normal Chinese subjects. HLA typing was performed with the standard NIH lymphocyte microcytotoxicity assay using a total of 196 antisera.

The frequency of HLA-B17 was higher among the leprosy patients as a group than among controls. Twenty-three (29.9%) of 77 leprosy patients had B17 compared with 34 of 238 (14.3%) controls ($\chi^2 = 9.53$; $p < 0.005$, RR = 2.6). This difference was not significant when corrected for the 26 antigens typed for. The high frequency of B17 was particularly marked in the patient subgroup of tuberculoid leprosy. Fifteen (40.5%) of 37 tuberculoid leprosy patients had B17 compared with 34 of 238 (14.3%) controls ($\chi^2 = 15.07$; $p < 0.0001$, corrected $p < 0.003$, RR = 4.09). This difference was significant even after corrected for the number of antigens typed for. Lepromatous leprosy patients had a higher frequency of B13 and a lower frequency of A2 than tuberculoid leprosy patients or controls, but these differences were not statistically significant.—(Adapted from article)

Cole, G. W. and Gebhard, J. *Mycobacterium avium* infection of the skin resembling lepromatous leprosy. *Br. J. Dermatol.* **101** (1979) 71–74.

A patient on systemic therapy developed a cutaneous papule which histologically resembled lepromatous leprosy. Cultures of this lesion grew *Mycobacterium avium*. Since there was no evidence of disseminat-

ed infection, the lesion was excised, and the patient continues to do well.—Authors' Summary

Dawson, D. M., Richardson, E. P., Jr. and Colvin, R. B. Peripheral neuropathy and renal failure in a young Mexican woman. *N. Engl. J. Med.* **300** (1979) 546–553.

A thirty-one year old Mexican woman, presenting to the Massachusetts General Hospital with a peripheral neuropathy, was the subject of a weekly clinicopathologic exercise. The patient apparently lacked dermatologic signs but presented with what appeared to be a typically lepromatous type sensory loss, accompanied by motor weakness affecting primarily the hands. The patient had concomitant renal disease, the etiology of which was not established. The differential diagnoses entertained included primary amyloidosis as well as leprosy. The detailed workup and discussions make for interesting reading to a leprologist. It is with some sense of reassurance that, near the end of the discussions, the reader learns that the patient is now under the care of Professor Fernando Latapí in Mexico City.—RCH

Dutta, R. K. A study of patients with erythema nodosum leprosum syndrome. *Lepr. India* **51** (1979) 209–212.

Twenty-five cases of erythema nodosum leprosum (ENL) syndrome have been clinically evaluated. The majority of 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 pronounced in patients having higher clinical scorings.—Author's Summary

Kelkar, S. S., Mondkar, A. D. and Warawdekar, W. Serum immunoglobulins in leprosy. *Lepr. India* **51** (1979) 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.—Authors' Summary

Khoubesserian, P., Taelman, H., Flament-Durand, J., Moriamé-Roussel, N., Stoupel, E., Kravtman, M. and Coers, C. A propos d'un cas de lèpre nerveuse: revue des données récentes. (Review of recent findings concerning a case of leprosy affecting the nerves.) *Acta Clin. Belg.* **33** (1978) 117–128. (in French).

A white male patient 38 years old contracted leprosy in Africa. After several years of incubation, dermatological manifestations occurred (erythematous-squamous patches mainly located on the trunk) together with neurological signs (distal anesthesia of lower limbs going up to the thighs and localized zone of thermoanalgesia around the right forearm). Histological and immunological findings allowed classification of the disease within the "border-line" group, with a lepromatous tendency. A review of recent data concerning leprous neuritis emphasizes its close relationship with the immunological response of the host. The therapeutic prescriptions resulting from this relationship are described.—Authors' Summary

Lichtman, D. M., Swafford, A. W. and Kerr, D. M. Calcified abscess in the ulnar

nerve in a patient with leprosy. *J. Bone Joint Surg.* **61** (1979) 620-621.

Leprosy, primarily a disease of peripheral nerve trunks and cutaneous nerves, classically presents with neural or dermal signs and symptoms, or both. In the tuberculoid form of leprosy, the host has a high degree of resistance, and most of the pathological changes are secondary to the immune response. The case presented here is one of borderline tuberculoid leprosy with the highly unusual finding of a calcified abscess of the ulnar nerve.—Authors' Summary

McDougall, A. C. Dermal neuroma simulating leprosy. *Int. J. Dermatol.* **18** (1979) 46-49.

A 45-year-old Pakistani woman reported to a clinic in Karachi with a one-year history of hypopigmented lesions on the left side of the face and neck. On first presentation, the lesions were rough-surfaced and hypoaesthetic; the clinical findings in this highly endemic area of the world suggested macular tuberculoid leprosy. The patient was treated with dapsone for a period of 5 years but with no change in the appearance or size of the lesions. Subsequent biopsies revealed an unusual neuromatoid pathology in the dermis, in which axons were absent on light and electron microscopy, with neurilemmoma being considered as a possible diagnosis.—Author's Summary

Rea, T. H. Lucio's phenomenon: an overview. (editorial) *Lepr. Rev.* **50** (1979) 107-112.

The editorial is a concise review of Lucio's phenomenon, intended for leprologists outside North and Central America, who would lack clinical experience with this entity. After a brief historical background dealing with the initial description by Lucio and Alvarez in 1852 and the rediscovery of the phenomenon by Latapí, *et al.*, in 1948, the author describes his experience with 11 cases seen in Los Angeles, California.

A description of the pure and primitive diffuse lepromatous type leprosy is provided. The clinical and histopathologic characteristics of the reaction, Lucio's phenom-

enon, are provided. In this series, the onset of the Lucio's phenomenon did not occur in association with dapsone. The reactions were not accompanied by fever or leukocytosis in contrast to ENL patients. No immediate response to lepromin was found in four patients tested. Direct immunofluorescent studies of skin lesions demonstrated immunoglobulin and complement components in vessel walls, and evidence for circulating immune complexes was found, including positive Raji cell tests, positive latex fixation tests, and cryoglobulinemias of a mixed type containing IgG, IgM, IgA, and complement components. Of ten patients followed for 3 months or longer, in seven, new lesions of Lucio's phenomenon ceased with dapsone as the sole therapeutic agent. Three patients continued to have new lesions while on dapsone; none responded to thalidomide; but each responded within one week of beginning rifampin. The author hypothesizes that Lucio's phenomenon occurs only in pure and primitive diffuse lepromatous patients because these patients have a singularly deficient defense mechanism, which permits replication of *M. leprae* in endothelial cells, and that this enhanced exposure of *M. leprae* antigens to circulating antibody results in vasculitis and infarction.—(Adapted from article)

Sharda, D. P., Parvez, M., Jain, A. K., Bhargava, N. C. and Misra, S. N. A study of serum fibrinolytic activity in leprosy. *Lepr. India* **51** (1979) 203-208.

