# CURRENT LITERATURE

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

## General and Historical

**Pereira, A. C., Jr., and Gurfinkel, A. C. M.** Positioning of borderline and indetermined groups in the hanseniasis classification. Hansen. Int. **6** (1981) 63–70.

The authors discuss the present conceptions of the hanseniasis classification, establish the main clinical, histological, bacterioscopic, and immunological characteristics of the borderline and indeterminate groups. They also believe that the borderline group is genetically predetermined and show the importance of the indeterminate forms and its evolutionary aspects. They try a schematic process of classification from Rabello's polar concept, and conclude that the borderline group, with special characteristics, oscillates within itself in a defined spectrum without touching the extremes T and V (L).—Authors' Abstract

**Revankar, C. R., Jha, S. S., Dongre, V. V., Deshpande, S. S. and Ganapati, R.** Integration of leprosy into general health services in an urban area—a feasibility study. Lepr. Rev. **53** (1982) 297–305.

To study the feasibility of integrating leprosy treatment into the general health services in Bombay, 198 doctors (essentially private medical practitioners), 120 interns, 32 nurses, and 126 other auxiliary health staff were involved in intensive orientation programs of various types, and doctors were offered a free consultative service and guidance, with a free supply of dapsone. They were encouraged to treat leprosy patients in their own set-up without referring them elsewhere.

After 18 months' follow-up, it was found that 108 doctors (59%) suspected 771 leprosy cases, of which 724 (94%) were labelled as leprosy. The investigators confirmed personally 129 of 158 (82%) which were seen by these doctors: 70% were of tuberculoid type, 6% were lepromatous, and 22% borderline type. Out of 50 whose skin smears could be taken, 25 (50%) were positive for AFB. At the end of the study, it was found that 42% of all cases were under regular treatment.

Short-term follow-up assessment showed that 58% of doctors treated cases in their clinics as compared to 8% before study. Similarly the percentage of doctors who referred cases to leprosy clinics or dermatologists was reduced to 42%. Ninety-two percent of patients expressed their desire to continue treatment from their doctors only. It is concluded that if proper diagnostic guidance and encouragement is given, doctors may be able to manage uncomplicated leprosy cases. Integration is feasible in the urban situation so that leprosy patients get the benefit of health care at the level of "first contact" with the peripheral service.—Authors' Summary

**Sansarricq, H.** The WHO leprosy programme. Ann. Microbiol. **133B** (1982) 5–12.

During the last decade there has been an increased interest in leprosy on the part of the governments of many endemic countries as reflected in five resolutions calling on Member States and the Organization to intensify leprosy control and research activities.

The WHO leprosy program operates at three levels of the WHO structure: a) country, b) regional, and c) global.

The country level corresponds to the national programs where the national WHO program coordinator or the WHO program coordinator is the focal point for all activities involving WHO cooperation. There are some 70 countries with a leprosy problem.

The regional level is represented by six regional offices in the different WHO regions (Africa, the Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific). In each regional office a medical officer is responsible for the coordination of leprosy activities.

The global level is symbolized by the WHO headquarters in Geneva. In headquarters the leprosy unit, which was established in 1958, is part of the Division of Communicable Diseases. The leprosy unit is responsible for overall coordination and ensures particularly that technical orientations are maintained in conformity with the most recent advances in knowledge through meetings of the WHO Expert Committee on Leprosy or study groups.

The different components of the WHO program for leprosy are under the following headings: a) assessment of the leprosy problem, b) policy guidance, c) coordination, and d) technical cooperation.—(*From* the article)

## Chemotherapy

**Beeching, N. J. and Ellis, C. J.** Leprosy and its chemotherapy. J. Antimicrob. Chemother. **10** (1982) 81–87.

The chemotherapy of leprosy must be considered within the context of the overall management of the patient. Although in many ways analogous to the treatment of tuberculosis, the time-scale of treatment is altogether different and means that it has taken years for controlled trials to establish the most practical and effective regimes. During this time, the emergence of organisms resistant to dapsone, and latterly, rifampin, has meant that reevaluation of second-line drugs in various combinations must now take place. It is a sobering thought that in the last 40 years only two agents—dapsone and clofazimine—have become established for long-term treatment of leprosy. A cheap, new agent is desperately needed.—(*From* the article)

**Belaube, P., Devaux, J., Boutboul, R., deMicco, C., Pizzi, M. and Privat, Y.** Enteropathie exsudative a la clofazimine: a propos d'une observation. (Exudative enteropathy due to clofazimine: about a case.) Acta Leprol. **88** (1982) 61–67. (in French)

The authors report a case of a 46-year-old woman suffering from generalized prurigo nodularis. This dermatosis was associated with a cellular immunodeficiency; therefore clofazimine therapy (300 mg/day) was instituted for six months.

Ten months after the cessation of the clofazimine therapy, there appeared a malabsorption syndrome that was temporarily improved by a gluten-free diet. The real etiology was only ascertained during laparotomy, when masses of crystals in the small intestine mucosa as well as in mesenteric lymph nodes were observed.

Therefore when it is necessary to prescribe clofazimine to take advantage of its immunoregulating properties, one must always bear in mind that an intestinal complication may ensue: this is well recognized in articles appearing in journals devoted to leprosy.—Authors' Summary

**Koticha, K. K., Pade, S. S., Chulawala, R. G. and Juwatkar, P. S.** Rifampicin (RFP) trial in lepromatous leprosy. Lepr. India **54** (1982) 441–447.

A rifampin trial in 66 lepromatous cases is reported. Some of these cases were previously treated with dapsone and some were fresh cases, the main criterion for selection being high BI and MI. The cases were divided into seven groups, depending on the dosage and frequency of administration of RFP. Dapsone was given in all the cases. Whenever the MI became zero, rifampin was stopped but dapsone continued. In those cases when the MI remained high, RFP was stopped either because of non-improvement or reactions or the patient dropped out. Only two groups showed good improvement: RFP 900 mg once a week and

RFP 600 mg six times a week. The latter group is preferable and the average period required to render MI zero was about 45 days.—Authors' Summary

**Li Wenzhong, Ye Ganyun, Zhang Yongfa, Feng Bi, Ma Lin, Ma Bukuan, Jiang Jun and Gu Shenggui.** Preliminary study on R761 treatment for leprosy. Acta Acad. Med. Sinicae **4** (1982) 293–295. (in Chinese)

Ten cases of BL and LL leprosy including dapsone-resistant cases were treated with R761 [3 (4-isobutyl-1 piperazinyl) rifamycin SV] 150 mg daily for six months. All of them showed significant improvement clinically, bacteriologically, and histologically. In the course of treatment, no obvious toxicity was found. As compared with previous reports, the therapeutic effect of R761 was similar to that of rifampin during the first half-year of treatment. Since R761 was cheaper than rifampin, it would be possible to use the former instead of the latter in combination with other chemotherapeutics in the treatment for leprosy, especially dapsone-resistant cases.—Authors' Summary

**Manungo, J. and Thomas, J. E. P.** A comparison of the incidence of type 2 reactions in lepromatous leprosy with two regimens of treatment. Cent. Afr. J. Med. **28** (1982) 209–211.

In this paper we have detailed a comparison of the incidence of Type 2 reactions in lepromatous leprosy with a clofazimine/dapsone regimen and an isoniazid plus thiacetazone ($HT_3$)/dapsone regimen. Type 2 reactions were more common on the $HT_3$/dapsone regimen but the difference was not great. We therefore recommend the $HT_3$/dapsone regimen as the most cost/effective treatment in Zimbabwe at the present time in the first year of combined treatment of lepromatous leprosy.—Authors' Summary

## Clinical Sciences

**Andersen, J. G.** Malignant degeneration in chronic ulceration of the leg and foot in leprosy patients; two case reports. Lepr. Rev. **53** (1982) 265–269.

The development of squamous cell carcinoma in long-established ulcers is described in two patients with leprosy, one on the lower leg in a patient with borderline-tuberculoid (BT) leprosy and the other on the sole of the foot in a patient with lepromatous (LL) leprosy. Although sometimes stated by clinicians to be rare, and infrequently reported in the literature, it is suggested that malignant change in chronic ulcers in leprosy may be found more often if patients are examined with care and the possibility kept in mind.—Author's Summary

**Carayon, A.** La reaction reverse ou inverse—point actuel. (The reversal or inversal reaction—present point.) Hansen. Int. **6** (1981) 10–18. (in French)

The reversal or inversal reaction, well studied in some research centers, is still imperfectly known, even contested or denied. This lack of knowledge has been one of the hindrances in the understanding of the mechanism of the hansenic neuritis. The evolution of the concepts about this question is studied, starting with Souza Lima and Souza Campos (1950), followed by Tajiri (1955), up to the present "I reaction" of Jopling, involving the "upgrading" and "downgrading" reactions. An interpretation of the reactional mechanism is given, with better possibilities for the understanding of clinical aspects and for therapy.—Author's Summary

**Duncan, M. E. and Oakey, R. E.** Estrogen excretion in pregnant women with leprosy: evidence of diminished fetoplacental function. Obstet. Gynecol. **60** (1982) 82–86.

Estrogen excretion was assayed in 64 women with leprosy and 15 healthy control women. The mean estrogen excretion was lower in women with leprosy than in controls, and the incidence of subnormal estro-

gen values was higher in the leprosy patients than in the controls. There was an association between infant birth weight and frequency of subnormal estrogen excretion. These features were most marked in women with lepromatous leprosy and are further evidence of diminished fetoplacental function in women with leprosy.—Authors' Summary

**Jonguierès, E. D. L., Sánchez Caballero, H.** Involución baciloscópica en dimorfos Virchowianos tratados con sulfonas—comparación con pacientes Virchowianos tratados con iguales dosis. (Bacteriologic involution in dimorphous Virchowian patients treated with sufones—comparison of Virchowian patients treated with the same doses.) Hansen. Int. **6** (1981) 19–22. (in Portugese)

The authors compare the bacilloscopic involution in 37 dimorphous Virchowian (DV) patients and in 47 Virchowian (V) patients with definite polarity treated with 200 mg daily of DDS for up to 20 years. After five years of treatment the DV patients presented negative bacilloscopy of the nasal mucus in 93% of the cases and of the skin in 81%. The control group of V patients showed, at the same time, negative bacilloscopy of the nasal mucus in 81% of the cases and of the skin only in 29.7%. After ten years of treatment 19.21% of the DV patients and 32% of the V cases showed positive skin bacilloscopy. It was concluded that the DV patients presented better responses to the sulfone therapy although a Virchowian aggravation had been observed in about one fifth of the DV cases. Considering that the DV patients represent 25% of the group of 150 D patients studied and that the DD and DT did not present a Virchowian aggravation, it was concluded that of the whole D group (DV, DD, DT) 4% of the patients presented Virchowian aggravation in spite of the sulfone treatment.—Authors' Abstract

**Krishnamoorthy, K. V.** Congenital absence of sensation. Lepr. India **54** (1982) 499–504.

Congenital absence of sensation which is described as a rare condition was met in the field and misled paramedical workers to include them as cases of leprosy. Further, eight persons having such a condition were traced from the same family.—Author's Summary

**Kundu, S. K., Hazra, S. K., Ghosh, S. and Chaudhuri, S.** Corticosteroids and lepromin sensitivity. Lepr. India **54** (1982) 489–498.

Corticosteroids are known to influence the hypersensitivity reaction in a number of diseases involving hypersensitivity of tissues and alter the antigen antibody reactions *in vivo*. Corticosteroids administered in 30 tuberculoid cases for a period of three weeks showed negative response in the lepromin-positive cases uniformly thereby proving suppression of cell-mediated immunity in tuberculoid cases under the influence of corticosteroids; hence the polar concept of the tuberculoid type may be under question with continuous and prolonged corticosteroid therapy under necessity.—Authors' Summary

**Manungo, J. and Thomas, J. E. P.** A study of type 2 reactions in lepromatous leprosy. Cent. Afr. J. Med. **28** (1982) 211–213.

The clinical picture and degree of leukocytosis are good guides to the onset, progress and response to treatment of Type 2 reactions in lepromatous leprosy. The hemoglobin level is less reliable, though anemia is common in reactions. Proteinuria is not a constant finding in reactions. A reactive thrombocytosis occurs in many reactions.—(*From* the article)

**Nigam, P., Goyal, B. M. and Saxena, H. N.** Eosinophilia as a result of rifampicin therapy. J. Indian Med. Assoc. **77** (1981) 158–159.

Eosinophilia can result from the therapy with rifampin but this has never been definitely established as the drug is usually given with isoniazid, which itself may result in an increase in eosinophils. Two cases (one with tuberculosis and one with leprosy) are being reported who developed eosinophilia during therapy with rifampin, which regressed on stopping rifampin.—(*From* Trop. Dis. Bull.)

**Petri, V.** Um caso pouco comum de erythema nodosum leprosum. (An unusual case of erythema nodosum leprosum.) Hansen. Int. **6** (1981) 51–54. (in Portugese)

An unusual manifestation of erythema nodosum leprosum (ENL) in a female, 24 years old, whose clinical history and picture were suggestive of acute systemic erythematosus lupus rather than hanseniasis, is described and commented. The diagnosis of ENL was made only after acid-fast bacilli were demonstrated in the ulcerated lesions.—(*From* the Author's Abstract)

**Rao, S. S. L., Rao, T. D. and Rao, T.** Immunological status of maculo-anaesthetic leprosy: T and B lymphocytes and serum immunoglobulins. Lepr. India **54** (1982) 471–478.

