CURRENT LITERATURE

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

General and Historical

Gregory, D. R. AIDS—the leprosy of the 1980s. Is there a case for quarantine? J. Legal Med. **9** (1988) 547–560.

Decades from now, society may well look back and conclude that AIDS was indeed the "leprosy of the 1980s." It is impossible for us, at this point, to so characterize it, although there are some remarkable parallels between the two diseases. Perhaps the most striking are the early societal perceptions of the two diseases and of the groups who seemed to constitute the majority of their victims. These perceptions, and the emotions they generated, dictated the societal behaviors toward those victims. As for quarantine, the parallel between leprosy and AIDS should not exist. Leprosy sufferers were readily identifiable and their disease was transmitted by direct contact. We do not yet know all who have been infected with AIDS nor can we identify those who may be infectious. Therefore, there is no reasonable ground to establish a quarantine when there is little likelihood that such a drastic measure would be effective in controlling the spread of the disease. Nor is there a case for general isolation, since mere physical contact without "high-risk behaviors" is not a factor in its transmission.—(*From the* Author's Conclusion)

Segredo, A. B. G., Castells, E. G.-A., Rodriguez, A. V.-P., Moreno, O. S. and Sabournin, R. O. [Leprosy: a brief overview of the topic.] Rev. Cubana Med. Trop. **40** (1988) 67–81. (in Spanish)

Some history and current concepts on leprosy, as well as the most conspicuous aspects of the investigational work developed at the National Reference Laboratory for Leprosy in Pedro Kourí Institute of Tropical Medicine (Cuba), are described.—Authors' English Summary

Sukumaran, K. D. The status of leprosy control in Malaysia. Southeast Asian J. Trop. Med. Public Health **19** (1988) 519–524.

The declining incidence of leprosy in Peninsular Malaysia can be attributed to improved management and supervision, intensive health education and training as well as the use of multiple drug regimen. However, leprosy is still a public health problem in Malaysia and, therefore, leprosy surveillance on all fronts is essential to ensure that its incidence declines to the target of 1:100,000 population. Research has to be conducted vigorously: on the application of effective early diagnostic tools, development of a good leprosy vaccine, screening of new chemotherapeutic compounds, understanding all the many "grey" areas in the pathogenesis of the disease, transmission dynamics of leprosy bacilli and *in-vitro* culture technique. With the introduction of biotechnology tools, recombinant DNA technology and the production of the monoclonal antibodies specific to *Mycobacterium leprae,* it is possible to accelerate research in leprosy on all fronts for the effective control of the disease. The present research activities which are directed mainly to the application of suitable effective early rapid diagnostic tools for field application and the development of a good leprosy vaccine will also contribute for the effective control of the disease.—Author's Discussion and Conclusion

Chemotherapy

Anderson, R., Beyers, A. D., Savage, J. E. and Nel, A. E. Apparent involvement of phospholipase A_2, but not protein kinase C, in the pro-oxidative interactions of clofazimine with human phagocytes. Biochem. Pharmacol. **37** (1988) 4635–4641.

The antileprosy agent clofazimine, at concentrations of 0.1–5 μg/ml, caused a dose-related, stimulus-nonspecific (*N*-formyl-methionyl-leucyl-phenylalanine, calcium ionophore, opsonized zymosan, arachidonic acid and phorbol myristate acetate) potentiation of superoxide generation by human neutrophils *in vitro* without affecting basal oxidative responses. The pro-oxidative interactions of clofazimine with neutrophils were eliminated by the phospholipase A_2 inhibitor 4-*p*-bromophenacyl bromide but not by the protein kinase C (PKC) inhibitor H-7. In support of these observations clofazimine promoted the release of radiolabeled arachidonic acid from neutrophil membrane phospholipids but did not influence the activity of PKC in cytosolic extracts of neutrophils or of purified PKC from rat brain. Pro-oxidative interactions of clofazimine with human phagocytes may contribute to the intraphagocytic antimycobacterial activity of this agent.—Authors' Abstract

Bhainagar, P., Kumar, B., Kaur, S., Kaur, I. and Seghal, S. Dapsone drug compliance study among leprosy patients: a comparison between qualitative and quantitative methods. Indian J. Lepr. **61** (1989) 373–378.

The methods currently employed to monitor self-administration of dapsone (DDS) have been evaluated by comparing the results of the qualitative spot test and quantitative DDS/creatinine ratio test. Random urine samples of 242 leprosy patients periodically attending the leprosy clinic were tested. Although a good correlation between the results of the two tests was evident, the DDS/creatinine ratio technique appeared to be more sensitive than the spot test. The concentration of DDS and its metabolites in urine specimens found to be negative by the spot test ranged from 3.32–12.37 μg of DDS/mg creatinine. The spot test was found to be more specific and stays the method of choice, when rapidity and reproducibility are the prime objectives, and sensitivity can be marginally compromised. Acidification of urine prior to the spot test was found to be desirable to rule out false-negative and false-positive reactions.—Authors' Abstract

Chaudhury, S., Hazra, S., Podder, G. C., Poddar, S., Sarkar, S., Das, S., Chaudhury, S. N. and Majumder, V. New multidrug regimen with indigenous drugs and dapsone in the treatment of lepromatous leprosy (preliminary report). Indian J. Dermatol. **32** (1987) 63–67.

The treatment of leprosy by the multidrug regimens (MDR) of WHO is not the final answer to the problem of managing leprosy patients. MDR is only a transitional phase in our search for optimum treatment for leprosy. There continues to be a need to develop new antileprosy drugs and new antileprosy drug regimens, and this need is an urgent necessity. We have evaluated the efficacy of a combination of two indigenous drugs and dapsone in the treatment of leprosy patients. Preliminary results indicate that this combination is as good as MDR clinically. There were negligible reactional episodes in the patients treated with the combination compared to those in patients treated with MDR.—(*From the* Authors' Abstract)

Dhanapaul, S. DDS-induced photosensitivity with reference to six case reports. Lepr. Rev. **60** (1989) 147–150.

Photosensitivity as an adverse reaction to dapsone (DDS) was recognized in 6 patients of our hospital during the summer of 1988. The clinical manifestations and also the management of those patients are given in detail. All doctors and health workers involved with leprosy need to be aware of such a problem and to make correct decisions after weighing the risk of photosensitivity against the potential benefit of DDS.—Author's Summary

Freerksen, E., Rosenfeld, M. and Spannuth, G. New forms of multidrug therapy for the treatment of leprosy. First report for the practice on rifampicin + sulfamethoxazole-thrimethoprim + prothionamide and rifampicin + sulfamethoxazole-trimethoprim + isoniazid. Chemotherapy **35** (1989) 133–139.

Since 1970, when the lifelong monotherapy with dapsone (DDS) in leprosy could be replaced by short-term combination therapy with rifampin + isoniazid + prothionamide + DDS (Isoprodian-RMP), chemotherapeutic research was faced with two problems: a) to find alternative treatment regimens for cases of intolerance, and b) to work out forms of therapy allowing a further reduction of the average treatment time of 2 years. The present paper describes the attempts made to find solutions to these problems. With two new combinations, alternatives have become available, and the average treatment time is shortened to 6 months. Both combinations are also effective in tuberculosis.—Authors' Abstract

Goloshchapov, N. M., Bazurov, G. I., Khromova, E. B., Steklovsky, V. K. and Goloshchapova, E. N. [Diuciphone and dimociphone in combined therapy of lepra (*sic*) (a 14-year follow-up study).] Vestn. Dermatol. Venerol. 7 (1988) 18–22. (in Russian)

A 14-year administration of diuciphone and dimociphone together with present-day antileprosy drugs to 169 patients suffering from leprosy has proved the biologic compatibility of such drug combinations. The addition of diuciphone to a combination of antileprosy drugs, including the "isoprodian" combination, has resulted in an elevation of T-lymphocyte count and has drastically reduced the side effects of therapy, such as leprous nodular erythema, hypochromic anemias, toxic hepatitides.—Authors' English Summary

Millan, J. P. and Moulia-Pelat, J. P. Antagonism between dapsone and rifampicin in experimental *Mycobacterium leprae* infections in mice. Res. Microbiol. **140** (1989) 143–150.

In experimental infections of normal mice with *Mycobacterium leprae,* the bactericidal activity of four consecutive weekly doses of rifampin (RMP) was suppressed when this treatment was preceded, for 1 month, by daily administration of dapsone (DDS), and then the latter. Up until now, it has been impossible to detect this antagonism between the action of RMP and DDS, since all studies involved the simultaneous administration of these two drugs, and such a phenomenon would therefore have been masked by the rapid and potent action of RMP. Previous clinical observations suggest that such a delayed antagonistic effect may also occur in humans. The demonstration of this antagonism between RMP and DDS raises the problem of the long-term efficacy of therapeutic regimens currently used in leprosy and that of the role of DDS in induction of bacillary persistence. It is suggested that this particular methodology, the delayed combination of RMP with a less-active drug, should be applied to the study of other drug combinations recommended in the treatment of leprosy.—Authors' Summary

Pattyn, S. R., Bourland, J., Grillone, S., Groenen, G. and Ghys, P. Combined regimens of one year duration in the treatment of multibacillary leprosy—I. Combined regimens with rifampicin administered during one year. Lepr. Rev. **60** (1989) 109–117.

In 1981, 1982 and 1983, 216 multibacillary patients in Anjouan (Comores) and Burundi were treated for 8 weeks with daily rifampin (600 mg), ethionamide (500 mg), and dapsone (100 mg) or clofazimine (100 mg), followed for 44 weeks by once-weekly rifampin (600 mg) and daily ethionamide (500 mg) and dapsone (100 mg) or clofazimine (100 mg). There were 109 previously untreated patients and 107 patients who had had dapsone monotherapy, 16 of whom were infected with proven dapsone-resistant *Mycobacterium leprae.* Clinical and bacteriological results were excellent but hepatotoxicity of this regimen remains a problem. No relapses were observed during a 2 to 6 year (mean: 4.29 years) follow-up period after the end of treatment (upper 95% confidence limit of 0.40 per 100 persons years).

It is concluded that multibacillary leprosy can be successfully treated with a regimen of 1 year duration but less toxic regimens, more easily applicable in the field, are necessary.—Authors' Summary

Pattyn, S. R., Groenen, G., Janssens, L., Deverchin, J. and Ghys, P. Combined regimens of one year duration in the treatment of multibacillary leprosy—II. Combined regimens with rifampicin administered during 6 months. Lepr. Rev. **60** (1989) 118–123.

From 1981 to 1983 all multibacillary patients presenting at the collaborating centers in Zaire and Rwanda were treated with one of the following regimens: 6 months' supervised daily rifampin (RMP) 600 mg, ethionamide (ETH) 500 mg and dapsone (DDS) 100 mg or clofazimine (CLO) 100 mg followed by 6 months' unsupervised daily DDS 100 mg or CLO 100 mg with ETH 500 mg added or not. These regimens gave rise to hepatotoxicity, reversal and erythema nodosum leprosum reactions as described previously. Bactericidal activity was excellent. Among the 289 patients in the trial, with a mean follow-up period of 3.88 years, no relapses were observed, with an upper 95% confidence limit of 0.35 per 100 person years. Because of the hepatotoxicity, alternative short-course therapies need to be tested.—Authors' Summary

Revankar, C. R., Karjivkar, V. G., Gurav, V. J. and Ganapati, R. Clinical assessment of paucibacillary leprosy under multidrug therapy—three years followup study. Indian J. Lepr. **61** (1989) 353–359.

Four-hundred-eight skin-smear-negative, paucibacillary leprosy cases who had completed 6 months' MDT were kept under surveillance for 3 years. The clinical assessment at the end of surveillance showed that 276 (82%) of all the cases attained inactivity. Two patients who were inactive showed signs of relapse. Five patients showed more activity although they were regressing under treatment. The inactivity rate was much higher among the patients with 1 to 3 skin lesions (88%) as compared to the patients with $\geq$ 4 lesions (60%). The difference was statistically significant ($p <$ 0.001). The past treatment before MDT did not appear to influence the clinical course of the disease; 17% of the patients essentially borderline type continued to show signs of activity even after 3 years' surveillance, indicating the need for triple-drug therapy (to be treated as multibacillary). However, large-scale data on the relapse rate would be essential before the efficacy of the WHO short-term therapy for paucibacillary leprosy is evaluated.—Authors' Summary

Revankar, C. R., Sorensen, B. H. and Kielstrup, R. W. Delivery of MDT through blister calendar packs in leprosy eradication programmes—a multicentre field study (Phase I). Lepr. Rev. **60** (1989) 135–138.

To overcome operational problems and improve patient compliance in leprosy program. DANIDA introduced blister calendar packs (BCP) to deliver MDT in four districts in India. A questionnaire study of 1470 patients from these districts showed that more than 90% accepted BCP and found them to be very convenient for domiciliary treatment. A similar study of 127 treatment providers indicated that delivery of MDT through BCP was found convenient to overcome logistic problems.—Authors' Summary

Venkatesan, K. Clinical pharmacokinetic considerations in the treatment of patients with leprosy. Clin. Pharmacokinet. **16** (1989) 365–386.

On the basis of the efficacy of the available agents, the World Health Organization has recommended only four drugs for combined chemotherapy of leprosy: rifampin, dapsone, clofazimine, and ethionamide/prothionamide. Thiacetazone and isoniazid are also used to a lesser extent by some physicians. Pyrazinamide may find a place in treating "persister" bacilli.

Dapsone is absorbed slowly after oral administration. Peak plasma drug concentration is reached at about 4 hr, absorption half-life is 1.1 hr, elimination half-life is about 30 hr. Oral availability is around 90%. Dapsone is approximately 70% protein-bound, while its monoacetylated metabolite is amost entirely bound. Dapsone crosses

the placenta and is excreted into breast milk. It is metabolized via acetylation and *N*-hydroxylation, but acetylation polymorphism has no effect on dapsone handling by leprosy patients. Dapsone penetrates into sciatic nerves of experimental animals but its presence has not been demonstrated in Schwann cells.

Oral doses of rifampin are rapidly and completely absorbed. The bioavailability is greater when the drug is given before meals; peak concentrations occur at 1 to 2 hr, 80% to 90% of rifampin is bound to plasma proteins, and the drug is found in saliva, cerebrospinal fluid and breast milk. Its main metabolite, desacetyl rifampin, also exhibits antimycobacterial activity in tuberculosis. Rifampin induces its own metabolism, as well as that of dapsone and steroids. Absorption of dapsone and rifampin is reported to be reduced in leprosy patients.