Fibrinolytic activity was studied in 50 patients with leprosy and 30 healthy individuals who served as controls. Fibrinolytic activity was determined by measuring euglobulin lysis. No significant alteration in fibrinolytic activity was observed in patients with non-lepromatous leprosy, the levels being approximately similar to the control group. However, fibrinolytic activity was found to be significantly decreased in patients with lepromatous leprosy and in the lepra reaction group. The observed decrease in fibrinolytic activity can be explained on the basis of the presence of tissue destruction and vasculitis seen in leprosy, more so in patients with lepromatous leprosy and lepra reaction.—Authors' Summary

Smith, W. C. S. Screening for diabetes mellitus in leprosy patients with complicated ulcers. *Lepr. India* **51** (1979) 236–238.

All patients admitted to an ulcer ward in a leprosy hospital 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.—Author's Summary

Venkatesan, K., Bharadwaj, V. P., Ramu, G. and Desikan, K. V. Serum beta-glucuronidase in leprosy—a preliminary report. *Indian J. Med. Res.* **69** (1979) 553–556.

Serum beta-glucuronidase was estimated in 58 patients with lepromatous leprosy. The patients included cases of lepra reaction in the reactive as well as subsided phases, and those with lepromatous leprosy with severe painful neuritis. In all cases the enzyme activity was elevated as compared to normal control values. In lepra reaction

the level was very high. With the subsidence of reaction, the enzyme activity was found lowered by 50 per cent approximately. Patients with lepromatous leprosy with neuritis also exhibited high serum beta-glucuronidase activity.—Authors' Summary

Weissman, J. B. and Neu, H. C. Lepromatous leprosy masquerading as disseminated tuberculosis. *Am. J. Med.* **67** (1979) 113–116.

A patient with disseminated leprosy is described. A 57 year old man from Cuba presented with fever and pancytopenia. Bone marrow aspirate showed numerous acid-fast bacilli and a liver biopsy specimen contained multiple granulomas. The patient was considered to have tuberculosis and was treated with isoniazid and rifampin, with initial clinical improvement, only to have the fever recur and to show deterioration in hematologic and hepatic function. Failure to grow *M. tuberculosis* suggested a diagnosis of leprosy which was proved by skin biopsy. How lepromatous leprosy can masquerade as disseminated tuberculosis is discussed.—Authors' Summary

Immuno-Pathology

Anthony, J., Vaidya, M. C. and Dasgupta, A. Immunoglobulin deposits in erythema nodosum leprosum (ENL). *Hansenologia Internationalis* **3** (1978) 12–17.

Erythema nodosum leprosum (ENL) skin lesions observed by fluorescence microscopy were found to contain immune complexes. While biopsies taken from at least 7 ENL lesions contained deposits of immunoglobulin in their vessel walls, 12 of the lesions contained such deposits in the perivascular cell infiltrate. However, immunoglobulin deposits were observed in the dermis of all 25 ENL lesions studied. On the basis of localization of these fluorescent deposits, the 25 skin lesions were classified under groups I to III and were correlated with the onset of the reaction. Control biopsies taken from the lepromatous leprosy patients without ENL

were uniformly negative for immunoglobulin deposits.—Authors' Summary

Çöloğlu, A. S. Immune complex glomerulonephritis in leprosy. *Lepr. Rev.* **50** (1979) 213–222.

Twenty patients with lepromatous or borderline leprosy selected at random were investigated for evidence of immune complex glomerulonephritis. Light, immunofluorescence and electron microscopy findings suggested that glomerulonephritis in leprosy results from the accumulation of immune complexes in glomeruli. Fluorescence and electron microscopy findings may be attributed to the fact that the deposits are less soluble immune complexes. A comparison was made between glomerulonephritis in the BSA-rabbit system and leprosy.—Author's Summary

Dastur, D. K. Leprosy (An infectious and immunological disorder of the nervous system). In: *Handbook of Clinical Neurology*, P. J. Vinken, and G. W. Bruyn, eds., Vol. 33, *Infections of the Nervous System*, (Part I edited in collaboration with H. L. Kalwans), Amsterdam: North Holland Publishing Co., 1978, 421–468.

Epidemiological details have not been considered here, but the far greater prevalence of the high-resistance tuberculoid form of leprosy in the more crowded and less nourished populations of the East, constitutes a feature as impressive as the preponderance of the more infectious lepromatous variety among the fair-skinned peoples, where the prevalence of the disease is very small.

The individual susceptibilities to the disease appear even more important and interesting than the racial. Our knowledge both of the general pathology and the neuropathology of leprosy, and on which naturally depends our understanding of the clinical features of the disease, has increased on account of a better appreciation of its immunology, during the past one and a half decades. In fact, leprosy has now become a model for the study of immunology; as in the past it has been successively a model for the study of bacteriology, general pathology, rehabilitative surgery and neuropathology. This has become possible through the realization that the two polar types of leprosy, the tuberculoid and the lepromatous, behave almost like two separate diseases. In the former the host is able to mount a strong cell mediated immunity (CMI) and in the latter the CMI is deficient or paralyzed, while the humoral factors—the antibodies developing against mycobacterial antigens and the immunoglobulins—are augmented. The evidence for disturbed CMI in lepromatous leprosy has come through methods such as the histological examination of cells in the para-cortical and central parts of lymph nodes; the leukocyte migration inhibition test; the differentiation between T and B lymphocytes; and the response of cells in tissue culture to mitogens such as phytohaemagglutinin (PHA), and to incorporation of tritiated thymidine. The immunological differences between the two polar types account for the

million fold heavier bacillation in the low resistance lepromatous type of leprosy, and for the unique macrophage, the lepra cell, which develops here, as against the tuberculoid histology of tuberculoid leprosy.

It is now common knowledge that leprosy, with its global population of over 15 million patients, constitutes the largest single disorder of the peripheral nervous system, considering the involvement of intradermal nerves, other sensory nerves, the mixed nerve trunks and the intramuscular nerves, in all types of the disease. The nerve damage in tuberculoid leprosy may be more severe in onset and faster in progression, but is more localized initially. The subtler but more extensive spread of the infection in lepromatous leprosy arises out of the blood-borne dissemination of *M. leprae*. This is made possible by the bacillation of endothelial cells of blood vessels throughout the body. The pathogenesis of lepromatous leprosy is best understood by keeping in mind the constant operation of the dual mechanism of a neural spread and a vascular spread. In the tuberculoid types of leprosy the neural spread appears to predominate.

In either type the entry of *M. leprae* into the body appears to occur through the body surfaces, either dermal or mucosal, especially of the upper respiratory tract, or both. In any situation the predilective involvement of nerves, i.e., primarily of the Schwann cells, is the "fact of life" in leprosy. The neural spread thus amounts to a spread of organisms along the Schwann cells. This is again easier to understand in lepromatous leprosy where the bacilli can actually be traced in their vertical spread, mainly but not exclusively centripetally; centrifugal, lateral from one nerve bundle to another, and ramificatory (from a larger nerve to its smaller branches) spreads have also to be considered. With the parasitization of Schwann cells the first nerve constituent to suffer is logically the myelin, with segmental demyelination occurring in the early stages of lepromatous leprosy, and being reflected in reduced nerve conduction velocity. Unless the disease is arrested with early and effective chemotherapy, damage to the axis cylinder and consequent axonal degeneration distally are inevitable and indeed occur. Quantita-

tive histology has confirmed the loss of myelinated fibers and heavier bacillation of their Schwann cells and of perineurial cells, in lepromatous leprosy. A variety of degenerative and proliferative changes in Schwann cells are seen, depending on the stage and type of the disease, and leprosy neuritis provides rich material for studying Schwann cell pathology. Similar features have been noted in experimental leprosy in the mouse and armadillo, and in the mouse a disturbance in the blood-nerve barrier has been demonstrated consequent to damage to the perineurium. The latter seems to serve a protective function for the intrafascicular contents.