Peripheral blood T and B lymphocyte percentage and serum immunoglobulin levels were evaluated in 36 maculo-anesthetic (MA) leprosy patients using E and EAC rosette techniques and single radial immuno-diffusion, respectively. Twenty-one tuberculoid, 13 indeterminate, 16 borderline, 13 lepromatous, and 20 healthy controls were also studied for comparison. The results showed that the peripheral blood T lymphocyte percentages and humoral immune responses of maculo-anesthetic leprosy are not significantly different from either tuberculoid or indeterminate leprosy types or from control group.—Authors' Summary

**Sharma, V. D., Ramu, G., Dutta, A. K., Katoch, K. and Ramanathan, U.** Solid, fragmented and granular index as one of the parameters in drug trials. Lepr. India **54** (1982) 448–453.

A bacteriological study of the skin smears of 108 bacteriologically positive cases of leprosy, 30 of them untreated, has been undertaken. In each case solid, fragmented and granular (SFG) index, Bacteriologic Index (BI), and Morphological Index (MI) of skin smears from four sites were calculated. The results show that SFG index together with BI can be used as one of the parameters in drug trials. The importance of SFG index in research and as a routine laboratory procedure in leprosy control units undertaking multidrug therapy is discussed.—Authors' Summary

**Shilo, S., Livshin, Y., Zylber-Haran, E., Sheskin, J. and Spitz, I. M.** Gonadotropin, prolactin, and thyrotropin secretion in lepromatous leprosy. J. Androl. **3** (1982) 320–325.

Gonadotropin, prolactin (PRL), and thyrotropin (TSH) secretion was determined in 14 patients (27 to 56 years of age) with lepromatous leprosy and in 28 controls. Each subject received leutinizing hormone releasing hormone (LHRH) (100 $\mu$g), thyrotropin releasing hormone (TRH) (200 $\mu$g), and the dopaminergic antagonist, metoclopramide (10 mg), at 30-min intervals, with periodic blood sampling. On the basis of the LH response to LHRH, the patients were divided into two groups. Group I consisted of nine patients with an exaggerated LH response to LHRH. The remaining five patients of Group II had a normal response to LHRH. Mean basal and peak follicle stimulating hormone (FSH) responses to LHRH were increased in both groups, but were greater in Group I. Mean 17 $\beta$-estradiol ($E_2$) levels were increased in both groups; whereas testosterone values were normal. Basal PRL levels were similar to those in controls, but there was an increased PRL response to both TRH and metoclopramide in Group I patients. In contrast, Group II patients had PRL responses identical to controls. Both groups had increased TSH responses to TRH in the presence of normal basal thyroxine ($T_4$) and triiodothyronine ($T_3$) levels. The PRL response to TRH correlated with both basal and peak FSH responses to LHRH, but not with LH, $E_2$, or testosterone. The TSH response did not correlate with either gonadotropins, $E_2$, or thyroid hormone levels. Similar abnormalities in PRL and TSH secretion have been described in patients with primary testicular failure.—Authors' Summary

**Shulman, D. G., Wilkinson, R. D. and Nguyen, N.** Leprosy downgrading reaction associated with griseofulvin. Arch. Dermatol. **118** (1982) 909–912.

A dramatic alteration from clinically subpolar tuberculoid leprosy toward subpolar lepromatous leprosy was observed during

griseofulvin therapy in a 29-year-old man, despite apparently normal cell-mediated immunity. To our knowledge, this is the first reported case of a downgrading reaction associated with griseofulvin. It is possible that this reaction was due to inhibition of polymorphonuclear leukocyte chemotaxis by griseofulvin.—Authors' Summary

**Terencio de las Aguas, J.** Diabetes y lepra. (Diabetes and leprosy.) Rev. Leprologia **13** (1982) 523–529. (in Spanish)

The common symptoms of diabetes and leprosy are outlined regarding the skin and peripheral nervous system. The neurological damage can be a particular problem in differential diagnosis. The incidence of diabetes among 250 leprosy cases in the Fontilles Hospital (Spain) was determined. A total of 28 cases were observed, 15 men and 13 women. Twenty-five of the diabetes patients were lepromatous and three were tuberculoid. The prevalence of diabetes was 11.2% among this population, leading to the conclusion that there is a higher frequency of diabetes among patients with leprosy.—(*Adapted from* Author's Summary)

**Zhang, Jun-Tan, *et al.*** Preliminary observation on 20 cases of histoid leproma. Chin. J. Clin. Dermatol. **11** (1982) 183–184. (in Chinese)

Clinical and histopathological studies on 20 cases of histoid leproma were made. There were 12 cases of LLs, 4 cases of LLp, and 4 cases of BL. The development of disease, clinical course, and response to specific therapy were different from the lesions of conventional lepromatous leprosy. Histopathologically, typical and atypical cases could be differentiated and a transitional process could be found between them. The atypical form resembled lesions of lepromatous leprosy, in some instances similar to lesions in reaction. Therefore it was indicated that some relationship might exist between them. Further studies are necessary to understand the pathogenesis of histoid leproma.—Authors' Abstract

## Immuno-Pathology

**Bahr, G. M., Rook, G. A. W., Stanford, J. L., Lydyard, P. M. and Bryceson, A. D. M.** The effect of delayed addition of antigen and "E" rosetting on the proliferative response to mycobacterial antigens of peripheral blood lymphocytes from normal individuals or from patients with tuberculosis or leprosy. Immunology **44** (1981) 585–591.

Some suppressor cells are reported to lose their activity when precultured without stimulus *in vitro*. We have investigated the role of such suppressors in responsiveness to mycobacterial antigens of peripheral blood mononuclear cells (PBMNC) from patients with leprosy or tuberculosis, or from normal donors.

Delayed addition of mycobacterial antigens (*Mycobacterium leprae, M. vaccae,* and *M. tuberculosis*), but not of a fungal antigen (*Candida albicans*) caused enhanced responses using PBMNC from most normal donors, or tuberculoid leprosy (TT/BT) patients. However, the effect was less common using PBMNC from the lepromatous leprosy (BL/LL) group ($p < 0.01$, using *M. leprae,* relative to the TT/BT group), suggesting that this type of suppression reflects a normal mechanism, which is diminished rather than increased in anergic patients.

Delayed addition of antigens to "E"-rosetting cells did not result in enhanced responses. However, the different effects of "E"-rosetting on the responses to the mycobacterial antigens of cells from normals, TT/BT and BL/LL patients, suggested that there may be two types of proliferative response to these antigens.—Authors' Summary

**Botasso, O. A., Amerio, N., Puig, N., Corona, C. J. and Morini, J. C.** Estudio de parametros inmunologicos en enfermos de distintas formas clinicas de lepra; influencia del tratamiento. (Study of immunological parameters in patients with

different clinical forms of leprosy; the influence of treatment.) Leprologia **23** (1981) 135–139. (in Spanish)

Immunologic studies were performed in 64 patients with different forms of leprosy and in 13 healthy controls. The results were as follows:

a) Mitsuda reaction: Negative in patients with lepromatous leprosy but slightly positive in six of 17 treated patients. There was no variation in 12 patients with untreated lepromatous leprosy. There was a small percentage of positive responses in patients with indeterminate leprosy. The 15 patients with tuberculoid leprosy under treatment were more reactive than the 12 untreated tuberculoid patients.

b) There was a reduction in the number of lymphocytes in the peripheral blood of patients with tuberculoid leprosy under treatment and in those with lepromatous leprosy both with and without treatment in comparison to the controls.

c) EA rosettes: Indeterminate patients with a positive Mitsuda reaction had significantly higher EA rosettes than did lepromatous patients under treatment.

d) EAC rosettes showed no significant changes among the groups.

The two mechanisms for the immunologic disturbances in leprosy could be: a) a genetic defect in the processing of *Mycobacterium leprae* and b) tolerance caused by excess antigen (in the lepromatous type of disease).—(*Adapted from* the Authors' Summary)

**Chakrabarty, A. K., Maire, M. A. and Lambert, P. H.** SDS-PAGE analysis of *M. leprae* protein antigens reacting with antibodies from sera from lepromatous patients and infected armadillos. Clin. Exp. Immunol. **49** (1982) 523–531.

Studies have been conducted to characterize *M. leprae* antigens from purified leprae bacilli derived from infected armadillos. First, the proteins of the mycobacterial extracts were fractionated by SDS-PAGE. Subsequently, the proteins in the gel were electrophoretically transferred on a strip of nitrocellulose paper by the technique of "electrophoretic blotting." The separated bacterial protein bands immobilized on the nitrocellulose paper were made to react immunologically with sera from the lepromatous patients, infected armadillo sera, and other experimental mycobacterial antisera. It was observed that a majority of *M. leprae* proteins contained antigenic determinants also present on proteins of BCG. In addition, only two specific antigen bands of 33KD and 12KD were conspicuously detected by the patients' sera and the infected armadillo sera. These substances were further identified as polysaccharides or glycoproteins since they could only be stained by Schiff's reagent or alcian blue. Only the 12KD glycoprotein band reacted with concanavalin A; whereas wheat germ agglutinin (WGA) did not show any reaction with them. These 33KD and 12KD glycoprotein antigens were found to lose their antigenicity after pepsin treatment and can be considered as glycoproteins. Further, radiolabelling experiments showed that the 12KD antigen underwent radioiodination under usual conditions, but the 33KD glycoproteins failed to be similarly radiolabelled. It is suggested that these protein antigens have *M. leprae*-specific determinants on a cross-reacting component.—Authors' Summary

**Harikrishnan, S., Balakrishnan, S. and Bhatia, V. N.** Serum immunoglobulin profile and C3 levels in lepromatous leprosy patients. Lepr. India **54** (1982) 454–460.

A study of the serum levels of IgA, IgG, IgM and C3 in well-defined cases of lepromatous leprosy has been undertaken. The serum levels of IgA, IgG and IgM were significantly raised in the group of lepromatous leprosy patients (20) compared to healthy controls (20). The C3 level also tends to be increased in these patients. In the 15 cases of LL, studied before and after ENL reaction, the levels of all the immunoglobulins as well as C3 were found to be further increased during ENL and showed a fall during subsidence.—Authors' Summary

**Humphres, R. C., Gelber, R. H. and Krahenbuhl, J. L.** Suppressed natural killer cell activity during episodes of erythema nodosum leprosum in lepromatous leprosy. Clin. Exp. Immunol. **49** (1982) 500–508.

Natural killer (NK) cell activity was in-

vestigated in peripheral blood mononuclear cells of patients with leprosy. The NK activity of patients with borderline or lepromatous leprosy did not differ significantly from that of normal subjects. However, in a group of patients with lepromatous leprosy undergoing an episode of erythema nodosum leprosum (ENL), NK activity was significantly depressed. In four patients with ENL, NK activity was virtually abolished. Depressed NK activity could not be attributed to the effects of corticosteroid therapy, nor did a serum factor appear to be responsible. Evidence was obtained that depressed NK activity in patients with ENL was not due to dysfunction of the NK cells themselves; they functioned normally when separated from the individual's total mononuclear cell population. Additional cell depletion studies suggested that the patients' monocytes were responsible for the observed depression of NK activity.—Authors' Summary

**Kodjovi, M., Arnold, J., Massoni, F., Stach, J.-L. and Husser, J.-A.** Diminution du taux des T lymphocytes circulants dans la lèpre lépromateuse: Étude préliminaire. (Impairment in the number of circulating T lymphocytes in lepromatous leprosy. Preliminary study.) Bull. Soc. Path. Exot. **75** (1982) 384–389. (in French)

An impairment was found in the number of circulating T lymphocytes in lepromatous leprosy.

This defect is not correlated with the bacterial load, the severity of the disease, or with the length of treatment.—Authors' Summary

**Kurup, I. G. and Mahadevan, P. R.** Cholesterol metabolism of macrophages in relation to the presence of *Mycobacterium leprae*. J. Biosci. **4** (1982) 307–316.

