CURRENT LITERATURE

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

Chemotherapy

Ganapati, R., Revankar, C. R. and Naik, S. S. Field application of combined therapy for infectious leprosy cases. A feasibility study in Bombay. Lepr. India **55** (1983) 485–489.

The practical problems related to dapsone monotherapy for a prolonged period for infectious leprosy patients are well known to the scientific community and combined treatment of dapsone with clofazimine, rifampin or prothionamide has been successfully carried out by several workers in hospitalized leprosy patients. The application of polytherapy in field conditions was hindered by the cost of the drugs and fear of the side effects.

Forty-two infectious leprosy patients attending five field leprosy clinics in the slums of Bombay city were put on a combined drug schedule. The drug compliance of these patients was judged along with their regularity in attendance at clinics by the persons in charge and periodic and frequent check up of urine; 27 (65%) were regular in treatment from the beginning, 8 (19%) were initially irregular after motivation and 7 (17%) remained irregular throughout the period. The urine samples collected from leprosy patients on monotherapy and attending the same centers revealed 31% irregularity in drug consumption.

The study indicates that advocating combined therapy in field conditions by paramedical workers is quite feasible. Patients on multiple drugs are more regular in drug consumption as compared to monotherapy patients. The frequent check up of urine for drug content, and advice to patients who are irregular in treatment improve their regularity in drug consumption.—Authors' Abstract

Irudaya Raj, P. O., Lourdumary, S., Aschhoff, M. and Balakrishnan, S. A comparison of screening tests for dapsone in urine. Lepr. India **55** (1983) 528–538.

The comparative merits and limitations of three qualitative tests for dapsone (DDS) screening in urine (the spot test, using modified Ehrlich's reagent; tile test, employing Bratton-Marshall reagents; and the ELISA test) were assessed with regard to their sensitivity and operational feasibility. Investigations were carried out on a total of 716 urine specimens of which 268 specimens were collected during surprise visits paid to the patients' homes. The others were specimens collected from patients at different time intervals, following the administration of 25, 50 and 100 mg of dapsone. The findings were evaluated against their corresponding ratios of the urinary concentrations of dapsone and its diazotizable metabolites to creatinine (C). A good correlation was found between the three qualitative tests in general and also in relation to the DDS/C ratios. Operational feasibility under field conditions for spot and tile tests are discussed.—Authors' Abstract

Ji Ban-Hong, *et al.* The activity of thirty-five drugs in suppressing experimental *Mycobacterium leprae* infection in mice. Chin. J. Clin. Dermatol. **12** (1983) 230–231. (in Chinese)

By means of the mouse foot pad technique and using continuous administration of drug incorporated into mouse diet, 35 drugs have been tested for their ability to suppress experimental *Mycobacterium leprae* infection. Although all of these drugs had been shown to have antituberculous activity *in vitro,* none of them revealed any significant activity in suppressing the multiplication of *M. leprae* in the mouse foot pad. Therefore, the activity against *M. leprae* in a given drug has not been predictable

from its activity against *M. tuberculosis in vitro*. The drug screening studies by means of the mouse foot pad model are cumbersome and time consuming. The drugs should be tested as primary screening in an *in vitro* system composed of several species of cultivable mycobacteria. If any drug has been shown to have broad activity against mycobacteria *in vitro*, some necessary pharmacologic studies, including the absorption and metabolism of the drug in mice, should be undertaken before the evaluation of its antileprosy activity in the mouse foot pad model.—Authors' English Abstract

Kumar, A. and Balakrishnan, S. Operational study to monitor the regularity of dapsone intake by leprosy out-patients. Lepr. India **55** (1983) 521–527.

Three hundred nineteen leprosy patients attending our mobile treatment unit were monitored for their regularity of dapsone (DDS) intake by 1) verification of DDS tablets, and 2) spot test in the field. The consistency in regularity of DDS intake by these patients was monitored at two more occasions at the interval of about two months.

Only 36% of patients were regular in attending the clinics. On an average, one patient would miss about one third of the clinics in a year. The number of patients taking regular treatment increased from 62% (first round) to 79% (third round). Approximately 10% of patients collected DDS tablets from the clinic but never ingested them, and 3%–7% of patients removed the dapsone tablets regularly but ingested none of them, as indicated by negative spot tests. The spot test was found to be positive in about 86% of the patients and has a very good correlation (98%) with the DDS/creatinine ratio. Both methods of monitoring were found to be operationally very feasible and reliable under field conditions, hence they can be used together to monitor the dapsone intake by leprosy patients in the National Leprosy Control Programme (India).—Authors' Abstract

Leprosarium of Hai-an County, *et al.* Liver toxicity in leprosy with combined therapy. Chin. J. Clin. Dermatol. **12** (1983) 237–239. (in Chinese)

Eighty-nine leprosy patients, 39 in Hai-an Leprosy Hospital and 50 in Shanghai Zeng-yi Hospital, were treated with combined therapy. The incidence of hepatitis caused by drugs was 56.4% and 22%, respectively. After starting combined therapy for 3–4 months, one patient in each hospital developed acute yellow atrophy of the liver and hepatic coma, and eventually died. It was not yet clear what drug caused the drug hepatitis, most probably the prothionamide. Liver function tests should be done monthly in the course of combined therapy in order to avoid irreversible hepatic damage.—Authors' English Abstract

Li Huan-Ying. Correlation of the chemotherapy of leprosy and tuberculosis. Chin. J. Clin. Dermatol. **12** (1983) 258–259. (in Chinese)

The action of the different drugs in short course of antituberculosis therapy is complementary. It is not yet possible to eliminate all viable bacilli from lepromatous leprosy. The purpose of the combined treatment is to prevent the appearance of drug resistance and to shorten the course of treatment. The rational basis of combined therapy for all types of leprosy as recommended by WHO in 1981 is reviewed, and the importance of training of personnel and laboratory examinations, as well as regular follow-ups, in modern leprosy control is stressed.—Author's English Abstract

Mathur, N. K., Bumb, R. A. and Mangal, H. N. Oral zinc in recurrent erythema nodosum leprosum reaction. Lepr. India **55** (1983) 547–552.

Oral zinc sulfate was tried in eight cases of recurrent erythema nodosum leprosum (ENL). To control ENL, they required high dosage of clofazimine and steroids for prolonged periods. After instituting oral zinc, the dose of clofazimine could be reduced to 100 mg twice a week and steroids could be withdrawn completely. Four out of five patients who were not tolerating dapsone earlier started tolerating dapsone. Incidence and severity of subsequent ENL was also reduced.—Authors' Abstract

Moore, V. J. A review of side-effects experienced by patients taking clofazimine. Lepr. Rev. **54** (1983) 327–335.

The incidence of specific side effects experienced by 65 patients taking clofazimine was assessed. All but one had suffered side effects; skin and conjunctival pigmentation being the commonest. Abdominal pain was a complaint in one third of the patients. The 57 patients who were still taking clofazimine were divided into two groups according to dosage. The incidence of side effects was similar in both groups. The average times of onset of the side effects since starting clofazimine, in all instances, were greater in the lower dosage group. The possible significance of this is discussed. Eight patients who had discontinued clofazimine therapy were seen. The disappearance of the side effects was, in the majority of cases, six months or more after stopping therapy. The difficulties associated with assessing dimness of vision and time intervals retrospectively are discussed. No patients had stopped clofazimine due to side effects. Five patients expressed dislike of the side effects; three of these patients were in the lower dosage group. One patient asked for an increase in dosage to control an ENL reaction. The tolerance of side effects, in general, was very good. No patients suffered serious adverse reactions.—Author's Summary

Stanley, J. N. A., Pearson, J. M. H. and Ellard, G. A. An investigation of dapsone compliance using an isoniazid-marked formulation. Lepr. Rev. **54** (1983) 317–325.

In a study conducted among outpatients in Hyderabad, India, it was shown that the precision of the dapsone/creatinine method for monitoring dapsone compliance could be improved if patients were prescribed specially formulated dapsone capsules containing 6 mg isoniazid as an innocuous marker. Urine samples were obtained by means of surprise home visits; the ingestion of the isoniazid marker was revealed by a simple colorimetric procedure which gives reliably positive results for about 18 hr. The study showed that such capsules were acceptable to the patients and, in the short run, were taken more regularly than the standard tablets. However, a small proportion of patients took both capsules and tablets very irregularly, indicating that poor compliance was not overcome by simply changing the dapsone formulation.—Authors' Summary

Valdes-Portela, A., Vazquez, A. M. and Finlay, C. M. The effect of clofazimine on the plaque-forming cell response. Lepr. Rev. **54** (1983) 309–325.

The plaque-forming cell (PFC) technique was used to assay the effect of clofazimine, an antileprotic drug, on the immune system. Inbred mice were force-fed the drug for different periods of time at concentrations of 1 mg/kg and 10 mg/kg of body weight per day. After 14 and 21 days of treatment, a significant increase in PFC response was observed. It is concluded that clofazimine exerts an effect on the early events involved in the antibody-forming cell response.—Authors' Summary

Clinical Sciences

Al-Karawi, M., Nawaz, S. and Beeching, N. J. Leprosy—a diagnosis that should still be considered in Saudi Arabia. Saudi Med. J. **4** (1983) 31–36.

This review of the literature on the epidemiology of leprosy in Saudi Arabia shows that most of the cases arise in the South West Province of the country and that almost half have lepromatous leprosy. This figure may reflect the true situation or decreased diagnosis of tuberculoid leprosy cases. Widespread ignorance and fear of the disease is noted. The overall prevalence of the disease in the country is not cited. Five cases of leprosy diagnosed in the Riyadh Military Hospital are described. [These cases are of interest but are by no means typical.]—P. R. Gully (*From* Trop. Dis. Bull.)

Baldrich Camino, J. F., Angulo, M. H., Rams, L. V., Ponce, G. T. and Marrero,

A. Sonoterpia en lepra ocular. [Sonotherapy for ocular leprosy.] Rev. Cubana Med. Trop. **34** (1982) 298–307. (in Spanish)

This is a preliminary report on the results obtained with ultrasonic therapy in eight patients with corneal opacity as a consequence of ocular lesions in Hansen's disease. In spite of the small sample size, a clear and valuable improvement in subjective symptoms of an irritative nature (photophobia and lacrimation) was found. No conclusions could be reached of an objective nature since only three (37.5%) of the eight patients showed a decrease in the density of the corneal opacity. A greater number of patients should be studied in order to provide definite evidence of the efficacy of this therapeutic method. It seems clear that the subjective improvement achieved by this therapy is valuable and represents a partial rehabilitation of these patients.—(*From* the Authors' English Summary)

Brandt, F. and Shrestha, K. B. Über den Wandel von ophthalmologischen Befunden bei Morbus Hansen unter Chemotherapie. [Changes of the ophthalmic findings in morbus Hansen during chemotherapy.] Fortschr. Ophthalmol. **79** (1983) 455–457. (in German)

Eighteen months after the introduction of chemotherapy in a leprosarium in Nepal, no new ophthalmic findings were found in patients with tuberculoid leprosy. In the lepromatous form of the disease, however, increasing numbers of ophthalmic findings—especially in the anterior part of the uvea—were observed.—Authors' English Summary

El-Saaiee, L., Abd-el Aal, H., El-Mahdy, H. and Abd-el Galil, S. Minerals in blood sera and scalp hair in patients with lepromatous leprosy and tuberculoid leprosy. J. Med. **14** (1983) 117–124.

Scalp hair and blood sera of three groups of individuals were studied for mineral contents by flame photometric and colorimetric procedures. Patients in one of the three groups were suffering from lepromatous leprosy; the second group comprised patients with tuberculoid leprosy and the third group consisted of normal controls. The results obtained revealed changes in the mineral content of the scalp hair of those suffering from lepromatous leprosy and tuberculoid leprosy. A possible relationship may exist between hair and serum minerals.—Authors' Abstract

ffytche, T. J. A computer form to aid in the collection of data on the ocular complications of leprosy. Lepr. Rev. **54** (1983) 271–281.