The most proximal extent of the infection appears to be up to the spinal posterior root ganglia, the CNS being apparently spared. In either form of leprosy, a retrograde degeneration of the posterior roots and ganglion cells can result from damage to the sensory fibers in the corresponding nerves.

The strong immunological reaction of the tissues, including the nerve, in tuberculoid leprosy is manifested through the histolytic activity of the epithelioid cells which destroy the nerve, and produce axonal degeneration predominantly. Both these and the Schwann cells show increased activity of lysosomal enzymes, as do the lepra cells in lepromatous leprosy. While the disease can be arrested at this stage by chemotherapy, the progression of the neuropathy in the face of extreme paucity of the organisms, raises the possibility of a hypersensitivity type of reaction. In this hypothesis while the bacillary proteins might provide the initial antigen, after the nerve damage has taken place myelin breakdown might supply the subsequent antigenic material that perpetuates the neuropathy.

The clinical manifestations of this varied neuropathology are loss of cutaneous sensibility, in the skin-patches or in diffuse infiltrates of lepromatous leprosy in the sensory territory of cutaneous nerves or mixed nerve trunks in the limbs and the face; the greater or lesser thickening or tenderness of such nerves; in the later stages weakness and wasting of muscles supplied by the motor fibres in the affected nerves; and, when treatment is delayed or discontinued, deformities and absorption of digits and ex-

tremities. Predilective sites of involvement of large nerves in the limbs result from the operation of factors inherent in the surroundings of the nerve, such as of the ulnar at the elbow or the lateral popliteal at the knee. Ischemia resulting from compression of swollen nerves in unyielding fibro-osseous tunnels, repeated stretching and minor trauma to the nerve at these sites where it becomes superficial and is over a joint, are some of the factors. The exposure of the nerve to cooler temperatures as it comes out into the subcutaneous tissues, appears to be an important factor in lepromatous nerves since the bacilli are known to thrive better in cooler temperatures; and a temperature-linked sensory loss prevails in this type of the disease.

Denervation atrophy of muscles is the very simple but devastating consequence of involvement of motor fibers in mixed nerve trunks by the leprosy process. Intramuscular neuritis is less frequent and an extension of this to produce local myositis is even less frequent. While bacillation of striated muscle fibers in experimental mouse leprosy is an important event, it must be considered a rare and inconsequential event in human lepromatous leprosy and is unheard of in tuberculoid leprosy. Even the invasion of smooth muscles in the skin, which does occur in man, is far less frequent than invasion of nerves. The overaction of normal muscles at distal joints, such as of the hand, where the opposing muscle groups have wasted or weakened, precipitates deformities. The situation is worsened by minor or major trauma to anesthetic extremities. Denervation and devascularization of bones, compounded by the demineralization of disuse, or secondary infection, completes the pathetic picture of a destroyed limb. Surgical rehabilitation is the only succour here and has of course to be accompanied by chemotherapy to control the infection. Diaminodiphenyl-sulphone (DDS) remains the sheet anchor of medical treatment, but rifampicin, clofazimine, thalidomide and steroids help in DDS-resistant cases, in nerve pain and in reactions.—Author's Summary

Dastur, D. K. The nervous system in leprosy. *In: Scientific Approaches to Clini-*

cal Neurology. E. Goldensohn and S. Appel, eds. New York: Lea & Febiger, 1977, 1456–1493.

Leprosy, the single most prevalent peripheral nerve disorder in the world, is discussed from a neurologic and neuropathologic viewpoint. A classification of the main types of the disease is presented from the immunologic and cytopathologic points of view. It is seen how the three main types—the tuberculoid, the borderline and the lepromatous—represent increasing degrees of immunologic inadequacy on the part of the host in combatting the multiplication and spread of the causative infective agent, *Mycobacterium leprae*. A breakdown particularly of cell-mediated immunity is evidenced from the newer immunologic methods. The striking differences in the bacterial content and in the histologic reactions in the two polar types of disease, characterized by the typical epithelioid and small mononuclear cells of tuberculoid leprosy on the one hand and by the large foamy bacteria-laden macrophage (the lepra cell) of the lepromatous variety on the other, are stressed.

The pathologic changes produced in sensory territories such as the skin, the mucosa and the eye, and some of the clinical effects of these, are then presented. The ingress of the bacilli and the spread of the inflammatory reaction seem to be mediated by the intradermal nerve twigs, as studied by special neurohistologic methods. Characteristic patterns of sensory loss, at times with dissociation between the sensory modalities, appear to develop in such cutaneous lesions. The colder areas of the body are shown to manifest greater sensory loss. It is suggested that both thermal and pain sense, which are affected earlier and more severely in early leprosy lesions of the skin, are transduced by fine nonspecific freely ending nerve filaments in the dermis. Histologic evidence of greater damage to these axons than to the deeper and thicker perifollicular nerve fibers suggests a centripetal mode of progression of the disease along the neural pathway. The implication of newer evidence on the heavy bacillation of the nasal mucous membrane in lepromatous leprosy to an easier dissemination of

the disease is reviewed. The significance of fine corneal nerves as a portal of entry of the infection is also drawn out.

The limited role of motor nerve conduction studies in the complex neuritides of leprosy is revealed and the artefact of normal conduction velocity in the presence of severely damaged nerves is explained. Sensory nerve conduction and electromyography of muscle appear to be the more reliable indices of the nerve change in leprosy.

Sites of predilective damage to large nerves in the limbs in leprosy appear to result from a combination of the primary intraneural leprosy infection and cellular reaction which makes the nerves swell, and secondary factors of the terrain of the nerve. The most important of these factors seems to be compression of the swollen nerve in narrow unyielding fibro-osseous tunnels through which it passes at these sites (the elbow, knee, wrist and ankle). The other secondary factors stem from the superficial subcutaneous location of the nerve in these areas, which renders it susceptible to major and minor trauma and colder temperatures, and from stretching of the nerves at the joints. Recent studies of intraneural topography of leprosy nerves reveal the interweaving and plexus formation of funiculi in the large nerve trunks, and provide further evidence of the initial involvement of sensory bundles distally, of a centripetal progression of the intraneural infection, and of the later involvement of the motor fibers higher up along the nerves where the sensory fibers mix with them. The apparently primary involvement of the facial, a motor, nerve is shown in fact to be secondary to preliminary involvement of the sensory branches of the trigeminal nerve in the face, especially in the region of the eyelids.