Clofazimine has been in use in leprosy treatment since 1960. In higher doses it exerts an anti-inflammatory action which is useful in treating leprosy patients in reaction. Oral absorption of the drug is slow and dose-dependent; fecal excretion also increases with dose. Single- and multiple-dose studies have shown a plasma half-life of around 10 days. Bioavailability of the drug is higher when given with food than when fasting; the peak plasma concentration occurs at 4 to 8 hr when the drug is administered with breakfast. After absorption, the drug is thought to circulate in protein-bound form, accounting for the fact that it is deposited in various tissues. Uneven distribution and prolonged retention in the tissues are special features of clofazimine metabolism. One unconjugated and two conjugated metabolites have been detected in urine, and the urinary excretion of both the parent compound and its metabolites is around 1% of the dose. Clofazimine crosses the placental barrier and is excreted into breast milk, but does not cross the blood-brain barrier. Small amounts of the drug are found in sebum and sweat.

The pharmacokinetic properties of ethionamide and prothionamide are similar in man. Both are absorbed rapidly and completely following oral administration. Peak plasma concentration of prothionamide occurs at around 18 min; plasma half-life is about 2 hr. The sulfoxide metabolite of the drug is active against *Mycobacterium leprae*. The pharmacokinetics of thiacetazone, isoniazid and pyrazinamide are reviewed briefly. All three drugs are well absorbed after oral administration.

Hematological, dermatological and neurological effects and gastrointestinal symptoms are some of the side effects of the drugs reviewed. These may not pose serious problems at therapeutic dosages in leprosy, but the increased incidence of hepatotoxicity on combining rifampin and ethionamide/prothionamide causes serious concern.

Rifampin increases the excretion of dapsone, although this is not of therapeutic significance. Dapsone plus clofazimine reduces the absorption of rifampin, while rifampin plus dapsone does not affect absorption of clofazimine. Isoniazid treatment lowers the tissue concentration of clofazimine and increases its urinary excretion.—Author's Summary

Wille, R. C. and Morrow, J. D. Case report: dapsone hypersensitivity syndrome associated with treatment of the bite of a brown recluse spider. Am. J. Med. Sci. **296** (1988) 270–271.

Dapsone (4-4-diaminodiphenylsulfone) is a member of the sulfone group of antibiotics used in the treatment of leprosy and various dermatitidies and more recently employed in the management of local reactions to the bite of the brown recluse spider, *Loxosceles reclusa*. A dapsone-hypersensitivity syndrome, consisting of fever, headache, nausea, vomiting, lymphadenopathy, hepatitis, hemolysis, leukopenia, and mononucleosis, has been described in patients treated with the drug for leprosy. A case report of the hypersensitivity syndrome occurring in a patient being treated with dapsone for a brown recluse spider bite is presented.—Authors' Abstract

Clinical Sciences

Adala, H. S. and Kagame, K. Ocular leprosy in Kenya. East Afr. Med. J. **65** (1988) 593–601.

Clinical examination on 199 patients was done to determine the prevalence of ocular leprosy and categorize the different forms of clinical presentations of ocular leprosy. The western and coastal regions of Kenya were visited, including the Infectious Diseases Hospital, Nairobi. It was found that 53% of the patients examined had ocular complications. Lagophthalmos, keratitis and uveitis were considered potentially blinding lesions and existed in 22.1% of the 199 patients. Blindness (i.e., visual acuity of less than 3/60) was noted in 3%. Age and sex distribution are discussed, while a correlation is sought between duration of the disease and presentation of ocular complications. Socio-psychological and economical implications of leprosy are discussed, including practical recommendations for eye care in leprosy.—Authors' Summary

Adallah, S. O., Orege, P. A. and Owili, D. M. Eleven years of follow-up of the pattern of leprosy complications at Alupe Leprosy Hospital. East Afr. Med. J. **64** (1987) 656–664.

A retrospective follow-up study was done to find out the pattern of leprosy complications at Alupe Leprosy Hospital during the period 1973–1983. The total number of first admissions during the study period were 1371 cases out of which 59.4% were males and 40.6% were females; 5.3% of the admitted cases were nonleprosy cases. Out of 1299 leprosy cases, 775 (59.7%) were males and 524 (40.3%) were females. The majority of the patients were aged 50 years and above, and the predominant type of leprosy was borderline tuberculoid; 18.8% of the complications were medical, i.e., due to reactions; 64.2% of the complications were physical and 17.0% of the complications were found on the eyes; 53.7% of the surgical complications were found on the feet and 46.3% of the surgical complications were found on the hands; 59.9% of the patients with hand complications had anesthesia and/or claw fingers; 35.4% had ulcers and 4.7% had absorption of the fingers. In contrast, 26.0% of the patients who had feet complications had anesthesia and/or claw feet; 65.1% had ulcers and 8.9% had absorptions of the toes.

As for the medical complications, 63.3% of the patients had type 1 (reversal) reaction and 36.7% had type 2 (erythema nodosum leprosum) reaction. This study therefore shows that male patients have more complications than female patients, and that borderline tuberculoid (BT) patients are the ones at greatest risk of developing leprosy complications. The study also shows that 64% of the bed-occupancy at Alupe Leprosy Hospital is due to ulcers. This study also shows that surgical complications are still predominant in leprosy, hence leprosy control efforts should be intensified, and physical rehabilitation of leprosy patients should also be intensified, since leprosy ulcers are still a major cause for admission of leprosy cases into the hospital.—Authors' Summary

Anandi, V., Suryanwanshi, N. B., Koshi, G., Padhye, A. A. and Ajello, L. Corneal ulcer caused by *Bipolaris hawaiiensis*. J. Med. Vet. Mycol. **26** (1988) 301–306.

Following an injury to the right eye, a corneal ulcer with hypopyon developed in a leprosy patient. Direct examination of the corneal scrapings on three occasions showed septate, branched, dematiaceous hyphal elements. When scrapings were cultured on Sabouraud's glucose and brain heart infusion agars, *Bipolars hawaiiensis* was isolated repeatedly. The patient responded successfully to treatment with nystatin ointment, although the central opacity of the cornea remained and visual acuity did not improve.—Authors' Abstract

Cristofolini, L., Axcar, S. R., Bix, L. P. and Vieth, H. [Nursing routine in the evaluation of ocular injuries in hansensiasis.] Rev. Bras. Enf. **39** (1986) 86–89. (in Portuguese)

The acceptance of a great number of patients having eye injuries and the lack of an ophthalmologist at Hospital Lauro de Souza Lima (Brazil) has motivated the improvement of the ophthalmology work with the participation of the nursing staff. The following objectives were established: to offer a permanent and systematic assistance on the ophthalmological prevention and treatment; to increase the specific knowledge of the nurses; to develop and apply simple techniques on prescription and treatment; to offer a field for professional training. The basic element for the success of the unit was the disposition of the nurses in assuming the work, the cooperation and availability of the ophthalmologist and settlement on the work routines. The routine evaluation of injuries of the eye adopted by the nurses has two phases: 1) interview for identification of the subjective symptoms for the eye injury and 2) sequence of examinations: superciliary and ciliary area; lacrimal ducts; eyelids; orbicular muscles; conjunctivae; episclera; sclera; cornea; pupil; crystalline; intraocular pressure. In the described routine a minimum of resources are used and it is possible for the nursing staff to identify the main ophthalmologic problems of the patients, introducing preventive and curative actions.—(*From* Authors' English Abstract)

Font, R. L., Sobol, W. and Matoba, A. Polychromatic corneal and conjunctival crystals secondary to clofazimine therapy in a leper (*sic*). Ophthalmology **96** (1989) 311–315.

A 67-year-old man had a diagnosis of dapsone-resistant lepromatous leprosy. He received clofazimine (Lamprene) at a dosage of 100 mg twice daily. After 3 years of therapy, results of slit-lamp examination disclosed myriad polychromatic crystals diffusely involving the cornea and perilimbal conjunctiva of both eyes. Thick sections (1 μm) from a conjunctival biopsy showed numerous rectangular-to-rhomboidal crystals within stromal fibroblasts and macrophages. By electron microscopy, these cells contained elongated, membrane-bound, cleft-like spaces that corresponded to the sites where crystals had been present previously. Additionally, complex lipid inclusions were observed in mesenchymal cells as well as in endothelial cells and pericytes of blood vessels. The ocular side effects of clofazimine therapy are reviewed. Clofazimine-induced keratopathy should be included in the differential diagnosis of patients with polychromatic crystalline deposits in the corneas. To the best of the authors' knowledge, this complication of clofazimine therapy has not been described previously.—Authors' Abstract

Freitas, J. A. de S., Santos, W. M., Opromolla, D. V. A. and Alle, N. [New criteria for the characterization of *facies leprosa.*] Hansen. Int. **11** (1986) 7–23. (in Portuguese)

Facies leprosa was characterized by a combination of nasal change and resorption of nasal bone, anterior nasal spine, supraincisive alveolar region and anterior alveolar process of the maxilae, associated with the loss of upper incisors teeth, according to the criteria of radiographic interpretation.—Authors' English Abstract

High, A. S. and Lansley, C. V. Labial and gingival enlargement in leprosy. Br. Dent. J. **165** (1988) 371–372.

A patient is described in whom marked labial and gingival enlargement was the presenting feature. Clinical and laboratory investigations confirmed a diagnosis of leprosy, while further examinations revealed less obvious sites of disease activity. Background information on leprosy and a discussion of differential diagnoses are given, with particular emphasis on oral manifestations. Although rare in the United Kingdom, this disease is common worldwide, and the importance of vigilance with immigrants is stressed.—Authors' Abstract

Holcombe, D. J. A case of leprosy in central Louisiana. J. Louisiana State Med. Soc. **140** (1988) 33–35.

Indigenous cases of Hansen disease do appear sporadically in Louisiana, a traditional focus of infection. An 87-year-old white woman from central Louisiana presented with a short history of arthritic complaints and painless swelling of the left forehead and ear. Biopsy results showed a

nonspecific granuloma; sarcoidosis was considered. Specialized stains demonstrated the presence of innumerable acid-fast bacilli strongly compatible with the diagnosis of leprosy. The patient responded well to treatment with dapsone and rifampin.—Author's Abstract

Ishaque, M. Direct evidence for the oxidation of palmitic acid by host-grown *Mycobacterium leprae*. Res. Microbiol. **140** (1989) 83–93.

Oxidation of palmitic acid by whole-cell suspensions of *Mycobacterium leprae* free from host tissues was investigated using manometric techniques. After a lag period of about 6–8 hr, *M. leprae* suspensions catalyzed an active oxidation of palmitic acid, and the oxidative process (oxygen uptake) was quite sensitive to rotenone, atabrine, amytal, antimycin A, and cyanide. The spectrophotometric observations indicated that the *M. leprae* cytochrome system, under anaerobic conditions, was reduced in the presence of palmitic acid which was completely oxidized by oxygen. These data provide direct evidence that *M. leprae* cells are capable of oxidizing palmitic acid, and that oxidation is mediated by the electron transport system using oxygen as the terminal electron acceptor.—Author's Summary

Kaplan, G. The efficacy of a cell-mediated reaction in the disposal of *M. leprae* in human skin. Immunol. Lett. **19** (1988) 223–228.

The inability of lepromatous leprosy patients to mount a cellular immune response against *Mycobacterium leprae* antigens is not understood. The extensive intracellular replication of bacilli in the phagocytes and the relative paucity of T lymphocytes in the lesions suggest that these patients might be incapable of generating normal delayed-type hypersensitivity responses in their skin. In order to elucidate this problem we evaluated the patient's response to local antigen administration.

Our observations suggest that the majority of lepromatous patients can respond normally to intradermal injections of a soluble antigen such as purified protein derivative of tuberculin. The underlying lepromatous lesions do not inhibit mononuclear cell infiltration or differentiation. Moreover, the generation of a cellular immune response in the lesions appears to modify the lepromatous lesion to a lesion resembling the tuberculoid type. This process involves local T cell recruitment, granuloma formation and a reduction in the bacterial load at the antigen-responsive site.—Author's Summary

Levis, W. R., Lanza, A. P., Swersie, S., Meeker, H. C., Schuller-Levis, G. B. and Bardin, C. W. Testicular dysfunction in leprosy: relationships of FSH, LH and testosterone to disease classification, activity and duration. Lepr. Rev. **60** (1989) 94–101.

Luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone levels were determined by radioimmunoassay (RIA) in leprosy patients and analyzed for the effect of disease classification, disease activity and duration of disease. LH and FSH levels were found to be significantly elevated in lepromatous patients compared to borderline lepromatous, mid-borderline and borderline tuberculoid patients. A positive correlation was seen between LH and FSH, and a negative correlation was seen between testosterone and both LH and FSH. No correlation was seen between the hormone levels and measures of disease activity: bacillary index and IgM to phenolic glycolipid-I, a *Mycobacterium leprae* antigen. A significant correlation was seen between duration of disease and FSH when age was taken into account, indicating that testicular dysfunction is probably cumulative and irreversible. It is recommended that LL patients be routinely screened for hypogonadism using FSH, LH, and testosterone levels.—Authors' Summary

Looi, L. M., Jayalakshim, P., Lim, K. J. and Rajagopalan, K. An immunohistochemical and morphological study of amyloidosis complicating leprosy in Malaysian patients. Ann. Acad. Med. Singapore **17** (1988) 573–578.

Congo red screening of tissue blocks from 37 consecutive autopsies on leprosy pa-

tients revealed 7 cases of systemic amyloidosis, indicating a prevalence rate of 19%, 5 were males and 2 females. All were ethnic Chinese. Their ages ranged from 52 to 85 years with a mean of 69 years. Six had lepromatous leprosy while the remaining 1 had tuberculoid leprosy. In all 7 cases, the amyloid was AA in type, being permanganate-sensitive and immunoreactive with anti-human AA protein antiserum. Hepatic deposition was limited to blood vessels, a pattern typical of AA (secondary) amyloidosis. With regard to renal involvement, 4 showed a predominantly vascular pattern of infiltration while 3 exhibited the more ominous glomerular pattern. Three died of chronic renal failure and 2 of congestive cardiac failure attributable to renal and cardiac amyloidosis, respectively. One patient succumbed to septicemia and the remaining 1 to acute myocardial infarction. AA amyloidosis remains a serious and significant complication of leprosy among Malaysians.—Authors' Abstract

Mahakul, K. C., Nandy, S. C., Gill, N. S., Biswal, S. K., Mahapatra, B. N. and Barik, B. K. Tuberculous basal meningitis with multiple cranial nerve palsies and leprosy. J. Indian Med. Assoc. **86** (1988) 244–246.

A very rare case of tuberculous basal meningitis with multiple cranial nerves involvement (bilateral I, II, VI cranial nerve palsies, V nerve palsy on left side, VII nerve palsy on right side) and a tuberculoid leprotic patch over the left wrist joint in a 26-year-old male patient is presented.—Authors' Summary

Malaviya, G. N., Girdhar, A., Mishra, B., Husain, S. and Girdhar, B. K. Nerve abscess simulated by a lipoma in a leprosy patient. J. Hand Surg. **14B** (1989) 115–116.