Macrophages phagocytose *Mycobacterium leprae* and live bacilli inside such macrophages alter the lipid metabolism. There is increased accumulation of cholesterol ester in the bacteria infected cells. This increase appears to be due to the decreased level of esterase enzyme that could hydrolyse cholesterol esters. Associated with the decreased level of this enzyme is a reduced amount of protein synthesis. Increased cholesterol ester may be responsible for conversion of macrophages into foamy cells in the presence of *M. leprae*.—Authors' Abstract

**Liu Zijun, *et al.*** A study of histopathologic lesions on peripheral nerve trunks in tuberculoid leprosy. Chin. J. Clin. Dermatol. **11** (1982) 169–171. (in Chinese)

Peripheral nerves from biopsies of 210 cases and autopsies of 21 cases of tuberculoid leprosy were studied. The frequency of nerve trunks affected in order was ulnar nerve, median nerve, fibular nerve, radial nerve, and auricular nerve. In some cases we could also find lesions in the axillary nerve, ischiadic nerve, intercostal, and vagus nerves. One hundred thirteen pairs of bilateral peripheral nerve trunks were studied. Generally bilateral involvement was twice as frequent as unilateral involvement. Histologically, the evolution of the nerve lesions may be divided into three stages: active stage with active granuloma and active nerve abscess, regressive stage with regressive granuloma and regressive nerve abscess, and the quiescent stage with fibrosis and/or calcification. This division was closely related to the duration of the disease. The shorter the duration of illness the more active the nerve lesions. In the majority of cases, the activity of the nerve lesions corresponded with the activity of the cutaneous lesions. Deformity of the limbs was more frequently associated with quiescence of the nerve lesions. The authors believe that biopsy of the peripheral nerve in tuberculoid leprosy is of value in the diagnosis and the assessment of therapy as well as in the study of the pathogenesis of leprosy.—Authors' Abstract

**Liu Zijun, *et al.*** Analysis of pathological changes of peripheral nerve trunks in 70 autopsies of lepromatous leprosy. Chin. J. Dermatol. **15** (1982) 149–152. (in Chinese)

A total of 807 tissue blocks of various peripheral nerve trunks taken from 70 autopsied cases of lepromatous leprosy have been studied. The incidences of lesions in various nerve trunks were quite different, with the highest in ulnar nerve (98.2%), common fibular nerve (97.8%), and median

nerve (90.2%). Three hundred fourteen pairs of bilateral tissue blocks taken from the same level of the same nerve have been examined, and the ratio of unilateral nerve lesions to bilateral nerve lesions was generally 1:5. This means that the lesions in nerve trunks of lepromatous leprosy were not generalized, symmetrically distributed, at least not diffusely affecting the entire length of the nerve. From the difference in cellular infiltrates of a given nerve, we can divide the lesions of nerve trunks into progressive stage, regressive stage, and quiescent stage. Correlating nerve trunk lesions to skin lesions in 57 cases studied, we found that the process of regression in skin lesions was faster than that in peripheral nerve trunks.—Authors' Abstract

**Mehra, V., Convit, J., Rubinstein, A. and Bloom, B. R.** Activated suppressor T cells in leprosy. J. Immunol. **129** (1982) 1946–1951.

Leprosy is a spectral disease in which the patients at the lepromatous end display selective immunologic unresponsiveness to antigens of *M. leprae*. We have previously explored the possibility that the anergy in lepromatous leprosy is mediated by suppressor cells. An *in vitro* system was developed in which lepromin induces suppression of the mitogenic response of lepromatous and borderline but not tuberculoid leprosy patients to concanavalin A. Two populations, an adherent cell and a T lymphocyte, were responsible for this lepromin-induced *in vitro* suppression. All the T cell suppressor activity was associated with a 20%–30% subset of human T cells recognized by a $TH_2$ xenogeneic antithymocyte serum or OKT8 monoclonal antibodies.

That the lepromin-induced $TH_2^+$/$OKT8^+$ subset may be involved in suppressing the specific antigenic response of peripheral blood lymphocytes of some lepromatous and borderline leprosy patients to *M. leprae* antigens was established by showing that OKT8-depleted cells from 6 of 21 lepromatous patients showed markedly enhanced $^3$H-thymidine incorporation at six days upon stimulation with lepromin, compared to the unresponsiveness of their unfractionated cells.*

The expression of Ia determinants and Fc receptors (FcR) on T cell subsets was examined as a potential marker for *in situ* activation. In contrast to normal subjects, there were significantly elevated numbers of $Ia^+$, $TH_2^+$/$OKT8^+$ T cells in lepromatous leprosy patients. There was a similar elevation in $FcR^+$ cells in the same subset, and the expression of Ia and of FcR were highly correlated. The possibility that the Ia and Fc markers may serve as an index of active T cell suppressor activity *in vivo* was strengthened by studies in a small number of lepromatous patients vaccinated with living BCG and killed *M. leprae* who showed marked clinical improvement and conversion to skin test positive reactivity. In 10 such patients examined over a treatment period of 1–2 years, the suppressor activity returned to normal levels, and the number of $Ia^+$, T cells in 7 of 8 similarly returned to normal levels.—Authors' Summary

* *Editor's Note: All six were classified as borderline or subpolar lepromatous.*—RCH

**Melsom, R., Harboe, M. and Duncan, M. E.** IgA, IgM and IgG anti-*M. leprae* antibodies in babies of leprosy mothers during the first 2 years of life. Clin. Exp. Immunol. **49** (1982) 532–542.

IgA, IgM and IgG anti-*M. leprae* antibody activity was estimated by solid phase radioimmunoassay in repeated serum samples from cord sera to sera taken two years after birth from 29 babies of mothers with lepromatous leprosy (Group 1) and 16 babies of mothers with tuberculoid leprosy and non-leprosy control mothers (Group 2). IgA anti-*M. leprae* antibody activity could be detected in 30% and IgM anti-*M. leprae* antibody activity in 50% of cord sera from Group 1, but not in any of the cord sera from Group 2. After birth, there was a significantly higher increase of IgA and IgM anti-*M. leprae* antibody activity in sera taken 3–6 months after birth from babies of Group 1 compared to Group 2, but the IgA and IgM activity in sera taken after six months of age showed the same increase in the two groups. IgG anti-*M. leprae* antibody activity showed a marked decrease in sera from both Groups 1 and 2 taken 3–6 and 6–9 months after birth compared to the activity in the cord sera. No increase of the IgG activity could be demonstrated even in sera taken 15–24 months after birth in any

of the two groups. These findings are discussed in relation to possible transfer of *M. leprae* bacilli across the placenta, the influence of *M. leprae* and other mycobacteria exposure on the antibody activity, the poor IgG anti-*M. leprae* antibody response and subclinical leprosy infection in babies exposed to leprosy below two years of age.—Authors' Summary

**Prasad, H. K., Singh, R. and Nath, I.** Radiolabelled *M. leprae* resident in human macrophage cultures as an *in vitro* indicator of effective immunity in human leprosy. Clin. Exp. Immunol. **49** (1982) 517–522.

Twelve strains of human-derived, freshly extracted *M. leprae* maintained within human macrophages showed a 2.1–13.2-fold increase in the incorporation of $^{3}$H-thymidine compared to parallel cultures containing heat-killed bacilli of the same strain. The addition of antigen stimulated lymphokines from five paucibacillary, tuberculoid leprosy patients resulted in the inhibition of the uptake of the radiolabel by 49%–87%. Minimal or no inhibition was noted in the presence of similar culture supernatants from five bacilliferous lepromatous leprosy individuals. The results indicate that in contrast to lepromatous leprosy, tuberculoid patients possess antigen reactive lymphocytes which modulate macrophage function through soluble products. Attention is drawn to a rapid and sensitive *in vitro* method with potential for studying the immunological mechanisms leading to bacterial killing in human leprosy.—Authors' Summary

**Ramos-Zepeda, R., Ortega-Araiza, M. E., Gamboa-Márquez, A., Barba-Gómez, J. F. and González-Mendoza, A.** Perfil inmunologico del enfermo con lepra lepromatosa nodular. (Immunologic profile in patients with nodular lepromatous leprosy.) Dermatologia Rev. Mex. **26** (1982) 12–22. (in Spanish)

Seventy patients with nodular lepromatous leprosy observed at the Dermatologic Institute of Guadalajara, México, were studied concerning their immunologic status. Patients were divided in two groups. In the first one (50 patients) the humoral immunity was studied measuring the serum levels of immunoglobulins G, A, M, D, E, and C3 complement; the presence of abnormal serum proteins, rheumatoid factor, and reactive C protein were also looked for. In the second group (30 patients) cellular immunity was evaluated. For this purpose the amount of lymphocytic transformation induced by stimulation with phytohemagglutinin was measured.

Results showed that 70% of the patients from the first group had hypergammaglobulinemia for IgG, IgA or IgM. In addition, 34% of the patients showed rheumatoid factor and 38% C reactive protein in their sera. On the other hand, 40% of the patients of the second group had in their sera a depressive factor for lymphocytic transformation. This effect was exerted in the lymphocytes obtained from lepromatous patients as well as in those obtained from the control subjects.—Authors' Summary

**Ridley, M. J. and Ridley, D. S.** Unique expression of HLA-DR (Ia-like) antigen in the lesions of polar tuberculoid leprosy. Lepr. Rev. **53** (1982) 249–252.

HLA-DR antigen was demonstrated in the skin lesions in leprosy in 11 out of 11 polar tuberculoid (TT) cases, in 3 of 6 near-tuberculoid cases in reaction, and in 0 out of 38 other cases covering the spectrum from BT to LL. This antigen is therefore a good marker for the TT group. It is suggested that genetic markers may be associated with the rare TT group alone because, among those susceptible to leprosy, they denote the strong immune response that is needed to sustain this position in the spectrum. Susceptibility has not been explained.—Authors' Summary

**Rook, G. A. W.** Suppressor cells of mouse and man. What is the evidence that they contribute to the aetiology of the mycobacterioses? Lepr. Rev. **53** (1982) 306–312.

The author succinctly reviews and critiques current hypotheses that suppressor cells are involved in the pathogenesis of the mycobacterioses. There is no doubt that

suppressor cells are one of the most exciting areas of contemporary immunology, and it is now clear that, in mouse and man, suppressor cells can be triggered by mycobacterial antigens. In both species suppressor cells with non-specific suppressor effects accompany disseminated disease, but it will be extremely difficult to prove that they are important for its pathogenesis. All immune responses are regulated, and the demonstration of regulatory mechanisms in the laboratory does not prove that they were behaving in an abnormal manner in the donor. The initial defect which leads to the susceptibility of a lepromatous leprosy patient may not be over-active suppression. We can equally well hypothesize that overactivity of an inappropriate effector system leads to a failure to destroy bacilli, and that the increasing bacterial load secondarily activates a normal suppressor response.—(*Adapted from* the article)

**Saha, K., Chakraborty, A. K., Sharma, V. and Sehgal, V. N.** An appraisal of third complement component (C3) and breakdown product (C3d) in erythema nodosum leprosum (ENL). Lepr. Rev. **53** (1982) 253–260.

Sera from 20 patients with erythema nodosum leprosum (ENL) were collected at the first visit, and four weeks after successful therapy. The levels of C3, C3d, C1q, and C4 were measured in 20 paired samples. Acute phase reactants—alpha-1-antitrypsin (AAT), alpha-2-macroglobulin (AMG), and C-reactive protein (CRP)—were also estimated to monitor the activity of ENL. The mean serum C3 level showed a decrease during ENL, while after remission it showed a significant increase. Even then, the C3 level after remission was less than that in healthy controls. The mean level of C3d increased remarkably during ENL, and this increase persisted in most patients even after the clinical remission. An inverse relationship between C3d and C3 suggests that the determination of C3d forms a better indicator of C3 hypercatabolism during ENL. Clofazimine treatment resulted in a remarkable decrease of C3d, in contrast to those treated with prednisolone and chloroquine. Mean levels of AAT were greatly elevated during ENL but decreased significantly after its clinical remission.

Serum levels of C1q, C4, AMG, and CRP did not alter significantly during ENL and also showed no difference in patients on ENL therapy.—Authors' Summary

**Saha, K., Sehgal, V. N. and Sharma, V.** High incidence of IgG class of Epstein-Barr virus capsid antibody in Indian patients of lepromatous leprosy. Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 311–313.

Low levels of Epstein-Barr virus capsid (EBVC) antibody of the IgG class were detected in the sera of 19 of 23 (82.6%) lepromatous leprosy patients and 6 of 38 (16%) healthy controls. In contrast, heterophile antibody was found in only 6 of 43 (14%) lepromatous patients and 3 of 41 (7%) normal subjects. Overlap of the two types of antibody occurred only in one normal serum. It is inferred that the presence of EBVC antibody against an unbiquitous virus in lepromatous patients who often suffer from impairment of cell-mediated immunity might be due to past infection leading to persistence of the virus in their lymphoid cells and subsequent production of specific anti-viral antibody. Further, the striking finding of low incidence and titer of EBVC antibody in the normal Indian adults is consistent with the rarity of EB virus-associated disease, such as Burkitt's lymphoma, nasopharyngeal carcinoma, and infectious mononucleosis in India.—Authors' Summary

**Shepard, C. C., Walker, L. L., Van Landingham, R. M. and Shunzhang Ye.** Sensitization or tolerance to *Mycobacterium leprae* antigen by route of injection. Infect. Immun. **38** (1982) 673–680.

Aqueous suspensions of heat-killed *Mycobacterium leprae* in a dose of $10^7$ organisms were highly immunogenic when injected intradermally (i.d.). The same dose of bacteria did not sensitize when given intraperitoneally (i.p.) or intravenously (i.v.), and did so only minimally at best when given subcutaneously. The i.d. route was the most immunogenic for sheep erythrocytes also. *M. leprae* injected i.p. or i.v. stimulated immune tolerance to *M. leprae* challenge i.d. In older mice (≥8 weeks), the i.v.

injections gave more complete tolerance. Mice that had been rendered tolerant by i.v. injections maintained their tolerance for at least 168 days. Prior UV irradiation of intact mice prevented sensitization by the i.d. route. In normal mice, living *M. bovis* BCG given i.d. produced good sensitization to *M. leprae*. Mice that had been made tolerant by i.v. injection of *M. leprae* could be partially sensitized to *M. leprae* by i.d. immunization with BCG; mixtures of living BCG and heat-killed *M. leprae* were no more effective than BCG alone. These findings appear to have relevance to the pathogenesis of lepromatous leprosy and its immunoprophylaxis.—Authors' Summary

**Skinsnes, O. K.** Infectious granulomas: Exposit from the leprosy model. Annu. Rev. Med. **33** (1982) 47–67.

Dr. Skinsnes masterfully reviews leprosy as a model of infectious disease. The immunopathologic spectrum of leprosy is explained and the causes of lepromatous disease are explored. The pathogenesis of deformity in leprosy is reviewed. The natural history of the disease and epidemiologic considerations conclude the paper. The wealth of information and perspective provided in the paper deserve careful study.—RCH

**ten Dam, H. G. and Pio, A.** Pathogenesis of tuberculosis and effectiveness of BCG vaccination. Tubercle **63** (1982) 225–233.