Pathologic studies on large and cutaneous nerves in the limbs have revealed the difference in the reactions and modes of damage to nerves in tuberculoid and lepromatous processes. In the former type of disease the nerve is infiltrated and disorganized by a typical tuberculoid exudate which can totally destroy the parenchyma and produce irregular fibrous scarring. In the lepromatous nerves the profuse infection of the Schwann cells results in "met-

abolic'' damage to the myelin, with slow degeneration of the axon and fibrosis; intra- and interfunicular inflammation is generally less. The intraneural progression of the infection seems to stop short where the Schwann cells cease to exist, at the level of the posterior root ganglion, the capsule cells of its large sensory neurons appearing to be the most proximal outpost of *M. leprae*. This parasitization of Schwann cells by *M. leprae* appears unique in neurology, and lepromatous leprosy emerges as a classical disorder of the Schwann cell. The axon damage is severe and often commensurate with that of myelin in tuberculoid nerves, but less severe than myelin loss in nerves of lepromatous cases. Axonal type of degeneration appears to occur in tuberculoid leprosy almost invariably and in lepromatous leprosy frequently, segmental demyelination being infrequent. Swelling, thickening and tenderness of large and small nerves result from these histopathologic changes and constitute an important diagnostic sign in leprosy.

The muscle disorder in leprosy is essentially neurogenic and the denervation patterns on the EMG find their counterpart in the histologic changes of varying severities of group atrophy of muscle fibers. Intra-neural granulomas infrequently spread into the surrounding muscle tissue and produce a variety of leprosy myositis. In contrast to the frequent presence of AFB in the smooth muscle fibers of the skin, the striated muscle fibers of man rarely contain *M. leprae*.

Quantitative data in the form of nerve fiber counts and measurement of fiber diameters with observation of deviations from the normal bimodal pattern provide most useful information. Assessed this way even nerves that are clinically not thickened show pathologic changes in both tuberculoid and lepromatous cases. Usually irregular patterns with loss of both large and small myelinated fibers, a relative prominence of medium sized fibers and, rarely, clusters of small regenerative fibers are seen.

Electron microscopy (EM) has contributed considerably to the peripheral neuropathology of leprosy. Thus, in addition to confirming the above-described light microscopic changes, the bacillated cell in all types of leprosy has been confirmed to be

the Schwann cell mainly of unmyelinated fibers; reactive and degenerative changes in it have been demonstrated, intact and degenerating forms of *M. leprae* have been shown and the early increase of endoneurial collagen established. Moreover, the perineurial cell has been shown to behave similarly to the Schwann cell in respect to phagocytic propensity. The possible protective function of the perineurium has been another highlight of these EM studies. Increase of Schmidt-Lantermann clefts has been shown as an early change of axonal type degeneration, especially in tuberculoid leprosy.

In addition to this Schwannian passage, an important route of dissemination of the bacilli, especially in lepromatous leprosy, is the bloodstream; both large and small vessels, including those running within the nerves, show many AFB in the endothelial and subendothelial tissues. Fine structural examination has confirmed the constant and heavy bacillation of the endothelial cell and demonstrated its distension into the lumen of the blood vessel, thereby suggesting the mode of hematogenous dissemination of leprosy infection. Increased formation of lysosomes and phagolysosomes is seen, though not invariably, in all these cells and also in the lepra cells infiltrating the nerves and skin lesions of lepromatous leprosy.

Augmented lysosomal activity has been demonstrated in the bacillated cells of lepromatous leprosy and the large mononuclear cells of tuberculoid leprosy, using acid phosphatase (AcPh) as a marker on frozen sections. By the same procedure, the AcPh activity in Schwann cells of tuberculoid nerves has been shown to vary from almost nil in the normal state to increased activity in the stage of Schwann cell proliferation, and to loss of activity with severe nerve degeneration setting in. AcPh activity has been demonstrated in Schwann cells derived from human acoustic schwannomas, in tissue cultures. The ready growth of these cells and their avid phagocytosis of *M. leprae* and related mycobacteria have been achieved. Long-term cultures hold promise for future experimental work.

In the treatment of leprosy neuritis, the main drug used, diaminodiphenylsulfone, is now being reinforced by clofazimine or ri-

fampicin, and by cortisone or thalidomide in lepra reactions. Decompression of swollen nerves by appropriate procedures of release from surrounding adherent tissues or slitting of the epineurium is a useful surgical measure for relief of nerve pain in selected cases. Deformity in leprosy is a result of a combination of imbalance of paralyzed and intact muscle groups, trauma to anesthetic extremities, and infective necrosis or disuse osteoporosis of bone. Protection of insensitive hands and feet is of paramount therapeutic importance.

Considerable fillip has been given to research in human leprosy by the development of experimental models in the mouse and, recently, in the armadillo. Situations comparable to human lepromatous leprosy have been produced in the former by destruction of immunity and in the latter without any such adventitious procedure. The blood-nerve barrier appears to be breached in lepromatous mouse leprosy. Leprosy comparable to human tuberculoid leprosy has been more difficult to reproduce experimentally. The experimental models seem particularly favorable for studying bacillary metabolism and susceptibility to various chemotherapeutic agents. The recent report of development of lesions simulating those of tuberculoid leprosy, in the rabbit, through the use of myelin extracts of sensory nerves combined with Freund's adjuvant, merits attention.—Author's Summary

Hirschberg, H. The role of macrophages in the lymphoproliferative response to *Mycobacterium leprae* *in vitro*. Clin. Exp. Immunol. **34** (1978) 46–51.

Peripheral blood lymphocytes from patients suffering from lepromatous leprosy do not normally react *in vitro* to stimulation by *Mycobacterium leprae* antigens. In contrast, we found that T cells from non-responding patients in combination with macrophages from responding patients or healthy contacts did respond well to *M. leprae*. Conversely, T cells from responding patients or healthy contacts in combinations with macrophages from non-responding patients failed to respond. It seems, therefore, that the lack of response normally observed in *in vitro* tests using cells

from lepromatous leprosy patients is due to a failure of their macrophages to present *M. leprae* antigens in an immunogenic form.—Author's Summary

Lowrie, D. B., Aber, V. R. and Jackett, P. S. Phagosome-lysosome fusion and cyclic adenosine 3':5'-monophosphate in macrophages infected with *Mycobacterium microti*, *Mycobacterium bovis* BCG or *Mycobacterium lepraemurium*. J. Gen. Microbiol. **110** (1979) 431–441.

When ingested by mouse peritoneal macrophage monolayers, live *Mycobacterium microti* caused a sustained increase in monolayer cyclic AMP content, and fusion of lysosomes with the bacterium-containing phagosomes was impaired. Ingested live *M. bovis* BCG caused a transient increase in cyclic AMP and the defect in phagolysosome formation was less pronounced. Dead mycobacteria and live *M. lepraemurium* neither enhanced monolayer cyclic AMP content nor inhibited phagolysosome formation. *Mycobacterium microti* and BCG exceeded *M. lepraemurium* in cyclic AMP-synthesizing activity *in vitro*, but the question of whether bacterial cyclic AMP contributed substantially to the increments in infected macrophages was not resolved. Antibody-coated BCG retained the ability to synthesize cyclic AMP and to enhance monolayer cyclic AMP but lost the ability to inhibit phagolysosome formation in macrophages. The observations are discussed in terms of possible control of phagolysosome formation by cyclic nucleotides.—Authors' Summary

Mehra, V. and Bloom, B. R. Induction of cell-mediated immunity to *Mycobacterium leprae* in guinea pigs. Infect. Immun. **23** (1979) 787–794.