A case of suspected giant nerve abscess near the radial nerve in the upper arm of a patient with borderline leprosy is reported. On exploration, it turned out to be a deep seated lipoma. Consideration should be given to exploring nerve masses in leprosy.—Authors' Abstract

Nigam, P., Pant, K. C., Mukhija, R. D., Sharma, S. P., Saxena, S. P., Kumar, A., Kapoor, K. K. and Gupta, A. K. Rapidly progressive (crescentric) glomerulonephritis in erythema nodosum leprosum: case report. Hansen. Int. **11** (1986) 1–6.

A middle-aged man (48 years) with short duration of illness (7 days) was admitted in the state of acute renal failure with erythema nodosum leprosum (ENL). He had repeated episodes of ENL in the past. His blood pressure was normal (150/80 mm Hg). During his hospital stay he was in the state of progressive anemia (Hb = 8.8 g/dl to 7.2 g/dl), oliguria (urine out-put = 250–350 ml/day), azotemia (blood urea = 198 mg/dl to 218 mg/dl) and impaired renal function tests with fatal outcome. Kidneys were smooth, congested and weighing 150 g each with histological features of rapidly progressive (crescentric) glomerulonephritis, a result of immune complex deposition from recurrent ENL episodes.—Authors' Abstract

Ponce, P., Ramos, A., Ferreira, M. L., Pinto, G. and Lacerda, M. H. Renal involvement in leprosy. Nephrol. Dial. Transplant. **4** (1989) 81–84.

Renal involvement in Hansen's disease was evaluated in 94 Portuguese patients, with an average age and duration of disease of 47.6 and 6.8 years, respectively. Sixty-seven were studied retrospectively and 27 prospectively; renal biopsy was obtained in 4, fat-tissue needle aspiration for amyloidosis in 20, and tubular function was tested in 10. Mild proteinuria and/or hematuria was found in 33 patients, the severity increasing during erythema nodosum leprosum (ENL) reactions, but without overt nephritic or nephrotic syndrome. Two patients had renal amyloidosis on biopsy and two more were confirmed by fat biopsy, a 10.5% incidence in those studied prospectively; all but one were of the lepromatous type, with frequent bouts of ENL. The two other renal biopsies showed mesangial glomerulonephritis, and one unexplained acute tubular necrosis; none had immune deposits by immunofluorescence. Proximal acidification was always normal, distal acidification tested by bicarbonate infusion was abnormal in 1 of 9 patients, and 6 of 9 patients had con-

centration defects. Leprosy causes frequent urinary sediment changes and concentration defects, usually without clinical expression; proteinuria and/or glomerular involvement is mainly due to amyloidosis.—Authors' Abstract

Prasad, A. S. Relative efficacy of commonly used clinical and laboratory methods for the diagnosis of leprosy. Indian J. Dermatol. **31** (1986) 7–11.

Sixty suspected cases of leprosy were studied; 12 case were bacteriologically positive. The remaining 48 cases were studied to evaluate the relative efficacy of commonly used clinical and laboratory methods of diagnosis. Diminution of sensation is the best criterion and results are comparable to the histopathological findings. Its limitations are the unpredictable information received in cases of children and mentally retarded patients. The sweat test, which was modified by the author, and the histamine flare test were found to be very effective, with 95% accuracy.—Author's Abstract

Saha, K. and Rao, K. N. Undernutrition in lepromatous leprosy: nutritional deficit in lepromatous patients co-infected with pulmonary tuberculosis. Eur. J. Clin. Nutr. **43** (1989) 117–128.

We have compared the nutritional status of patients with lepromatous leprosy coinfected with pulmonary tuberculosis (18 cases) with that of lepromatous leprosy (239 cases) and of pulmonary tuberculosis (21 cases) and with that of healthy controls. There was a severe weight loss and reduction of skinfold thickness in the patients with pulmonary tuberculosis as well as in lepromatous patients with associated pulmonary tuberculosis, but not in patients with lepromatous leprosy.

Levels in sera of diet-dependent proteins, such as albumin, prealbumin and retinol binding protein, were significantly decreased in all three groups of patients; on the other hand, levels of the diet-independent proteins, such as the immunoglobulins, were raised in all the groups, particularly in the pulmonary tuberculosis patients as compared with healthy controls. Serum transferrin levels were decreased only in the tuberculosis patients with or without lepromatous leprosy, but not in patients with leprosy alone. While hemoglobin levels decreased in all patient groups, serum iron concentrations were reduced most in lepromatous patients concomitantly infected with pulmonary tuberculosis. Serum ferritin levels increased in the sera of pulmonary tuberculosis and lepromatous leprosy patients, but was severely reduced in lepromatous patients with associated pulmonary tuberculosis. Mean serum zinc and calcium levels were decreased in all three groups of patients, while the serum copper concentration was increased in all of them compared with healthy controls. Also, inorganic phosphorus was elevated in tuberculosis and lepromatous patients coinfected with pulmonary tuberculosis, but not in lepromatous patients. Serum calcitonin levels were increased in all patient groups indicating an inverse correlation between serum calcium and calcitonin levels.

This is the first comparative report describing the status of macro- and micronutrients in two most important mycobacterial diseases of the Third World countries.—Authors' Abstract

Sehgal, V. N. and Sharma, V. Reactions in leprosy—a prospective study of clinical, bacteriological, immunological and histopathological parameters in thirty-five Indians. J. Dermatol. **15** (1988) 412–419.

The clinical manifestations of types 1 (lepra) and 2 (erythema nodosum leprosum; ENL) reactions are now well appreciated. The correlation of clinical expression to bacterial index, lepromin response and histological features has hardly been attempted. In a study of 35 reaction patients, 18 type 1 (lepra) and 17 type 2 (ENL), the preceding parameters were studied in detail. Their incidence among leprosy patients was 20%. Males in the age group 20–30 years were frequently affected, the ratio of males to females being 6:1. The mean age at onset in type 2 (ENL) was younger than in type 1 (lepra) reactions. However, the duration of the reactions was variable. They were frequently precipitated by antileprosy drugs. The clinical features were cardinal. The bacteriological features reflected wide variations, but were considered imperative. Early

Fernandez and late Mitsuda reactions were useful adjuvants for monitoring progress. The utility of changing microscopic pathology in determining the swing toward the lepromatous or tuberculoid end of the leprosy spectrum are emphasized.—Authors' Abstract

Sehgal, V. N. and Srivastava, G. Histoid leprosy: a prospective study in 38 patients. Dermatologica **177** (1988) 212–217.

Histoid leprosy is a fascinating expression of multibacillary leprosy, the incidence of which was 3.6%. It was seen predominantly in males of the younger age group, who were on inadequate and irregular dosage of diaminodiphenylsulfone. Papules, cutaneous and/or subcutaneous nodules, and plaques appearing over apparently normal skin were its exquisite prospective clinical features. It was invariably supported by enormous, uniformly solid-staining discrete bacilli from the lesions, in contrast to their virtual absence from the surrounding normal-appearing skin. Encapsulated tumorous masses, formed primarily by spindle-shaped histocytes, displayed either in intertwining, criss-cross or whorled fashion in hematoxylin-eosin-stained sections, were supplementary. The morphology of acid-fast bacilli was, however, similar to skin-slit smears.—Authors' Abstract

Shorey, P., Krishnan, M. M., Dhawan, S. and Garg, B. R. Ocular changes in reactions in leprosy. Lepr. Rev. **60** (1989) 102–108.

A study of ocular changes in reactions in leprosy was undertaken to assign these changes their proper place in the wide spectrum of ocular morbidity in leprosy; 76.1% of eyes of type 1 reaction and 89.7% of eyes with type 2 reaction showed some ocular involvement. Corneal hypoesthesia, superficial punctate keratitis, a decrease of corneal film break up time (BUT), prominent corneal nerves, pigment on the endothelium of the cornea and a pigmented trabecular meshwork were the common ocular findings. The incidence of iridocyclitis in type 2 reactions was low (8.1%). The significance of the ocular involvement in reactions in leprosy and the pathogenesis of iridocyclitis in type 2 reactions are discussed.—Authors' Summary

Thornton, Y. S. and Bowe, E. T. Neonatal hyperbilirubinemia after treatment of maternal leprosy. So. Med. J. **82** (1989) 668.

Leprosy occurs rarely in women of reproductive age. Until this report, the treatment of leprosy with dapsone has not been associated with any adverse fetal or neonatal side effects. We have reported what we believe to be the first case of neonatal hyperbilirubinemia after maternal dapsone therapy for leprosy.—Authors' Summary

Vieth, H., Sallotti, S. R. A. and Passerotti, S. [Evaluation and treatment of the dry eye in hanseniasis.] Rev. Bras. Enf. **39** (1986) 118–122. (in Portuguese)

The authors have done this piece of work because there are a lot of dry cornea patients and very few publications about it. They have examined 150 patients from February to March (1986); 66% type V, 16.6% type B, 16.6% type T. Sixty-two percent of the examined patients had dry cornea and the main causes were: low tear production trichiasis, lagophthalmia I (initial and advanced) and ectropium. The treatment of the patients during that period was divided into two levels according to the gravity of the problem: a) simple and total lubrication of the cornea using synthetic lubricant; b) removal of the eyelashes from patients who had trichiasis. Putting that treatment into practice, the authors have observed a 100% recovery in dry cornea patients.—Authors' English Abstract

Weiner, I. D. and Northcutt, A. D. Leprosy and glomerulonephritis: case report and review of the literature. Am. J. Kidney Dis. **13** (1989) 424–429.

Membranoproliferative glomerulonephritis (MPGN) is a common form of glomerulonephritis and frequently is associated with chronic infections. Leprosy, one of the most common infections worldwide, was found in conjunction with MPGN, type 1, in a patient. Serological abnormalities typical of MPGN, improvement in renal

function with therapy of acute complications of leprosy, and long-term renal improvement with antileprosy therapy, all occurred in this patient. Others have found that MPGN is found in 11% to 43% of leprosy patients undergoing renal biopsy. Serological abnormalities typical of MPGN frequently are found in patients with lepromatous leprosy. The association of MPGN and leprosy, and the susceptibility of the glomerulonephritis to therapy, should be emphasized.—Authors' Abstract

Westblom, T. U. and Roller, J. A. Leprosy in Missouri. Missouri Med. **84** (1987) 699–701.

Two case reports demonstrate that leprosy still occurs in this country [U.S.A.]. World travel to countries where the disease is prevalent, and immigration from those locales, would account for most of the cases Missouri physicians are likely to encounter.—Authors' Abstract

Zimmermann, V. R., Wurdel, C. and Kaben, H. [Think of leprosy again and more frequently.] Dermatol. Monatsschri. **174** (1988) 753–761. (in German)

International cooperation and tourism cause diseases of other latitudes—so leprosy, too—to appear more frequently in our regions. Three cases of leprosy observed within one year (two tuberculoid, one borderline-lepromatous leprosy) are presented. Special attention was given to securing the diagnosis as well as the differential diagnosis and therapy. Possible leprosy reactions under therapy and an increase of resistance of *Mycobacterium leprae* to dapsone are pointed out.—Authors' English Summary

Immuno-Pathology

Agrewala, J. N., Ghei, S. K., Sudhakar, K. S., Girdhar, B. K. and Sengupta, U. HLA antigens and erythema nodosum leprosum (ENL). Tissue Antigens **33** (1988) 486–487.

Until now no specific genetic relationship has been identified for erythema nodosum leprosum (ENL). This study was carried out for the first time to examine such a possibility of correlation with HLA antigens.

The frequencies of HLA antigens tested for appeared more or less similar in normal control and LL groups. A nonsignificant ($p > 0.05$) association of HLA-DR2 (28.16%) and DQwl (26.76%) was observed in LL as compared to those (15.06% and 7.21%) of controls.

The frequency of HLA-A11 was 53.84% in ENL patients; whereas it was only 16.90% in LL patients. This difference in the frequency of HLA-A11 was statistically significant ($pc = 0.0035$). For the remaining HLA antigens there was no statistically significant difference. The occurrence of 53.84% of HLA-A11 in the ENL group compared to 16.90% of non-ENL group indicates a possible relationship between A11 positivity and proneness to develop ENL.—(*From the* Article)

Bahr, G. M., Sattar, M. A., Stanford, J. L., Shaaban, M. A., Al Shimali, B., Siddiqui, Z., Gabriel, M., Al Saffar, M., Shahin, A., Chugh, T. D., Rook, G. A. W. and Behbehani, K. HLA-DR and tuberculin tests in rheumatoid arthritis and tuberculosis. Ann. Rheum. Dis. **48** (1989) 63–68.

Responses to four new tuberculins were found to be significantly reduced in 46 patients with rheumatoid arthritis in comparison with a control group of 79. Except for tuberculin itself, the same was found in 111 patients with tuberculosis. In common with patients with tuberculosis and leprosy, those with rheumatoid arthritis did not respond to common mycobacterial (group i) antigen. Three DR haplotypes were found to have significant effects on skin-test responsiveness of the rheumatoid patients but had little or no effect on that of the patients with tuberculosis and none on that of the healthy

control group. Rheumatoid patients with the HLA-DR4 haplotype had significantly greater responses to all four reagents than did non-DR4 patients, but their responses to leprosin A and scrofulin remained significantly lower than those of the control group. Possession of HLA-DR3 haplotype was associated with skin-test positivity approaching normal, but the sizes of responses were reduced. Possession of DR7 was associated with an unexpected reduction in skin-test positivity, especially in the case of tuberculin. These results support the hypothesis that mycobacteria, or autoantigens crossreactive with mycobacteria, may be involved in the etiology of rheumatoid arthritis. The results also show that the regulation and specificity of responsiveness to mycobacterial antigens are different in patients with rheumatoid arthritis with different HLA-DR haplotypes.—Authors' Summary

Bottasso, O., Puig, N., Amerio, N. and Morini, J. C. [Study of T lymphocyte subpopulations in patients with leprosy, using incubation with theophylline.] Med. Cutan. Ibero. Lat. Am. **16** (1988) 397–401. (in Spanish)

T cells and the theophylline resistant cells (The-R helper cells) in peripheral blood of patients with different forms of leprosy were studied. Active lepromatous patients (LL+) showed a significant decrease in T lymphocytes and The-R cells. Nevertheless, in LL+ developing a reactional episode of erythema nodosum (LL-ENL) a restoration in the level of The-R cells was observed. It is concluded that in LL+ patients the depression of T cells and The-R cells represents an imbalance in the T-T cellular cooperation with a defective cellular immune response. On the other hand, the recovery of The-R cells in LL-ENL support the hypothesis of a cell-mediated immune mechanism in the immunopathology of this reactional episode.—Authors' English Summary

Chanteau, S., Plichart, R., Boutin, J.-P., Roux, J. and Cartel, J.-L. Finger-prick blood collection and computer-assisted enzyme-linked immunosorbent assay for large-scale serological studies on leprosy. Trans. R. Soc. Trop. Med. Hyg. **83** (1989) 414–416.