Among the hypotheses offered to explain the conflicting results of various trials of BCG vaccination, the one invoking gross differences in the immunogenic properties of the various BCG vaccines (strains) has received most attention. Indeed, for many years research in BCG vaccination has been directed almost entirely towards improving the quality of vaccines. The anticipated benefit of this work, however, is not borne out by the results of the latest trial in India.

Whereas it cannot be excluded that technological advances may have resulted in the worst vaccines ever, it also remains possible that the basic hypothesis was less relevant than presumed. The quality of the vaccine may be of little importance and a different explanation should be sought for the observed differences in protection.

One possible lead is the observation that BCG vaccination consistently appeared to be of poor efficacy under conditions where, in a vaccination program, even an effective vaccine would have little impact on the tuberculosis problem, i.e., where the majority of cases originated from the population already infected. The hypothesis offered is that in such populations the pathogenesis of tuberculosis is different from that prevailing under the clearly exceptional conditions under which BCG vaccination was effective. Rather than being the direct result of primary infection, tuberculous disease (observed) may be the result of reinfection. In this case BCG vaccination cannot be expected to have a protective effect.—Authors' Summary

## Microbiology

**Abou-Zeid, C., Voiland, A., Michel, G. and Cocito, C.** Chemical composition of cell-wall polysaccharides from leprosy-derived corynebacteria. Fems Microbiol. Lett. **15** (1982) 185–188.

Two kinds of microorganisms have been recognized in human leprosy lesions: a) *Mycobacterium leprae*, acid-fast Gram-positive, which does not replicate *in vitro*; and b) some non-acid-fast Gram-positive bacteria which multiply in axenic culture and were previously indicated as "diphtheroids" because of their resemblance to *Corynebacterium diphtheriae*. These microorganisms were recently characterized as true corynebacteria according to their DNA base composition (56%–58% GC) and mycolic acid structure (polyunsaturated corynomycolic acids). Consequently, "diphtheroids" were renamed as "leprosy-derived corynebacteria" (LDC) according to Barksdale.

The aim of the present study was the purification and analysis of cell-wall polysaccharides of three LDC and two reference microorganisms, *C. hoffmannii* and *M. smegmatis*.

Cell-wall polysaccharides from the LDC strains Nos. 4, 8, and 15, and two reference bacteria of the CMN group, *M. smegmatis* and *C. hoffmannii*, were purified by column chromatography. Upon acid hydrolysis of purified polysaccharides, the alditol derivatives of the resulting monosaccharides were prepared, and the mixture was analyzed by gas liquid chromatography.

Arabinose and galactose were present in the expected molar ratio of 5:2 in *M. smegmatis*. The proportion of the two main monosaccharides was different in *C. hoffmannii* (3:1) and, moreover, the amount of the additional sugars, mannose and glucose, was close to that of galactose. In the LDC strains 4, 8, and 15 the arabinose-galactose ratio was similar to that of *M. smegmatis*. In addition, mannose was present in a proportion equal to 15%–50% of the amount of galactose.

Three of the tested LDC strains have a fixed amount of mannose in the wall polysaccharide fraction. We propose, therefore, the occurrence of arabinogalactomannan in these organisms: this contributes to the biochemical uniqueness of this group of bacteria. The structure of LDC polysaccharide is now being analyzed.—(*From* the article)

**Cocito, C., Abou-Zeid, C., Danhaive, P., Fontaine, F., Gailly, C., Gueur, M. C., Janczura, E. and Delville, J.** Biochemical studies of leprosy-derived corynebacteria. Acta Leprol. **88** (1982) 33–46.

Data related in the present communication indicate that leprosy-derived corynebacteria (LDC) represent an homogeneous yet unique cluster of microorganisms within genus *Corynebacterium sensu stricto*. The structure of the wall polymers of these bacteria has been partly unravelled; they account for the antigenic and immunomodulating activity of their components. The immunological relatedness of LDC and mycobacteria has been demonstrated, and the correspondence of the M. component of LDC with major antigen 7 of *M. leprae* has been proven.—(*From* the article)

**David, H. L., Clavel, S. and Clément, F.** Adsorption of mycobacteriophages on *Mycobacterium leprae*: taxonomic significance. Ann. Microbiol. **133B** (1982) 93–97.

". . . The phages used in our experiments were specific for bacteria in the genus *Mycobacterium*, and therefore our observations showed that the leprosy bacilli synthesized substances typical of other mycobacterial species."—(*From* Trop. Dis. Bull.)

**Delville, J., de Sloovère, T., Fontaine, F., Gueur, M. C., Rajjan, W., Spina, A. and Cocito, C.** Biological properties of diphtheroid bacteria (LDC) isolated from human leprosy lesions. Acta Leprol. **88** (1982) 47–59.

Data summarized in the present paper indicate that "diphtheroid" microorganisms (LDC), non-acid-fast bacteria now identified as true corynebacteria, have been isolated in numerous cases of leprosy, from cutaneous lesions as well as from blood. These organisms proliferating in axenic culture behave as a homogeneous group of bacteria from the morphological and immunological viewpoints. Their possible pathogenic role is shown under experimental conditions in which the injection of small numbers of viable LDC in the foot pad of mice facilitates the multiplication of *M. leprae*. However, the administration of a large number of unviable LDC inhibits locally the proliferation of *M. leprae*. On the other hand, an immunosuppressive effect of LDC on humoral immunity seems ruled out. Finally, the immunological relatedness of LDC and *M. leprae* has suggested the use of LDC antigens for cutaneous tests. Preliminary data seem indeed to indicate a good correlation between lepromin and LDC antigens both in patients and in controls.—(*From* the article)

**Dhople, A. M.** Effect of freezing *Mycobacterium leprae* in tissues. Lepr. India **54** (1982) 461–470.

*Mycobacterium leprae*-infected tissues from armadillos and human patients have been stored at −76°C and have shown that the bacilli harvested from such tissues re-

tain their original metabolic activity as well as infectiousness.—Author's Summary

**Mori, T. and Nyein, M-M.** Study of a growth factor for *Mycobacterium lepraemurium* grown in the Ogawa yolk medium. II. Egg yolk protein fraction and effect of reducing reagents. Jpn. J. Lepr. **50** (1981) 105–115. (in Japanese)

One of the growth factors of *M. lepraemurium* in 1% Ogawa yolk medium might be a reducing action of the yolk protein fraction. Egg white medium containing the water insoluble fraction of egg yolk did not permit the good growth of *M. lepraemurium*. However, growth of *M. lepraemurium* corresponding to egg yolk medium was seen on the above medium supplemented with a high molecular fraction of water boiled extract of egg yolk which did not accelerate the growth of *M. lepraemurium* on the minimal medium. Since the water insoluble fraction of egg yolk was a high molecular lipoprotein particle, purification of growth factor could not be achieved. Thioglycolate, reduced glutathione, or cysteine accelerated the growth of *M. lepraemurium* on the Kirchner agar medium containing 10% bovine serum.—Authors' Summary

**Nakamura, M.** Growth stimulation of *Mycobacterium lepraemurium* by liposome in cell-free liquid medium. Jpn. J. Lepr. **51** (1982) 40–43. (in Japanese)

Effect of lipid complex, lecithin-cholesterol liposome, on the growth of *M. lepraemurium* in cell-free liquid medium (ND-5 and NDD-5) was studied, and the following results were obtained:

1) It was indicated that liposome was more effective than lecithin or cholesterol on growth stimulation of *M. lepraemurium*.
2) Optimal concentration of liposome was 1.4% (v/v). No significant stimulating effect was observed even if the doses of liposome were increased. If the liposomes were increased, turbidity and sedimentation took place in the medium.
3) Among the sources of lecithin for preparation of liposomes, egg lecithin showed the most effective function.
4) It was considered that the suitable ratio of lecithin and cholesterol in the mixture might be 8:1.—Author's Summary

**Nakamura, M.** Stimulating effects of lecithin and cholesterol on the growth of *Mycobacterium lepraemurium* in cell-free liquid medium. Jpn. J. Lepr. **51** (1982) 35–39. (in Japanese)

Effects of lecithin and cholesterol on the growth of *Mycobacterium lepraemurium* in cell-free liquid medium were studied and the results obtained were as follows:

1) The growth of *M. lepraemurium* was stimulated by addition of either lecithin or cholesterol.
2) Optimal concentration of lecithin for stimulation was 0.02% in NCS-5 medium, and 0.005% in NDD-5 medium, respectively.
3) Phosphatidyl choline dipalmitoyl had a stimulating effect quite similar to that of lecithin. On the contrary, the growth of *M. lepraemurium* was inhibited by palmitic acid.
4) It was determined that an optimal concentration of cholesterol for stimulating the growth was 0.005%.—Author's Summary

**Portaels, F., Francken, A. and Pattyn, S. R.** Bacteriological studies of armadillo livers infected with *Mycobacterium leprae*. Ann. Soc. Belg. Med. Trop. **62** (1982) 233–245.

Non-mycobacterial contaminants and *in vitro* cultivable mycobacteria have been isolated in large numbers from two out of four armadillo livers infected with human-derived *Mycobacterium leprae*. The organisms were "difficult to grow mycobacteria" and their *in vitro* multiplication was only successful if the following three conditions were fulfilled: 1) inocula should contain high numbers of viable organisms ($>10^5$); 2) suspensions should be pretreated with NaOH or HCl; 3) acid media, with a very precise pH (5.4–5.7) and containing autoclaved mycobacterial suspensions should be used.

The presence of these mycobacteria in armadillo livers may influence the results of studies performed on *M. leprae* purified

from such organs. The relationship of these mycobacteria with *M. leprae* remains to be elucidated.—Authors' Summary

**Portaels, F., Pattyn, S. R. and Francken, A.** *In vitro* sensitivity of *Mycobacterium lepraemurium* for antimycobacterial drugs. Arzneim.-Forsch. **32** (1982) 1123–1124.

The sensitivity of *Mycobacterium lepraemurium* for isoniazid, dapsone, ethionamide, pyrazinamide, rifampin, p-aminosalicylic acid, ethambutol, and various sulfonamides was determined using Ogawa medium. The sensitivities of *M. lepraemurium* for these drugs are different from those obtained with *M. leprae.* Our results illustrate that *M. lepraemurium* is not a model for the drug sensitivities of *M. leprae.*—Authors' Summary

**Portaels, F., Van den Breen, L. and Pattyn, S. R.** Sensitivity of mycobacteria to dapsone. Arzneim.-Forsch. **32** (1982) 1124–1125.

Dapsone sensitivity was tested on Löwenstein-Jensen medium on 164 mycobacterial strains belonging to 32 different species. A minimum inhibitory concentration as low as that of *M. leprae,* as determined "*in vivo,*" was never observed. The most sensitive strains belong to the species *M. kansasii, M. ulcerans, M. gordonae, M. szulgai,* and *M. gastri* with minimal inhibitory concentrations varying between 0.3 μg/ml and 0.1 μg/ml, still approximately 10 times the value known for wild strains of *M. leprae.*—Authors' Summary

**Rastogi, N. and David, H. L.** Morphology of bacteriophages from *Mycobacterium lepraemurium.* Ann. Microbiol. **133B** (1982) 303–309.

The two phages obtained from *Mycobacterium lepraemurium,* strain Douglas, by using *M. segmatis* ATCC 607 as a non-lysogenic indicator (kindly supplied by L. Sula and named as $AL_1$ and 1/1) were adsorbed on *M. smegmatis* ATCC 607 with a P 45′/$P_o$ of 0.016 and 0.01, respectively. Ultrastructural studies showed that these phages could be classified as Bradley type $B_1$.—Authors' Summary

**Rotberg, A.** An inquiry into the adoption of the term *Mycobacterium hansenii.* Hansen. Int. **6** (1981) 71–82.

An inquiry was made among various organs of the Public Health Service of the State of Sao Paulo, Brazil, members of the Scientific Council and Editorial Board of HANSENOLOGIA INTERNATIONALIS, and professors of dermatology, bacteriology, neurology, pathology and preventive medicine of Brazil, having in view the possibility of using the term *Mycobacterium hansenii* in that periodical, as a substitute for *M. leprae.* The results were considered favorable to the change and led to the adoption of the new term by the Institute of Health, which publishes the periodical. The First Congress of Hansenology of the Endemic Countries and the Third Brazilian Congress of Hansenology, held in Rio de Janeiro, November 1980, were informed of the change and resolved to introduce *M. hansenii* as a synonym for *M. leprae,* upon a recommendation of their workshop on bacteriology. Appeals are made to the International Committee of Systematic Bacteriology and societies of bacteriology of the whole world to study the grave moral, social, medical, and preventive problems caused by the "bacteriological stigma" in endemic Christian countries.—Author's Abstract

**Sathish, M., Prasad, H. K., Mittal, A. and Nath, I.** Lack of correlation between morphological index and viability as assessed by the uptake of $^3$H-thymidine by macrophage resident *M. leprae.* Lepr. India **54** (1982) 420–427.