Guinea pigs immunized with intact or disrupted armadillo-grown human *Mycobacterium leprae* administered in aqueous or oil vehicles were tested with various dilutions of *M. leprae* suspended in saline, water-soluble *M. leprae* extract, purified protein derivative, and a water-soluble extract of normal armadillo tissue. The results demonstrated the following. (i) Under no conditions was any skin test reactivity found to normal armadillo tissue extract.

(ii) Positive sensitization to both *M. leprae* and its water-soluble extract was achieved by sensitizing guinea pigs with *M. leprae* suspended in Hanks solution or saline. Autoclaved *M. leprae* in Hanks solution or saline inoculated intradermally was an effective immunogen. Oil suspensions or emulsions were effective at sensitization, but appeared to be no better and, in general, slightly weaker, than simple inoculation in aqueous suspension. (iii) Living BCG failed to reveal a significant adjuvant effect on sensitization to *M. leprae*. However, cord factor appeared to potentiate slightly the sensitization to *M. leprae* in aqueous suspension. (iv) The minimum dose required for sensitization with *M. leprae* in aqueous suspension was 55 μ g of purified bacilli. (v) Animals inoculated with *M. leprae* in saline or with *M. leprae* together with BCG showed positive skin test reactivity to the first skin test application made fully 1 year after the initial sensitization. The efficacy of autoclaved, irradiated *M. leprae* in aqueous, oil-free medium suggests a relatively safe approach to human vaccination studies.—Authors' Summary

Sharma, S., Ganguly, N. K., Kumar, B., Kaur, S. and Chakravarty, R. N. T and B lymphocytes and blastogenesis in leprosy. *Lepr. India* **51** (1979) 194–202.

T and B cell percentages and their blastogenic response to PPD and lepromin have been studied in 107 patients with 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.—Authors' Summary

Vilaseca, J., Guardia, J., Cuxart, A., Clotet, V., Martinez-Vasquez, J.-M., Bernardo, L., Masana, L., Garcia-Vanrell, G. and Bacardi, R. Hépatite granulomateuse: étude étiologique de 107 cas. (Granulomatous hepatitis: etiological study of 107 cases.) *Nouv. Presse Méd.* **7** (1978) 3323–3325. (in French)

In this series, the commonest etiology was tuberculosis (30 cases, 28%), followed

by sarcoidosis (18 cases, 17.7%), Mediterranean fever (Olmer's disease) (13 cases, 12.1%), brucellosis (8 cases, 7.4%), typhoid fever (7 cases, 6.6%), and idiopathic forms (8 cases, 7.4%). These were followed by Hodgkin's disease, toxoplasmosis, adenocarcinoma, and leprosy. Finally, there were single cases due to infectious mononucleosis, BCG reaction, hypogammaglobulinaemia, coeliac disease and temporal arteritis. Half of the patients had hepatomegaly and an increase, in general moderate, in hepatic enzymes (transaminases, alkaline phosphatase). The highest enzyme levels were seen in cases of brucellosis, hepatic enzymes being normal in patients with sarcoidosis.—Authors' Summary

Watson, S. R., Morrison, N. E. and Collins, F. M. Delayed hypersensitivity responses in mice and guinea pigs to *Mycobacterium leprae*, *Mycobacterium vaccae*, and *Mycobacterium nonchromogenicum* cytoplasmic proteins. *Infect. Immun.* **25** (1979) 229–236.

Antigenic relationships between *Mycobacterium vaccae*, *M. nonchromogenicum*, and *M. leprae* were examined in mice and guinea pigs injected with *M. vaccae* or *M. nonchromogenicum* suspensions. The growth of both organisms in outbred ICR and four inbred mouse strains was followed up to 30 days. *M. nonchromogenicum* persisted in the livers and spleens of the inbred mice substantially better than did the *M. vaccae* population in the same mouse strains. A translucent colony variant of *M. vaccae* isolated from the opossum survived *in vivo* better than the opaque colony isolated from opossums and cattle. Persistence of *M. vaccae* and *M. nonchromogenicum* was not markedly increased in T-cell-depleted (nude) mice. Normal mice infected with increasing numbers of *M. vaccae* did not develop delayed-type hypersensitivity to the homologous *M. vaccae* cytoplasmic protein antigen. When heat-killed *M. vaccae* were incorporated into Freund adjuvant, both mice and guinea pigs developed delayed hypersensitivity to cytoplasmic antigens prepared from *M. vaccae*, *M. nonchromogenicum*, and *M. leprae* but not to purified protein derivative. Both *M. nonchromogenicum* and *M.*

vacciae vaccines cross-sensitized guinea pigs to the *M. leprae* cytoplasmic antigens.—Authors' Summary

Yoder, L., Naafs, B., Harboe, M. and Bjune, G. Antibody activity against *Mycobacterium leprae* antigen 7 in leprosy: studies on variation in antibody content throughout the spectrum and on the effect of DDS treatment and relapse in BT leprosy. *Lepr. Rev.* **50** (1979) 113–121.

Antibodies against *Mycobacterium leprae* antigen 7 were determined by a specific

radioimmunoassay. The median value of 4 groups of patients decreased gradually from the lepromatous to the tuberculoid end of the spectrum, but there was a striking variation between the antibody content of individual sera in each group. Prolonged DDS treatment led to only a moderate decline of this antibody activity in lepromatous leprosy. In borderline tuberculoid leprosy, DDS treatment led to a marked decrease in antibody activity and a relapse is associated with renewed synthesis and increased antibody content.—Authors' Summary

Microbiology

Goren, M. B., Brokl, O. and Roller, P. Cord factor (trehalose-6,6'-dimycolate of *in vivo*-derived *Mycobacterium lepraemurium*. *Biochim. Biophys. Acta* **574** (1979) 70–78.

Harvests of *Mycobacterium lepraemurium* obtained from livers of moribund infected mice yielded *M. lepraemurium* cell walls that were extracted with solvent to provide crude *M. lepraemurium* cell wall lipids. By solvent fractionation and chromatography on DEAE cellulose and cellulose, a cord factor-like glycolipid contaminated with mycoside C was obtained. Additional solvent treatment provided the purified glycolipid, which was identified as 6,6'-trehalose dimycolate, by infrared and chromatographic comparison with authentic samples from *M. tuberculosis*, by identification of trehalose and specific mycolates of *M. lepraemurium*, and by permethylation analysis. This constitutes the first unequivocal identification of cord factor as a product of *in vivo*-derived mycobacteria.—Authors' Summary

Goyle, S. and Virmani, V. *In vitro* studies on biopsies from leprosy cases. *Indian J. Med. Res.* **69** (1979) 919–925.