An immunoglobulin M anti-phenolic glycolipid-I assay was standardized and optimized using specimens of dried blood collected on commercial precut filter paper discs, followed by a computer-assisted enzyme-linked immunosorbent assay (ELISA). The correlation between venipuncture and finger-prick methods, the calibration of the quantity of absorbed blood, and the reproducibility of the ELISA test were excellent. A slight decline of activity was observed when the samples were stored for 3 months at +4°C. Skimmed milk can be used as diluent instead of bovine serum albumin, contributing to lessening the cost of the test. Using the method described, as many as 300 samples can be collected in the field and 480 ELISAs per day can be run in the central laboratory by one trained person.—Authors' Abstract

Cooper, C. L., Mueller, C., Sinchaisri, T.-A., Pirmez, C., Chan, J., Kaplan, G., Young, S. M. M., Weissman, I. L., Bloom, B. R., Rea, T. H. and Modlin, R. L. Analysis of naturally occurring delayed-type hypersensitivity reactions in leprosy by in situ hybridization. J. Exp. Med. **169** (1989) 1565–1681.

Analysis of tissue lesions of the major reactional states of leprosy was undertaken to study the immune mechanisms underlying regulation of cell-mediated immunity (CMI) and delayed-type hypersensitivity (DTH) in man. *In situ* hybridization of reversal reaction biopsy specimens for INF-γ mRNA expression revealed a tenfold increase in specific mRNA-containing cells over that observed in unresponsive lepromatous patients. Expression of huHF serine esterase, a marker for T cytotoxic cells, were fourfold increased in reversal reaction and tuberculoid lesions above that detected in unresponsive lepromatous individuals. Immunohistology of reversal reactions confirmed a selective increase of Th and T cytotoxic cells in the cellular immune response. Of interest, the microanatomic location of these serine esterase mRNA-containing cells was identical to the distribution of CD4+ cells.

Analysis of erythema nodosum leprosum

(ENL) lesions revealed differences in the underlying immune processes in comparison with reversal reaction lesions. Although phenotypic Th cells predominated in ENL lesions, IFN-γ and serine esterase gene expression were markedly reduced. We suggest that reversal reactions represent a hyperimmune DTH response characterized by a selective increase of CD4+ IFN-γ-producing cells and T-cytotoxic cells, which result in the clearing of bacilli and concomitant tissue damage. In contrast, ENL reactions may be viewed as a transient diminution of Ts cells and activity leading to a partial and transient augmentation in CMI, perhaps sufficient to result in antibody and immune complex formation, but insufficient to clear bacilli from lesions.—Authors' Summary

de Vries, R. R. P., Ottenhoff, T. H. M. and van Schooten, W. C. A. Human leukocyte antigens (HLA) and mycobacterial disease. Springer Semin. Immunopathol. **10** (1988) 305–318.

In this chapter we will first review the epidemiological studies demonstrating the HLA class II-linked control and the association with certain HLA class II types of the course of mycobacterial infections. Next, we will discuss what is presently know on HLA class II Ir-genes, their products and their regulation of the immune response. Finally, we will review the studies indicating HLA class II Ir-gene control of the immune response against mycobacterial antigens and its implications for the pathogenesis of leprosy and tuberculosis as well as for the development of an effective vaccine. Because most information is available for leprosy, that disease will be discussed in greater detail. However, we think that the main conclusions drawn for leprosy also apply to tuberculosis and other mycobacterial diseases.—(*From the* Chapter)

Dersimonian, H., McAdam, K. P. W. J., Macworth-Young, C. and Stollar, B. D. The recurrent expression of variable region segments in human IgM anti-DNA autoantibodies. J. Immunol. **142** (1989) 4027–4033.

RNA sequences for the V regions of human hybridoma-produced autoantibodies were determined by primer extension will reverse transcriptase. The sequencing of IgM autoantibodies from a leprosy patient revealed examples of recurrent use of V region gene segments in different autoantibodies from this patient and a previously studied patient with systemic lupus erythematosus (SLE). Moreover, several gene segments used in these autoantibodies show little alteration from germ-line sequences. mAb TH3, from a patient with leprosy, binds denatured DNA and poly(dT). The center of its H chain CDR3[5] has a sequence identical to that found previously in two anti-DNA antibodies from a lupus patient; these identities and their overlapping with two other published sequences define a human D-gene segment of approximately 25 nucleotides. Autoantibody TH9, from a leprosy patient, does not bind DNA. Its V_H sequence has 87% identity with a V_HI anti-DNA antibody, but differs from it markedly in the CDR1 region. TH9 also has a different H chain CDR3. The closely related J_H4 or J_H5 gene segments are expressed in five lupus or leprosy autoantibodies. In four of the antibodies, examples of Vκ1, Vκ3, or Vκ4 and Jκ2, or Jκ5 segments were found. Two distinct leprosy-derived anti-DNA antibodies, 8E10 and TH3, share a completely identical Vκ sequence. This sequence differs in only two positions from that of a germ-line RF L chain gene. Several gene segments that are close to the germ line in sequence encode Ig V regions with autoantibody reactivity. These results provide a baseline for determining whether these genes are precursors of more highly diversified antibodies that may be pathogenic in patients with SLE.—Authors' Abstract

Dhandayuthapani, S., Anandan, D., Vasanthi, B. and Bhatia, V. N. Use of eluates of filter paper blood spots in ELISA for the serodiagnosis of leprosy. Indian J. Med. Res. **89** (1989) 150–157.

Blood samples were collected from 59 leprosy patients and 35 normal healthy subjects by the venipuncture and finger-prick methods to obtain serum samples and blood spots on filter paper, respectively. The serum samples at 1:300 dilutions and the eluates of dried blood spots at 1:40, 1:80, 1:160 and 1:320 dilutions were applied in

ELISA to measure the antibody levels (IgM) against synthetic ND-O-BSA antigen. The antibody levels were found to be higher in the multibacillary leprosy patients than the paucibacillary patients, irrespective of whether serum samples or eluates were used. The OD values obtained at a 1:160 dilution of the eluates were equivalent to that of values obtained at the 1:300 dilution of the serum samples. The positivities differ in different dilution of the eluates, showing the highest in the 1:40 dilution and the lowest in the 1:320 dilution.—Authors' Abstract

Dockrell, H. M., Stoker, N. G., Lee, S. P., Jackson, M., Grant, K. A., Jouy, N. E., Lucas, S. B., Hasan, R., Hussain, R. and McAdam, K. P. W. J. T-cell recognition of the 18-kilodalton antigen of *Mycobacterium leprae*. Infect. Immun. **57** (1989) 1979–1983.

The 18-kilodalton (kDa) antigen of *Mycobacterium leprae* was expressed as a fusion protein with a 2-kDa leader peptide and used in proliferation assays with peripheral blood cells. Fifty percent of untreated tuberculoid leprosy patients and 93% of long-term leprosy contacts responded to the recombinant protein in lymphocyte transformation tests. Comparison of the stimulation indices in the two groups showed that the contacts responded more strongly than the tuberculoid leprosy patients. Seventy percent of *M. bovis* BCG-vaccinated European donors responded, although with low stimulation indices. The isolation of 18-kDa antigen-responsive T-cell lines from a BCG-vaccinated British donor confirmed that the 18-kDa antigen contains at least one crossreactive epitope. These results indicate that the 18-kDa protein is an important antigen in the immune response to leprosy.—Authors' Abstract

Filley, E., Andreoli, A., Steele, J., Waters, M., Wagner, D., Nelson, D., Tung, K., Rademacher, T., Dwek, R. and Rook, G. A. W. A transient rise in agalactosyl IgG correlating with free interleukin 2 receptors, during episodes of erythema nodosum leprosum. Clin. Exp. Immunol. **76** (1989) 343–347.

The proportion of oligosaccharide chains on the Fc fragment of IgG which terminate with *N*-acetylglucosamine and not galactose (%GO) has previously been shown to be raised in rheumatoid arthritis (RA), Crohn's disease (CD) and tuberculosis (TB), but to be normal in sarcoidosis (SA), and in both lepromatous and tuberculoid leprosy. However, we have now studied %GO in sequential serum samples collected from lepromatous leprosy patients undergoing episodes of erythema nodosum leprosum (ENL). During ENL %GO is transiently raised, and this rise parallels an increase in circulating interleukin 2 receptors (IL-2R). These findings confirm that changes in T-cell function occur during ENL. Moreover it appears that %GO rises when there is, simultaneously, T-cell-mediated tissue damage and an acute phase response (RA, CD, TB, ENL), but not when there is an acute phase response without major T-cell involvement, or chronic T-cell activity alone (SA, and tuberculoid leprosy). We suggest therefore that %GO is an indicator of a type of T-cell activity with broad immunopathological implications.—Authors' Summary

Filley, E., Abou-Zeid, C., Waters, M. and Rook, G. The use of antigen-bearing nitrocellulose particles derived from Western blots to study proliferative responses to 27 antigenic fractions from *Mycobacterium leprae* in patients and controls. Immunology **67** (1989) 75–80.

Antigens present in sonicates of *Mycobacterium leprae* were separated by SDS-PAGE, blotted electrophoretically onto nitrocellulose, and visualized with a colloidal gold stain. Six bands identified by existing monoclonal antibodies, and a further 21 bands not previously studied, were converted into antigen-bearing nitrocellulose particles for use in *in vitro* lymphoproliferation studies. Controls (putative noncontacts) responded poorly to the antigenic fractions presented in this way. Contacts responded variably to a wide range of the antigens, and most frequently (23%) to the 18,000 MW fraction. Responses to this, and to several other low molecular weight antigens, were not seen in noncontacts, and were very rare in all patient groups, which tended to respond to high-molecular-weight components. The most interesting individual band was at 36,000 MW. This caused

significant stimulation of cells from 25% of tuberculoid donors, but never stimulated the cells from lepromatous cases. Indeed, this fraction significantly suppressed the background proliferation of the cells from 30% of the lepromatous cases, although the significance of this observation is unclear. Responses to the 65,000 MW heat-shock protein did not differ significantly between the donor groups. Overall, the results suggest that the spectrum of clinical leprosy may not be determined by the response to any one antigen. However, this study cannot rule out the possibility that the response to one or a few antigens determines the outcome during the first few days after infection.—Authors' Summary

Gimenez, M. F., Gigli, I. and Tausk, F. A. Differential expression of Langerhans cells in the epidermis of patients with leprosy. Br. J. Dermatol. **121** (1989) 19–26.

Eighteen patients with lepromatous leprosy (LL) showed a significant reduction ($p < 0.001$) of Langerhans' cells (LC) irrespective of whether the biopsies were obtained from involved (398 ± 186) or healthy skin (304 ± 98). The cells showed morphological changes consisting mainly of loss of dendritic processes. Twenty-four controls (age-, sex- and race-matched) had a mean number of LC of 632 ± 138. In tuberculoid patients (TT) significant differences were observed, depending on the site of biopsy. Nine biopsies from involved skin had 993 ± 206 LC; whereas 11 from healthy skin had 448 ± 96 ($p < 0.001$). This difference was confirmed in six additional borderline tuberculoid (BT) and TT patients in whom biopsies were simultaneously obtained from involved (973 ± 179) and uninvolved skin (498 ± 99). In 10 patients with indeterminate leprosy the LC density did not differ from the control population (630 ± 261). The expression of LC numbers in BT and TT patients may represent migration of these cells from healthy skin to involved areas or mobilization of a central pool. The low density found in LL patients could interfere with adequate presentation of mycobacterial antigens leading to tolerance. Alternatively, the presence of T-helper cells in TT infiltrates may produce factors that recruit LC; their absence in LL lesions may account for the decrease in LC expression.—Authors' Summary

Hancock, G. E., Cohn, Z. A. and Kaplan, G. The generation of antigen-specific, major histocompatibility complex-restricted cytotoxic T lymphocytes of the CD4+ phenotype; enhancement of the cutaneous administration of interleukin 2. J. Exp. Med. **169** (1989) 909–919.

We have examined an *in vitro* system in which peripheral blood mononuclear cells (PBMC) from purified protein derivative (PPD)-sensitized patients generate cytotoxic T lymphocytes (CTL) after *in vitro* activation with antigen. These cells selectively destroy mycobacterial antigen PPD-pulsed monocyte targets. These CTL are of the CD4+ phenotype and exhibit MHC class II restriction. After exposure to antigen these cells require 5–7 days for maximal development; whereas a separate antigen-independent population is generated within 3–4 days. CD8+ cells are poorly, if not at all, cytotoxic under similar conditions. Cells with properties of the natural killer (NK) and lymphokine-activated killer (LAK) lineage are also present in these cultures and kill other specific targets. Human rIL-2 was injected into the skin of lepromatous patients at 10-μg doses, given at 48-hr intervals, for three doses. Peripheral blood cells obtained 8–14 days after the initiation of IL-2 injection demonstrated enhanced antigen-dependent destruction of monocyte targets. The efficacy of antigen-dependent and -independent populations and their amplification by IL-2-dependent mechanisms is discussed in terms of the local destruction of parasitized macrophages and the subsequent disposal of *Mycobacterium leprae*.—Authors' Summary

Harada, K. and Suzuki, K. Improved staining of leprosy bacilli in tissues. Lepr. Rev. **60** (1989) 124–128.

A technique which reliably demonstrates *Mycobacterium leprae, M. tuberculosis,* and fungi in tissues is described. It is based on the oxidation of cell-wall lipid substances by chromic or periodic acid, and the subsequent release of aldehydes which are then capable of reducing ammoniacal silver salt

solutions to metallic silver. The organisms so demonstrated appear uniformly solid. The sensitivity of the method and the ease of examination and recognition of bacilli and their products are recommendations for the use of the method in diagnosis and research, disregarding morphological appearances.—Authors' Summary

Harboe, M. Rheumatoid factors in leprosy and parasitic diseases. Scand. J. Rheumatol. Suppl. **75** (1988) 309–313.

Rheumatoid factors (RFs) occur with higher frequency and in higher titers in multibacillary forms of leprosy and several parasitic diseases than in healthy controls. The selection of controls is essential in studies of this kind. They should be individuals without signs of the disease under study living under similar socioeconomic conditions as the patients in the endemic country. In three studies where this matter was considered, RFs in lepromatous leprosy and Chagas' disease reacted more strongly with rabbit than human IgG, a feature generally considered to be quite restricted to rheumatoid arthritis. RFs interfere in various test systems, particularly in inducing false-positive reactions for specific IgM antibodies in parasitic and other infectious diseases. Model experiments in rats, *in vitro* culture studies, and observations in humans indicate that RFs may have a protective role in trypanosome infections, malaria and schistosomiasis, respectively.—Author's Abstract

Kaplan, G., Sampaio, E. P., Walsh, G. P., Burkhardt, R. A., Fajardo, T. T., Guido, L. S., Machado, A. de M., Cellona, R. V., Abalos, R. M., Sarno, E. N. and Cohn, Z. A. Influence of *Mycobacterium leprae* and its soluble products on the cutaneous responsiveness of leprosy patients to antigen and recombinant interleukin 2. Proc. Natl. Acad. Sci. U.S.A. **86** (1989) 6269–6273.