There is a need for data on the wide variety of ocular complications of leprosy that have been observed in patients in different parts of the world. Such data would be valuable in the planning of eye care and preventive measures. A computer form has been designed to collect information from groups of leprosy patients so that the results can be centralized and submitted for analysis. The form can be used by medical students as well as medical and paramedical workers, and guidelines on ophthalmic examination in leprosy and the recording of the findings are presented.—Author's Summary

Green, C. A., Katoch, V. M. and Desikan, K. V. Quantitative estimation of *Mycobacterium leprae* in exhaled nasal breath. Lepr. Rev. **54** (1983) 337–340.

A quantitative estimation of leprosy bacilli in exhaled nasal breath was undertaken in 20 patients of borderline and lepromatous leprosy. Out of the 20 patients, 8 were untreated, 6 had treatment for one month, and the remaining 6 were on treatment for a period of three months. Noncultivable acid-fast bacilli could be demonstrated in nasal breath in all the cases studied. The average number of bacilli excreted were 3.8×10^4, 2.9×10^4, and 2.8×10^4 per breath in the three groups, respectively. The quantum of bacilli exhaled increased with duration of the disease.—Authors' Summary

Hogeweg, M. and Leiker, D. L. Eye involvement in leprosy: a survey among patients in The Netherlands. Br. J. Dermatol. **109** (1983) 477.

Leprosy affects the eye in two ways: a)

Indirectly: through invasion of *Mycobacterium leprae* into the fifth or seventh cranial nerves, and immune response reactions in the nerve, causing lid weakness, lagophthalmos and possibly damage to the cornea by exposure keratitis, and corneal anesthesia, which may worsen corneal damage, respectively. b) Directly: through invasion of *M. leprae* into the eye and immune response reactions, or via circulating immune complexes (ENL). Chronic iritis is said to be the most frequent cause of blindness in leprosy. LL—and BL—patients are especially prone to direct eye involvement. In 1979–1980 a survey was done among 121 outpatients visiting the leprosy clinic of the Department of Dermatology, Amsterdam Medical Centre (former Binnengasthuis). Potentially blinding lesions were found only in long-standing LL—and BL—cases in this series. Lagophthalmos was the most frequent lesion in BT patients.—(*From* the article)

Lamba, P. A., Santoshkumar, D. and Arthanariswaran, R. Ocular leprosy—a new perspective. Lepr. India **55** (1983) 490–495.

The classification of ocular lesions in leprosy into academic and potentially sight-threatening (PST) lesions clears away much of the confusion engendered by the wide disparity in the reported incidences. It also enables one to project confidently the level of ocular morbidity in a given leprosy population with more precision. Based on the observation in the study, approximately 1.5 million leprosy patients are expected to be affected with PST lesions. Measures to be undertaken to prevent this morbidity and visual impairment in this vulnerable group can be better worked up. The incidence of blindness because of leprosy is reported to be 2.6%.—Authors' Abstract

Moll, V. M. Diabetes mellitus en enfermos de Hansen: un estudio epidemiológico. [Diabetes mellitus in leprosy patients: an epidemiologic study.] Fontilles **14** (1983) 137–141. (in Spanish)

The author has made a survey concerning the incidence of diabetes mellitus in leprosy patients from Fontilles (predominantly of the lepromatous type) and he has compared it with a control group of healthy people from the surrounding villages (Orba and Vall de Laguart). The two groups (122 individuals in each group) were closely matched for age. Among the leprosy patients, 18 were diabetic (14.8%), while 8 (6.6%) of the controls had diabetes.—(*Adapted from* Author's English Summary)

Prabhakar, M. C., Appa Rao, A. V. N., Krishna, D. R. and Ramanakar, T. V. How much non-infectious are the "non-infectious" lepromatous leprosy patients? Lepr. India **55** (1983) 576–583.

The nose forms an important site at which *Mycobacterium leprae* in lepromatous leprosy (LL) patients lodge and multiply. The nose forms an important reservoir for *M. leprae,* from where they may be transmitted to healthy contacts. In spite of this fact, the nose does not normally receive due importance during the chemotherapy of leprosy. LL patients, after regular treatment with dapsone or rifampin for about 20 wk and 3 wk, respectively, are normally considered noninfectious. From the present investigation it is clear that local treatment of the nose with a bactericidal agent should perhaps be necessary during chemotherapy of LL patients to make them noninfectious and to control the transmission of the disease.—Authors' Abstract

Ramu, G. The Indian classification of leprosy. Jpn. J. Lepr. **50** (1981) 226–232.

The author reviews a number of historical classifications used for leprosy. The clinical features of the six classes of leprosy in the Indian classification (indeterminate, maculo-anesthetic, tuberculoid, borderline, lepromatous, and polyneuritic) are presented. A comparison is made among the Indian, Madrid, Ridley-Jopling, and Japanese classifications. Differences in classifications could be due to differences in the types and manifestations of leprosy observed in different regions of the world. A commonly agreed classification is vital to the exchange of scientific information among different regions. The classification that has been recommended in a recent concensus in Bombay is aimed at such an approach.—(*From* the article)

Sandburg, P. and Shum, T. K. Lepromatous leprosy of the larynx. Otolaryngol. Head Neck Surg. **91** (1983) 216–220.

This case illustrates the classic features of lepromatous leprosy, including lesions of the oropharynx and larynx. The disease is rare in the United States, and the diagnosis must be suspected in persons from endemic areas who may have laryngeal signs and symptoms. The diagnosis is readily made with the combination of history, physical findings, and biopsy. Treatment is by chemotherapy for an extended period of time, with precautions taken at the initiation of therapy to avoid erythema nodosum leprosum because of its potential for edematous obstruction of the larynx.—Authors' Conclusions

Scrimgeour, E. M. Huntington's disease and leprosy in a New Guinea Highlander. J. Med. Genet. **20** (1983) 412–415.

Huntington's disease (HD) was observed in a 45-year-old male Melanesian patient from the Eastern Highlands Province of Papua New Guinea. The patient had multiple peripheral nerve palsies as a result of tuberculoid leprosy and had been resident in the leprosy ward of Goroka Base Hospital for over six years. During this time his HD had remained undiagnosed. This is the first report of HD in the Highlands of New Guinea.—Author's Summary

Sengupta, P., Raychowdhuri, D. and Haldar, B. Foot drop mimicking neuritic leprosy induced by a Baker's cyst. Lepr. India **55** (1983) 480–482.

A Baker's cyst of the left knee joint induced foot drop insidiously in a male, Hindu, aged 25 years. On clinical suspicion that this malady was caused by neuritic type of leprosy, he was administered antileprosy drugs for six months without any benefit. On exploration, a globular cystic mass containing gelatinous fluid was seen to be pressing over the left lateral popliteal nerve. Following removal of this mass, which on histology confirmed to be a Baker's cyst, foot drop and associated motor power impairment disappeared. This case thus highlights the importance of an early exploration and histological diagnosis of a suspected case of neuritic leprosy inducing foot drop and progressively deteriorating, in spite of regular antileprosy therapy.—Authors' Abstract

Shenoy, M., Somayajulu, G. L. and Bhaskaran, C. S. Haptoglobulin phenotypes in leprosy. Lepr. India **55** (1983) 566–569.

Haptoglobulin phenotyping was carried out in 50 controls and in 35 leprosy patients. In controls the incidence of Hp phenotypes 2-2, 2-1 and 2-1 (Mod) is 76%, 16% and 8%, respectively. In leprosy patients, the incidence of phenotypes 2-2, 2-1, 1-1 and 0-0 is 77%, 11%, 3% and 9%, respectively. The incidence of phenotypes 2-2, 1-1 and 0-0 is more in leprosy patients than in controls and is significant ($p < 0.05$). In none of the leprosy patients was phenotype 2-1 (Mod) recorded.—Authors' Abstract

Venkatesan, K., Kannan, K. B., Bharadwaj, V. P., Sritharan, V., Katoch, K., Usha, R. and Ramu, G. Serum copper & zinc in leprosy & effect of oral zinc therapy. Indian J. Med. Res. **78** (1983) 37–41.

Fifteen patients of active lepromatous leprosy (LL), 10 of borderline tuberculoid (BT) leprosy, 15 LL/BL patients during the reactional as well as the subsided states, and 15 family members of the patients were investigated for serum copper and zinc levels. Hypercupremia associated with hypozincemia was observed in active LL and LL/BL reactive patients as compared to controls and BT patients. Twelve patients in BL/LL reaction with blistering and ulcerations including varying degrees of arthritis and 12 active LL patients were given oral zinc sulfate therapy for two weeks and then subjected to copper-zinc analyses at the end of the therapy. Zinc sulfate therapy was found to restore the initial low zinc level while the copper level was lowered from the initial higher level. The possible beneficial effects of oral zinc therapy during reactions in LL/BL and also active LL patients have been indicated.—Authors' Abstract

Vinod Kumar, C. H. D., Harikrishnan, S., Bhatia, V. N. and Roy, R. G. Bacteriological study of trophic ulcers in leprosy

patients. (A preliminary study.) Lepr. India **55** (1983) 504–511.

Swabs from trophic ulcers from 108 cases were studied by culture: 37 cases yielded single organism (*P. aeruginosa,* 18; *Proteus* species, 11; *Staph. pyogenes,* 4; others, 4); 71 cases yielded mixed growth with two or more organisms. *P. aeruginosa, Proteus* species and diphtheroids were the predominant organisms in these cultures. *P. aeruginosa* was sensitive to gentamycin (96.6%), streptomycin (62.7%) and chloramphenicol (33.9%). Other organisms although comparatively more sensitive showed a similar pattern.—Authors' Abstract

Yuan Gyan-Qing. Lucio's phenomenon in leprosy: a case report. Chin. J. Clin. Dermatol. **12** (1983) 254. (in Chinese)

A case of leprosy with Lucio's phenomenon was reported with description of the clinical manifestations. Rather good therapeutic effect was obtained after the combined treatment of traditional Chinese medicine and Western medicine.—Author's English Abstract

Zawar, P. B., Holla, V. V., Patil, S. M., Zawar, M. P. and Chawhan, R. N. Bacillaemia in lepra reaction: its correlation with liver pathology. Lepr. India **55** (1983) 570–575.

Thirty patients with lepromatous leprosy in a state of reaction (ENL) were studied for bacillemia and a correlation was made with liver pathology. Buffy coat smears were examined in all, eliminating as far as possible the chances of contamination of blood by the skin bacilli. Thirteen out of 30 patients showed presence of acid-fast bacilli (AFB) in the buffy coat smear. Hepatic involvement in the form of leprous granuloma was observed in all, 93.3% of which showed the presence of AFB. It is concluded that during reaction the possibility of heightened bacillemia is less likely and that the systemic spread of infection is not accentuated during the bouts of reaction.—Authors' Abstract

Immuno-Pathology

Abdirov, C. A., Eshchanov, T. B., Vdovina, S. K. and Podoplelov, I. I. Some values of T and B system of immunity in patients with different types of leprosy. Vestn. Dermatol. Venerol. **5** (1983) 14–17. (in Russian)

In the Karakalpak endemic zone, the content of T and B cells and IgM, IgG, and IgA in the blood of patients with lepromatous and tuberculoid types of leprosy and of normal subjects (controls) was compared. Patients with lepromatous leprosy were found to have most marked changes in the blood including a significant decrease in the content of T lymphocytes, an increase of the content of B lymphocytes and IgG and IgA. In tuberculoid leprosy there was also a trend to changes in populations of T and B lymphocytes but only a minor increase in the content of IgM. The authors interpret the obtained results in the light of the proposed immunogenetic concept of leprosy and current data concerning the development of suppressor cells in leprosy.—Authors' English Summary

Bjune, G., Closs, O. and Barnetson, R. St.C. Early events in the host-parasite relationship and immune response in clinical leprosy: its possible importance for leprosy control. Clin. Exp. Immunol. **54** (1983) 289–297.

To learn more about protective mechanisms, which may also be non-immunological in nature, research should focus more on subclinical and indeterminate leprosy. We also need to know a) more about the antigenic composition of *Mycobacterium leprae,* b) about escape mechanisms of this organism, c) about the normal fate of bacilli in various human cells, and d) about genetic and environmental risk factors. This paper is an attempt to review some of the factors which are known, some which are suspected and to raise questions for further research. It is divided into three sections: 1) the caus-

ative organism, 2) the host response, and 3) diagnosis of subclinical infections.—(*From* the article)

Curtis, J. and Turk, J. L. Dissociation between allergy and immunity in leprosy. Practitioner **222** (1983) vii–ix.