Organotypic cultures of skeletal muscle, skin, and subcutaneous fat were set up from biopsies obtained from leprosy patients. This culture technique permits the growth, maturation, and survival of all the cellular elements from the respective tissues. Mac-

rophages grew profusely in all the cultures. Intracellular acid fast bacilli (AFB) were observed in the spindle cells and macrophages. The behaviour of AFB was studied by means of subcultures. When subcultured on Lowenstein Jensen medium up to a period of 5 months, these bacilli did not show any growth.—Authors' Summary

Kim, S. J., Ishaque, M. and Kato, L. *Mycobacterium leprae* and phenoloxidase activity. *Microbios* **22** (1979) 143–153.

Our earlier studies indicated that the enzyme *o*-diphenoloxidase was absent in *Mycobacterium leprae* separated from lepromatous human tissues. At that time the bacilli were not available from any other source. The existence or absence of this enzyme in *M. leprae* recovered from infected armadillo tissues was reinvestigated. The intact cells which were metabolically active failed to oxidize DOPA. Likewise, DOPA and its derivatives were not oxidized by the enzymatically active cell-free preparations from *M. leprae*. Upon incubation DOPA for more than 2 hr with whole cell suspensions or particulate fractions, there was no development of color with an absorption maximum of 540 nm as has been reported for an intermediate of DOPA oxidation. However, DOPA and several phenolic compounds were very actively oxidized by mushroom tyrosinase. The results suggested that *M. leprae* is deficient in *o*-diphenoloxidase, and this en-

zyme is not an intrinsic characteristic of this mycobacterium.—Authors' Summary

Nguyen, H. T., Trach, D. D., Man, N. V., Ngoan, T. H., Dunia, I., Ludosky-Diawara, M. A. and Benedetti, E. L. Comparative ultrastructure of *Mycobacterium leprae* and *Mycobacterium lepraemurium* cell envelopes. *J. Bacteriol.* **138** (1979) 552–558.

The structural properties of the cell envelopes of *Mycobacterium leprae* and *Mycobacterium lepraemurium* were investigated by freeze-fracture, freeze-etching, and negative-staining techniques. Freeze-fracture split the cell wall and exposed the internal features of the peptidoglycolipid mycosidic filamentous network. The cell membrane was also split into two asymmetric faces. The external fracture face was characterized by linear arrays of intramembranous particles, whereas the protoplasmic fracture face showed randomly distributed clusters of particulate entities. Comparative analysis of the ultrastructural features observed in *M. leprae* and *M. lep-*

raemurium indicated that the organization of the cell envelope in these two species differed particularly with respect to the amount and complexity of the superficial peptidoglycolipid and mycosidic integument, which is poorly developed in the mycobacterium responsible for human disease.—Authors' Summary

Sanabria, Kh., Smirnova, T. A., Kuri, Kh. and Almeida, Kh. A study of ultrastructure of *M. leprae* in human leproma. *Zh. Mikrobiol., Epidemiol., Immunobiol.* **1** (1979) 46–49. (in Russian)

The authors studied the ultrastructure of *M. leprae* in human leproma. Delicate morphology of *M. leprae* was described; fibrillar structures of the surface characteristic of mycobacteria were demonstrated on the ultrathin sections. Several types of interactions of *M. leprae* with tissue cells were revealed. Peculiarities of the ultrastructure of lepra cells characteristic of the given preparation were described.—Authors' Summary

Experimental Infections

Alexander, J. and Curtis, J. Development of delayed hypersensitivity responses in *Mycobacterium lepraemurium* infections in resistant and susceptible strains of mice. *Immunology* **36** (1979) 563–567.

C57BL mice are relatively resistant to a moderate subcutaneous infection with *Mycobacterium lepraemurium* while BALB/c mice are much more susceptible. Cutaneous delayed hypersensitivity reactions which develop in the first 3 weeks of infection were compared in these two strains of mice. Both strains gave a peak of delayed hypersensitivity between 6 and 10 days after infection which was followed by a period of low reactivity before the development, in the third week, of a stable persistent delayed hypersensitivity reaction. There was no difference between the strains in the size at 24 hr of the delayed hypersensitivity reaction, but the reactions differed in their kinetics. The low resis-

tance strain, BALB/c, gave a Jones-Motet-type of response while the high resistance strain gave a response which could be described as a tuberculin-type reaction.—Authors' Summary

Curtis, J. and Turk, J. L. Mitsuda-type lepromin reactions as a measure of host resistance in *Mycobacterium lepraemurium* infection. *Infect. Immun.* **24** (1979) 492–500.

The footpad reaction to autoclaved whole *Mycobacterium lepraemurium* organisms (MLM lepromin) in high-resistance (C57BL) and low-resistance (BALB/c) mice was studied. Infected C57BL mice gave a prolonged footpad response persisting for 4 weeks after skin testing with high and low doses of lepromin. This was accompanied by mononuclear cell infiltration. Uninfected C57BL mice gave no response. The majority of infected BALB/c mice gave

no increase in footpad thickness. However, a high proportion of infected and control BALB/c mice tested with the high dose showed mononuclear cell infiltration which resembled that in C57BL mice. The low dose caused little infiltration in infected or control BALB/c mice. The course of infection in the two strains was different. Dissemination of organisms from the infected footpad was minimal in C57BL mice 5 months after infection. In BALB/c mice, dissemination to the draining lymph node and to some extent to the liver had occurred by 5 months. The draining lymph node of BALB/c mice showed histological evidence of local antibody formation, which was not found in C57BL mice. On the basis of these findings, it was possible to fit murine leprosy in these two strains into a classification similar to that used for human leprosy.—Authors' Summary

Draper, P., Hart, D'A. and Young, M. R.

Effects of anionic inhibitors of phagosome-lysosome fusion in cultured macrophages when the ingested organism is *Mycobacterium lepraemurium*. *Infect. Immun.* **24** (1979) 558–561.

The mouse pathogen *Mycobacterium lepraemurium* is readily phagocytosed by cultured mouse peritoneal macrophages. Ingestion is normally followed by fusion between phagosomes and lysosomes. The influence of some anionic compounds known to inhibit fusion in other systems was investigated by transmission electron microscopy after ingestion of *M. lepraemurium*. Fusion was markedly, although temporarily, inhibited by suramin and moderately inhibited by poly-D-glutamic acid. The effects are, however, not sufficient to permit these agents to be used to study the long-term effects of shutting off the secondary lysosome-phagosome fusion system in cultured macrophages infected with *M. lepraemurium*.—Authors' Summary

Kawaguchi, Y., Matsuoka, M., Kawatsu, K., Sushida, K. and Tanemura, M.

Pathogenicity of cultivated murine leprosy bacilli of Hawaiian-Ogawa strain in mice. *Jap. J. Exp. Med.* **49** (1979) 27–32.

C3H and DDD strain mice were subcutaneously inoculated with 0.25 ml of a

1:1,000 saline suspension prepared from a malignant leproma in a nude mouse. The malignant leproma was induced with smooth colony variants (HO-S) of cultivated murine leprosy bacilli, strain Hawaiian-Ogawa. In C3H mice, no palpable lesions developed during the initial 35 weeks post-infection; however, at week 40, palpable lesions, which were identified as malignant lepromata, were found. In DDD mice, small benign lepromata were present at week 10, and examination at week 40 showed that they had not increased in size.