Experiments were carried out in the skin of patients with leprosy to examine whether suppressor-cell populations either exist in the skin of multibacillary lepromatous leprosy patients, can be activated with antigen, or are induced to emigrate into a cutaneous site from the circulation. For this purpose, purified protein derivative of tuberculin, a delayed-type antigen that generates a cell-mediated immune response, was introduced into the skin alone or with nonviable *Mycobacterium leprae* bacilli. Areas of induration and the resulting numbers and phenotypes of emigratory cells were not influenced by *M. leprae* and its products. Further studies examined the ability of *M. leprae* and its soluble products to modify the cutaneous response to intradermal injection of recombinant interleukin 2 (IL-2), a lymphokine that mimics a cell-mediated response. Neither the simultaneous injection of *M. leprae* and IL-2, nor the prior injection of *M. leprae* followed in 2 days by IL-2, nor the prior administration of IL-2 followed in 4 days by *M. leprae,* into the same skin site modified the zone of induration generated by IL-2. In addition, the immunocytochemical and histopathological evaluation of biopsy specimens of skin sites showed no difference between sites injected with IL-2 and sites injected with IL-2 and *M. leprae.* We conclude that suppressor-T cells, if they exist, do not influence the gross or microscopic responsiveness of a cell-mediated skin reaction to antigen and IL-2. IL-2 did, however, enhance the responsiveness of skin-test-positive tuberculoid patients and family contacts to *M. leprae* antigens by a synergistic effect on the zone of induration and local cell accumulation.—Authors' Abstract

Kaufmann, S. H. E. and Flesch, I. E. A. The role of T cell-macrophage interactions in tuberculosis. Springer Semin. Immunopathol. **10** (1988) 337–358.

Acquired resistance against tuberculosis paradigmatically depends on specific T lymphocytes and mononuclear phagocytes. The etiological agent, *Mycobacterium tuberculosis,* is capable of replicating in mononuclear phagocytes which act both as habitat and as effectors of protection. Upon interaction with antigen-specific T lymphocytes infected mononuclear phagocytes acquire tuberculostatic activities. Here, data from experimental tuberculosis studies in mice are summarized which show that: interleukins produced by cloned T cells and recombinant interferon-γ are capable of activating

tuberculostatic capacities in macrophages; both CD4 and CD8 T cells, after adequate stimulation, produce interferon-γ; CD8 T cells lyse macrophages in an antigen-specific way; not only CD8 but also CD4 T cells possess an antigen-specific cytolytic potential; lysis of infected macrophages results in mycobacterial growth inhibition. Evidence is also presented that tuberculostatic activities of activated macrophages depend on phagosome-lysosome fusion and are independent of reactive oxygen metabolites and that some strains of *M. tuberculosis* are resistant against interferon-γ-activated macrophages. These findings suggest that both helper- and cytolytic-T cells participate in the immune response to tuberculosis and that similar T-cell mechanisms contribute to resistance as well as pathogenesis. Protection against tuberculosis, therefore, depends on subtle coordination of the immune response.—Authors' Abstract

Kim, S. J., Choi, I. H., Cho, S. N., Kim, S. H. and Kim, J. D. The leukocyte inhibitory factor and circulating immune complex in leprosy patients. Yonsei Med. J. **29** (1988) 316–320.

To investigate leukocyte inhibitory factor (LIF) production and circulating immune complexes (CIC) in leprosy, peripheral blood mononuclear cells (PBMC) from 61 patients and sera from 60 patients were tested. The results indicate that there is a defect in LIF production in the lepromatous (LL) or borderline lepromatous (BL) types compared to the tuberculoid (TT) type (mean migration index = 66.0 ± 16.0 in LL, 61.1 ± 15.3 in BL, 51.9 ± 11.2 in TT) ($p < 0.05$). The number of patients with positive CIC was higher among the LL patients (30%) than the TT patients (20%). There was also positive correlation between the bacterial index (BI) and the CIC level ($r = 0.46$, $p < 0.05$). The correlation between CIC and LIF in LL patients and the possibility ($p = 0.06$) that the increase in CIC may account for the decrease in LIF production in LL patients and vice versa are discussed.—Authors' Abstract

Kingston, A. E., Bergsteinsdottir, K., Jessen, K. R., Van der Meide, P. H., Colston, M. J. and Mirsky, R. Schwann cells cocultured with stimulated T cells and antigen express major histocompatibility complex (MHC) class II determinants without interferon-γ pretreatment: synergistic effects of interferon-γ and tumor necrosis factor on MHC class II induction. Eur. J. Immunol. **19** (1989) 177–183.

Schwann cells (SC) do not express major histocompatibility complex (MHC) class II antigens under normal culture conditions. SC can, however, be induced *in vitro* to express MHC class II molecules by exposure to high concentrations of interferon-gamma (IFN-γ) and can present antigens to antigen-specific T-cell lines. In the present study, immunohistochemical labeling showed that most SC (> 90%) prepared from rat neonatal sciatic nerves expressed MHC class II molecules when cultured together with mycobacterial antigen and T cells, and as a consequence were able to function as antigen-presenting cells in lymphoproliferation assays, without requiring pretreatment with IFN-γ. Antigen or T cells alone were ineffective in stimulating MHC class II expression and induction of class II molecules was MHC restricted, requiring the presence of syngeneic T cells. Addition of monoclonal antibody DB1, directed against IFN-γ to cocultures of SC and T lymphocytes stimulated with antigen, prevented the induction of MHC class II antigen on SC. When SC were incubated with recombinant (r)IFN-γ alone, up to 50% of SC showed positive labeling for MHC class II antigen. This level of expression was enhanced to > 80% when recombinant tumor necrosis factor (rTNF) was also added. rTNF alone had no effect, and addition of DB1 antibody inhibited the synergistic effects of rTNF on MHC class II expression. The effects of rIL4 were also investigated but neither rIL4 alone nor rIL4 in combination with rIFN-γ induced MHC class II expression by SC. These results show that in the presence of sensitized T lymphocytes and antigen, SC do not require pretreatment with exogenous rIFN-γ to express MHC class II antigens and function as antigen-presenting cells. T-cell-derived TNF and IFN-γ appear to act as mediators of the T-cell-induced expression of MHC class II by SC.—Authors' Abstract

Kumar, R. Mast cells in histoid lepromatous lesions. Hansen. Int. **10** (1985) 1–4.

Ten patients with histoid lesions among the lepromatous leprosy cases, of both sexes in the age group of 35–65 years, were included in this study. Skin biopsy from the nodule with surrounding healthy skin of histoid lesion was taken. The biopsies were fixed in Susa solution and processed for light microscopy; 5–7 μ-thick sections were cut and stained with hematoxylin and eosin, toluidine blue and Fite-Faraco. Observations were made on the dermis to locate the mast cells and bacilli. Proliferation of mast cells and their degranulation were seen in the histoid nodule as compared to surrounding normal healthy skin where the cells were mainly intact. The study further investigates the role of mast cells in the histopathogenesis of the disease.—Author's Abstract

Lee, S. P., Stoker, N. G., Grant, K. A., Handzel, Z. T., Hussain, R., McAdam, K. P. W. J. and Dockrell, H. M. Cellular immune responses of leprosy contacts to fractionated *Mycobacterium leprae* antigens. Infect. Immun. **57** (1989) 2475–2480.

Antigens of armadillo-derived *Mycobacterium leprae* sonic extract were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, blotted onto a nitrocellulose membrane, and the unstained blot was converted into 20 fractions of antigen-bearing particles. These were tested in cellular proliferation assays, and reproducible results were obtained between batches of fractions. Peripheral blood mononuclear cells from healthy contacts of leprosy patients (presumed to have protective immunity) were tested with the fractions to investigate which antigens they recognized. A small group of tuberculoid leprosy patients were also tested. Both groups showed a wide range of responses. Almost every fraction stimulated proliferation with at least one donor, yet none was clearly immunodominant or inhibitory in either group. Thus, protective immunity did not appear to be associated with proliferation caused by any single fraction.—Authors' Abstract

Løvik, M. and Closs, O. Local reactivity, local resistance and systemic dissemination in *Mycobacterium lepraemurium* (MLM) infection. Clin. Exp. Immunol. **75** (1989) 461–465.

Local reactivity measured as swelling of the infected foot pad, local resistance to bacterial multiplication, and capacity to limit systemic dissemination were studied in C57BL, C3H/Bom, C3H/HeJ, and A/Sn mice inoculated with *Mycobacterium lepraemurium*. C57BL mice developed a strong local reaction with a sudden onset, and effectively limited local multiplication as well as systemic dissemination of bacteria to the liver and spleen as determined 19 weeks after the inoculation. C3H/Bom mice showed no local reaction, had high numbers of bacteria locally, and had extensive systemic dissemination of the infection. C3H/HeJ mice, on the other hand, developed a small local reaction and had less systemic dissemination of bacteria than C3H/Bom mice. In C57BL mice and in the two C3H substrains local reactivity, local resistance to infection, and resistance to systemic spread of the infection paralleled each other. In contrast, A/Sn mice showed a small local reaction, had the most extensive bacterial multiplication at the site of inoculation of the four mouse strains tested, and at the same time were the mice that most effectively restricted systemic dissemination of the infection. Thus, the mechanisms restricting local bacterial multiplication may be different from the mechanisms limiting bacterial dissemination. Neither bacterial growth locally at the site of subcutaneous inoculation in the foot pad, nor systemic dissemination of the infection, followed a mouse strain pattern consistent with the *Ity/Lsh/Bcg* gene model. In experimental mycobacterial infection both local bacterial growth at the site of inoculation and systemic dissemination should be determined.—Authors' Summary

Makonkawkeyoon, S. and Kasinrerk, W. *In vitro* suppression of interleukin 2 production by *Mycobacterium leprae* antigen. Clin. Exp. Immunol. **76** (1989) 398–403.

The suppressive activity of three different lots and sources of *Mycobacterium leprae* was studied by measuring the inhibitory ef-

fect on interleukin 2 (IL-2) production in normal subjects. All three *M. leprae* preparations had suppressive activity on IL-2 production when peripheral blood mononuclear leukocytes (PBML) were stimulated with the mitogens PHA-P or ConA in a dose response. *M. leprae* also had suppressive activity on IL-2 production when PBML were stimulated with the specific antigen, PPD. The inhibitory activity of *M. leprae* on IL-2 was not due to the direct interaction of *M. leprae* and IL-2 because direct mixing of IL-2 with different concentrations of *M. leprae* did not alter the activity of IL-2. Incorporation of *M. leprae* for 0, 6 and 12 hr in PHA-P and PBML cultures had no inhibitory effect on IL-2 production; however, after 14, 16 and 18 hr of *M. leprae* incorporation, significant inhibitory effects were noted on IL-2 production. The suppressive mechanism of *M. leprae* was studied by incorporating *M. leprae* into PBML or adherent cells. The suppressive activity could be detected in both *M. leprae*-stimulated PBML and *M. leprae*-stimulated monocyte supernatant fluids. The suppressive mechanism of *M. leprae* was further evaluated by incorporating 1 and 2 μg/ml of indomethacin in PBML containing PHA-P and *M. leprae*. The suppressive activity of *M. leprae* was significantly diminished by indomethacin, suggesting that the inhibitory effect of *M. leprae* may result from the induction of PBML and adherent cells to produce the immunosuppressive activity of prostaglandin(s).—Authors' Summary

Malarkannan, S., Chakkalath, H. R. and Muthukkaruppan, V. R. Impairment of alternate pathway (CD2) of T cell activation in leprosy. J. Biosci. **14** (1989) 29–36.

Recent studies in basic immunology have been directed toward the understanding of the mechanism of T-cell activation. T cells can be activated to proliferate via the classical pathway through the antigen receptor (CD3-Ti) or via the alternate pathway through the CD2 receptor. Since immunologic unresponsiveness in lepromatous leprosy is considered to be due to the inability of T cells to proliferate upon stimulation, we have been interested in the nature of these receptors and the activation pathways in lymphocytes of leprosy patients. In the present investigation we demonstrate: a) CD2 receptor (E-receptor) is downregulated in bacterial index positive lepromatous leprosy patients. b) The alternate pathway of T-cell activation is impaired in lepromatous patients as revealed by the inability of their lymphocytes to proliferate in response to a pair of mitogenic anti-CD2 monoclonals. c) The addition of recombinant interleukin 2 *in vitro* restores the ability of lymphocytes from lepromatous patients to proliferate in response to anti-CD2 antibodies. d) Interestingly, CD2 modulation and the associated functional impairment could be brought about in peripheral blood lymphocytes from normal subjects by prior treatment with *Mycobacterium leprae in vitro*. This approach would be useful in understanding the molecular events leading to the defective T-cell functions in leprosy.—Authors' Abstract

Maslov, A. K. and Yuschenko, A. A. [Assessment of leprous macrophages function.] Arkh. Patol. **50** (1988) 51–54. (in Russian)

Cytochrome oxidase (CCO), peroxidase, succinic dehydrogenase (SDG), and NADH-diaphorase were studied electron-cytochemically in leprous macrophages (LM) of granulomas of patients suffering from lepromatous leprosy. The LM peroxidase activity and location differed, this affecting the completeness of *Mycobacterium leprae* phagocytosis. High CCO activity in LM cytoplasm was not a factor essentially influencing *M. leprae* disintegration. SDG and NADH-diaphorase, locating predominantly in membraneous structures of *M. leprae*, show some activity in LM cytoplasm.—Authors' English Summary

Mittal, A., Mishra, R. S. and Nath, I. Accessory cell heterogeneity in lepromatous leprosy; dendritic cells and not monocytes support T cell responses. Clin. Exp. Immunol. **76** (1989) 233–239.

Dendritic cell (DC)-enriched cell populations from anergic lepromatous leprosy (LL) patients were found to be several-

hundred-fold more efficient than monocytes (MO) in promoting antigen-induced T-cell responses in autologous accessory + T-cell cultures. Whereas, the use of autologous monocytes over a wide concentration range failed to stimulate *Mycobacterium leprae*-induced T-cell proliferation, DC at concentrations as low as 0.1% induced significant proliferation in 9/15 and interferon-gamma (INF-γ) production in 14/15 LL patients. Four of the LL patients who failed to show proliferation were, however, able to secrete INF-γ in the same T cell + DC co-cultures. DC were able to present particulate leprae antigens to autologous T cells. This preference for DC as an accessory cell was not shown when the crossreacting antigen PPD was used in parallel co-cultures. Although tuberculoid leprosy patients showed some improvement in T-cell proliferation with DC as compared to MO-constituted co-cultures, this was not statistically significant. These results suggest that there is a heterogeneity in accessory cell requirement across the leprosy spectrum and that many lepromatous patients possess *M. leprae*-reactive functional T cells.—Authors' Summary

Modlin, R. L., Pirmez, C., Hofman, F. M., Torigian, V., Uyemura, K., Rea, T. H., Bloom, B. R. and Brenner, M. B. Lymphocytes bearing antigen-specific $\gamma\delta$ T-cell receptors accumulate in human infectious disease lesions. (Letter) Nature **339** (1989) 544–548.