Thirty strains of *M. leprae* derived from skin biopsies of lepromatous leprosy patients were scored for Morphological Index (MI) and concurrently maintained for two weeks in macrophage cultures containing $^3$H-thymidine. Selective and significant incorporation of the radioactive label was observed in cultures containing freshly extracted *M. leprae* as compared to control cultures containing autoclaved bacilli from the same biopsy. The percentage incorporation of $^3$H-thymidine ranged from 103% to 114%. The MI of the bacilli from these individuals varied from 0 to 8. Six cultures containing bacilli with MI of $\leq 1$ and 3 con-

taining bacilli with MI of 0 showed significant incorporation of $^3$H-thymidine. There was no correlation between the percent of solid or beaded bacilli in the inoculum and the ability of *M. leprae* to incorporate $^3$H-thymidine in the macrophage cultures.—Authors' Summary

**Wheeler, P. R.** Metabolism of carbon sources by *Mycobacterium leprae*: A preliminary report. Ann. Microbiol. **133B** (1982) 141–146.

Glucose was catabolized in *Mycobacterium leprae* by glycolysis in both the hexose monophosphate and pentose phosphate pathways; 30% was catabolized by the hexose monophosphate pathway alone. Glycerol was also catabolized to $CO_2$ at a similar rate to glucose. Key enzymes from the pathways for these metabolic activities were identified in cell-free extracts as enzymes of *M. leprae*.—(*Amended Author's Summary from* Trop. Dis. Bull.)

## Experimental Infections

**Brown, I. N., Glynn, A. A. and Plant, J.** Inbred mouse strain resistance to *Mycobacterium lepraemurium* follows the *Ity/Lsh* pattern. Immunology **47** (1982) 149–156.

Inbred mouse strains and their $F_1$ hybrids infected intravenously with *Mycobacterium lepraemurium* showed different mean survival times (MST). BALB/c and C57BL mice were particularly susceptible; whereas C3H, CBA and DBA/2 mice were relatively resistant. Resistance as judged by MST was dominant in the $F_1$ hybrids. A similar ranking order was obtained by comparing the doubling time of the bacillus in the bone marrow, the increase in spleen weight between four and 12 weeks after infection, and the pathology of the liver during infection. The general pattern suggests that mouse resistance to *M. lepraemurium* is, at least in part, controlled by a gene with the same strain distribution as the genes for resistance to *Salmonella typhimurium* (*Ity*$^r$) and *Leishmania donovani* (*Lsh*$^r$) and the gene controlling resistance to *M. bovis* BCG (*Bcg*). *Ity, Lsh* and *Bcg* are all known to be on chromosome 1, suggesting a center, controlling reactions to intracellular infections.—Authors' Summary

**Curtis, J., Adu, H. O. and Turk, J. L.** *H*-2 linkage control of resistance to subcutaneous infection with *Mycobacterium lepraemurium*. Infect. Immun. **38** (1982) 434–439.

The *H*-2 linkage of the gene or genes controlling resistance to subcutaneous infection with $10^7$ *Mycobacterium lepraemurium* organisms was investigated by using *H*-2 congenic strains on BALB and B10 backgrounds. Resistance was assessed by counting the organisms present at the infection site in the foot pad and in the draining (right popliteal) lymph node 20 weeks after infection. When mice of BALB and B10 backgrounds with the same *H*-2 haplotype were compared, the BALB mice were always more susceptible. However, BALB/K (*H*-2$^k$) mice were more susceptible than BALB/B (*H*-2$^b$) mice, and BALB/B mice were more susceptible than BALB/c (*H*-2$^d$) mice. There was no detectable difference in the resistance of B10.D2/n (*H*-2$^d$) mice and B10 (*H*-2$^b$) mice, but B10.BR (*H*-2$^k$) mice were more susceptible than mice of the other two B10 strains. BALB/K was the only strain in which a high proportion of mice showed significant dissemination of organisms to the liver and spleen.—Authors' Summary

**Galletti, G., Cavicchi, G. and Ussia, G.** Replication of *Mycobacterium leprae* in hibernating ground squirrels (*Citellus tridecemlineatus*). Acta Leprol. **88** (1982) 23–31.

Subcutaneous injections of $10^6$ acid-fast bacteria from human lepromatous tissue to hibernating ground squirrels (*Citellus tridecemlineatus*) is followed by generalized infection of the animals and spontaneous death. The number of mycobacteria is high in the skin of ground squirrels during winter and decreases during summer. Animals sur-

viving the first hibernation period invariably die during the second. The number of microorganisms in the visceral organs is low at all times. The system of infected hibernating ground squirrels is a valuable model for the experimental study of leprosy.—Authors' Summary

**Kawaguchi, Y., Matsuoka, M., Sushida, K. and Tanemura, M.** Susceptibility of *Mycobacterium avium* of various inbred strains of mice. IV. Comparative observations on virulence of four strains of *M. avium*. Jpn. J. Lepr. **50** (1981) 173–184. (in Japanese)

Comparative observations were made on the virulence of four strains of *M. avium*, Kirchberg, Nagoya #59, Flamingo and ATCC 19075, in five inbred strains of mice, C3H, C57BL/6, DDD, BALB/c and KK. The virulence was evaluated by the average survival time and also by the grade of visceral lesions following intraperitoneal infection with 0.5 mg and subcutaneous infection with 0.025 mg of 14 day-culture of *M. avium* grown on 1% Ogawa's medium.

Following the intraperitoneal infection, two strains, Kirchberg and Nagoya #59, were highly pathogenic for four strains of mice, C57BL/6, DDD, BALB/c and KK, causing a more severe infection than the others. Strain Flamingo was pathogenic for three strains, C57BL/6, BALB/c and KK, but slightly pathogenic for DDD strain. In contrast, in all the mice infected with ATCC 19075, only a few bacillus-containing cells were occasionally detected from their visceral organs even at 50 weeks, the end of this experiment. It is noted that C3H mice were very resistant to the infection with all the strains of *M. avium* tested throughout the observation period.

The similar tendencies on the pathogenicity of *M. avium* were also demonstrated in the cases with subcutaneous infection.

The results of these experiments revealed that Kirchberg and Nagoya #59 were highly virulent, Flamingo was moderately virulent and ATCC 19075 was of low virulence.—Authors' Summary

**Kawaguchi, Y., Matsuoka, M., Sushida, K. and Tanemura, M.** Susceptibility to *Mycobacterium avium* of various inbred strains of mice. V. Host resistance to *M. avium* of hybrids of C3H origin. Jpn. J. Lepr. **51** (1982) 1–8. (in Japanese)

As stated in our preceding reports, C3H mice were much more resistant than the other strains (DDD, BALB/c and KK) of mice following intraperitoneal infection with *M. avium*.

Then, comparative observations were carried out on the host resistance to *M. avium* infection in F1 hybrids obtained by crossing females of DDD, BALB/c and KK with males of C3H. After the intraperitoneal infection, all the F1 hybrids, (DDD × C3H) F1, (BALB/c × C3H) F1, and (KK × C3H) F1, showed approximately the same susceptibility to that of C3H, being resistant to *M. avium*.

Similar experiments were made in F2 hybrids from the mating between (DDD × C3H) F1 mice. The ratio of susceptible to resistant was 1 to 3 in males and 1 to 2 in females of the F2 hybrids.

In the intraperitoneally infected mice of (DDD × C3H) F3, obtained from random mating of the F2 hybrids, 1 of 11 females and 2 of 11 males were susceptible and the others resistant. None of them were ranked as intermediate.

The results of these observations suggest that resistance to *M. avium* infection in C3H mice is mainly controlled by a hereditarily dominant factor.—Authors' Summary

**Martinez, A. R., Resoagli, E. H., Millan, S. G. and Resoagli, J. P.** Nueva comunicacion de mycobacteriosis natural en armadillos *Dasypus novemcinctus* (Linneo). [A new communication on natural mycobacteriosis in armadillos (*Dasypus novemcinctus,* Linn.)] Leprologia **23** (1981) 129–134. (in Spanish)

The experimental transmission of leprosy in the armadillo and the natural infection of them provided by the bibliography are reviewed by the authors. They present the second Argentine case of "indigenous leprosy" in the armadillo.

It consists of a *Dasypus novemcinctus* female coming from Saladas (Corrientes) which, after passing through the different states of the syndrome of not adapting to captivity, died 35 days later.

The necropsy showed bacillary lesions in the lymph nodes, spleen and liver, resembling more those lesions of the infection in the human than those described in the experimental infection of the armadillo coming from human lesions.

Finally, it is proposed to use the name of "natural mycobacteriosis of the armadillo" until obtaining definitive identification.—Authors' Summary

**Tanemura, M.** Susceptibility to *Mycobacterium avium* of various inbred strains of mice. II. On the cases with subcutaneous infection. Jpn. J. Lepr. **50** (1981) 116–127. (in Japanese)

Avian tubercle bacilli, strain Kirchberg, were inoculated subcutaneously on the thorax of five inbred strains of mice, C3H, C57BL/6, DDD, BALB/c, and KK, in order to examine the development of local and visceral lesions at varying time intervals.

In almost all the mice of each strain, a small, hard and sharply defined nodular infiltrate developed at the inoculation site within two to three weeks. At about ten to 15 weeks, the nodule stopped growing and tended to regress spontaneously, and in all the mice examined the visceral lesions were slight at that time.

At the late stage of infection, however, there were remarkable differences in their visceral lesions among the tested strains of mice, while subcutaneous lesions were still slight. At 35 to 50 weeks, extensive involvement was found in the lung, liver, and spleen of KK and BALB/c mice, and many bacilli-loaded cells were found in the lung of C57BL/6 mice. On the contrary, visceral lesions of C3H and DDD mice were very slight even in the late stage of infection.

Mouse strain differences in visceral lesions of the subcutaneously infected mice showed similar tendencies to those of the intraperitoneally infected mice.—Author's Summary

**Tanemura, M., Sushida, K., Kawaguchi, Y. and Matsuoka, M.** Susceptibility to *Mycobacterium avium* of various inbred strains of mice. III. On the cases intraperitoneally infected with small dose. Jpn. J. Lepr. **50** (1981) 169–172. (in Japanese)

Male mice, approximately six weeks of age, of six inbred strains (C3H, C57BL/6, DDD, BALB/c, KK, and CF#1) were inoculated intraperitoneally with 0.005 mg of *M. avium*, strain Kirchberg. Susceptibility to *M. avium* was evaluated mainly by the average survival time and visceral lesions of experimental animals.

C3H strain mice were confirmed to be resistant to the infection with *M. avium*, and mice of the other strains were susceptible. However, there was a remarkable difference in average survival time between KK and CF#1 group and C57BL/6, DDD, and BALB/c group.

From the results of our earlier experiments with mouse leprosy, the above-mentioned difference in the susceptibility was assumed to be due to cell-mediated immunity developed in the hosts, excepting the C3H strain.—Authors' Summary

## Epidemiology and Prevention

**Asseis, E. A., Tornero, N., Magalhães, L. B., Priscinotti, T., Barth, Y. L. and Casagrande, N. A.** Alguns aspectos sobre a hanseníase no região de Londrino pr., 1968–1978—1. Características gerais. (Some aspects of hanseniasis in the region of Londrina, Paraná, 1968–1978—1. General characteristics.) Hansen. Int. **6** (1981) 55–62. (in Portugese)

The authors studied some characteristics of hanseniasis, through registered data, in the Public Health District of Londrina, in the State of Paraná, Brazil. As mean findings, they verified that 49.3% of the patients were V+D cases, 29.5% were I cases, and 21.2% were T cases. Incidence in Londrina city ranged between 6.6–18.7/100,000 and the prevalence rate, calculated by the last years, was even greater than 3.0/100,000. The authors concluded that the area is highly endemic for hanseniasis.—(*From* the Authors' Summary)

**Bale, U. M., Mehta, M. M., Contractor, N. M., Bhatia, H. M. and Koticha, K. K.** HLA antigens in leprosy patients. Tissue Antigens **20** (1982) 141–143.

The phenotype frequencies of HLA antigens in normal subjects and in leprosy patients were determined. There were significant differences in the distribution of A locus ($p < 0.0001$) as well as B locus ($p < 0.0001$) antigens between LL patients and the healthy controls. The difference in A locus antigens was mainly for Aw19, showing decreased frequency among patients ($\chi^2 = 13.03$ $p < 0.02$). The difference in B locus antigens was mainly for B40, showing increased frequency among patients ($\chi^2 = 20.38$ $p < 0.0027$). There was a borderline increase in the frequency of B40 among tuberculoid patients ($p < 0.05$) which on correction (Pc) was nonsignificant. Our results are in agreement with those of Youngchaiyud, *et al.* (1977) in the Thai population. However, B40 was also reported to be increased in their tuberculoid patients.