It appears that in leprosy patients standard tests both *in vivo* and *in vitro* of cell-mediated immunity correlate well with resistance at the lepromatous end of the spectrum. The lack of resistance of polar lepromatous patients is accompanied by low responses in all such tests. However, in borderline leprosy patients, particularly at the tuberculoid end of the spectrum, the size of their responses is often a measure of their state of allergy. Several defects in the immune systems of leprosy patients have been demonstrated in *in vitro* tests of cell-mediated immunity (CMI) but the causal relationship of such defects to low resistance have yet to be established.

The specificity and relationship to resistance of positive CMI reactions in healthy people in leprosy endemic areas is of great importance for any future leprosy vaccine trials. Perhaps even more important, however, is the relevance of negative responses in people with a high degree of contact with leprosy patients.—Authors' Conclusions

Gatti, J. C. and Raimondi, A. Infeccion subclinica en lepra. [Subclinical infection in leprosy.] Leprologia **24** (1982) 163–170. (in Spanish)

The subject of subclinical infection in leprosy is reviewed and the epidemiological, bacteriological, and immunological evidence of its existence is updated. Techniques for studying cell-mediated and humoral immunity are described along with the results that have been obtained, with special attention to the importance of some of these tests, especially the FLA-ABS, in the diagnosis of infection in leprosy and the usefulness of the application of both the FLA-ABS and the lepromin test for the detection of patients with a high risk of development of the lepromatous form of the disease.—(*Adapted from* Authors' English Summary)

Gonzalez-Amaro, R., Moncada, B., Loredeo, C. E. and Baranda, M. deL. T-lymphocyte subsets in leprosy. Int. J. Dermatol. **22** (1983) 305–306.

Immunologic abnormalities in T cells have been reported in patients with lepromatous leprosy. Ten patients with leprosy (8 lepromatous, 1 dimorphous, 1 tuberculoid) were studied in order to detect the proportions of total T lymphocytes and helper as well as suppressor subsets, using monoclonal antibodies in an indirect immunofluorescence test. Percentages of total T cells, suppressor cells, as well as helper subsets were similar in leprosy patients as compared with age-matched controls. This study could be considered a preliminary one to be followed by functional assays.—Authors' Abstract

Haregewoin, A. and Louis, J. Characterization and functional studies of the murine T-lymphocyte response to *Mycobacterium leprae* antigen. Scand. J. Immunol. **18** (1983) 225–233.

Mice were immunized with *Mycobacterium leprae* in incomplete Freund's adjuvant, and sensitized lymphocytes were obtained from draining lymph nodes. The lymphocytes thus obtained proliferated specifically *in vitro* in the presence of *M. leprae* antigen, and this response was shown to be both T cell and macrophage dependent. T cell blasts generated *in vitro* in response to *M. leprae* antigen were grown in the presence of interleukin 2 (IL-2). The proliferative response of these blasts to *M. leprae* antigen was strictly dependent on the presence of syngeneic spleen cells as antigen-presenting cells. *M. leprae*-immune F_1 blasts responding to the antigen in the context of either parental H-2 haplotype-bearing accessory cell could be obtained by positive selection from an F_1 hybrid-responding cell population. By means of flow microfluorometry the T cell phenotype of the *M. leprae*-specific T cell blasts was found to be Thy-1^+ and to be composed of Lyt-1^+ and Lyt-2^+ subpopulations. Functionally, the blasts were shown to transfer delayed-type hypersensitivity locally to nonimmunized recipients and to have cytolytic activity. Limiting dilution analysis showed the fre-

quency of *M. leprae*-responding cells from blasts grown in IL-2 to be approximately 1/333.—Authors' Abstract

Haregewoin, A., Yemaneberhan, T. and Belehu, A. The role of products of the human HLA-DR locus (Ia molecules) in *in vitro M. leprae* driven lymphoproliferation. Clin. Exp. Immunol. **53** (1983) 328–334.

[Peripheral blood lymphocytes were obtained from healthy contacts of leprosy patients in Ethiopia. Cells from such contacts are known to give a high proliferative response to *Mycobacterium leprae in vitro.*] We analyzed the role of Ia molecules in T cell activation with *M. leprae* by using two hybridoma monoclonal antibodies D1-12 and D4-22 with specificity for non-polymorphic isotypes NG-1 and NG-2, respectively, on the HLR-DR molecular framework. The results show that the addition of either monoclonal antibody up to three days after onset of culture significantly blocks the *in vitro M. leprae* driven lymphoproliferation. The mechanism of suppression appears to be due to a combination of steric hindrance and a vigorous suppressor signal from anti-Ia treated macrophages. The possible implications of these results are discussed.—(*From* Trop. Dis. Bull.)

Holla, V. V., Zawar, P. B., Desmukh, S. D. and Sardar, S. S. Leproma of heart—a case report. Indian Heart J. **35** (1983) 111–113.

An unusual occurrence of leprous granuloma with the presence of acid-fast bacilli (AFB) in a patient with lepromatous leprosy encountered at autopsy is reported. On autopsy the most interesting findings were encountered in the heart. On external examination, the heart appeared normal, weighing 230 g. On cutting open, a polypoidal, firm, irregular lesion was seen attached to the atrial surface of the lateral leaflet of the mitral valve which was extending over the lateral left atrial wall. It measured 2.5 × 1.5 × 1 cm and showed relatively pale, rough surface. On microscopic examination, the sections from the lesion showed subendocardial granuloma. The granuloma was composed of foamy histiocytes, epithelioid cells and few lymphocytes. Staining for acid-fast organisms revealed 0–2 bacilli per high power field within the foamy cells. These were also seen in the endothelial cells lining the blood vessels in the vicinity of the granuloma. These organisms were morphologically typical of *Mycobacterium leprae.* A few of them were fragmented, while others were irregularly stained indicating dead bacilli. Multiple sections studied from other sites of the heart showed areas of subendocardial and focal myocardial fibrosis with separation of myocardial fibers. These areas showed sparse lymphoid infiltration and mild vasculitis.—(*From* the article)

Kumar, B., Ganguly, N. K., Kaur, S., Vaishnavi, C. and Chakravarti, R. N. Effect of dapsone (DDS) on T-cells and their response to PHA and lepromin in tuberculoid leprosy patients. Lepr. India **55** (1983) 465–471.

T and B cell counts and their response to PHA and lepromin were studied in 46 patients of polar tuberculoid (TT) leprosy divided into two age- and sex-matched groups. Twenty-five normal, healthy controls were similarly investigated. While one group consisted of 26 untreated TT patients, the other included 20 individuals who had taken dapsone, 50 mg daily, for 12–14 months. There was significant decrease in the number of T lymphocytes and their response to PHA and lepromin was lower in the treated as compared to the untreated patients and normal persons. No significant change was found in the number of B lymphocytes in any of the groups.—Authors' Abstract

Kuzina, Z. A., Mezhova, L. I., Vilkov, G. A. and Khasabov, L. M. Circulating immune complexes in patients with lepromatous leprosy. Vestn. Dermatol. Venerol. **5** (1983) 11–14. (in Russian)

Circulating immune complexes (CIC) were determined by the method of Gashkova, *et al.* in 60 normal subjects and 104 patients with lepromatous leprosy. In 90.4% of the patients, the level of CIC was significantly higher than normal. The highest level of CIC was detected in patients in the active stage of the disease, with relapses and complications. CIC levels were found to depend

on the extent of mycobacterial content and efficacy of antileprous therapy.—Authors' English Summary

Lal, S., Natarajan, S., Veliath, A. J. and Garg, B. R. Does isopathic phenomenon occur in leprosy? Lepr. India **55** (1983) 495–499.

Twenty-five patients of leprosy classified according to the criteria of Ridley and Jopling were studied to verify the existence of isopathic phenomenon, using lepromin and autoclaved BCG as antigens. BCG as well as lepromin injection sites showed tuberculoid granulomas in all the cases of tuberculoid, borderline tuberculoid, mid-borderline, and indeterminate leprosy. In lepromatous and borderline lepromatous cases, BCG injection sites showed infiltration of foam cells containing acid-fast bacilli (AFB) and foci of epithelioid cells, while lepromin injection sites showed infiltration of foam cells containing AFB only. These findings in the present study do not support the occurrence of isopathic phenomenon in leprosy with BCG.—Authors' Abstract

Mor, N. Intracellular location of *Mycobacterium leprae* in macrophages of normal and immune-deficient mice and effect of rifampin. Infect. Immun. **42** (1983) 802–811.

Soon after more than 10^6 *Mycobacterium leprae,* freshly harvested from armadillo liver or harvested and ^{60}Co irradiated, were inoculated into the hind foot pads of either normal or thymectomized and irradiated (T900R) mice, the organisms were found to reside within phagosomes of polymorphonuclear and mononuclear cells. On the other hand, seven and eight months after 10^4 freshly harvested *M. leprae* were inoculated into the foot pads of normal or T900R mice and the organisms had multiplied to their maximum in the normal mice, many organisms, largely intact by electron-microscopic criteria, were found to reside free in the cytoplasm of the foot pad macrophages, whereas damaged organisms were contained within phagosomes. After 11 months, many intact organisms were found to lie free in the cytoplasm of the macrophages of T900R mice, whereas only damaged intraphagosomal *M. leprae* cells were observed in the macrophages of normal mice. Finally, a remarkably large proportion of damaged extraphagosomal *M. leprae* was found in T900R mice administered rifampin for two days in a bactericidal dosage. It appears that *M. leprae* multiplies free in the cytoplasm of the foot pad macrophages of infected mice, whereas the *M. leprae* cells resident within the phagosomes of the macrophages are dead. As the result of treatment with rifampin, the organisms appeared to have been killed in their extraphagosomal location, only afterwards being incorporated into phagosomes. However, the intracellular site in which *M. leprae* is killed in the course of an effective immune response remains unclear.—Author's Abstract

Mshana, R. N., Humber, D. P., Harboe, M. and Belehu, A. Demonstration of mycobacterial antigens in nerve biopsies from leprosy patients using peroxidase-anti-peroxidase immunoenzyme technique. Clin. Immunol. Immunopathol. **29** (1983) 359–368.

Peripheral nerve biopsies from patients with leprosy were stained with anti-*Mycobacterium bovis* (BCG) in a peroxidase-antiperoxidase (PAP) system to demonstrate intraneural mycobacterial antigens. Most *M. leprae* antigens have been shown to cross-react with BCG. Of the 30 biopsies from borderline tuberculoid (BT) patients, 18 had acid-fast bacilli while 26 of them had demonstrable mycobacterial antigens in their nerves. All borderline lepromatous (BL) and lepromatous leprosy (LL) nerve biopsies had both *M. leprae* and mycobacterial antigens within them. Most of the antigens in the BT patients were seen to be extracellular. In BL and LL patients antigens were seen both extracellularly and intracellularly in Schwann cells and infiltrating macrophages. Mycobacterial antigens in BT nerves were always seen to be surrounded by a mononuclear cell reaction, while in the BL and LL patients antigens could be seen with minimal cellular infiltrate and the neural architecture was more or less preserved. While bacilli could not be seen in BT patients who had been released from treatment for more than four years, mycobacterial antigens could still be seen in some

patients who had been released from treatment for up to five years. Patients with no skin lesions but with large, painful, or tender nerves were found to have intraneural inflammation surrounding mycobacterial antigens, while those with a similar clinical picture but without tender or painful nerves showed no marked inflammation within their nerves despite the presence of mycobacterial antigens. From these findings it was concluded that immunologically mediated inflammatory response toward intraneurally located *M. leprae* antigens in conjunction with other host factors may be necessary for nerve damage in the BT leprosy patients. In the BL and LL patients the mechanisms of nerve damage are still unknown with certainty but local effects and immune-complex damage secondary to abundant *M. leprae* antigens are worth exploring. The use of immunohistological techniques should offer a new approach in the study of the immunopathology of leprosy.—Authors' Abstract

Narayanan, R. B., Badenoch-Jones, P., Curtis, J. and Turk, J. L. Comparison of mycobacterial granulomas in guinea-pig lymph nodes. J. Pathol. **138** (1982) 219–233.