The majority of T cells bear the T-cell receptor (TCR) $\alpha\beta$ complex which recognizes foreign antigen peptides only in the context of self major histocompatibility complex (MHC) molecules. Such T cells function in a variety of effector roles and secrete cytokines that mediate the activation and differentiation of other cells in the immune system. Recently, a small subpopulation T cells was found to bear a distinct TCR composed of γ and δ subunits. In man, TCR $\gamma\delta$+ cells are distributed as ~5% of the CD3+ cells in all organized lymphoid organs as well as in the skin- and gut-associated lymphoid tissues. Although a limited number of germ-line genes encode the TCR γ and δ subunits, extensive junctional variation particularly in the δ gene, results in unprecedented diversity for this receptor. The nature of the specificity and immunological functions of these T cells remains enigmatic. We report here that in contrast to the normal low frequency of $\gamma\delta$-bearing cells in lymphoid tissues, peripheral blood, or normal skin, the frequency is increased five- to eightfold in particular granulomatous reactions of leprosy. TCR $\gamma\delta$+ lymphocyte lines from these leprosy skin lesions proliferate *in vitro* specifically to mycobacterial antigens. This reactivity to foreign antigens appears to require presentation in the context of self-molecules. Moreover, culture supernatants from activated $\gamma\delta$ T lymphocytes induce adhesion and aggregation of bone-marrow monocytes in the presence of granulocyte monocyte-colony stimulating factor (CSF), suggesting that products of $\gamma\delta$-bearing T cells may play a role in the immune response, possibly by stimulating granuloma formation.—Authors' Abstract

Mor, N., Goren, M. B. and Crowle, A. J. Enhancement of growth of *Mycobacterium lepraemurium* in macrophages by gamma interferon. Infect. Immun. **57** (1989) 2586–2587.

Gamma interferon, an immune lymphokine that protects mouse macrophages against infection by several parasites, was ineffective against *Mycobacterium lepraemurium*. On the contrary, it significantly stimulated multiplication of *M. lepraemurium* in the macrophages. Simultaneous treatment of macrophages with gamma interferon and interleukin-4 or interleukin-2, or a combination of all three, did not enhance the macrophage resistance to infection with *M. lepraemurium*, but instead stimulated growth of *M. lepraemurium*.—Authors' Abstract

Narayanan, R. B., Natarajan, M., Katoch, K. and Sengupta, U. CD1-positive epidermal Langerhans cells in skin reactions to autologous peripheral-blood-derived mononuclear cells in leprosy patients. Int. Arch. Allergy Appl. Immunol. **89** (1989) 38–42.

A comparison was made on the characteristics of the infiltrates, the number and

distribution of CD1-positive epidermal Langerhans' cells (LC) at the sites of skin reaction induced by autologous peripheral-blood-derived mononuclear cells (PBMC) in leprosy patients. Clinically and histologically, the skin reaction was well expressed in tuberculoid patients as compared to lepromatous patients, erythema nodosum leprosum (ENL) patients, and contacts. The quantum of lymphocytes in the infiltrates was maximal in the tuberculoid patients, and it was minimal in lepromatous and ENL patients. The number and distribution of LC in the tuberculoid patients was significantly higher in the PBMC-inoculated sites as compared to control sites over 24 hr. In contrast, no difference in the number and distribution of LC was noticed in the lepromatous and ENL patients. These observations indicate that the lymphocytes of tuberculoid patients in contrast to lepromatous leprosy patients are capable of sustenance in the local micro-environments of the skin and an effective interaction may be possible between LC and PBMC.—Authors' Abstract

Ottenhoff, T. H. M., Converse, P. J., Gebre, N., Wondimu, A., Ehrenberg, J. P. and Kiessling, R. T cell responses to fractionated *Mycobacterium leprae* antigens in leprosy. The lepromatous nonresponder defect can be overcome *in vitro* by stimulation with fractionated *M. leprae* components. Eur. J. Immunol. **19** (1989) 707–713.

Protective immunity against *Mycobacterium leprae* is dependent on *M. leprae*-reactive T lymphocytes. *M. leprae*-directed T-cell reactivity is high in the localized tuberculoid form of leprosy but specifically absent in the disseminated lepromatous type of the disease.

Two important questions that are relevant for the understanding of the immune response in leprosy as well as for the design of rational immunoprophylaxis and therapy strategies are: a) what are the antigens that trigger T-cell responses in tuberculoid patients and thus protect these individuals from developing lepromatous leprosy, and b) is it possible to restore T-cell responsiveness to *M. leprae* in lepromatous patients by rechallenging the immune system with selected antigens that will trigger help but not suppression? We have addressed these questions by directly probing the peripheral T-cell repertoire of 10 tuberculoid and 18 lepromatous patients with large numbers of different *M. leprae* and BCG antigenic components that had been separated on the basis of their relative molecular mass (M_r) by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and electroblotted onto nitrocellulose. This technique allows the identification of T-cell-stimulating antigens independent of the expression of B-cell epitopes by these antigens. So far, T-cell epitopes have only been mapped on *M. leprae* proteins that had previously been defined by antibodies. Our results show that: a) tuberculoid patients' T cells responded preferentially to *M. leprae* and BCG antigens in the lower (i.e., < 70 kDa) M_r range with a peak in the 10–25 kDa range; b) 6 out of 18 lepromatous patients who did not respond to whole *M. leprae* responded strongly to isolated *M. leprae* components; antigens in the lower M_r range were recognized by 5 out of these 6 patients and thus commonly seen by both tuberculoid and lepromatous patients' T cells; however, antigens in the higher M_r range, in particular > 150 kDa, were only recognized by lepromatous patients' T lymphocytes; c) furthermore, the T- and B-cell repertoires in leprosy patients are skewed toward different antigenic fractions.—Authors' Abstract

Ranade, A. and Mahadevan, P. R. A component of *Mycobacterium leprae* as a serodiagnostic tool for leprosy. Indian J. Biochem. Biophys. **25** (1988) 554–559.

It has been observed that the delipidified component of the cell wall of *Mycobacterium leprae* (DCW), when used as an antigen, can distinguish and show different binding ability to sera of lepromatous leprosy patients and of healthy normals or tuberculoid leprosy individuals. This was demonstrated by the ELISA technique. Long-term treated (> 4 years), bacteriologically negative lepromatous individuals showed no antibody in the sera for DCW. The level of antibody to DCW declined in patients undergoing treatment, and this appeared to happen rather rapidly. This could

be indicative of the reduction in the quantum of viable *M. leprae* as was demonstrated with patients who were followed through several months of chemotherapy. The test appears to be specific. It is possible that whole DCW or some antigens associated with it could function as a specific serodiagnostic reagent for lepromatous leprosy.—Authors' Abstract

Rasheed, F. N., Locniskar, M., McCloskey, D. J., Hasan, R. S., Chiang, T. J., Rose, P., de Soldenhoff, R., Festenstein, H. and McAdam, K. P. W. J. Serum lymphocytotoxic activity in leprosy. Clin. Exp. Immunol. **76** (1989) 391–397.

Sera from 167 patients across the spectrum of leprosy and 46 endemic controls were screened for lymphocytotoxic activity (LCA). The Terasaki microdroplet lymphocytotoxicity assay was performed at 37°C and 15°C to test sera for LCA against a panel of lymphocytes from 50 donors which represented most known HLA-ABC antigens. Raised complement-dependent LCA at 15°C was seen in leprosy patients with histories of erythema nodosum leprosum (ENL) or reversal/type 1 reactions. Eighty-six percent of lepromatous (LL) patients with a history of ENL ($N = 21$, $p < 0.001$), 83% of borderline lepromatous (BL), and 88% of borderline tuberculoid patients (BT) with a history of type 1 reactions ($N = 12$, $p < 0.01$ and $N = 24$, $p < 0.001$, respectively) had LCA compared to 39% of endemic controls ($N = 46$). LCA was attributed to IgM on the basis of reduced activity when serum was treated with both dithiothreitol or absorbed with antiserum for IgM. Removal of immune complexes and rheumatoid factor did not influence LCA. LCA-positive sera reacted similarly with allogeneic lymphocytes from either healthy donors or leprosy patients. Moreover LCA-positive sera reacted with autologous lymphocytes. Specificities for HLA-ABC antigens were not identified. The potential role of these autoantibodies manifested in leprosy patients with hypersensitivity reactions remains speculative.—Authors' Summary

Turcotte, R. and Lemieux, S. Unresponsiveness to ConA in spleen cell cultures of *M. lepraemurium*-infected mice is dependent on a defective expression of high-affinity IL-2 receptors rather than on a lack of IL-2 production. Clin. Exp. Immunol. **76** (1989) 126–131.

The production of interleukin-2 (IL-2) by ConA-activated spleen cells (SC) progressively declined and reached negligible values during the course of infection of C57BL/6 mice with *Mycobacterium lepraemurium*. In addition, the capacity of cultured SC to utilize IL-2 was highly reduced, as demonstrated by the accumulation of IL-2 activity in culture supernatants at 48 and 72 hr after ConA activation. The depressed IL-2 utilization started to be observed about 1 to 2 weeks prior to the onset of the depressed IL-2 production and was not reversed by the addition of exogenous IL-2; thus implying that a lack of IL-2 utilization rather than a lack of IL-2 production could be directly responsible for the inhibition of T-cell proliferative responses to ConA in SC cultures of infected mice. The utilization of IL-2 was found to be down-regulated, at least in part, by splenic suppressor cells since, in mixed-culture experiments, SC from infected mice actively depressed the capacity of normal splenocytes to consume IL-2. Finally, the depressed IL-2 utilization would result from a two- to threefold reduction of either or both the density of high-affinity IL-2 receptors and their affinity for IL-2.—Authors' Summary

Williams, R. C. Rheumatoid factors in subacute bacterial endocarditis and other infectious diseases. Scand. J. Rheumatol. Suppl. **75** (1988) 300–308.

Rheumatoid factors (RF) occur during the course of various infections, such as leprosy, infective endocarditis, tuberculosis, trypanosomiasis, visceral larva migrans, infectious mononucleosis, influenza A, hepatitis A or cytomegalovirus. When first described, it seemed logical to assume that host-selfimmunization with autologous immune complexes provided the initial stimulus for RF production. Subsequently, extensive characterization of bacterial, parasitic and viral Fc receptors has suggested an alternative explanation for RF associated with infections. It seems possible that patients make an ini-

tial immune response to infecting agent Fc receptors and that anti-anti-Fc receptors or anti-idiotypes either then directly stimulate RF production or are themselves rheumatoid factors. Such an hypothesis might also be applied to rheumatoid arthritis itself, where either infecting agent or autologous cell Fc receptors could be the initial immunizing epitopes involved in RF production.—Author's Abstract

Microbiology

Chakrabarty, A. N., Das, S., Bhattacharya, C. P. and Dastidar, S. G. Metabolism of fossil fuels by chemoautotrophic nocardioform bacteria from infectious leprosy tissues and its implications. Indian J. Exper. Biol. **26** (1988) 845–847.

Acid-fast nocardioform chemoautotrophic bacteria isolated from infectious human and animal leprous tissues were found to metabolize fossil fuels/derivatives, in addition to tetradecane and liquid paraffin reported earlier. These were: benzene, naphthalene, toluene, xylene, aniline and diphenylamine, derived from coal, and hexadecane from petroleum, as sole source(s) of C when added to NH_4-salts as sole source(s) of N in mineral salt minimal medium. Aniline or diphenylamine singly could meet both C and N requirements. Xylene/naphthalene minimal medium proved to be the most rapid enrichment culture medium for primary isolation and routine propagation of such bacteria from leprosy tissues.—Authors' Abstract

Chakrabarty, A. N., Das, S., Mukherjee, K., Dastidar, S. G. and Sen, D. K. Silicon (Si) utilisation by chemoautotrophic nocardioform bacteria isolated from human and animal tissues infected with leprosy bacillus. Indian J. Exper. Biol. **26** (1988) 839–844.

Acid-fast nocardioform chemoautotrophic bacteria from leprosy tissues, as well as several reference strains of mycobacteria and nocardia, tested could grow on minimal medium containing a small quantity of asparagine as the sole C source; this was conspicuously improved in the presence of silicon (Si) and the organisms could be trained to grow in absence of any obvious C source, which suggested that Si could probably partly/wholly replace C in the biosynthetic processes of these bacteria; electron probe microanalyzer data confirmed a significant Si uptake. These may explain the ecosystem of these bacteria involving man and the soil.—Authors' Abstract

Chan, J., Fujiwara, T., Brennan, P., McNeil, M., Turco, S. J., Sibille, J.-C., Snapper, M., Aisen, P. and Bloom, B. R. Microbial glycolipids: possible virulence factors that scavenge oxygen radicals. Proc. Natl. Acad. Sci. U.S.A. **86** (1989) 2453–2457.

Two important pathogens of developing countries, *Mycobacterium leprae,* the etiologic agent of leprosy, and *Leishmania donovani,* the protozoal parasite that causes kala-azar, persist in the human host primarily in mononuclear phagocytes. The mechanisms by which they survive in these otherwise highly cytocidal cells are presently unknown. Since the best understood cytocidal mechanism of these cells is the oxygen-dependent system that provides lethal oxidants including the superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical ($OH\cdot$), and singlet oxygen ($^1O_2$), we sought specific microbial products of these organisms that might enable them to elude oxidative cytocidal mechanisms. Phenolic glycolipid-I (PGL-I) of *M. leprae* and lipophosphoglycan of *L. donovani* are unique cell-wall-associated glycolipids produced in large amounts by the organisms.

In this study, PGL-I derivatives and lipophosphoglycan were examined for their ability to scavenge potentially cytocidal oxygen metabolites *in vitro*. Electron spin resonance and spin-trapping indicate that PGL-I derivatives and lipophosphoglycan are highly effective in scavenging hydroxyl radicals and superoxide anions. The results suggest that complex glycolipids and carbohydrates of intracellular pathogens that can scavenge oxygen radicals may contribute to their pathogenicity and virulence.—Authors' Abstract

Choudhury, A., Mistry, N. F. and Antia, N. H. Effects of a derivative of serotonin (deosyfructoserotonin) and other antileprosy drugs on attachment and uptake of *Mycobacterium leprae* by Schwann cells *in vitro*. Antimicrob. Agents Chemother. **33** (1989) 866–870.