The study of halplotypes of B40 with different A locus antigens indicated increased frequency of the haplotype A2,B40 in LL ($\chi^2 = 13.42$ $p < 0.00025$). However, the risk for both forms of leprosy is greater with the haplotypes A1,B40 and A11,B40. Our findings support the findings of Wolf, *et al.* (1980) on leprosy families from Tamil Nadu, India, showing increased frequency of haplotypes A1,B40 and A11,B40. Our results did not show any signficant differences in the frequency of ABO and Rho(D) antigens between the controls and the leprosy patients, and is thus in agreement with other reports.—(*Adapted from* the article)

**Barreyo, D. A., Baras, M., Squires, P., Walerstein, M., Yodfat, Y. and Levy, L.** Familial clustering of leprosy patients in an Israeli village. Lepr. Rev. **53** (1982) 277–283.

In an Israeli community of immigrants from Kurdistan, with a leprosy prevalence of 3.2 per 100, the leprosy patients were found to be clustered in a very few sibships.—Authors' Summary)

**Belda, W.** Aspectos da hanseníase na área urbana do município de São Paulo—hanseníase indiferenciada, 1963–1977. (Aspects of hanseniasis in an urban area in the city of São Paulo—indeterminate hanseniasis, 1963–1977.) Hansen. Int. **6** (1981) 23–50. (in Portugese)

The purpose of this work is to analyze the epidemiological changes that have occurred in São Paulo due to geographical and historical influences. This research was made during the period of 1963 to 1977, covering 6664 cases and two main aspects: origin and age. In 1977, São Paulo presented 5179 inhabitants per square kilometer and a percentage of 5.3 hanseniasis patients per square kilometer. The data compiled during the research have led to the following conclusions: São Paulo has become an important economical center and as such a point of attraction to intense migratory currents; this increase has caused the formation of unplanned and outnumbered populational centers in the outskirts which are obstacles to medical and social welfare assistance and to diagnosis and control as well; changes in the social and economical structures leading to a poorer family life; increase in the possibilities of transmission of hanseniasis either by non-intimate or long-term contacts; decrease in the number of cases in the same family and, finally, the characterization of hanseniasis as a grown-up and urban disease.—Author's Summary

**Bernardi, C. and Ferreira, J.** Epidemiologia da hanseniase no estado do Rio Grande do Sul. (Epidemiology of hanseniasis in the state of Rio Grande do Sul.) Leprologia **23** (1981) 85–98. (in Spanish)

The authors describe briefly the geographic, climatic, and population aspects of the state of Rio Grande do Sul, Brazil. They further do a short historic report about the problem of Hansen's disease in the region and show the present policy adopted in the control of this disease and its relation with the existent health system.

They point out the results of a six-year work after the implantation of a nominal index computer based file of ill persons and contacts.

They outline the distribution of new cases by the clinic, sex and age range ways, and by the coefficients of incidence during the

period of 1975 to 1980. They also describe the discharges given during this period, the variation of the coefficients of prevalence, and the rate of control of ill persons and contacts. Together with this description, the standards of classification, especially of the type I, the criteria of concession of discharges and the policy of internment of ill persons in the colony hospitals are analyzed.—Authors' Summary

**Fine, P. E. M.** Leprosy: the epidemiology of a slow bacterium. Epidemiol. Rev. **4** (1982) 161–188.

Although many questions remain unanswered, recent years have witnessed important advances in our understanding of the epidemiology of leprosy. The discovery of natural transmission of *Mycobacterium leprae* in New World armadillos has challenged the traditional view of man as the only maintenance host. There is as yet no evidence that an extrahuman reservoir determines disease patterns in human populations, but this discovery alerts us to the possibility that other unusual species may harbor the organism. It may also raise difficulties for efforts to eliminate the infection from some regions.

Available data suggest that most transmission within human populations originates from the upper respiratory tract of multibacillary cases. Bacteriologic evidence for massive excretion of viable organisms from the nose of the lepromatous patient contrasts dramatically with the difficulty of demonstrating *M. leprae* on the skin. It would indeed be surprising if this difference did not have implications for transmission of *M. leprae*. Transmission by percutaneous inoculation by arthropods probably occurs, but there is no evidence to suggest it is a major contributor to leprosy incidence.

There is growing evidence that infection occurs more readily than previously thought, and that the incidence of infection far exceeds that of clinical disease in endemic populations. This important inference is supported by several findings: 1) evidence of specific sensitization in a high proportion of persons in contact with leprosy cases as revealed by serum antibodies, *in vitro* lymphocyte tests, and skin tests with soluble *M. leprae* antigens; 2) observation of *M. leprae*-like bacilli in dermal tissues of 5% of clinically normal persons in endemic areas of India; 3) evidence that a considerable proportion of clinical cases resolve without trace, spontaneously, and thus many are never recognized under usual ascertainment conditions—a finding that implies a logical extension of the clinical spectrum to minimal and subliminal forms which are never recognized; and 4) analogies with tuberculosis, in which only 10% of infections may manifest as clinical disease. It may be noted that if some primary infections result in total self-cure, then the ratio of infection prevalence to disease prevalence may be far lower than the corresponding ratio of infection incidence to disease incidence.

The extent to which infection exceeds disease in the community reflects the extent to which factors other than infection itself are responsible for observed disease patterns. These determinants are still not well understood, but probably reflect the interaction of at least three factors: host genetics, immunologic background, and route of infection. Family segregation studies of HLA antigens provide convincing evidence for host genetic involvement, although the magnitude of the effect is still uncertain. BCG vaccination has been shown to reduce leprosy risk, and it is reasonable to expect that infections with other mycobacteria species, many of which share antigens with both *M. leprae* and BCG, also have important effects on host immunity to *M. leprae*. Arguments that route of infection is important in leprosy are based on basic immunology and animal studies, and have not yet been demonstrated in studies on human populations.

How well does this model explain the observed patterns of clinical leprosy? The age and sex pattern—in particular the male excess among adults—has traditionally been explained on the basis of contact with source cases in the community. Young boys and girls circulate equally in the community, but adult males circulate more widely than females. It is interesting to note the similarity between this pattern and that of tuberculin sensitivity found in many populations. The West African exceptions to the rule of more leprosy among adult males are of particular interest. The contact hypothesis predicts that adult females in these populations should have higher prevalences of tuberculin sensitivity than males.

On the other hand, it is possible that the general excess of clinical leprosy among adult males reflects their greater exposure to some determinant promoting establishment or expression of infection, rather than (or in addition to) exposure to infection itself. It might be possible to assess this by comparing the sex ratio of adult cases with and without a history of household exposure to multibacillary cases. If the adult male excess were observed among household-exposed incident cases, this would indicate some factor other than infection determining clinical expression. Prevalence cases may be misleading in that affected females may have difficulty in marrying and hence remain in their family households. This reviewer is aware of no appropriate data against which to test this hypothesis. The fact that clinical incidence rates fall after age 20 years may also be interpreted as evidence that factors other than contact determine disease among adults. The peak incidence around ages 15–25 years could be interpreted as primary disease, and clinical onsets among older individuals could reflect a mechanism analogous to endogenous reactivation or exogenous reinfection as discussed in the tuberculosis literature.

The evidence for household or familial aggregation is explicable in terms of multibacillary cases as the sole sources of infection. The slightly increased risk observed among contacts of paucibacillary cases is consistent with this hypothesis, since such individuals should have a greater probability of contact with multibacillary cases outside the home (e.g., with the sources of the household paucibacillary cases) than should individuals with no known exposure. This argument does not refute a limited infectious potential for paucibacillary cases, but it makes it unnecessary to assume such a potential.

Although contact may reasonably well explain the age, sex, and household distributions of clinical leprosy in endemic areas, the evidence for widespread subclinical infection and for the rarity of clinical cases among contacts of multibacillary cases in nonendemic areas suggests an important role for other factors in determining patterns of disease. Both of these anomalies could be satisfied if either a heavy or repeated inoculum were necessary for clinical expression, but such an assumption might lead one to expect a higher risk of lepromatous leprosy among close contacts of lepromatous cases than has been observed. It is likely that factors other than contact or dose are involved.

The observation that leprosy may be associated with rural environments is opposed to the simple contact interpretation of leprosy. Although evidence for a rural predilection is still provisional, it is nonetheless suggestive that leprosy may differ from tuberculosis in this respect. If valid, a rural preference for leprosy would suggest either environmental sources of *M. leprae* infection, a promoting role of some infection (atypical mycobacterium?) or transmission process (arthropods?) found in rural environments, or protection associated with some urban factor (which could even be *M. tuberculosis* itself). Furthermore, it might explain the apparent absence of transmission in northern Europe and northern United States in recent years, since most of the potential source cases are immigrants and live in urban areas.

Differences in clinical spectrum between populations probably reflect a combination of genetic factors and immunologic background. It is of interest that the order of BCG efficacy against leprosy—Uganda > New Guinea > South India > Burma—correlates with the proportion tuberculoid among leprosy cases in these populations. It also correlates with the degree of skin pigmentation in these groups, which might in turn be related to shielding of dermal Langerhans' cells from ultraviolet radiation. This is consistent with the limited data from immigrant populations (e.g., the evidence that tuberculoid leprosy is more common among people of African descent than among Caucasians in South America) and would indicate a genetic mechanism. In addition, the proven influence of BCG on leprosy risk demonstrates the importance of immunologic experience in determining the course of an infection, and further suggests that some of the differences between populations are attributable to the different arrays of "environmental" mycobacteria to which they are exposed.

Leprosy begins to appear less unique among infectious diseases in the light of recent information. Evidence that only a small

proportion of infected individuals manifest clinical disease, and for a spectrum of clinical response dependent upon genetic and immunologic background, reflects features common to many infectious diseases. The analogy with tuberculosis looks increasingly relevant. We might also note parallels with problems posed by the slow viruses, whose natural history has been so difficult to unravel because of an inability to identify the infected state and a long interval between exposure and clinical manifestation. But perhaps the slowness of *M. leprae*, manifested in the division time of the organism, the course of the disease, and the pace of leprosy research, is at last being overcome.—Author's Summary and Conclusions

**Guha, P. K.** Clinical epidemiology of non-lepromatous leprosy among service personnel. Lepr. India **54** (1982) 512–517.

Some aspects of the clinical and epidemiological presentation of 172 non-lepromatous leprosy patients, belonging to the Armed Forces of India have been presented. The tuberculoid type (TT) was the commonest form of the disease. The majority of the patients (59.8%) had a single lesion at the time of diagnosis. The age of onset of 62.2% of the patients was between 20 and 29 years.

The incidence of gross neurological deficit or deformity was rather low in these patients. Ulnar nerve involvement showed evidence of clinical symptons most often.—Author's Summary

**Kaur, S., Kumar, B. and Roy, S. N.** Endemicity of leprosy in the Union Territory of Chandigarh and surrounding states. Lepr. India **54** (1982) 428–440.

Data on 603 leprosy patients registered with the leprosy clinic at the Nehru Hospital attached to the Postgraduate Institute of Medical Education and Research, Chandigarh, India, were analyzed. The sample was collected over a period of six years in this area of very low endemicity. The overall average age at onset of the disease was 35.07 years. The majority of the patients had contacted the disease by the age of 39 years. Only 2% of the patients presented with the disease in the first decade. Males were more often seen with the disease than females (M: F, 3.6:1). The highest represented type of leprosy was borderline (47.7%) and least represented was lepromatous (24.4%) with the tuberculoid group in between (27.9%). The most common sites of first lesion were the exposed areas, i.e., hand, trunk, feet and forearm. Most of the patients came from high prevalence states of the country. There were, however, 118 Punjabis and 41 Haryanvis who had never been outside their home states to any endemic area. The findings are presented.—Authors' Summary

**Radhakrishna, S., Christian, M. and Nair, N. G. K.** A 20-year study of the leprosy control programme at the Government Leprosy Treatment and Study Centre at Tirukoilur in South India. Indian J. Med. Res. **76** (1982) 18–35.

An assessment of the leprosy control program between 1955 and 1974 was undertaken at the Government Leprosy Treatment and Study Centre in Tirukoilur, South India. This center covers a rural population of about 90,000, and had diagnosed nearly 9000 cases in this period. The profile of newly detected cases was compared in the periods 1955–57, 1958–60, 1961–64, 1965–69 and 1970–74. The ratio of males to females was stable (3:2), but the proportion of cases aged under 15 years increased from 36%–38% in 1958–64 to 46%–47% in 1965–74. The lepromatous rate declined substantially; the proportions in the five periods being 18%, 7%, 5%, 4% and 2%, respectively. About one fourth to one half of the diagnosed cases did not commence treatment, and of those that did, about 30% collected less than half their drug supplies. Over a five-year period from the start of treatment, 26%–30% migrated from the study area and 2%–5% died. Only 20%–30% were known to have inactive or arrested disease at the end of the five-year period. Total population surveys were undertaken once in every two or three years during 1955–66, but subsequently in only half the villages. The coverages attained were of the order of 90%. The overall prevalence of leprosy (all types) declined from 62.7 per thousand in 1955–57 to 45.3 per thousand in 1961–63; in the next decade, there was no decrease. Lepromatous leprosy, however, showed a

steady linear decrease from 11.7 per thousand in 1955–57 to 5.1 per thousand in 1967–73. It is concluded that field studies to explore methods for better caseholding and greater regularity in taking drugs, clinical trials for evolving shortcourse regimens, and continuous monitoring of the operational aspects of the program are urgently needed.—Authors' Summary

**Risso, H. I. and Giménez, M. M.** Consideraciones sobre un programa de control de lepra. (Considerations in a leprosy control program.) Leprologia **23** (1981) 119–123. (in Spanish)

The leprosy endemic in a great extension of the national territory establishes a severe problem of health. It is known from the beginning of this century, pointing out the special worry of the government in the last three decades and the anxiety to get the transfer of the direction of the program of control to a zone of high endemicity and to obtain the formation of specialist doctors in leprosy.