A study was made of mycobacterial-induced granulomas in guinea pig lymph nodes. Live BCG (Pasteur) induced a granuloma containing epithelioid cells, while cobalt-irradiated *Mycobacterium leprae* induced a granuloma comprised of phagocytic macrophages. The granulomas were quantitated by measurement of lymph node weight and the areas of infiltration in histological sections. The time course of granuloma formation induced by Co-irradiated *M. leprae* was very different from the time course of the granuloma formation induced by BCG. Collagen synthesis assessed by incorporation of ^{14}C-proline into collagenase sensitive protein was greater in lymph nodes draining the site of injection of Co-irradiated BCG than those draining the site of injection of Co-irradiated *M. leprae* during the first ten weeks. Collagen synthesis was delayed in the nodes from animals injected with live BCG for at least ten weeks. Single cell suspensions of draining lymph nodes containing granulomas consisted of lymphocytes and large cells (epithelioid cells and macrophages). A high proportion of the large cells were found to be non-adherent in the live BCG-induced epithelioid cell granuloma. In contrast, *M. leprae*-induced granulomas contained a high percentage of adherent large cells. In both the granulomas, the majority of large cells were esterase positive and showed the presence of fibronectin. Most of the large cells in the granulomas did not carry receptors for the Fc component of IgG or the C3 component of complement and did not exhibit peroxidase activity.—(*From* Trop. Dis. Bull.)

Rea, T. H. Suppressor cell activity and phenotypes in the blood or tissues of patients with leprosy. Clin. Exp. Immunol. **54** (1983) 298–304.

Suppressor cell activity has been demonstrated in the peripheral blood of patients with leprosy. Cells bearing the suppressor/cytotoxic phenotype have been enumerated in both peripheral blood and tissues, and microanatomical differences in tissue distribution have been observed. This first generation of studies has been characterized by considerable disagreement, a not unusual circumstance in the study of leprosy. In the case of blood suppressor cell activity, there appears to be no doubt as to its existence, but there is much uncertainty regarding its distribution. Concerning peripheral blood phenotypic suppressor cells, the observed differences in lepromatous and ENL patients may well reflect differences in methods used. Concerning phenotypic suppressor cells in tissue, there is no agreement as to their numbers or microanatomical distribution across the spectrum of leprosy or in its reaction states. Although these observational differences make firm conclusions impossible, this first generation of studies has provided new ways of considering old problems. For example, lepromin unresponsiveness might be a consequence of active cellular suppression. Differences in the numbers (or percentages) of the suppressor phenotype in blood or tissues of lepromatous patients with or without ENL reopens the door to the possibility of cell-mediated immune mechanisms in the pathogenesis of ENL. The identification of defective suppressor cells as important in the pathogen-

esis of hypergammaglobulinemia is of interest in and of itself, but also gives rise to the possibility that other kinds of phenomena may be the consequence of defective or effete suppressor mechanisms. The observation of microanatomical differences in the distribution of the suppressor phenotype in tuberculoid and lepromatous leprosy indicates that effective or ineffective immunity might be a sequela of particular interactions between the suppressor/cytotoxic and helper/inducer phenotypes, and that these interactions merit further study. These new perspectives may be subject to experimental testing by the next generation of studies, which will surely include the techniques of clonal expansion and limiting dilution, as well as the study of interleukins 1 and 2.—Author's Summary

Rook, G. A. W. The immunology of leprosy. Tubercle **64** (1983) 297–312.

Immunity to both leprosy and tuberculosis requires the recognition by T cells of antigens released by live organisms, followed by secretion of lymphokines and accumulation and activation of macrophages. However, this general description covers a complex family of related pathways. We do not yet know, for either disease, which antigens, T cells, lymphokines, or macrophage antimicrobial mechanisms are required. The answers may not be the same for both organisms.

The pathology of tuberculosis is characterized by necrotizing responses to otherwise nontoxic antigenic components, which may be attributable to the triggering of secretory functions of highly activated macrophages. This does not occur in leprosy.

Immunology does not yet offer any explanation for tuberculoid leprosy, in which cell-mediated responses to *Mycobacterium leprae* seem to be intact. There are at least two possibilities. First, there may be a delay before the onset of cell-mediated immunity (CMI), so that when it appears the bacilli are established in vulnerable tissues which are subsequently damaged by the inflammation. Secondly, the CMI could be directed towards antigenic components which are not released by live organisms, so that the immunological attack occurs in the wrong places, around dead or "leaking" bacilli.

In lepromatous leprosy there is a failure of macrophage activation. This is not due to a lack of antigen-recognizing T cells, which can be shown to be present in the peripheral blood, or to malfunction of macrophages. Therefore, suppressor T cells have been sought and according to some workers, demonstrated. It is not clear whether such suppression is related to the failure of CMI early in the disease, or merely a late response to increasing antigen load.—(*From* the article)

Sathish, M., Bhutani, L. K., Sharma, A. K. and Nath, I. Monocyte-derived soluble suppressor factor(s) in patients with lepromatous leprosy. Infect. Immun. **42** (1983) 890–899.

Peripheral blood monocytes from polar lepromatous leprosy (LL) patients were unable to support *Mycobacterium leprae*-induced *in vitro* lymphoproliferation of HLA-D-matched T cells from tuberculoid leprosy subjects, whereas those from responder individuals were able to do so. Monocyte-rich adherent cells from untreated LL patients released *de novo* soluble factors which inhibited antigen-induced lymphoproliferation to a greater extent and mitogenic responses to a lesser extent. Suppressive activity varied in different LL patients. However, the degree of suppression was similar in soluble factors obtained *de novo* and after treatment of adherent cells with heat-killed and freshly extracted, cryopreserved *M. leprae.* Treated patients showed less inhibition with *de novo* released soluble factors (27 $\pm$ 7.7%) as compared to parallel soluble factors obtained after antigen treatment (44 $\pm$ 4.8%) or with *de novo* soluble factors from untreated LL patients (62 $\pm$ 14.2%). Similar supernatants from tuberculoid individuals showed no or insignificant effects on antigen-induced lymphoproliferation. The suppressive acitivy of LL soluble factors was produced for up to 72 hr, was heat stable at 56°C for 30 min, was indomethacin resistant, and resided in the >25,000 molecular weight fraction.—Authors' Abstract

Schroh, R. G., Ravettini, B. A., Magnin, P. H. and Casas, J. G. Inmunomarcacion de lisozima en granulomas hansenianos. [Immunoreactive liposozyme in Hansen's disease granulomas.] Abstract in Reunion Argent. Dermatol. **64** (1983) 347. (in Spanish)

Se realizó un estudio inmunohistoquímico con técnica de peroxidasa-antiperoxidasa con el objeto de demostrar la presencia de lisozima en granulomas de lepra. Esta enzima es sintetizada por histiomonocitos y neutrófilos, o sea, células con capacidad fagocítica.

Se inmunomarcaron 37 biopsias de enfermos que representaron el espectro de la lepra desde TT a LL. Asimismo se estudiaron ENL, lepromas histoides y lepra indeterminada.

La intensidad de la marcación mostró picos en las regiones TT, BT y LL con un valle en la región BB.

Se definió un tipo de depósito de lisozima para LL cuyo patrón es sacular y otro para TT cuyo patrón se definió como granular.

Los granulomas correspondientes a lepromas histoides poseen una carga de lisozima mucho menor a sus homónimos de lepra lepromatosa y con un patrón de depósito similar a los fibrohistiocitomas.

Los resultados sugieren la posibilidad de un defecto común desde BT a LL en el cual la generación de factores inmunológicos dentro de las lesiones es una respuesta secundaria a la carga antigénica.—Authors' Summary

Singh, K., Iyenger, B. and Singh, R. Histopathological evidence of indeterminate leprosy in apparently uninvolved skin of entire spectrum of leprosy. Lepr. India **55** (1983) 500–503.

Indeterminate histopathology with nerve involvement was seen in clinically uninvolved skin in 100% of leprosy cases, irrespective of clinical type. This was an interesting observation for TT and BT cases; in such cases, it might be a reflection of the disease process which is generalized right from the beginning.—Authors' Abstract

Singh, K., Iyenger, B. and Singh, R. Variations in clinical and histopathological classification of leprosy—a report and a plausible explanation. Lepr. India **55** (1983) 472–479.

Biopsies of macular hypopigmented lesions, in 21 untreated cases, representing the whole spectrum of leprosy, revealed a high incidence of disagreement between clinical and histopathological classification. It was not observed in macular tuberculoid and indeterminate cases but was seen in borderline and lepromatous leprosy, with highest incidence in borderline leprosy. This has been explained on the basis of a complex nervous system with a mosaic of anatomical and physiological subunits modulating different types of responses, including inflammation, through release of peptides and/or enzymes at the nerve endings in the peripheral tissues including skin.—Authors' Abstract

Singh, P. K., Ratna, Jain, P. K. and Mital, V. P. Status of T and B lymphocytes in peripheral blood. Lepr. India **55** (1983) 560–565.

T and B lymphocyte percentage was studied by erythrocyte (E) and erythrocyte antibody complement (EAC) rosette formation respectively in 90 cases including 65 cases of different types of leprosy and 25 healthy controls. The patients with different types of leprosy were classified according to Ridley and Jopling. The mean percentage of T lymphocytes was observed in gradually decreasing number from the tuberculoid pole to the lepromatous pole. The fall in T lymphocyte percentage was highly significant when control cases were compared with total cases of leprosy and different histological types of leprosy. This indicates that there is a gradually increasing loss of cell-mediated immune response from tuberculoid to lepromatous pole.—Authors' Abstract

Su Liaoyuan, *et al.* Determination of cell-mediated immunity in leprotics by ^{14}C-valine. Chin. J. Dermatol. **16** (1983) 158–159. (in Chinese)

Protein synthesis during the course of T lymphocyte transformation to PHA was measured *in vitro* by ^{14}C-valine incorporation. Whole blood was incubated for 32 hr

at 37°C and ^{14}C-valine was added for the final 24 hr before the cells were harvested. The cells were harvested by a filter film method and were counted by liquid scintillation.

The technique was used to study 26 LL and BL leprosy patients, 20 BT and TT patients, and 26 normal persons as controls. The amount of ^{14}C-valine incorporation expressed as radioactivity/0.2 μl of whole blood was normal in leprosy patients compared to controls. On the other hand, incorporation expressed as radioactivity/10^5 lymphocyte was significantly ($p < 0.01$) reduced in both types of leprosy patients in comparison with that of normal subjects. These results seem to reflect an impairment of cell-mediated immunity in leprosy patients. This experimental technique has the advantages of a shorter incubation time, the lack of need for added serum in the culture medium, and its precision.—(*Adapted from* Authors' English Summary)

Young, D. B. and Buchanan, T. M. A serological test for leprosy with a glycolipid specific for *Mycobacterium leprae.* Science **221** (1983) 1057–1059.

A phenolic glycolipid from *Mycobacterium leprae* was purified and used as antigen in an enzyme-linked immunosorbent assay. Antibodies directed against the lipid were seen in serums from leprosy patients but not in serums from uninfected controls or patients infected with other mycobacteria, including *M. tuberculosis.* The antibody response distinguished between the *M. leprae* lipid and the structurally related phenolic glycolipid from *M. kansasii.* This assay has considerable potential as a specific serodiagnostic test for leprosy infection.—Authors' Abstract

Microbiology

Chatterjee, B. R. Growth of *Mycobacterium leprae* in a redox system. Lepr. India **55** (1983) 426–449.