BALB/c mice were subcutaneously inoculated with 0.25 ml of a suspension prepared from the homogenate of subcutaneous tissue from the HO-S bacilli inoculation site of C3H mice. This suspension contained the same number of bacilli as a 1:2,000 leproma suspension. Three of 4 BALB/c mice developed typically intermediate mouse leprosy, and similar results were obtained in BALB/c mice infected with HO-S bacilli grown *in vitro*.

These observations confirmed our previous results and led us to conclude that the pathogenicity of HO-S bacilli grown *in vivo* is identical to that of *in vitro* cultivated HO-S bacilli and that HO-S bacilli do not revert to the more highly virulent parent bacilli of the rough colony (HO-R).—Authors' Summary

Preston, P. M. 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.* **73** (1979) 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 (C57BL) 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.—Author's Summary

Shepard, C. C., Walker, L. L. and Van Landingham, R. Heat stability of *Mycobacterium leprae* immunogenicity. Infect. Immun. **22** (1978) 87–93.

The protection provided to mice by vaccines administered intradermally was measured after footpad challenge with *Mycobacterium leprae*. The protection offered by *M. leprae* suspensions was not de-

creased when the vaccines were killed by 60°C heat or at the higher temperatures tested, which included 215°C (autoclave). Even highly purified suspensions retained their immunogenicity. In contrast, the vaccine protection provided by intradermal *M. bovis* (strain BCG) was markedly reduced when heated to 60°C. The enlargement of the lymph nodes regional to the intradermal vaccines was measured and found generally to parallel the vaccine protection provided by *M. leprae* and by BCG.—Authors' Summary

Epidemiology and Prevention

Faber, W. R. Leprosy in The Netherlands: a review of leprosy patients registered at the Department of Dermatology, University of Amsterdam in the years 1972–1976. Dermatologica **158** (1979) 38–45.

Recently, there has been a sharp increase in the number of leprosy patients in The Netherlands, due to an increased immigration from Surinam where leprosy is hyperendemic. The patients registered at the Dermatological Department of the University of Amsterdam during the years 1972–1976 were reviewed. It was found that 28% of the untreated patients had recently suffered a relapse. A substantial percentage took the medication irregularly or discontinued treatment prematurely, and quite a few patients required other types of treatment besides chemotherapy such as surgical treatment and physiotherapy.—Author's Summary

Fine, P. E. M., Wolf, E., Pritchard, J., Watson, B., Bradley, D. J., Festenstein, H. and Chacko, C. J. G. HLA-linked genes and leprosy: a family study in Karigiri, South India. J. Infect. Dis. **140** (1979) 152–161.

The evidence for a genetic determination of susceptibility to leprosy is reviewed. To test the hypothesis that an HLA (histocompatibility leukocyte antigen)-linked gene is

associated with such susceptibility, the association between the distribution of leprosy within a family, and the segregation of HLA haplotypes was investigated among 72 families who lived in Karigiri, Tamil Nadu State, South India. A statistically significant association was found for families in which siblings had tuberculoid leprosy and in which neither parent had leprosy. The findings from the data of this study agree with those of two previous studies carried out among smaller populations in Surinam and Wardha, Maharashtra State, India. Such an agreement suggests that a genetic determinant, which is linked to the major HLA locus on chromosome 6 and which is probably recessive, affects susceptibility to tuberculoid leprosy in humans.—Authors' Summary

Prost, A., Nebout, M. and Rougemont, A. Lepromatous leprosy and onchocerciasis. Br. Med. J. **1** (1979) 589–590.

Some recent reports mention a striking impairment of cell-mediated immunity in heavily infected patients, especially in areas where onchocerciasis is hyperendemic. As a similar disturbance occurs in the lepromatous form of leprosy we tried to compare the prevalence of leprosy in districts with and without a high prevalence of

severe onchocerciasis in the Republic of Upper Volta, in West Africa.

Our results indicate that in the two populations in which the overall prevalence of leprosy is similar, the prevalence of lepromatous leprosy is about twice as high in the areas where onchocerciasis is hyperendemic.

This finding seems to agree with observations of a reduced level of immunity because of onchocerciasis and with the hypothesis that a highly infected patient with onchocerciasis is more likely to develop the lepromatous form of leprosy and any other infection.—Authors' Summary

Russell, D. A., Worth, R. M., Jano, B., Fasal, P. and Shepard, C. C. Acedapsone in the prevention of leprosy: field trial in three high prevalence villages in Micronesia. *Am. J. Trop. Med. Hyg.* **28** (1979) 559–563.

The 1659 non-leprous people in a Micronesian population experiencing an annual leprosy incidence rate of about 7/1000 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 2/1000, 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.—Authors' Summary

Touw-Langendijk, E. M. J. and Naafs, B. Relapses in leprosy after release from control. *Lepr. Rev.* **50** (1979) 123–127.

In 1974, 678 patients, originally classified as suffering from various types of leprosy

from LL to TT, were released from control. During the next 3 years, 105 of them reported back on their own accord, with evidence of relapse which was confirmed by clinical, bacteriological and electrophysiological observations. During this period the overall relapse rate was 15%, but patients in the LL/BL group, the indeterminate group, and the BT group treated for less than 5 years had a relapse rate of over 30%. Reasons for these disconcertingly high figures are discussed and a plea is made for the collection of more data on relapse rates in similar groups of patients from different countries, in order to revise the criteria for releasing patients from treatment.—Authors' Summary

Varkevisser, C. M. Methodology of research into social aspects of leprosy control. *Lepr. Rev.* **50** (1979) 223–229.

Given the goal of optimal dapsone intake, social scientific research needs to take into consideration *both* the socio-cultural and socio-medical settings in which dapsone is available.

Various techniques can help reveal what factors determine prompt self-reporting and regular clinic attendance, and what factors retard them. In our project (Western Province, Kenya and Mwanza Region, Tanzania 1974–76) we combined a factor analysis of data on patient registration cards (limited in value because of the low quality of the data) with in-depth interviewing (patients, relatives, neighbors, false-alarmists, community leaders, traditional doctors). With a set of "test" statements, we measured prevailing community attitudes towards leprosy patients and then compared the results with our observations. At the same time we interviewed health personnel intensively and observed patient–staff interactions.

In-depth research is able to generate valuable suggestions for strengthening the leprosy services available, for training and retraining health personnel, and for educating patients and communities about leprosy control essentials.—Author's Summary

Rehabilitation

Enna, C. D. Skeletal deformities of the denervated hand in Hansen's disease. *The Journal of Hand Surgery* **4** (1979) 227-233.

Skeletal deformities of the denervated hand are subtle in their development and pose a more formidable problem than do primary deformities of Hansen's disease. Basic osseous changes consist of concentric, longitudinal, or the longitudinal varying methods of absorption. Knowledge of their pathogenesis provides the basis for their management. Prevention of deformity and conservative management of secondary complications are necessary to salvage as much of the hand as possible.—Author's Summary

Gupte, M. D. Dapsone treatment and deformities: a retrospective study. *Lepr. India* **51** (1979) 218-235.

Gandhi Memorial Leprosy Foundation conducted a study from 1963 to 72. Records of 2608 patients pertaining to type of leprosy, year of detection and registration, involvement of nerves, treatment, reactions, and deformities were available for a retrospective study.