The actual state of the endemic and the control of leprosy in the country is terrible. There has not been a continuity in the development of the national program of leprosy that allows an evaluation.

It is necessary to finish this situation with the longitudinal development of one program of control that provides the norms and coordinates the development of provincial programs of control.—Authors' Summary

**van Eden, W., de Vries, R. R. P., D'Amaro, J., Schreuder, I., Leiker, D. L. and van Rood, J. J.** HLA-DR-associated genetic control of the type of leprosy in a population from Surinam. Hum. Immunol. **4** (1982) 343–350.

The relationship between HLA phenotype and leprosy classification was studied in 73 unrelated patients and 92 healthy controls from a mixed Negroid-Caucasoid population originating from Surinam, South America. Heterogeneity in the distribution of HLA-DR (but not A, B, and C) was detected between tuberculoid (TT+BT) leprosy and lepromatous (BL+LL) leprosy patients ($p = 0.024$). This heterogeneity appeared to be caused almost exclusively by DR3. Most significantly, the frequency of DR3 was increased among polar tuberculoid (TT) leprosy patients as compared to the rest of the patients ($p = 0.0003$). Compared with healthy controls the frequency of DR3 was increased among TT patients ($p = 0.006$), unchanged in BT patients, and decreased among lepromatous (BL+LL) patients ($p = 0.027$). These data indicate that in this population a DR3-associated factor controls the type of the disease that develops after infection with *Mycobacterium leprae*.—Authors' Abstract

**Xu Keyu, *et al.*** HLA and leprosy. I. Frequency incidence of HLA–A, B antigens among leprosy patients of Han nationality. Chin. J. Dermatol. **15** (1982) 145–148. (in Chinese)

HLA–A, B typing was performed on 109 unrelated leprosy patients (L 61 and T 48) of Jiangsu Han nationality, with 116 healthy persons as controls.

Decreased frequency of HLA–A1, Aw30+w31, and B17 was found both in all patients and in lepromatous groups, especially HLA–B17 showed statistical significance even after correction for the number of antigens tested. In tuberculoid leprosy, decreased frequency of HLA–Bw54(w22), Bw60(B40) were observed but showed no significance when corrected.

A total of 162 parameter of third order linkage disequilibrium between HLA–A, B haplotype and supposed leprosy susceptible gene was calculated by the Porta-McHugh formulas on a programmable ALGOL calculator under AR model. Four relatively susceptible haplotypes to leprosy were found, namely A9–B13 and A11–B17 to lepromatous, A11–B15 and A28–Bw54 to tuberculoid.

The above results indicated that susceptible and/or resistant genes to leprosy were linked with HLA region, and that the associations between L or T leprosy and HLA were multi-antigenic and weak. Their relative antigens and haplotypes are different. It is suggested that lepromatous and tuberculoid leprosy are heterogeneous diseases.—Authors' Summary

**Younger, B., Michaud, R. M. and Fischer, M.** Leprosy; our Southeast Asian refugee experience. Arch. Dermatol. **118** (1982) 981–984.

In the past two years, we have diagnosed four cases of leprosy at the St. Paul-Ramsey Hospital Dermatology Clinic, St. Paul, Minnesota, U.S.A. This is a markedly increased incidence for the state of Minnesota. All of these cases have been found among recently arrived Southeast Asian refugees not noted to have their disease by previous screening examinations. The purpose of this study is to report these four cases (2 tuberculoid, 1 lepromatous, and 1 borderline leprosy) and to review the Southeast Asian Refugee Resettlement Program, focusing on medical screening programs. We recommend refugee health education, health personnel training, and refugee medical screening centers as ways to detect leprosy among refugees entering the United States.—Authors' Summary

## Rehabilitation

**Boyle, A. and Ramu, G.** Assessment of cutaneous autonomic nerve functions in leprosy. Lepr. India **54** (1982) 518–524.

Thirty-one cases of established leprosy were studied for sweat response to acetylcholine and adrenaline injected intradermally and compared with normal areas of skin on the contralateral side in a total of 40 lesions. Sweating was measured by counting the number of blue dots which appeared on the yellow background of a filter paper soaked in 1% bromophenol blue solution which represented sweat pores. Whereas there was decreased, or absent sweat response in 31 lesions, there was an increased response to acetylcholine in 7 lesions, and normal response in 2 lesions. A sweat response to adrenaline was obtained in 29 lesions. It was increased in 13 lesions all of which were anesthetic or analgesic. Adrenergic sweating in these cases is probably a result of a direct effect of adrenaline on sweat glands. Biopsy sections of 20 cases were reviewed for the histological appearance of the nerves. It was found that out of the cases with increased sweat response one had partially destroyed nerves while two others had intact nerves. Sweat function tests are of limited value in the diagnosis of leprosy and some autonomic function may continue in leprosy despite loss of somatic nerve function.—Authors' Summary

**Charosky, C. B.** Premio "Guillermo Basombrio año 1981"—Cirugia neural en el mal de Hansen. (1981 Guillermo Basombrio Prize—neural surgery in Hansen's disease.) Leprologia **23** (1981) 99–118. (in Spanish)

A new classification based on multiple simultaneous clinical and anatomical patterns is proposed for neuropathies in patients with Hansen's disease.

Three basic nerve lesion producing physio-pathological mechanisms are identified: a) intrafascicular, b) extrafascicular-intraneural, and c) extraneural, with discussion of their diagnostic and therapeutic approach.

Different surgical techniques are proposed according to the nerve lesion classification and its postulated physio-pathology:

1. perineurolysis: in extrinsic compression neuropathies;
2. endoneurolysis: in tuberculoid neural abscesses with partial paralysis;
3. epineurotomy: in reactional neuropathies secondary to intraneural edema within fibrotic epineural walls;
4. epineurectomy: in paralytic syndromes due to choking of the nerve fibers by a scarred fibrotic epineural sheath without acute inflammatory signs;
5. neurectomy: in the exceptional cases of recurrent focal neuritis on nerve trunks completely and irreversibly damaged.

Finally, a series of 54 cases operated upon following the aforementioned criteria is discussed.

It is strongly emphasized that the all encompassing terms such as "leprotic neuritis" should be abandoned and replaced by

a nomenclature based on physio-pathological mechanisms.—Author's Summary

**Chauhan, N. S., Ramu, G. and Dhar, U.** Leprosy as a correlate of anxiety on the self-erosion dimension. Lepr. India **54** (1982) 505–511.

To see how the growth of the disease and feelings of worthlessness in patients associates with enhancing psychic pain, i.e., anxiety, an attempt was made to study the anxiety levels in persons with and without leprosy with a multi-group–experimental–control group design. The 60 leprosy patients belong to the Central JALMA Institute for Leprosy and constitute two equal-sized experimental groups with a control group of 30 non-leprosy people who remain matched on variables of age and sex. Anxiety scores of the study are obtained with the help of an objective tool that has been administered after proper rapport-formation. Elements for the two experimental groups have been cautiously selected after proper clinical verification.

Results show that the non-lepromatous patients possess a higher level of anxiety than the lepromatous ones, and people of the control group possess the lowest level of anxiety.

The implications are that anxiety is an intimate correlate of leprosy and that while clinical hazards of the disease are negative correlates of anxiety, physical disabilities and deformities promote anxiety.

A paradox exists between the clinical dimension and the psychological one. The fact that resolves it is that physical disabilities and deformities of the patient contribute to greater exposure to people, with lesser chances of self-defense and hiding from them. The enhanced psychic pain induces self-erosion.—Authors' Summary

**Cook, A.** An urban community's thoughts about leprosy: a survey of Guyana. Lepr. Rev. **53** (1982) 285–296.

Leprosy is regarded as a serious and fearful disease by urban Guyanese. This does not appear to be a function only of the characteristics of the disease but results from a perception of leprosy as stigmatizing. A vicious circle is thereby created: people "scorn" leprosy because of the stigma attached and the stigma is attached to leprosy because people "scorn" it. Thus leprosy belongs to that group of diseases that "discredit" their victims. What makes leprosy particularly frightening, especially for older people, is the prevalent notion that it is incurable, yet not fatal. At this point we would mention the fact that during the course of the interviews not a single respondent indicated a knowledge of the fact that treatment renders a patient non-infectious. The treatability of leprosy is the point which can be stressed most profitably in education programs. It seems reasonable to expect that once the view of leprosy as untreatable is corrected, then fears about contagion may be more easily allayed, domiciliary treatment may be more acceptable, and gradually the stigma may begin to fade. This would seem to be the area where education is most needed and where there is the greatest chance of effecting a break in the "vicious circle" of stigma.

Younger people, as a group, seem less aware of, and less afraid of, leprosy. Perhaps health programs addressed to them in schools and universities can capitalize on this and emphasize the treatment of leprosy along with those of other diseases.—(*From* the article)

**Enna, C. D.** Rehabilitation of leprous deformity. Ann. Rev. Med. **33** (1982) 41–45.

The neuropathic bases for the development of deformity in leprosy are loss of sensation, dysautonomia, and impaired motor function. These changes are not unique to leprosy; they are also encountered as manifestations of physical injury inflicted directly or by traction and/or compression, of infectious diseases, nonspecific infections, alcoholism, industrial poisons, drugs, metabolic diseases, nutritional and vitamin deficiencies, peripheral circulatory disturbances, hereditary and immunological deficits, and neurological changes of congenital origin.

The pattern of involvement depends upon the site of the nervous system lesion and the extremity affected. Syringomyelia, scleroderma, and Raynaud's disease usually affect the upper extremity; whereas diabetes mel-

litus, tabes dorsalis, and lesions of the lower spine such as spondylolisthesis involve the lower extremity. Diseases in which both upper and lower extremities are commonly affected include leprosy, poliomyelitis, and congenital insensitivity to pain.

The consequences of a neuropathy in either the hands or the feet are similar and the principles and methods of prophylaxis and treatment are fundamentally the same regardless of the disease that causes them.—(*From* the article)

**Kumar, R. P.** Evaluation of "power grip and pinch tests" in relation to claw hand disability. Lepr. India **54** (1982) 478–484.

To test power, the spring balance and the sand bag methods are more accurate and consistent than the dynamometer test. In these two, the former method is useful to test a patient's ability as a whole; whereas the latter is useful to test specifically the power of forearm and intrinsic muscles. None of these tests are useful to find out the pressure areas while applying force.—(*From* the article)

**Pring, D. J. and Casiebanca, N.** Simple plantar ulcers treated by below-knee plaster and moulded double-rocker plaster shoe—a comparative study. Lepr. Rev. **53** (1982) 261–264.

Fifty-five simple plantar ulcers in patients with Hansen's disease were treated in plaster for six weeks as outpatients. A conventional below-knee plaster of Paris (BK POP) was applied to 24 ulcers. Eighteen ulcers healed, 3 nearly healed and 3 failed to heal. Thirty-one ulcers were treated with a moulded double plaster of Paris (MD POP) shoe, 18 were healed, 8 almost healed and 5 failed to heal. The MD POP shoe was better accepted by patients and proved more economical; it also provides an acceptable and effective alternative to the BK POP for the outpatient treatment of simple plantar ulcers.—Authors' Summary

**Söderberg, T., Hallmans, G., Stenström, S., Lobo, D., Pinto, J., Maroof, S. and Vellut, C.** Treatment of leprosy wounds with adhesive zinc tape. Lepr. Rev. **53** (1982) 271–276.

In two hospitals in India 90 leprosy patients with a total of 128 ulcers on the soles of their feet were treated with local applications of zinc or gauze soaked in Eusol. The patients were selected on a random alternate basis. The average healing time was shorter for the tape-treated ulcers compared to the gauze-treated ulcers in both hospitals. The zinc tape was easy to apply, could be worn under shoes without causing pressure, and was socially acceptable because no bandages were needed.—Authors' Summary

**Srinivasan, H.** Correction of the paralytic claw-thumb by two-tailed transfer of the superficialis tendon through a window in the flexor retinaculum. Plast. Reconstr. Surg. **69** (1982) 90–94.

The results of correction of 39 paralytic claw-thumbs in 34 leprosy patients with combined ulnar and median nerve paralysis by transfer of the flexor superficialis tendon through a small window in the flexor retinaculum are reported. The motor tendon was split into two slips, one passed lateral and the other volar to the metacarpophalangeal joint of the thumb. Both slips were sutured to the tendon of the extensor pollicis longus. The volar slip was used in an attempt to restore muscle balance at the metacarpophalangeal joint. Satisfactory abduction was obtained in 90% of the cases, and excessive tip flexion during abduction-opposition was abolished in 85% of the cases. However, undesirable flexion of the proximal phalanx occurred in 10 thumbs when held actively in abduction-opposition.—Author's Summary

**Srinivasan, H., Rao, K. S. and Shanmugam, N.** Steroid therapy in recent "quiet nerve paralysis" in leprosy. Lepr. India **54** (1982) 412–419.