Mycobacteria recovered from human lepromatous nodules and presumably *M. leprae,* have been grown in a medium that ensured a minimal oxygen tension at initiation of growth, and an increasing availability of oxygen as bacillary growth increased requiring marginal increments in oxygen tension. This physico-chemical environment was achieved by the addition of strong biological reductants in the medium, and a combination of partial vacuum and alkaline pyrogallol in the culture vessel. In addition, n-tetradecane, a straight chain hydrocarbon, and lipids like cholesterol and lecithin, all three substances mixed in the aqueous medium as liposomes, were added and found to be useful. Menadione, or vitamin K_3, added to the medium considerably improved growth efficiency. Growth occurred initially as non-acid-fast coccoids and bacilli that gradually changed to acid-fast bacilli and globi, and cell-wall deficient, spherical L-form elements. Appearance of growth in any form was perceptible within 1–2 weeks and optimal growth as acid-fast bacilli took up to three months. Both the acid-fast and non-acid-fast bacilli could not be grown in conventional media, but the non-acid-fast coccoids could be readily isolated from these cultures in a specially enriched liquid medium. The problem of harvesting of the growth free of lipid-hydrocarbon substances has still not been solved, as also an optimum oxidation-reduction potential. The growth is transferable.—Author's Abstract

Dhople, A. M. Effect of lysozyme on *Mycobacterium leprae.* Lepr. India **55** (1983) 455–464.

The *in vitro* effect of lysozyme on *M. leprae* has been studied and shown that *M. leprae* exposed to up to 500 micrograms of lysozyme retain all their original metabolic activity and viability.—Author's Abstract

Katoh, M. and Matsuo, Y. Adherence of *Mycobacterium lepraemurium* to tissue culture cells. Hiroshima J. Med. Sci. **32** (1983) 285–290.

Adherence of *Mycobacterium lepraemurium* to tissue culture cells was examined and compared with that of *M. microti*. *M. lepraemurium* used in the present study was maintained on Ogawa egg yolk medium. This microbe adhered to HEp-2 cells much more than A31 or McCoy cells, although the adherence was unusally low compared with the large infectious dose. Frequency distribution of the number of bacteria agreed closely with Polya-Eggenberger distribution. The pretreatment of *M. lepraemurium* with heat or protease increased the adherence of the bacteria to HEp-2 cells; whereas the pretreatment with lipase or hyaluronidase retained the adhering ability. The pretreatment of *M. microti* with heat or protease produced the same effect on the adherence as that of *M. lepraemurium*. These results suggest that adherence of *M. lepraemurium* to HEp-2 cells is prevented by protein-like material on the surface of the bacteria, and that the adherence is independent of specific adhesion-receptor interaction.—Authors' Abstract

Prabhakar, R., Hari, L. and Herbert, D. Observations on the culture of *M. leprae* in medium V. A preliminary report. Lepr. India **55** (1983) 450–454.

This paper reports the preliminary findings of an investigation using medium V for culture of *Mycobacterium leprae*. The medium was prepared adhering to the procedures adopted by Veeraraghavan. Tissues from seven cases of lepromatous leprosy (bacteriologic index of 3 or more) were inoculated into medium V and incubated at 8°–10°C for 72 hr. Quantitative estimation of leprosy bacilli was made employing the enumeration technique of Veeraraghavan. There was no evidence of multiplication in any of the cultures. The findings are in conformity with those of Kato and of Katoch and Desikan.—Authors' Abstract

Saha, K., Chakraborty, A. K. and Prakash, N. A quick method of demonstrating bacillaemia in patients with lepromatous leprosy and ultrastructural studies of the circulating acid-fast bacilli. Trans. R. Soc. Trop. Med. Hyg. **77** (1983) 660–664.

While studying circulating immune complexes (CIC) in the sera of lepromatous patients by the polyethylene glycol (PEG) precipitation technique, we found (by light microscopy) abundant acid-fast bacilli (AFB), morphologically similar to those seen in slit skin smear preparations from these patients, precipitated with the PEG precipitated materials. Both solid and non-solid AFB could be readily identified. Ultrastructures of these AFB in the PEG aggregates showed some similarity with those detected in the PEG precipitates prepared from armadillo-derived lepromin under identical conditions. The most striking difference between the AFB in the test sera and that in the armadillo-derived lepromin was the absence of any transverse band in the former. This suggested that the AFB in the patients' circulation were not in division stage. Furthermore, electron-dense material was deposited on the AFB co-precipitated from the patients' sera, which were not found on the AFB co-precipitated from the armadillo-derived lepromin.—Authors' Summary

Silva, M. T. and Macedo, P. M. A comparative ultrastructural study of the membranes of *Mycobacterium leprae* and of cultivable mycobacteria. Biol. Cell **47** (1983) 383–386.

The characterization by microdensitometry and by ultrastructural cytochemistry of the membrane of *Mycobacterium leprae* in comparison with the membrane of several cultivable species of *Mycobacterium* (pathogenic and nonpathogenic) showed that, under the experimental conditions used, the membrane of *M. leprae* is 7.04–7.08 nm thick and has PAS-positive (Thiéry reaction) components in both layers, while the membranes of the other species studied are 6.36–6.37 nm thick and have PAS-positive components only in the outer layer. These characteristics of *M. leprae* represent the first distinctive ultrastructural marker for this unique bacterium.—Authors' Summary

Sun Zheng-De, *et al.* Superoxide dismutase activity in the peripheral blood cells of leprosy patients. Chin. J. Clin. Dermatol. **12** (1983) 177–180. (in Chinese)

Superoxide dismutase activity in the pe-

ripheral blood cells of 40 leprosy patients and 26 normal subjects was determined. The superoxide dismutase activity in 1 ml extract from 0.5 ml peripheral blood hematocrit cells was 658 U in the patients, and 1376 U in the normal subjects. In addition, we have also measured the superoxide dismutase activity of leprosy bacilli. We found that the superoxide dismutase activity in one leprosy bacillus was twice that in one normal leukocyte.—Authors' English Abstract

Vithala, K., Talati, S. and Mahadevan, P. R. An *in vitro* system to study drug sensitivity of *Mycobacterium leprae* using infected human tissue. J. Biosci. **5** (1983) 235–241.

A reliable screening technique for assessing the sensitivity of *Mycobacterium leprae* to drugs has been developed. The method is based on the susceptibility or otherwise of *M. leprae*–infected tissues from lepromatous leprosy patients to the action of diaminodiphenyl sulfone (dapsone) or rifampin on the incorporation of [^{14}C]-acetate into lipids. The extent of inhibition or lack of inhibition correlated very well with the drug sensitivity or resistance of the bacteria isolated from the patients to the above drugs. A similar trend was observed when the incorporation into individual fractions of neutral lipids was measured. There was no incorporation by heat-killed tissues. This method correlates well with the 3,4-dihydroxyphenylalanine uptake studies.—Authors' Abstract

Experimental Infections

Balina, L. M., Valdez, R. P., de Herrera, M., Costa Cordova, H., Bellocq, J., Garcia, N. and Sarciat, C. Lepra diseminada en *Dasypus hybridus* (armadillo 7 bandas). Informe preliminar. [Disseminated leprosy in seven-banded armadillos (*Dasypus hybridus*). Preliminary results.] Leprologia **24** (1982) 103–116. (in Spanish)

We report two seven-banded armadillos (*Dasypus hybridus*) inoculated with *Mycobacterium leprae.* Each animal received not less than 1.32×10^8 bacilli by intravenous and subcutaneous routes. Thirteen months after inoculation we observed acid-fast bacilli in the ears. The animals were sacrificed 14.5 months after inoculation and histopathological studies showed a picture similar to human lepromatous (LL) leprosy. The bacilli were not cultivable on culture media for mycobacteria. Acid-fastness was lost after pyridine treatment. These results suggest that the acid-fast bacilli found in these animals were *M. leprae.* Mouse foot pad results are not available.—(*Adapted from* Authors' English Summary)

Balina, L. M., Valdez, R. P., de Herrera, M., Costa Cordova, H., Bellocq, J. and Garcia, N. Reproduccion experimental de lepra en *Dasypus hybridus.* [The experimental reproduction of leprosy in *Dasypus hybridus.*] Reunion Argentina de Dermatologia, 1983. Abstract in Rev. Argent. Dermatol. **64** (1983) 348.

La inoculación de *M. leprae* en armadillos argentinos del género *Dasypus* tiene por objeto reproducir experimentalmente la lepra lepromatosa en estos animales con el fin de disponer de un "banco de bacilos." El *M. leprae* a inocular se obtiene de pacientes LL vírgenes de tratamiento y se procesa separando la epidermis y macerando manualmente. Se diluye en cloruro de sodio al 5% pero cuidando de obtener uns suspensión final no menor de 10^8 bac./cc. El recuento de bacilos se hace según técnica de Shepard. Se inocula por vía endovenosa y subcutánea. Hemos encontrado BAAR en *Dasypus hybridus* después de 12 a 16 meses de inoculados. Las necropsias mostraron cuadros histopatológicos que corresponden a lepra lepromatosa diseminada y los estudios bacteriológicos de comprobación sugieren que efectivamente se trata de *M. leprae.*

Botasso, O. A., Pentinalli, M. I., Poli, H., Amerio, N. and Morini, J. C. Estudio histopatologico de la infeccion experimental

con *Mycobacterium lepraemurium* en rationes inmunizados especificamente. [Histopathologic study of experimental infection in mice immunized with *Mycobacterium lepraemurium*.] Leprologia **24** (1982) 117–120. (in Spanish)

In order to study protective immunity in murine leprosy, adult Rockland mice were immunized with heat-killed *M. lepraemurium*, either alone or mixed with incomplete Freund adjuvent. Thirty days later, the experimental and control groups were challenged with a viable *M. lepraemurium* suspension. The resulting disease was followed histopathologically by the size and type of granuloma developing in the liver and spleen. The results showed no significant differences between immunized and control animals.—(*Adapted from* Authors' English Summary)

Chehl, S., Ruby, J., Job, C. K. and Hastings, R. C. The growth of *Mycobacterium leprae* in nude mice. Lepr. Rev. **54** (1983) 283–304.

Armadillo-derived *Mycobacterium leprae* were inoculated in graded doses into the left hind foot pads of 160 nu/nu mice and the same number of BALB/c mice. The course of the infection was followed for 18 months. The nu/nu mice developed massive foot pad enlargements with eventual dissemination of the bacilli in virtually all organs outside the central nervous system. The acid-fast bacilli were identified as *M. leprae*. BALB/c mice showed a characteristic localized infection. In the nu/nu mice, bacilli were found in large numbers free in the cytoplasm of striated muscle cells and in macrophages, both free in the cytoplasm and within phagosomes. With time, the *M. leprae* in the nu/nu mice showed a tendency to stain more and more non-solidly, suggesting that death of *M. leprae* occurs in these animals despite their lack of the capacity to develop cell-mediated immunity. This model of disseminated leprosy seems useful for a number of studies of the disease.—Authors' Summary

Ha, D. K. K., Gardner, I. D. and Lawton, J. W. M. Characterization of macrophage function in *Mycobacterium lepraemurium*-infected mice: sensitivity of mice to endotoxin and release of mediators and lysosomal enzymes after endotoxin treatment. Parasite Immunol. **5** (1983) 513–526.

Mycobacterium lepraemurium (MLM) infection increases the sensitivity of mice to lipopolysaccharide (LPS) as do infections with other intracellular parasites. Tumor necrosis factor (TNF), lymphocyte activating factor (LAF) and increased levels of various lysosomal and cytoplasmic enzymes were found in serum samples taken 2 hr after intravenous injection of a small dose of LPS suggesting that damage to a variety of cell types, including macrophages, had occurred. Sera from moribund MLM-infected mice not injected with LPS also demonstrated significant levels of TNF compared with controls. Intravenous injections of silica into leprous mice also led to increased levels of serum lysosomal and cytoplasmic enzymes but did not give rise to a significant amount of TNF or LAF. Moreover, in contrast to LPS treatment, the injection of silica did not lead to the death of leprous mice. These findings suggest that the phagocytic cells of the infected animals did not contribute to the production of these mediators after LPS challenge. Rather, the non-phagocytic granuloma macrophages or other unidentified cell types seemed to provide the main source of the monokines TNF and LAF *in vivo* in the present model. These mediators may have important implications for the immunopathology of MLM infection.—Authors' Summary

Job, C. K., Chehl, S., Hastings, R. C. and Ruby, J. R. Invasion of liver parenchymal cells by *Mycobacterium leprae* in an experimentally infected nude mouse. An electron microscopic study. Am. J. Trop. Med. Hyg. **32** (1983) 1088–1095.