Patients having problems like neuritis and deformities and of the lepromatous and borderline types were the ones who tended to be regular clinic attenders.

Lepromatous, borderline, and polyneuritic types and the N3 group were prone to develop deformities.

There seemed to be association between reaction and causation of deformities.

Because of the neurotoxic effect and ability to concentrate in the affected nerves, dapsone might enhance the risk of deformities.

Low deformity rates in N1 and N2 types of nerve involvement reaffirmed the necessity of early diagnosis of leprosy.—Author's Summary

Lakhan Pal, V. P., Yadav, S. S. and Nair, M. N. Reconstructive surgery of claw hand in leprosy. *Lepr. India* **51** (1979) 213-217.

Thirty-two hands in 31 known cases of leprosy were operated on, using the Paul Brand technique for the intrinsic minus deformity. Twenty-nine hands revealed good results whereas the remaining three also had definite improvement in their function and cosmesis. Bunnel's opponens plasty was performed in seven cases to restore the power of opponens in the thumb. Meticulous pre- and postoperative management proved to be very necessary.—Authors' Summary

The Fact of Stigma. New York: IYC Secretariat, 1979, 101 pp.

This booklet, prepared by the Sub-Group on Stigmatized Children of the Working Group on the Handicapped Child of the NGO Committee for the International Year of the Child, 1979, deals with the physical, mental, cultural, religious, and semantic elements which create stigma, i.e., "a negative emotional response to differentness," in the lives of children with special reference to leprosy. It points out that the consequence of stigma is to turn a relatively simple clinical problem into a difficult one because adults hide the disease in themselves or in their children out of fear of stigma until the clinical complications of the disease are very obvious, and treatment is much more difficult. It is pointed out that leprosy becomes a serious health problem in children between 5 and 14 years of age in highly endemic areas and that the incidence in these areas in children may approach that of the whole population. The booklet provides a highly useful and exhaustive bibliography (157 references) dealing with all aspects of the subject of stigma. Register of activity sheets are included, pointing out activities dealing with the International Year of the Child and the theme of leprosy and children which have been carried out by ILEP, L'Association Française des Fondations Raoul Follereau, the ILA, and the ALM as well as the text of the ILEP resolution of 23 November 1978 supporting the rights of children with leprosy or related to leprosy patients.—G. Gordon

Other Mycobacterial Diseases and Related Entities

Katz, P., Goldstein, R. A. and Fauci, A. S. Immunoregulation in infection caused by *Mycobacterium tuberculosis*: the presence of suppressor monocytes and the alteration of subpopulations of T lymphocytes. *J. Infect. Dis.* **140** (1979) 12–21.

This study was designed to characterize qualitative and quantitative alterations, occurring before and during chemotherapy, in the mononuclear cells of patients with infections caused by *Mycobacterium tuberculosis*. A hemolytic plaque-forming (PFC) assay indicated that the production of antibody to sheep red blood cells by pokeweed mitogen (PWM)-stimulated lymphocytes was suppressed in treated and untreated patients as compared with that in normal adult donors ($p < 0.001$). The removal of adherent cells from the suspensions of mononuclear cells significantly enhanced the responses to the PFC assay for both the untreated ($p < 0.01$) and treated ($p < 0.05$) patients. Mononuclear cells from patients with tuberculosis, however, did not suppress the PFC responses of allogeneic normal mononuclear cells ($p > 0.02$). Thymus-derived (T) lymphocytes were proportionally reduced in untreated subjects ($p < 0.001$) but returned to normal levels after four to six weeks of therapy ($p > 0.2$). Both groups of patients had a consistent reduction in the absolute number of circulating T cells. However, untreated patients had a relative increase in the percentage of T_G cells (the subpopulation of T cells with receptors for the Fc portion of IgG) ($p < 0.001$) and a concomitant decrease in T_M cells (the subpopulation with Fc receptors for IgM) ($p < 0.05$). These alterations in the subsets of T cells were reversed after four to six weeks of therapy.—Authors' Summary

Nakamura, R. M. and Tokunaga, T. Strain difference of delayed-type hypersensitivity to BCG and its genetic control in mice. *Infect. Immun.* **22** (1978) 657–664.

Delayed-type hypersensitivity to BCG was remarkably different in two inbred strains of mice, SWM/Ms and C3H/He, when measured by the spleen index, the

disappearance of peritoneal macrophage, or the footpad reaction. High responsiveness in the SWM/Ms strain appeared to be dominant over low responsiveness in the C3H/He strain. Results of the footpad reaction test in F1, F2, and backcross hybrids of these two strains of mice suggested that the delayed-type hypersensitivity was mainly controlled by a gene which was transmitted under Mendel's laws and was possibly non-*H-2* linked. The spleen cells and their nylon wool nonadherent fraction from BCG-infected C3H/He mice were not reactive to purified protein derivative *in vitro*, whereas both the spleen cells and the nylon wool nonadherent fraction from BCG-infected SWM/Ms mice reacted well to purified protein derivative. Possible mechanisms of the different responses in the delayed-type hypersensitivity to BCG were discussed.—Authors' Summary

Narain, R., Gothi, G. D., Ganapathy, K. T. and Shyama Sunder, C. V. Effect on tuberculin allergy of tuberculin tests given 18 months earlier. *Indian J. Med. Res.* **69** (1979) 886–892.

The enhancing effect of tuberculin allergy as a result of repeat tests with 1 TURT 23 on groups tested with 1 TU, 20 TU and a placebo was studied by random allocation among a population not vaccinated with BCG in 8 villages. Tuberculin test reactions were found enhanced in an earlier study when the tests were repeated within two months in a group administered a dose of 20 TU. The study did not show an enhancing effect due to a previous tuberculin test with 1 TU alone among groups tested once, twice or thrice after an interval of 18 months. There was no increase in reaction even among those who were tested with a higher dose of 20 TU earlier. The boosting effect on account of an earlier tuberculin test observed after 2 months of the previous test shown in an earlier report seemed to disappear between the second and eighteenth month, when they were retested with a normal dose. It is inferred from the study that boosting with higher dose or repeat tests with the same dose does not per-

sist after 18 months. Hence, for classifying positive tuberculin reactors, no correction is required to overcome the boosting effect when repeated tuberculin tests are given to the same individuals/population after an interval of 18 months or more, as no boosting effect after 18 months has been observed on the basis of this analysis.—Authors' Summary

Smith, C. C., Barr, R. M. and Alexander, J. Studies on the interaction of *Mycobacterium microti* and *Mycobacterium lepraemurium* with mouse polymorpho-

nuclear leucocytes. J. Gen. Microbiol. **112** (1979) 185–189.

When polymorphonuclear leucocytes (PMN) elicited in mice were infected with *Mycobacterium microti* or *Mycobacterium lepraemurium*, phagosome-lysosome fusion occurred with both species. This contrasts with the situation in macrophages where phagosome-lysosome fusion is inhibited by *M. microti* but not *M. lepraemurium*. No evidence was found for killing of *M. microti* or *M. lepraemurium* when the bacteria were isolated from PMN and their viability tested in cell-free medium or macrophages.—Authors' Summary