Nerve trunks may "quietly" get paralyzed in a proportion of leprosy patients without going through a stage of acute or subacute neuritis. A study of 25 male patients with quiet paralysis of 57 nerves shows that such paralysis, which may be complete or incomplete, can occur in any type of leprosy and may involve any nerve trunk. Steroid ther-

apy for six months reversed the motor paralysis to a satisfactory extent in about 75% of the nerves. The recovery rate was higher in nerves other than the ulnar nerve, and when paralysis was incomplete or of short duration. There was no recurrence of paralysis after stopping steroid therapy. Except for mooning of the face noticed in two patients, no serious side effects attributable to prolonged steroid therapy occurred in the subjects included in this trial.—Authors' Summary

## Other Mycobacterial Diseases and Related Entities

**Bhardwaj, O. P. and Shriniwas.** Soluble antigen fluorescent antibody test in the serodiagnosis of tuberculosis: selection of antigenic preparation. Indian J. Med. Res. **76** (1982) 5–9.

Six antigenic preparations, used in different serological techniques for serodiagnosis of tuberculosis, were evaluated. The serological technique adopted was the modified soluble antigen fluorescent antibody (SAFA) test. Antigens were tested against panels of sera from healthy controls and confirmed cases of tuberculosis. Most of the antigens elicited negative results against non-tuberculous sera by SAFA test. The discrimination between the tuberculous and the control subjects was best elucidated by using mycobacterial saline extract antigen. The sera highly reactive with one antigen did not react equally well against other antigens, and each antigen appeared to react with different combinations of antibodies. The correct choice of an antigen is thus as important as the technique used for serological diagnosis.—Authors' Summary

**Cassels, A., Heineman, E., LeClerq, S., Gurung, P. K. and Rahut, C. B.** Tuberculosis case-finding in eastern Nepal. Tubercle **63** (1982) 175–185.

Two methods of case-finding used in eastern Nepal have been compared. The differences in terms of outcome and patient compliance in one district have been examined in detail and compared with results in four other neighboring districts. The two methods compared were active case-finding (ACF) carried out by mobile teams and self referral (SR) of patients to the existing services. The results can be summarized thus:

1) In a district with established tuberculosis services an active case-finding campaign revealed patients that had not presented for treatment of their own accord.
2) These patients tended to be older than self-referred patients and there was a higher proportion of women.
3) ACF patients defaulted from treatment more than SR patients and older women were more likely to default than older men.
4) Proximity to a health facility or treatment at a health post (HP) did not decrease the proportion defaulting in the ACF group but both these factors positively influenced the default rate in SR patients.
5) Over 90% of ACF patients had their first period of default within six months of starting treatment, and if they returned they were more likely than SR patients to default again.
6) The number of ACF patients completing one year's treatment with sputum conversion was significantly lower than SR patients in this and three other districts.
7) In a district where no separate tuberculosis services existed the cure rate among ACF patients was significantly lower than in four districts where separate services had been established.—Authors' Summary

**Chaparas, S. D.** Immunity in tuberculosis. Bull. WHO **60** (1982) 447–462.

Tuberculosis continues to be one of the most prevalent and serious diseases in the world. The varied and sometimes profound immune responses induced by *Mycobacterium tuberculosis* are not only responsible for immunity but can cause considerable tissue damage and metastasis. For many years the cellular and humoral immunity

induced by *M. tuberculosis* has served as a valuable model but, despite this, many questions concerning the pathogenicity of the organism and protection against tuberculosis remain unanswered. In this review, various aspects of tuberculoimmunity and of the pathogenesis and diagnosis of tuberculosis are examined in the light of current immunological knowledge.—Author's Summary

**Deshpande, J. M., Sharma, K. D. and Kamat, R. S.** Delayed hypersensitivity eliciting lipoprotein antigen of *Mycobacterium tuberculosis* H37Rv. Indian J. Med. Res. **76** (1982) 10–17.

The protein antigens of *M. tuberculosis* H37Rv showed physiochemical properties of lipoproteins. The antigens responsible for delayed hypersensitivity (DH) response were also of similar nature and their antigenic activity was associated with the apoprotein moiety. Employing controlled papain digestion followed by repeated Sephadex G-200 chromatography, a 150,000 dalton fraction capable of eliciting DH response was isolated. This fraction showed on polyacrylamide gel electrophoresis (PAGE) two very close and sharp bands corresponding to 150,000 daltons. On 2D-IEP against anti-H37Rv antiserum the fraction showed two distinct peaks with a line of identity and a minor peak overlapping the first peak. Thus it could be concluded that at least one of the mycobacterial antigens associated with DH response is a lipoprotein of approximately 150,000 dalton molecular weight.—Authors' Summary

**Kiran, U., Shriniwas and Rohatgi, M.** Laboratory diagnosis of tuberculous lymphadenitis using soluble antigen fluorescent antibody test. Indian J. Med. Res. **76** (1982) 1–4.

A total of 136 patients aged between 1 month and 12 years with chronic enlarged lymph nodes were examined during the period January 1978–August 1979 for tuberculous etiology. Detailed clinical history and laboratory investigations including histopathological and microbiological examination of lymph nodes were carried out. Presence of antitubercular antibodies was studied using the modified soluble antigen fluorescent antibody (SAFA) test. Mantoux test was also carried out in all these cases. The data indicate that it is difficult to demonstrate mycobacteria in lymph nodes. SAFA test using mycobacterial saline extract antigen appears to be a more useful serological test in establishing the diagnosis of tuberculous lymphadenopathy, especially when the histopathological picture is non-specific.—Authors' Summary

**Ligresti, D. J., Neff, J. C. and Lowney, E. D.** Increased helper-suppressor T-cell ratio in psoriasis. Arch. Dermatol. **118** (1982) 966–970.

Numerous investigations have suggested an immunologic pathogenesis of psoriasis and diminished suppressor T cell activity of psoriatic blood. Consequently, a study was undertaken to explain whether diminished suppressor cell activity was a result of quantitative alterations of the T lymphocyte subpopulation. Twenty patients with psoriasis and 20 normal control subjects were randomly selected. Our findings demonstrated a significant decrease in the percentage of suppressor cells ($T\gamma$), a significant elevation of helper cells ($T\mu$), and a highly significant increase in the helper-suppressor T cell ratio ($T\mu/T\gamma$) of psoriatic blood compared with that of normal control subjects. Our study gives further support to the possible role of immunologic factors in the pathogenesis of psoriasis.—Authors' Summary

**Nash, D. R. and Steingrube, V. A.** Selecting drug combinations for treatment of drug-resistant mycobacterial diseases. J. Clin. Pharmacol. **22** (1982) 297–300.

Mixtures of antituberculosis drugs were evaluated for their *in vitro* effects on drug-resistant isolates of *Mycobacterium tuberculosis* and *M. avium-intracellulare.* The response of individual isolates to representative drug combinations was not always predictable from the results of single-drug sensitivity assays. For the case of *M. tuberculosis,* combinations of drugs were often bactericidal even under conditions where two or more drugs were without effect when tested singly. The more widely drug-resis-

tant *M. avium-intracellulare* demonstrated increased growth inhibition when subcultured in the presence of single drugs, particularly rifampin and streptomycin. However, these conditions favored the selection of highly resistant strains. Alternatively, multiple drugs were often bacteriostatic, and under conditions where isolates demonstrated growth inhibition, the selection of highly drug-resistant strains was delayed. These results suggest a role for multiple-drug sensitivity assays in selecting drug combinations to be used in the treatment of drug-resistant mycobacterioses.—Authors' Abstract

**Nouri-Arai, K. T., Hegarty, J. E., Alexander, G. J. M., Eddleston, A. L. W. F. and Williams, R.** Effect of corticosteroids on suppressor-cell activity in "autoimmune" and viral chronic active hepatitis. N. Engl. J. Med. **307** (1982) 1301–1304.

We detected a severe defect in concanavalin A-induced suppressor cell activity in 22 patients with "autoimmune" chronic active hepatitis and in 26 patients with hepatitis B surface antigen (HBsAg)-positive chronic active hepatitis, as compared with 20 control subjects ($p < 0.01$). Normal values were observed in 21 patients with "autoimmune" hepatitis in whom a remission had been induced and maintained by treatment with prednisolone. When lymphocytes from patients with autoimmune chronic active hepatitis were preincubated with low-dose prednisolone *in vitro,* suppressor cell activity was substantially improved ($p < 0.01$), but no clear effect of prednisolone was seen in cells from patients with HBsAg-positive chronic active hepatitis. The loss of suppressor cell activity in chronic active hepatitis may allow liver damage to continue, and the reversal of the defect in the autoimmune form of the disease by administration of low-dose prednisolone provides a plausible explanation for the efficacy of this treatment. The contrasting *in vitro* responses to prednisolone in autoimmune and HBsAg-positive chronic active hepatitis suggest that the fundamental nature of the suppressor cell defect may be different in these two forms of the disase.—Authors' Abstract

**Piessens, W. F., Partono, F., Hoffman, S. L., Ratiwayanto, S., Piessens, P. W., Palmieri, J. R., Koiman, I., Dennis, D. T. and Carney, W. P.** Antigen-specific suppressor T lymphocytes in human lymphatic filariasis. N. Engl. J. Med. **307** (1982) 144–148.

Immune responses to parasite antigens are much lower in patients with microfilaremia than in persons with other manifestations of brugian filariasis. To determine whether hyporeactivity is associated with changes in populations of lymphocytes that regulate immune responses, we quantitated helper and suppressor T cells in the blood of patients infected with *Brugia malayi.* Increased numbers of suppressor T cells were present in 15 of 17 patients with microfilaremia and in 6 of 11 patients with elephantiasis. This increase correlated with hyporeactivity to filarial antigens but not to nonparasite antigens. Removal of suppressor T cells activated *in vivo* or *in vitro* improved reactivity to filarial antigens.

These results suggest that immunosuppression induced by filarial parasites is a possible mechanism of survival of these organisms in an immunocompetent host.—Authors' Abstract

**Sanders, W. E., Jr., Hartwig, C., Schneider, N., Cacciatore, R. and Valdez, H.** Activity of amikacin against mycobacteria *in vitro* and in murine tuberculosis. Tubercle **63** (1982) 201–208.

Amikacin was found to be a potent inhibitor of clinical isolates of *Mycobacterium tuberculosis in vitro.* The drug was also active against some, but not all, strains of *M. intracellulare, M. kansasii,* and rapidly growing mycobacteria in concentrations that may be attained clinically. Activity was independent of susceptibility or resistance of the isolates to commonly used antituberculosis agents. Groups of mice were infected intravenously with *M. tuberculosis* H37Rv and then treated daily with amikacin, streptomycin, isoniazid, or kanamycin. One third of the mice in each group were killed 30, 60, and 90 days after infection. Extent of pulmonary disease was recorded and tubercle bacilli were enumerated in the lungs. Isoniazid eradicated tubercle bacilli from the

lungs within 90 days. The remaining drugs were suppressive. Amikacin was more efficacious than streptomycin or kanamycin given in equivalent or greater dosages. Because of its potent activity *in vitro,* efficacy in experimental tuberculosis, and activity against drug-resistant mycobacteria, amikacin merits further study as a potential therapeutic agent for tuberculosis and other mycobacterial infections.—Authors' Summary

**Speiser, F.** Serodiagnosis of tissue dwelling parasites: Application of a multi-antigen enzyme-linked immunosorbent assay (ELISA) for screening. Ann. Soc. Belg. Med. Trop. **62** (1982) 103–120.

Results obtained with the enzyme-linked immunosorbent assay (ELISA) and the indirect immunofluorescent antibody test (IFAT) in the routine laboratory for serology of parasitic diseases are presented. About 10,000 sera were simultaneously tested against different parasitic antigens in a multi-antigen ELISA plate. The antigens were crude extracts of: *Entamoeba histolytica, Leishmania donovani, Dipetalonema viteae,* metabolic antigen of *Toxocara canis, Echinococcus granulosus* hydatid fluid, *Schistosoma mansoni,* and *Fasciola hepatica.* ELISA proved to be generally more sensitive than IFAT and therefore suitable as a screening test. Testing a single serum dilution against several antigens in the same plate makes it possible to compare directly the extinction values obtained with different antigens and crossreacting sera. Thus it is often possible, even with crude antigen-preparations, to detect the homologous antibody-antigen system of such crossreacting sera. Up to 90 sera can be tested against eight different antigens within 1½ hours by one person.—Author's Summary

**Zimmer, B. L., DeYoung, D. R. and Roberts, G. D.** *In vitro* activity of ethambutol, isoniazid, kanamycin, rifampin, and streptomycin against *Mycobacterium avium-intracellulare* complex. Antimicrob. Agents Chemother. **22** (1982) 148–150.

Strains of *Mycobacterium avium-intracellulare* complex often exhibit *in vitro* resistance to common antimycobacterial agents. Combinations of ethambutol, isoniazid, kanamycin, rifampin, and streptomycin were tested to determine if synergism occurred. Ninety-six percent of the strains was susceptible to a combination of ethambutol and rifampin at concentrations attainable clinically. Other combinations of antimycobacterial agents inhibited 4% to 82% of the isolates tested.—Authors' Summary