Liver tissue from a nude mouse infected with *Mycobacterium leprae* for 18 months was examined using light and electron microscopes. Numerous microgranulomas composed of macrophages were present throughout the liver. *M. leprae* in large numbers were present in Kupffer cells, macrophages, endothelial cells, and liver parenchymal cells. The study shows that the lower

temperature of about 31°C optimal for the growth of *M. leprae* is relative rather than absolute, and that *M. leprae* can invade even liver cells.—Authors' Abstract

Meier, J. L., Folse, D. S. and Smith, J. H. Leprosy in wild armadillos (*Dasypus novemcinctus*) on the Texas Gulf Coast. Lab. Invest. **49** (1983) 281–290.

Recent studies have established that the "naturally-occurring leprosy-like disease of wild armadillos" is, indeed, caused by *Mycobacterium leprae* indistinguishable from *M. leprae* from human lepromatous leprosy. The present study reports the ultrastructure of the mycobacteria and host response in deep viscera, liver and spleen, in Texas armadillos with sylvatic leprosy. Evidence for acid-fast bacillary proliferation in these organs and penetration of hepatocytes is given. Acid-fast bacilli concentrated in activated macrophages in Billroth cords and sheaths of Schweigger-Seidel of the spleen and in Kupffer cells of the liver. Both mycobacteria and host response seen in lepromata of sylvatic leprosy, lepromatous lesions produced by injection of inocula from human lepromata and human lepromata, are compared.—Authors' Abstract

Epidemiology and Prevention

Costamagna, L. B. La lepra en la cuidad de San Francisco (CBA). Nueva contribucion a su estudio 38 anos despues. [Leprosy in San Francisco City (Córdoba). New contribution to its study 38 years later.] Leprologia **24** (1982) 145–162. (in Spanish)

Interested in the continuous increase in the leprosy endemic in the department San Justo de la Provincio de Córdoba, I studied the actual situation in San Francisco City, the head of that department. We made two inquiries, one among the public and the other among physicians, to investigate the degree of consciousness of leprosy and the importance which both of them have in the campaign against this illness. Various conclusions have come to light, such as: there are 191 cases of leprosy among 52,006 inhabitants for a high endemic of 3.67 cases/1000 inhabitants. Tuberculoid cases account for 88 (46.1%), indeterminate for 38 (19.9%), lepromatous for 55 (28.8%), and dimorphous for 10 (5.2%) of the cases. While the population increased 1.85 fold in the last 38 years, the number of patients increased 4.6 fold. Neither the weather, the physical aspects of the zone, the city or its people seemed to be related to the spread of the disease. The abundance of mosquitos during most of the year should be pointed out. The department of Córdoba lacks a permanent leprosy control program and the national program has not as yet extended to San Francisco or to San Justo. We were unable to find other reasons for this increase in the prevalence of leprosy in this area.—(*Adapted from* Author's English Summary)

Folse, D. S. and Smith, J. H. Leprosy in wild armadillos (*Dasypus novemcinctus*) on the Texas Gulf Coast: anatomic pathology. J. Reticuloendothel. Soc. **43** (1983) 341–357.

Recent studies of the naturally occurring leprosy-like disease of wild armadillos establish that the causative bacillus is genetically identical to *Mycobacterium leprae* from human sources, and thus the disease is a zoonosis, sylvatic leprosy. A recent survey of 451 wild armadillos from the Texas Gulf Coast demonstrated sylvatic leprosy in 4.66%. This companion study reports the anatomic pathologic changes seen in the 17 leprous and 17 nonleprous armadillos necropsied in that survey. Findings support previous studies on the histopathology and pathogenesis of sylvatic leprosy, but a broader spectrum of histologic changes are noted.—Authors' Abstract

Ganapati, R. Urban leprosy control. Trop. Doct. **13** (1983) 76–78.

There is a need for energetic application of a specialized urban approach to the control of leprosy. Failing this, rapidly proliferating urban slums and leprosy colonies in

them will continue to act as foci for the dissemination of the disease and cause considerable morbidity.—(*From* the article)

Harboe, M. The work and concepts of Armauer Hansen: how do they stand today? Ethiop. Med. J. **21** (1983) 123–126.

The principle of reducing the load of infection in the society to break the chain of infection is also the cornerstone of leprosy control work today. It implies early diagnosis and early adequate drug treatment to make the patient noninfectious. The greatest efforts should be concentrated on the lepromatous, multibacillary patients, who are the most dangerous with regard to the spread of the disease. It is truly remarkable that Armauer Hansen's concepts and work of more than 100 years ago are so valid today.—(*From* the article)

Lechat, M. F. Leprosy in a global context. Proceedings of the 5th International Workshop on Leprosy Control in Asia, Singapore, 24–27 October 1983.

Leprosy as a global health problem is today attracting considerable attention. Apart from the actual number of persons affected by it, the major importance of leprosy stems from the deformities it produces. As a single disease entity, it is at the moment one of the foremost causes of disablement and crippling. Thus, on purely epidemiological grounds, leprosy remains a health priority in the countries where it is endemic. Nevertheless, there is no doubt that leprosy is but one among the many health problems affecting the developing countries.

There is ample evidence that the transmission and spread of the *Mycobacterium leprae* is related to socio-economic conditions. Two observations militate in favor of an association between socio-economic conditions and leprosy. They are, first, the decline of leprosy in Europe and, second, the relative absence of transmission following migrations.

There are two epidemiological essentials in leprosy, prevalence and incidence. Prevalence measures the total number of patients in a community; it is a reflection of the past; it is dependent on how many caught the disease and how many are still with us now. Incidence, and incidence only, reflects the dynamics of the disease. It measures the number of new cases occurring during an interval of time (generally one year), indicating to what extent transmission still takes place. Due to the long incubation of the disease, however, incidence will reflect changes in transmission only with a delay of several years. Prevalence is an image of the past. Incidence is a window on the future. There is, therefore, no reason to despair even when actual figures for the total number of patients are high. What matters is the decline in the number of new cases.—(*From* the report)

Reddy, N. R., Kolumban, S. L. and Fritschi, E. P. The results of lumbrical replacement by extensor to flexor many tail operation—a retrospective study. Lepr. India **55** (1983) 539–546.

A follow-up study was carried out on 61 leprosy patients who had extensor to flexor many tail surgery at Schieffelin Leprosy Research and Training Centre, Karigiri, India, from 1957 to 1976.

After analyzing the data, it was noticed that the amount of clawing reduced considerably. Secondly the over-all assessment was good for 70% of the hands. But the deformities, such as intrinsic plus, deviation of fingers, M.P. extension, limitation, I.P. flexion limitation and loss of fingers, showed an increase in number post-operatively when compared to the pre-operative deformities. The reasons for these effects are discussed in this paper.—Authors' Abstract

Styblo, K. Tuberculosis and its control: lessons to be learned from past experience, and implications for leprosy control programmes. (The Kellersberger Memorial Lecture, 1982). Ethiop. Med. J. **21** (1983) 101–122.

Adequate chemotherapy of leprosy containing rifampin is the key to control and eradication of leprosy. It must be stressed, however, that unlike tuberculosis, leprosy has a very limited number of potent drugs; development of secondary resistance to rifampin and dapsone might become a severe obstacle in combatting the disease.—(*From* the article)

Tello, E. F. La lepra infantil en el dispensario dermatologico del patronato del enfermo de lepra. Córdoba. [Leprosy in children in the dermatologic dispensary of the Patronato del Enfermo de Lepra, Córdoba.] Leprologia **24** (1982) 137–144. (in Spanish)

This statistical work on childhood leprosy compares data obtained from the dermatologic clinic supported by the Patronato del Enfermo de Lepra in Córdoba, the second city in Argentina, with data from other areas (Buenos Aires and Rosario) which are as similar as possible regarding professional education (universities), population, and influences from agriculture, cattle-breeding and industry. The data show that from age 0–4 years, there is a clear predominance of tuberculoid and some indeterminate cases; from 5–9 years of age this predominance of tuberculoid and indeterminate cases continues but some lepromatous cases now appear; from 10–14 years of age high percentages of tuberculoid and indeterminate cases continue but lepromatous cases become more evident. In these periods, the sum of the tuberculoid and indeterminate cases demonstrates an early diagnosis. The lepromatous form appears only exceptionally from 0–4 years of age. During this period, tuberculoid forms are frequent and in these the nodular variety is seen in only a low proportion of cases in contrast to what is reported by some Brazilian authors.—(*Adapted from* Author's English Summary)

Rehabilitation

Charosky, C. B. Resultados de endoneurolisis cubital. [Results of ulnar nerve endoneurolysis.] Leprologia **24** (1982) 121–128. (in Spanish)

Eleven cases of ulnar nerve endoneurolysis are presented. The indication for this technique was restricted to patients with neural abcesses or with radiographic blockage observed at intraoperative neurography. The results showed that the operation corrects very satisfactorily the early neural deficits, but serves only as a means of relieving pain in cases with long-term paralysis. The procedure does not improve long-standing motor and/or sensory disturbances. Endoneurolysis is the only surgical procedure which relieves nerve fascicles compromised by intraneural scar tissue or caseation. However, it is considered potentially dangerous and it should be limited to these indications. The indiscriminate application of the procedure should be avoided in situations that can be controlled with less aggressive techniques.—Author's English Summary

Corn, J., Franceschini, G., Vaquero, N. and Ortiz, M. C. Estudio de la resistencia electrica cutanea en hanseniasis. (Communicacion previa.) [Study of the electrical cutaneous resistance in leprosy. (Preliminary communication.)] Leprologia **24** (1982) 129–135. (in Spanish)

Electrical cutaneous resistance primarily reflects the activity of sweat glands. The possibility of using such a bloodless, quick and simple method to detect the early alterations of sweat gland function is pointed out. Results to date do not allow definitive conclusions but are encouraging.—(*Adapted from* Authors' English Summary)

Gill, A. K. Social aspects of leprosy in Malaysia. Southeast Asian J. Trop. Med. Public Health **14** (1983) 25–28.

This paper attempts to explain both the persistence of traditional misconceptions about leprosy as well as the relative ineffectiveness of the leprosy control program. It has been pointed out that leprosy is a disease with tremendous social significance. To improve the program, therefore, the human element which is of paramount importance must be identified and rectified. It is felt, however, that we the providers should set our own house in order first. We need to find out the knowledge, attitudes and practices of the medical personnel and auxiliaries relating to leprosy, and identify the

factors that contribute to their lack of motivation and undesirable attitudes which in turn deter patients from seeking and continuing treatment. Interventions based on the findings of such studies will contribute considerably towards the successful implementation of the program.—Author's Summary

Kulkarni, V. N. and Mehta, J. M. Splinting of the hand in leprosy. Lepr. India **55** (1983) 483–484.

Clawing of the hand in leprosy, which is caused by paralysis of intrinsics, can often be prevented and corrected to some extent if treated properly. Splints can contribute greatly to this. This article emphasizes the use of a variety of splints prepared from a lumafoam, hexcelplast and other such materials, as an adjunct to other physiotherapy measures such as wax baths, massage, and exercises.—Authors' Abstract

Valencia, L. B. Socio-economic research in the Philippines with special references to leprosy. Southeast Asian J. Trop. Med. Public Health **14** (1983) 29–33.

This brief paper presents the need for studies on the social aspects of leprosy; it also describes a current research project in the Philippines with a multidisciplinary team consisting of medical doctors and social scientists. Moreover, it tries to show what the research data might do to improve leprosy control programs. The research team hopes that these pioneering efforts in the study of the social aspects of leprosy, which is a highly stigmatized disease, will encourage other scientists to follow suit.—Author's Summary

Vasundhra, M. K., Siddalingappa, A. S. and Srinivasan, B. S. A study of medico-social problems of the inmates of a leprosy colony in Mysore. Lepr. India **55** (1983) 553–559.