The association (attachment and/or uptake) of *Mycobacterium leprae* with cultured Schwann cells was studied at 8 hr and 72 hr in the presence of a new antileprosy compound, deoxyfructoserotonin (DFS), as well as conventional antileprosy drugs such as rifampin (RFP) and 4,4′-diaminodiphenyl sulfone (DDS). DFS significantly inhibited bacterial association with Schwann cells at 8 hr. RFP also affected the association of *M. leprae* but not to the same extent as DFS. A similar inhibition at 8 hr was noted when *M. leprae* but not Schwann cells were pretreated with DFS or RFP for 5 days before infection of cultures, implying that modulation was achieved through some form of drug action on bacteria. DDS had no effect on *M. leprae* association; however, the combination of DFS and DDS was neither antagonistic nor additive. At 72 hr postinfection, when attached but noninternalized bacteria were removed with trypsin-EDTA from Schwann cell cultures containing DFS or RFP, a 50% reduction in the number of bacteria in the drug-treated group was obtained as compared with the numbers in drug-free cultures. This indicated a slow entry of *M. leprae* into Schwann cells in the presence of these drugs. Collectively, these observations point to differing requirements for late and early association of *M. leprae* with Schwann cells, besides suggesting a role for DFS and RFP in the prevention and minimization of *M. leprae*-induced nerve damage *in vivo*.—Authors' Abstract

Daffé, M. and Lanéelle, M.-A. Diglycosyl phenol phthiocerol diester of *Mycobacterium leprae*. Biochim. Biophys. Acta **1002** (1989) 333–337.

A diglycosyl phenol phthiocerol diester that had not been previously detected was isolated from *Mycobacterium leprae*-infected armadillo tissues. Spectroscopy methods allowed the elucidation of its structure. The diglycoside was a 2,3-di-*O*-methylrhamnopyranosyl(α1 → 2)3-*O*-methylrhamnopyranosyl (α1-linked to the phenolic hydroxyl of phthiocerol dimycocerosates). It differs from the major phenolic glycolipid (PGL-I) only by the absence of the terminal 3,6-di-*O*-methylglucopyranosyl unit. The diglycoside could be an intermediate in the synthesis of the latter antigen or a degradative product in the host detoxification process.—Authors' Abstract

Katoch, V. M., Katoch, K., Shivannavar, C. T., Sharma, V. D., Patil, M. A. and Bharadwaj, V. P. Application of ATP assay for *in vitro* drug screening testing against human derived *M. leprae*. Indian J. Lepr. **61** (1989) 333–344.

In this study, the ATP content of *Mycobacterium leprae* exposed to various antimicrobial agents has been measured to evaluate its usefulness in drug sensitivity screening. Purified *M. leprae* suspensions from human biopsies have been incubated at 30°C in a modified Dubos medium in the presence of different concentrations of various drugs: rifampin, ethionamide, ethambutol, cycloserine, dapsone, clofazimine, erythromycin and tetracycline. ATP levels were estimated at 0, 7 days, 14 days of incubation by the procedures modified and standardized at this laboratory. ATP decay was accelerated by ethionamide, rifampin, clofazimine, dapsone, erythromycin and, to a lesser extent, by cycloserine; whereas ethambutol and tetracycline did not have any significant effect. The rate of decay depended on the concentrations of these drugs.

ATP assay promises to be a useful system for *in vitro* drug-sensitivity screening against *M. leprae* isolated from patients.—Authors' Abstract

Mistry, Y., Antia, N. H. and Mukherjee, R. Correlation of bacterial viability with uptake of [^{14}C]acetate into phenolic glycolipid-1 of *Mycobacterium leprae* within Schwannoma cells. J. Biosci. **14** (1989) 37–45.

The viability of *Mycobacterium leprae*, maintained within 33B Schwannoma cells, was estimated in terms of incorporation of [^{14}C]acetate into its specific phenolic glycolipid-I (PGL-I). This measure of viability was correlated with two other assays, fluorescein diacetate/ethidium bromide staining and mouse foot pad growth. Observation of a twofold increase in the number of intracellular *M. leprae* over an experimental period of 12 days also corroborated this contention. Furthermore, on addition of antileprosy drugs to these intracellular *M. leprae* there was significant decrease in PGL-I synthesis indicative of loss of viability of the organisms. This study also established the importance of the host cell for active bacillary metabolism, as *M. leprae* maintained in cell-free conditions showed no incorporation into PGL-I. Moreover, compromising the host's protein synthesis capacity with cycloheximide also led to reduction in bacillary metabolism. Since this system measures the metabolic synthesis of a unique *M. leprae* component, it would be useful for development and screening of compounds acting against specific bacillary targets.—Authors' Abstract

Rivière, M., Fournié, J. J., Vercellone, A. and Puzo, G. Particular matrix for fast atom bombardment mass spectrometric analysis of phenolic glycolipid antigens isolated from pathogen mycobacteria. Biomed. Environ. Mass Spectrom. **16** (1988) 275–278.

Phenolic glycolipids play a key role as an antigenic probe for serodiagnosis of some human pathogen mycobacterial infections. The lipidic part which corresponds to a phenolphthiocerol dimycocerosate molecule, and the presence of partial *O*-methylated sugars, confer a high hydrophobicity to this kind of molecule. Fast atom bombardment (FAB) mass spectrometric analysis with standard matrices such as glycerol or thioglycerol was unsuccessful. Using a new matrix—monobutyltriethylene glycol—FAB analysis allows molecular weight determination and partial structural elucidation of the saccharidic and the lipidic part of those compounds.—Authors' Abstract

Seydel, U. and Lindner, B. Monitoring of bacterial drug response by mass spectrometry of single cells. Biomed. Environ. Mass Spectrom. **16** (1988) 457–459.

The application of the laser microprobe mass analyzer LAMMA 500 to the solution of problems in the field of microbiology is reported. The special features of this instrument allow the analysis of single bacterial cells, and questions can be answered which are not accessible to the normally applied integral methods. Thus it is possible to establish distributions of, for instance, elemental concentrations within a bacterial population and of correlations between measured characteristics of a bacterium with its morphology. The mass spectrum of a single bacterial cell comprises information on its intracellular cation contents as well as on the organic matrix. The relation between the sodium and potassium contents can serve as a criterion of the physiological state of a cell and of its viability. The information from the organic matrix can be extracted from the complex spectra of fragment ions produced by the interaction of the laser with the cell by applying multivariate data analysis, thus rendering additional information. Examples will be given for *in vitro* drug screening and *in vivo* therapy control in leprosy, an infection which is caused by a mycobacterial species, *Mycobacterium leprae*; this organism does not multiply in artificial growth media so that only limited numbers of organisms are available for microbiological investigations.—Authors' Abstract

Siqueira, L. F. G., Almeida, R. G., Francisco, W., Santos, M. F. Q., Jr. and Belda,

W. [Stable solution of fuchsin—new method of preparation for Ziehl-Neelsen staining.] Hansen. Int. **11** (1987) 8–11. (in Portuguese)

The fuchsin salts currently available in the Latin American market have shown some instability when in solution, according to the classic Ziehl-Neelsen method, resulting in a total precipitation of the salt. The authors indicate a new technique for the preparation of this solution, in order to minimize the action of interfering factors responsible for the precipitation, obtaining thus a greater solubility of the salt, as well as the solution stability. The method's effectiveness is reinforced by the utilization of a smaller amount of the salt and the attainment of a larger storage period for the solution.—Authors' English Abstract

Experimental Infections

Foster, R. L., Facs, C. B., Sanchez, A., Small, P. H. C., Lau, B. H. S., Stuyvesant, W., Foster, F. N. and Baldwin, B. E. Effect of diet on growth of *M. leprae* in mouse footpads. Indian J. Lepr. **61** (1989) 360–366.

Semipurified diets, with equal amounts of vitamins, minerals and fiber, but varied in protein and fat content from pork, barbel fish or soya beans, were tested for their possible effect on the growth of *Mycobacterium leprae* in mouse foot pads; 105 BALB/c male weanling mice were randomly divided into five diet groups of 21 mice each and fed for 6 months. Differences between bacterial counts of diet groups were found. The mouse foot-pad model is suitable for dietary study in leprosy.—Authors' Abstract

Epidemiology and Prevention

Fine, P. E. M. The BCG story: lessons from the past and implications for the future. Rev. Infect. Dis. **11** Suppl. 2 (1989) 5353–5359.

BCG (bacille Calmette-Guérin) vaccines are at once among the least satisfactory and yet the most widely used of all vaccines today. Their variable efficacy against tuberculosis and leprosy is still not understood and points to a fundamental unsolved problem in vaccine immunology. The extensive use of BCG vaccines means that there are few BCG-free populations in the world that would be suitable for trials of future antimycobacterial vaccines. These facts have implications with regard to strategies for the development and testing of new vaccines against mycobacterial diseases.—Author's Abstract

Galvão, E. C. [Epidemiological aspects of hanseniasis in the 10th Regional Department of Health of Presidente Prudente, State of São Paulo in December 1984.] Hansen. Int. **10** (1985) 53–71. (in Portuguese)

This paper relates the epidemiological situation of hanseniasis at the Health Region of Presidente Prudente, São Paulo State, Brazil. It was observed a high percentage from 1974 to nowadays, of diagnosed early forms of the disease (I). In 1984 were diagnosed 132 patients, V and D cases 36 (27.28%), I cases 62 (46.96%) and T cases 34 (25.15%). The rate of incidence in 1984 was 0.19‰ and the rate of prevalence was 1.83‰.—Authors' English Abstract

Gobel, M., Gobel, M. B. B. and Ghidella, C. C. [The status of the hanseniasis endemic in the city of Rondonópolis-MT.] Med. Cut. Ibero Lat. Am. **16** (1988) 331–333. (in Portuguese)

Here we report the incidence of leprosy in Rondonópolis, State of Mato Grosso, Brazil. We direct attention to the fact that the contemporary index of prevalence in Brazil does not correspond to our reality when one makes a program of dynamic research of new cases and clearances to the population, medical staff and co-workers, through lectures and programs on radio and television, besides articles in local papers.—Authors' English Summary

Gonçalves, N. N. S. [Human resources in hanseniasis.] Hansen. Int. **11** (1986) 55–73. (in Portuguese)

In the control of endemic leprosy in Brazil, a qualitative and quantitative lack of human resources was felt as one of its most serious difficulties. Consequently, a systematical review on the practices of human resources on leprosy was carried out, covering the period between 1940 and 1980. An interesting paradox was then observed: sectorial authorities always recognized that courses and training are an important tool in order to improve the conditions for operating leprosy control but when they are put in practice, their result is transitory and ineffective. The maintenance of this fact, associated to low salaries and inadequate working conditions, indicated the necessity of formulating and implanting a policy for the development of human resources in leprosy at a nationwide level. The experience consisted of setting up a scheme of encouragement and support to state health departments for training at the local level; at the regional level, extension courses were organized by the National Department, in Amazonia, Mid-west, South, Northeast and Southeast. The strengthening and/or development of a referral system at the state level were reached through the national specialization course of sanitary dermatology; international qualifications were obtained, as a complement, by joint action with Pan-American Health Organization. Results, details, characteristics and strategies of this process are presented and discussed by discursive and tabular forms.—Authors' English Abstract

Misra, R. S., Ramesh, V. and Nigam, P. K. Leprosy in low endemic areas of India: an appraisal and suggested measures for control. Indian J. Lepr. **61** (1989) 345–350.

Prevalence of leprosy in the low-endemic areas of India is described based on the observations of patients attending an Urban Leprosy Centre in the Union Territory of Delhi from the neighboring states. The rising incidence in these so-called, low-to-moderate endemic places is closely linked to factors related to urbanization, movement of people in search of employment, etc., which necessitate fresh surveys in these areas. A significant number of leprosy patients attending the Centre were irregular (37.7%) in therapy and many absconded after the initial visit (35.3%), the reasons for which are discussed. These figures are compared to those from similar low-endemic areas and known high-endemic parts of the country. Suitable modifications to the control program in these areas are suggested under the purview of the National Leprosy Eradication Programme.—Authors' Abstract

Montreewasuwat, N. and Peerapakorn, S. Leprosy situation in Thailand. Southeast Asian J. Trop. Med. Public Health **19** (1988) 515–517.

The prevalence rate of leprosy in Thailand was approximately 5 per 1000 in 1953. A specialized leprosy control program was first launched in 1956 in Khon-Kaen Province and gradually expanded to cover the whole country in 1972. After successful control, it was partially integrated into provincial health services in 1971 and fully integrated into the primary health care system in 1976. Effective case finding in combination with chemotherapy using WHO multidrug therapy regimen and health education have brought about a decline in the prevalence of the disease to only 0.537 per 1000 in 1987. However, the estimated prevalence rate by random survey is approximately twice the number of registered cases. Reduction in the number of lepromatous

leprosy patients, particularly the new cases, decrease in the number of patients with deformities caused by leprosy and increased numbers of patients who voluntarily attend at the treatment centers imply the successful control at a certain level. It is then justified to aim at the goal of eradication of leprosy by combination of chemotherapy, immunotherapy and immunoprophylaxis with antileprosy vaccines in the future.—Authors' Summary

Revankar, C. R., Goyal, N. and Sorensen, B. H. Management information system for leprosy eradication programme—an alternative information system. Lepr. Rev. **60** (1989) 129–134.

For efficient monitoring of multidrug therapy (MDT) programs for leprosy both at the microlevel (individual patient monitoring) as well as the macrolevel (program monitoring), DANIDA decided to develop an alternative, simple and quick information system using a computer. A patient data base system was designed using dBase III Plus package. The field workers of the National Leprosy Eradication Prgramme were trained in transcribing data onto coded data sheets. The data of 1750 patients of six leprosy control units from the four MDT districts were processed and feedback reports were sent to paramedical workers and program managers. The initial experience in the field over the past year has shown that a computerized management information system is feasible and well accepted by the field staff for the purpose of improving monitoring.—Authors' Summary

Revankar, C. R., Gupta, V., Deshpande, S. S., Pai, R. and Ganapati, R. Leprosy survey in industries in Bombay. Indian J. Lepr. **61** (1989) 367–372.

Population surveys for leprosy in industrial cities like Bombay revealed that about 60% of adult subjects, especially males, could be examined. The fact that the prevalence rate of leprosy, particularly multibacillary type, is much higher in this segment of population as compared to other groups indicates the importance of examining this population at their workspot like industries; 22,287 industrial workers were examined for leprosy by paramedical auxillaries in their establishments and 270 leprosy cases were detected (P.R. 12/1000). However, only 13 multibacillary cases (P.R. 0.5/1000) could be unearthed; 12 patients were with grade II and above; 184 (83%) were untreated; 161 (60%) patients reported for treatment. With available resources, case-holding of patients who are not within the control area of the project becomes a challenging job for paramedical workers although a large number of leprosy cases are detected among industrial workers. If industrial management arranges treatment for leprosy patients without dislocating them from their service, the pool of infection in the urban community will be reduced and can contribute tremendously toward urban leprosy control program.—Authors' Summary

Rose, P. Changes in epidemiological indices following the introduction of WHO MDT into the Guyana leprosy control programme. Lepr. Rev. **60** (1989) 151–156.