A study of the inmates of a leprosy colony in Mysore revealed that there were more male cases and that the deformities were also more common among the male patients. There were no cases among inmates below 20 years of age. Most were in the age group 31–50 years; 93.2% of the inmates were illiterate and 96.6% of the patients were ignorant of the cause, spread, prognosis of the disease, and prevention of disabilities. This indicated an urgent need for health education among the leprosy patients and their families. All the inmates, including the apparently healthy relatives, reported loss of income due to disease and disabilities. Rehabilitation of the inmates must be encouraged.—Authors' Abstract

Volinn, I. J. Health professionals as stigmatizers and destigmatizers of diseases: alcoholism and leprosy as examples. Soc. Sci. Med. **17** (1983) 385–393.

Two disease entities are used for the analysis of stigmatization processes within the health care system. It is shown how overall cultural norms, specific professional role interpretations, and certain characteristics of the disease are contributory factors. Cultural norms of devaluating persons with disabilities are considered. The relative powers of the medical profession within the health care system are assessed in order to evaluate their potentially stigmatizing impact. Previously formulated theoretical concepts and findings of empirical studies provide the overall framework for the discussion.

The conclusions include implications which might lead to the improvement of treatment and rehabilitation of currently stigmatizing diseases.—Author's Abstract

Other Mycobacterial Diseases and Related Entities

Benjamin, R. G. and Daniel, T. M. Serodiagnosis of tuberculosis using the enzyme-linked immunoabsorbent assay (ELISA) of antibody to *Mycobacterium tuberculosis* antigen 5. Am. Rev. Respir. Dis. **126** (1982) 1013–1016.

The serologic response to purified mycobacterial antigen 5 was examined using an enzyme-linked immunoabsorbent assay in 75 patients with pulmonary tuberculosis and 150 control subjects. Two patient and six control groups were studied. The serums

from the patient groups had significantly higher IgG antibody concentrations than infected control subjects with good specificity. In patients living in low-prevalence areas where the results of skin tests in the majority of the population are negative, an antibody titer greater than or equal to 1:40 would have a 95.8% specificity for active disease. For patients living in a high-prevalence area where the results of skin tests in the majority of the population are positive, then an antibody titer greater than or equal to 1:40 would have a 79.9% specificity for active disease. Serums from patients with active nontuberculous mycobacterial infection had intermediate mean titers.—Authors' Summary

Blackwell, J. M. Genetic control of recovery from visceral leishmaniasis. Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 147–151.

Bradley and Kirkley noted that both inbred NMRI mice and outbred PO mice were strains innately susceptible to *Leishmania donovani* as judged by their parasite loads 2–4 weeks after infection. Over a longer period of observation, however, it was noted that NMRI mice but not PO mice resolved their infections. When the livers of the infected mice of both strains were examined histologically two weeks after infection they were full of granulomata comprising mainly parasitized and unparasitized macrophages. In NMRI mice, by 80 days after infection, however, the granulomata contained macrophages, many lymphocytes and very few parasites and after 4–5 months there were few granulomata and the liver was almost back to normal. In contrast, the PO mice had heavily parasitized livers with numerous granulomata for more than two years. This pattern of "cure" or "non-cure" in the innately susceptible mice was also seen in the innately resistant mice. In this paper Blackwell discusses the genetic control of the later stages of *L. donovani* infection in innately susceptible mouse strains.

To start with she examined the possible role of the major histocompatibility complex of the mouse, H-2, using congenic strains of mice such as B10 and B10.D2. B10 mice are haplotype H-2^b and B10.D2 are haplotype H-2^d. In crossing experiments the curing trait behaved as a recessive Mendelian trait. There was a 100% correlation between homozygous b/b haplotype with cure and between homozygous d/d and heterozygous b/d haplotypes with non-cure. Experiments with other haplotypes on a B10 genetic background confirmed that H-2 exerts a major influence in controlling the course of *L. donovani* infection. When H-2^b and H-2^d haplotypes were put onto other genetic backgrounds such as BALB/c, again H-2^b correlated with a reduction of parasite load while H-2^d mice were non-curing. There was, however, considerable variation between strains suggesting that non-H-2 linked genes influence the rate of recovery in some strains.—R. S. Phillips (*From* Trop. Dis. Bull.)

Bowers, P. W. and Powell, R. J. Effect of thalidomide on orogenital ulceration. Br. Med. J. **287** (1983) 799–800.

Severe recurrent oral and genital ulceration may be difficult to treat, but a recent report suggested that thalidomide may be used in Behçet's syndrome.

Mascaro, *et al.* reported improvement in six patients with severe recurrent aphthous ulcers when treated with thalidomide, and recently Saylan and Saltik reported good results in 26 patients with Behçet's syndrome, although iritis and arthritis did not improve. We have confirmed these findings and also that ulcers recur when treatment is withdrawn, although they are not as severe or as frequent as before treatment.

It is important that the possible development of neuropathy and teratogenesis is not forgotten and that informed consent is obtained. With this caveat we believe that thalidomide is a valuable adjunct to the treatment of severe orogenital ulcers.—(*From* the article)

Bradley, D. J. Genetics of resistance to infection with special reference to leishmaniasis. Introduction, and genetics of susceptibility to *Leishmania donovani.* Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 143–146.

The severity of a tropical parasitic infection shows considerable variation between individuals within a community. The factors which contribute to this variation in-

clude differences in virulence of the parasite, in the size of the parasite challenge, and in the host's susceptibility to the parasite. Differences in the host's susceptibility may reflect changing environmental factors such as nutritional levels, but host susceptibility is also controlled by genetical factors.

In early work on the genetic control of susceptibility to infection it was shown that tuberculosis in rabbits and typhoid in the mouse were genetically controlled but the number of genes involved was not elucidated. Subsequently a few viral infections in the mouse were shown to be under single gene control. Further work in this field is well illustrated by the work on *Leishmania donovani* in mice. Bradley found that different strains of mice infected with the same strain of *L. donovani* may carry different parasite burdens. In 25 inbred strains of mice, during weeks 2–4 of infection, the different strains of mice either contained a few hundred amastigotes or many thousands: there was no intermediate degree of infection. Further studies demonstrated that a single major gene or tight linkage group, called *Lsh,* controls initial susceptibility of mice to visceral leishmaniasis. The *Lsh* gene was then mapped using specially bred recombinant inbred strains of mice. These studies enabled Bradley and colleagues to allocate *Lsh* genes to an appropriate linkage group which was confirmed by classical linkage experiments: *Lsh* gene was located on chromosome 1 of the mouse.

Not only do different inbred strains of mice differ in their initial resistance to infection with *L. donovani* but among the strains which rapidly become heavily parasitized some eventually reduce the parasite load and others do not.—R. S. Phillips (*From* Trop. Dis. Bull.)

Bradley, D. J. Host genetics and tropical disease. Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 155–156.

It has been shown that for *Leishmania donovani* and *L. tropica* in mice variation in resistance to these parasites is genetically controlled and that a limited number of genes have significant effects upon the course of infection. The author considers the value of the kind of genetic analysis such as described in the previous papers where a single gene has been shown to exert considerable influence. If the genetic basis of the response to infection is known it may be easier to understand the biochemical or immunological basis of the particular disease.

In man there are two situations where resistance clearly has a single gene basis: the sickle cell trait where heterozygosity is associated with resistance to *Plasmodium falciparum* and the Duffy blood group antigen whose absence confers resistance to *P. vivax.*

Leishmaniasis and leprosy resemble each other in many respects. In mice the major histocompatibility locus plays an important role in determining resistance to visceral leishmaniasis, and it was therefore of interest to find evidence for involvement of the HLA locus in determining susceptibility to leprosy. HLA may also be involved in malaria. In a Tanzanian study individuals with HLA types A2 and AW30 together had an unusually high frequency of high antimalarial antibody titers.

Bradley concludes that through a continuing examination of the role of genetics and environment in tropical disease ultimately the balance between host and parasite may be tipped in favor of the host.—R. S. Phillips (*From* Trop. Dis. Bull.)

Flavin, D. K., Fredrickson, P. A., Richardson, J. W. and Merritt, T. C. Corticosteroid abuse—an unusual manifestation of drug dependence. Mayo Clin. Proc. **58** (1983) 764–766.

A depressed 44-year-old man presented with a 2½-year history of use of a synthetic glucocorticoid (prednisone) as the only psychoactive drug. The pattern of use strongly suggested drug dependence; secondary Cushing's syndrome was noted. We call attention to the potential abuse of neuroendocrine agents and, more specifically, corticosteroid preparations.—Authors' Abstract

Gardner, J. D., Ousley, M., Godfrey, W., Lindsey, N. J. and Abdou, N. I. *Mycobacterium fortuitum* infection: evidence of bactericidal defect due to hyperactive antigen-specific suppressor cells. Correction *in vitro* and *in vivo* by cholinergic

agonist and indomethacin. Am. J. Med. **73** (1982) 756–764.

Immunologic studies in a patient with long-standing *Mycobacterium fortuitum* infection revealed normal numbers of T cells, T inducers, T suppressors, B cells, and monocytes, significant *in vitro* proliferative response to *M. fortuitum* antigen, and poor bactericidal activity against *M. fortuitum* but not against *Escherichia coli*. *M. fortuitum* antigen-activated suppressor cells contributed to the bactericidal defect. The activity of these suppressor cells could be eliminated by the *in vitro* treatment of blood mononuclear cells with a combination of a cholinergic agonist and indomethacin, but not with either alone. Administration of the two drugs to the patient resulted in reversal of the bactericidal defect and dramatic clinical improvement. Systemic atypical (nontuberculous) mycobacterial infection may activate specific suppressor cells that could compromise the host's phagocytic cell function. Modulation of those suppressor cells by a combination of a cholinergic agonist and prostaglandin synthetase inhibitor could reverse this abnormality and may be beneficial to the patient.—Authors' Abstract

Hewitt, J., Coates, A. R. M., Mitchison, D. A. and Ivanyi, J. The use of murine monoclonal antibodies without purification of antigen in the serodiagnosis of tuberculosis. J. Immunol. Methods **55** (1982) 205–211.

A serum diagnostic test for tuberculosis has been devised on the basis of competitive inhibition by human sera of the binding of ^{125}I-labelled murine monoclonal antibodies (Mabs) to a solid-phase bound pressate of *Mycobacterium tuberculosis*. Five monoclonal antibodies binding to distinct antigenic determinants of the organism were used as structural probes which conferred their stringent combining site specificities to the polyclonal mixture of human antibodies. Sera from patients but not from healthy controls competed effectively with the binding of ^{125}I-labelled Mabs to *M. tuberculosis*-coated polyvinyl plates. This inhibition technique eliminated the need for elaborate purification of antigen used in previous serological methods. Some Mabs gave considerably more positive results than others. The best combination of tests used two Mabs and yielded a positive result in 71% of 41 patients with smear-positive pulmonary tuberculosis. This approach is applicable in principle to the serodiagnosis of other human bacterial diseases.—Authors' Abstract

Howard, J. G., Hale, C. and Liew, F. Y. Genetically determined response mechanisms to cutaneous leishmaniasis. Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 152–154.

Although in most clinical cases of *Leishmania tropica major* in man the skin lesions are self healing, in a small proportion of cases the lesions persist and may become more widely spread. The variable clinical picture apparently reflects differences in both parasite and patient. All the clinical forms of cutaneous leishmaniasis can be induced in different strains of inbred mice.

BALB/c mice are unusually susceptible to *L. tropica*. A very small infective dose of promastigotes initiates an infection which follows a progressive course and, after metastasing to the viscera, proves fatal. In many other strains of mice cutaneous lesions heal within two months, whereas in yet others there is sufficient acquired resistance to contain the lesion but not to eliminate it. Using congenic mice Howard and colleagues found that the differences between strains in the course of *L. tropica* infections are independent of H-2, unlike resistance to *L. donovani*.

BALB/c mice are very susceptible to *L. tropica*, whereas C57BL/6 mice are resistant. By infecting F_1, F_2 and backcross generations from these two strains and measuring their resistance or susceptibility in terms of lesion size after infection with *L. tropica*, Howard and colleagues demonstrated that BALB/c susceptibility segregated according to Mendelian inheritance of a single major autosomal gene.

The outcome of a *L. tropica* infection is thought to be the result of two levels of regulation: 1) the relative innate susceptibility of infected macrophages, and 2) the subsequent development of T cell-mediated immunity. The authors review the evidence which supports the existence of these two

levels of regulation. When chimeric mice were established of pairs of strains compatible at H-2 but which differed widely in their susceptibility to *L. tropica* (chimeric mice were prepared by lethally irradiating mice of one of the strains and reconstituting them with allogeneic bone marrow from the other strain), the chimeras after infection showed the susceptibility or resistance characteristic of the donor indicating that the major regulatory gene is expressed intrinsically in some property or properties of a hemopoietically derived cell, probably the macrophage. Cell transfer experiments showed an important role for T cells in acquired immunity to *L. tropica*. These T cells were not cytotoxic cells but were analogous to the T cells that mediate delayed type hypersensitivity (DTH). Although BALB/c mice are susceptible, early on in the *L. tropica* infection they do show DTH reactivity but this is lost due to specific suppression by the induction of suppressor T cells. Sublethal irradiation of BALB/c mice before infection, however, enabled the mice to recover from the infection and express strong DTH reactivity.

In summary, in mice infected with *L. tropica* two subsets of T cells are stimulated, namely DTH T cells and suppressor T cells and the outcome of the disease depends on the balance between these two subsets. A single major regulatory gene determines susceptibility to *L. tropica*. Where there is a primary macrophage defect, amastigotes rapidly accumulate and this high antigen load leads to induction of specific suppressor T cells.—R. S. Phillips (*From* Trop. Dis. Bull.)

Lavy, A. and Yoshpe-Purer, Y. Isolation of *Mycobacterium simiae* from clinical specimens in Israel. Tubercle **63** (1982) 279–285.

Mycobacterium simiae was first isolated from monkeys in 1965, was subsequently grouped in the Kansasii group B (photochromic mesophiles) and has rarely been identified as the cause of human disease. The tuberculosis laboratory of the Public Health Laboratory in Tel Aviv, Israel, isolated 399 strains of *M. simiae* from 287 persons and one monkey over a seven-year period. Eighteen patients had three or more isolates. All patients except one resided in the coastal plain, and the 18 patients described were middle-aged or elderly. Predisposing factors were present in most patients, consisting of tuberculosis (healed in 11, recently treated in 3, and active in 1); cancer in 1 patient; and unknown in 2. Ten strains were studied for drug sensitivity by the resistance ratio method and found to be highly resistant to most anti-tuberculous drugs, and sensitive to cycloserine only. None of the patients received treatment. One patient died of tuberculosis and three died of other causes. Two patients have undergone spontaneous conversion of the sputum, and ten continue to excrete *M. simiae* without significant clinical or radiological change. Two patients were lost to follow up. There is little evidence of the pathogenicity of *M. simiae,* although clearly it can colonize damaged lungs.—G. H. Rée (*From* Trop. Dis. Bull.)

Madzhidov, A. V. and Madzhidov, U. V. Study of the functional activity of natural killer cells in autoimmune processes in mice. Zh. Mikrobiol. Epidemiol. Immunobiol. **10** (1983) 65–67. (in Russian)

The functional activity of natural killer cells in mice with experimentally induced autoimmune (adjuvant) arthritis and in NZB mice with genetically determined autoimmune disturbances has been studied. A sharp suppression of natural killer cells has been shown to occur in the process of the development and in the course of adjuvant arthritis. A similar picture has been noted in the study of natural killer cells in NZB mice, suppression in these mice occurring simultaneously with the appearance of the signs of autoimmune disturbances. The activity of natural killer cells in the lymph nodes of NZB mice has proved to be absent practically during the whole period of the study. The preventive role of natural killer cells in autoimmunity is suggested.—Authors' English Abstract

Mason, U. G., III, Greenberg, L. E., Yen, S. S. and Kirkpatrick, C. H. Indomethacin-responsive mononuclear cell dysfunction in "atypical" mycobacteriosis. Cell. Immunol. **71** (1982) 54–65.

To evaluate cellular immunity in purified protein derivative (PPD) skin test-negative patients with "atypical" mycobacterioses, mononuclear cells from nine patients were examined for *in vitro* proliferative responses to PPD, candida (CAN), and phytohemagglutinin (PHA). The cell cultures received one of the following inhibitors of arachidonic acid metabolism: indomethacin, a preferential inhibitor of cyclooxygenase; nordihydroguaiarectic acid, a preferential inhibitor of lipoxygenase; or phenidone, an inhibitor of both enzymes; control cultures received no inhibitors. Every patient's lymphocyte responses to PPD and CAN were found to be significantly lower ($p < 0.01$) than those of skin test-positive healthy controls. However, in six of nine PPD skin test-negative patients, there was significant ($p < 0.05$) improvement in thymidine incorporation (TI) in PPD-stimulated cultures that contained indomethacin (1.0 μM). A similar effect was noted with CAN in three of nine patients and with PHA in three of three patients. In contrast, blockade of the lipoxygenase pathway produced even greater suppression ($p < 0.01$) of PPD-induced TI in five of nine patients, of CAN-induced TI in six of nine patients, and in all PHA-stimulated cultures. Phenidone produced no effects. This study supports the hypothesis that some patients with "atypical" mycobacterial disease have abnormal immunoregulation which may be mediated by an imbalance of the metabolic products of arachidonic acid, an abnormality similar to that noted in Hodgkin's disease and chronic coccidioidomycosis.—Authors' Abstract

Radin, R. C., Zeiss, C. R. and Phair, J. P. Antibodies to purified protein derivative in different immunoglobulin classes in the diagnosis of tuberculosis in man. Int. Arch. Allergy Appl. Immunol. **70** (1983) 25–29.

The sera of patients with active tuberculosis (TB) and sera from control groups were assayed for IgG, IgA, secretory IgA, IgM and IgE antibody activity to purified protein derivative (PPD) using the enzyme-linked immunosorbent assay. Patients with active TB clearly had higher levels of IgG antibody activity to PPD antigen than did healthy patients who were skin test positive or negative. There was a clear separation between the diseased and healthy groups. Similar, but not as marked increases were seen in IgA and secretory IgA antibody activity in diseased patients. No correlation between the presence of disease and antibody levels was found with IgM, and no IgE antibodies were found. The method presented is a rapid reproducible assay using commercially available materials, and may offer a clinically useful test for the diagnosis of TB.—Authors' Abstract

Rouillon, A. The International Union Against Tuberculosis. Tubercle **63** (1982) 247–253.

The International Union Against Tuberculosis (IUAT) was founded in 1920; over 60 years later there are 114 national associations affiliated to the Union, and over 6000 individuals—medical or lay—from 120 countries are individual members. The headquarters of the Union are in Paris, and it is governed by an executive committee of 17 members from different countries, and by a council comprising two representatives from each member association. The present activities of the IUAT are fourfold: namely, the exchange and dissemination of information, applied (basic) research, field research, and cooperation with other agencies including WHO, the International Union for Health Education, and the International Children's Centre.

Yet despite all the work that IUAT and other agencies have done, there are more cases of tuberculosis in the world today than ever before, even though the knowledge and means to cure the disease and break the transmission chain already exist. Dr. Rouillon calls this "a scandal and a paradox," but hopes that the future is not entirely gloomy.—G. H. Rée (*From* Trop. Dis. Bull.)

Seth, V., Kukreja, N., Sundaram, K. R., Malaviya, A. N. and Seth, S. D. *In vivo* and *in vitro* correlation of cell mediated immune response in preschool children after BCG in relation to their nutritional status. Indian J. Med. Res. **75** (1982) 360–365.

Existing tuberculin sensitivity may be depressed or suppressed by certain well known factors which include malnutrition. The present study in India was designed to correlate the results of both the Mantoux test and of the estimation of leukocyte migration inhibition in children of known nutritional state eight weeks after vaccination with BCG. All were tested with 5 TU of PPD plus Tween 80 before and after vaccination. The criterion of a positive reaction was induration of 5 mm or over; 154 children aged 1–6 years took part in the trial. They were distributed according to their nutritional status: normal, 39.6%; undernourished, 44.8%; severely undernourished (diminished protein energy), 15.6%.

The Mantoux test was positive after vaccination in 61.1% of the total and the leukocyte test in 68.2%. In the normally nourished children the respective rates were 68.8% and 55.7%, the difference not being statistically significant. In the severely undernourished children the Mantoux reactor rate was only 37.5% compared with 83.4% for the rate in the leukocyte test. The positivity of the leukocyte test was significantly higher (73.9%) in those with a mild-to-moderate degree of protein malnutrition than in the normally nourished group (55.7%). A mild-to-moderate degree of malnutrition did not however interfere with the positive Mantoux reaction. Comparison of the well-nourished and the severely malnourished showed that with the significant decrease in positive Mantoux reactions there was a significant increase in positive results with the leukocyte test.

Using both tests it was possible to elicit positive reactions in 83.3% of the severely malnourished children and in 88.6% of the well- and undernourished groups. The conclusion reached is that even severely malnourished children may be successfully vaccinated with BCG even if they fail to react to the post-vaccinal tuberculin test.—H. C. Calwell (*From* Trop. Dis. Bull.)

Stanford, J. L. The use of a sonicate preparation of *Mycobacterium tuberculosis* (new tuberculin) in the assessment of BCG vaccination. Tubercle **64** (1983) 275–282.

Six hundred sixty-four children attending elementary schools in and around the town of Butajira in the Shoa district of Ethiopia have been skin tested with a sonicate tuberculin and the responses have been divided into two different types. One of these types is believed to indicate protective immunity and the other, tissue-damaging hypersensitivity. On the basis of these responses, previously administered BCG vaccination has been assessed for its protective efficacy which, it is suggested, is above 80%. This system of assessment also indicated that school entry age would be a very suitable time for BCG vaccination in the region. If the system can be established as useful, its potential value in planning BCG campaigns in developing countries is considerable.—Author's Summary

Thorns, C. J., Morris, J. A. and Little, T. W. A. A spectrum of immune responses and pathological conditions between certain animal species to experimental *Mycobacterium bovis* infection. Br. J. Exp. Pathol. **63** (1982) 562–572.

Guinea pigs, rabbits, rats, ferrets and hedgehogs were infected with a recent field isolate of *Mycobacterium bovis.* The cell-mediated and antibody responses were studied up to eight weeks after infection at which time the animals were killed and pathological, histological and bacteriological examinations were carried out. Guinea pigs and rabbits produced an intense cell-mediated response and strong tissue reactions around the lesions. This appears, in part, to be responsible for the susceptibility of these animals to *M. bovis.* The strong cell-mediated response was also related to the small numbers of organisms in the tissues. Ferrets produced very little cell-mediated response and only minor tissue reactions. The lack of any cell-mediated response was related to the large numbers of organisms in the tissues which produced an acute disseminated disease. The antibody response produced by ferrets, rabbits and guinea pigs was variable within and between the species and could not be related to numbers of organisms in the tissues. In rats and hedgehogs a specific cell-mediated and humoral response was difficult to detect but the growth of the organism was controlled by the host, resulting in a persistent subclinical infection with no mortality.—Authors' Summary

Valero-Guillén, P. L. and Martin-Luengo, F. A gas-liquid and thin-layer chromatographic study of *Mycobacterium fortuitum*. Tubercule **64** (1983) 283–290.

Forty-two strains of *Mycobacterium fortuitum* were examined for fatty acid composition by gas-liquid chromatography and for mycolic acid pattern by two-dimensional, thin-layer chromatography of whole cell acid methanolysates. The strains studied contained saturated and mono-unsaturated fatty acids from 12 to 24 carbon atoms and tuberculostearic acid, and they showed a thin-layer chromatographic pattern of mycolic acids similar to the pattern previously reported for this species and characterized by the presence of α and α'-mycolates and several more polar components. The heterogeneity within the species *M. fortuitum* of its antigenic, biochemical and chemical properties, previously noted by several authors was slightly reflected (but not correlated) in the fatty acid composition found in the strains studied; the mycolic acid pattern of all of them was, however, very stable.—Authors' Summary