In December 1981 the multidrug regimen, recommended by the WHO Study Group of October 1981, was introduced into the Guyana Hansen's Disease Programme. This paper examines the changes that occurred in epidemiological indices over the 6 years following the introduction of MDT, and also evaluates changing work loads and staffing patterns.—Author's Summary

Stes, P. and Malâtre, X. Will the leprosy endemic in Rwanda soon be under control? Lepr. Rev. **60** (1989) 139–146.

It appears that leprosy in Rwanda is becoming a rather rare disease. By the end of 1987, 1142 cases were still under treatment, a prevalence rate of 0.17 per thousand. Prevalence rates declined from 0.26 per thousand in 1982, by an average of 0.018 per thousand a year. However, it is necessary to know whether the number of known patients reflects reality, and if case-finding has been adequate. In other words: has the detection rate been a reliable indication of the incidence rate? This paper studies the problem, and tries to see if any conclusions can be made about the transmission of leprosy in the Rwandan population.

The three criteria studied, the detection/incidence rate, the age and sex distribution of new cases, and the new cases among household contacts of leprosy patients, suggest that leprosy transmission in Rwanda is low—certainly outside the family clusters—and still diminishing. Taking into account the decreasing prevalence rates, we believe that the leprosy endemic in Rwanda can be controlled within a limited period of time, certainly before the goal of the World Health Organization for leprosy control worldwide by the year 2000. As to our own strategy in the field, we conclude that there should be more emphasis on contact survey and on informing the public and the medical staff of the first signs of the disease so as to make early detection easier. In this way, we hope to prevent more patients from becoming disabled.—(*From the* Article)

Walter, J. The post-lepromin scar and its significance in the control of HD. Indian J. Lepr. **61** (1989) 379–386.

In the past, little attention has been paid to the post-lepromin scar (PLS) and its use in controlling Hansen's disease (HD), particularly in the prognosis, classification and measurement of the cell-mediated immune (CMI) response. The immuno-information of the Mitsuda reaction is thought to be informative only in the extreme range of 10+ mm or in its absence. Previous studies have shown that the range of PLS formation increases proportionally to the degree of lepromin positivity. PLS-positive HD patients have a stable form of the disease with good prognosis. Those unable to form a PLS have a marked tendency to downgrade toward the lepromatous form of HD. PLS formation appears to indicate a CMI response to *Mycobacterium leprae,* implying immunity. It is thought that there exists a correlation between the PLS and the lymphocyte transformation test (LTT), both reaching their optimum measurement 3 months after the *M. leprae* injection, either with lepromin or *M. leprae* suspension used for the anti-HD vaccine. It is proposed to study the use of the PLS in HD control programs on a trial basis with the objective of its general introduction as part of the management of HD control. Considerable improvements in the prognosis, classification and application of treatment can be expected from such a measure. The discovery of the armadillo as a source of *M. leprae* by Kirchheimer and Storrs facilitates the availability of lepromin A and its purified version, lepromin Ap. The relevant studies have shown that a 40 M/bact/ml lepromin A suspension should be used for the application of lepromin in control programs. It is concluded that the routine reading of the PLS, particularly under field conditions where alternative tests are difficult to perform, will be of considerable benefit for the HD patient.—Author's Summary

Rehabilitation

Bourrel, P. [Surgical treatment for neurotrophic lesions of leprosy. Application to other types of neuropathy.] Chirurgie **114** (1988) 545–560. (in French)

In leprosy, hypertrophic leprous neuropathy only affects the extremities. The resulting paralyses can be fairly easily corrected by a number of palliative surgical techniques. However, the major, irreversible complication is the sensory loss of these extremities. This is responsible for painless trauma and microtrauma, leading to infections and progressive mutilations when the leprous patient does not know how to protect the extremities from aggressions. Surgery plays a role in this situation for incisions, drainage, regularization and, most importantly, amputations. Perforating ulcers of the foot are frequent; preventive surgery is possible by correcting deformities of the foot and by decreasing pressure points under the tubercles of the 5th metatarsal and calcaneum, by resecting them. Pathogenic surgery consists of decompression of large posterior tibial and plantar nerves in the tarsal tunnel, which can be applied to other neuropathies of large nerves.—Author's English Summary

Kaada, B. and Emru, M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct. Electrother. Res. **13** (1988) 165–176.

Low-frequency (2 Hz) transcutaneous electrical nerve stimulation (TNS) may produce widespread and prolonged increases in skin temperature in patients with peripheral vascular insufficiency due to improved microcirculation. The method has previously been used successfully to potentiate healing of chronic ulcers of various etiology. The present report describes a similar study, using TNS treatment in attempts to accelerate healing of chronic leprous ulcers that had resisted treatment for several months or years. All other treatment, local and systemic chemotherapy, and daily regime remained as far as possible unaltered. The study was limited to ulceration in the soft tissue of the foot or lower leg. Eleven TNS sessions, each of 30 min duration, were applied per week. In 19 patients (6 outpatients and 13 inpatients), in whom the TNS treatment was not interrupted, all ulcers healed completely within a mean of 5.2 weeks (range 3–12 weeks). The mean size of the ulcers was 5.2 cm^3 (range 0.2–48.3 cm^3), and they had persisted for a mean of 15.8 months (range 2–60 months). The "healing index," i.e., the mean reduction of the ulcer cavity per week, was 1.0 cm^3 week. The study demonstrates a clear therapeutic effect for low-frequency TNS in patients with leprous ulcers. The mechanisms involved in the accelerated healing are assumed to be increased microcirculation due to sympathoinhibition and release of endogenous corticosteroids.—Authors' Abstract

Lamba, P. A., Srinivasan, R. and Rohatgi, J. Surgical management in ocular leprosy. Indian J. Ophthalmol. **35** (1987) 153–157.

One-hundred-sixty patients of leprosy with or without visual disability were submitted to various surgical procedures as prophylactic or curative measures. The various procedures undertaken included cataract surgery, ectropion correction, trabeculectomy, tarsorrhaphy and keratoplasty. The utility of repositioning of pupil achieved by xenon arc photocoagulation for cases of centrally situated corneal opacity has been introduced with encouraging results. Such a procedure is of particular benefit in patients who are poor risks for keratoplasty. Surgery in leprosy offers a new hope to patients with advanced ocular complications due to this crippling disease.—Authors' Abstract

Shats, E. I. and Yushchenko, A. A. [Neurotrophic plantar ulcers in leprosy patients.] Vestn. Dermatol. Venerol. **12** (1988) 37–41. (in Russian)

Neurotrophic plantar ulcers remain to be among the main factors responsible for invalidism in leprosy. High prevalence, complicated etiopathogenesis, and severe clinical manifestations of such a complication of the leprosy process necessitate a complex approach to the prevention and treatment of them. The clinical and epidemiological observations of 69 neurotrophic plantar ulcers in 50 leprosy patients are presented. It has been found that leprosy ulcers are localized on bone prominences of the soles, mainly on the anterior part of the foot (83%). Chronic osteomyelitis of the feet is the main cause of long-standing and frequently relapsing ulcers. The authors stress the necessity of search for and introduction of new, more effective measures to prevent and manage neurotrophic ulcers of a leprosy etiology as an important component of rehabilitation of leprosy patients.—Authors' English Summary

Other Mycobacterial Diseases and Related Entities

Andersen, A. B. and Hansen, E. B. Structure and mapping of antigenic domains of protein antigen b, a 38,000-molecular-weight protein of *Mycobacterium tuberculosis*. Infect. Immun. **57** (1989) 2481–2488.

Only a limited number of proteins from *Mycobacterium tuberculosis* have so far been shown to possess species-specific epitopes as defined by monoclonal antibodies. One such protein is protein antigen b (Pab) of

molecular weight 38,000, which binds the monoclonal antibodies HYT 28, HAT 2, HBT 12, HGT 3, TB 71, and TB 72. The gene encoding this protein was isolated from a λ gtll *M. tuberculosis* DNA library. The nucleotide sequence of the recombinant mycobacterial insert was determined, and an open reading frame of 374 amino acids was identified. The amino-acid sequence exhibited 30% homology to a phosphate-binding protein, PstS, from *Escherichia coli*. The *pab* gene was subcloned into pBR322 in conjunction with the *lacZ* gene, and deletions were obtained from the 3′ end. The anti-Pab monoclonal antibodies were used to probe crude protein lysates of *E. coli* transformed with the deletion plasmids. The monoclonal antibodies showed two reactivity patterns; one group of antibodies were dependent on the presence of the ultimate 91 amino acids of the protein, whereas another group of antibodies recognized an antigenic domain located on the middle portion of the molecule. None of the antibodies bound to the *N*-terminal 117-amino-acid peptide.—Authors' Abstract

Beck, J. S., Morley, S. M., Lowe, J. G., Brown, R. A., Grange, J. M., Gibbs, J. H., Potts, R. C. and Kardjito, T. Diversity in migration of CD4 and CD8 lymphocytes in different microanatomical compartments of the skin in the tuberculin reaction in man. Br. J. Exp. Pathol. **69** (1988) 771–780.

The lymphocytes in the perivascular foci of tuberculin skin tests have a similar CD4:CD8 ratio to those in the peripheral blood, suggesting that these subsets do not show bias in their initial emigration. By contrast, the diffusely infiltrating lymphocytes show a relative preponderance of CD4 cells which is progressively greater in successive 250 μm layers into the dermis. A generally similar pattern is seen in healthy controls and in patients with untreated pulmonary tuberculosis, treated leprosy, hemophilia A, and chronic obstructive lung disease (COLD) patients treated with prednisolone, but the gradient of increasing CD4: CD8 ratio with depth into the dermis is significantly less steep in patients with tuberculosis, hemophilia, and prednisolone-treated COLD than in the healthy controls. Selective migration results in a relative preponderance of CD4 cells in the diffuse infiltrate, and it is suggested that this is a mechanism likely to potentiate defensive reaction to *Mycobacterium tuberculosis*: any deficiency in selective migration may make immunological defenses less effective and so contribute to the chronicity of the lesions of tuberculosis.—Authors' Summary

Buschman, E., Apt, A. S., Nickonenko, B. V., Moroz, A. M., Averbakh, M. H. and Skamene, E. Genetic aspects of innate resistance and acquired immunity to mycobacteria in inbred mice. Springer Semin. Immunopathol. **10** (1989) 319–336.

In murine models of mycobacterial diseases, natural or innate resistance genes control early growth of the bacteria in the unprimed, unvaccinated host. If the infection follows a chronic course, many host immune responses are elicited, such as the formation of granulomas, the activation of macrophages, T and B cells, DTH responses, and the production of lymphokines and antibodies. The various responses may or may not be effective in eliminating the infection. Thus, the genetic control of acquired immunity is very complex, and consequently it is difficult to link a certain trait with a single gene or haplotype. Moreover, natural resistance gene expression can modify the immune response, as has been shown for the *Bcg* alleles. However, several conclusions can be made from analysis of the presently available data: a) Innate resistance and susceptibility to BCG, *Mycobacterium lepraemurium* (MLM), and *M. intracellulare* is controlled by the *Bcg* gene. b) The trait of extreme sensitivity to *M. tuberculosis* (H37Rv) infection is under control of the *Tbc-1* gene. The possible identity of *Bcg* and *Tbc-1* is presently being analyzed. c) In several models of mycobacterial infection, the immune response was shown to be quantitatively different in different mouse strains (HR/LR phenotypes). In studies of BCG-induced granuloma reaction, HR and LR phenotypes were associated with protective and suppressive immunity, respectively. d) Although in several studies B6 and C3H strains seemed to typify HR/LR phenotypes, respectively, few studies could link

the trait with a particular H-2 allele or other genetic system. In MLM infection, an enhanced granulomatous reaction was linked to expression of the H-2^b allele at the K-Eβ region. In H37Rv infection, the H-2^f haplotype was linked with the development of suppressive immunity. c) In a study of H-2^d-identical, *Bcg*-congenic mice, the *Bcg*^{f} allele exerted a positive influence on BCG immunity by promoting earlier T-cell activation. The *Bcg*^{f} allele seems to act at the level of macrophage priming for activation.—Authors' Conclusions

Caplin, M., Grange, J. M., Morley, S., Brown, R. A., Kemp, M., Gibson, J. A., Kardjito, T., Hoeppner, V. and Beck, J. S. Relationship between radiological classification and the serological and haematological features of untreated pulmonary tuberculosis in Indonesia. Tubercle **70** (1989) 103–113.

Immunological and metabolic responses were studied in 110 patients with newly diagnosed pulmonary tuberculosis and 32 healthy controls from similar socioeconomic backgrounds. The severity of lung involvement was assessed radiologically, but this was not related to the current features of the cell-mediated immunity or to those of many aspects of the serological response to *Mycobacterium tuberculosis.* However, the patients with more extensive pulmonary tuberculosis showed higher titers of IgG_2 antibody to whole killed *M. tuberculosis* and to the ML34 epitope shared by many species of mycobacteria. The patients with more extensive pulmonary tuberculosis showed a more marked metabolic response to infection as manifested by changes in serum levels of acute phase reactant proteins. Accordingly, the metabolic responses are considered to be more likely to prove of value in clinical monitoring of patients for severity of infection, or of reactivation of infection with *M. tuberculosis,* than immunological responses.—Authors' Summary

Cooper, G. L., Grange, J. M., McGregor, J. A. and McFadden, J. J. The potential use of DNA probes to identify and type strains within the *Mycobacterium tuberculosis* complex. Lett. Appl. Microbiol. **8** (1988) 127–130.

DNA was extracted and purified from 11 strains of *Mycobacterium bovis* isolated from cattle in Ireland. After digestion with restriction endonuclease *Pvu*II and electrophoresis on an agarose gel, the separated DNA fragments were transferred to a nylon membrane and sequentially hybridized with three DNA probes derived from BCG. None of the three probes detected restriction fragment length polymorphism (RFLP) within the 11 *M. bovis* strains, indicating a very close genetic relationship. One probe, pBCG12, detected RFLPs between the *M. bovis* strains and a reference *Pvu*II digest of DNA from *M. tuberculosis* R37Rv, confirming that *M. bovis* and *M. tuberculosis* are closely related though genetically distinct.—Authors' Abstract

Gonzalez, A. H., Berlin, O. G. W. and Bruckner, D. A. *In-vitro* activity of dapsone and two potentiators against *Mycobacterium avium* complex. J. Antimicrob. Chemother. **24** (1989) 19–22.

The efficacy of dapsone against *Mycobacterium avium, M. intracellulare, M. kansasii, M. fortuitum* and *M. tuberculosis* was determined by disc elution in agar. The minimal inhibitory concentrations at which 90% of the colony forming units were inhibited (^{90}MIC) by dapsone was 8 mg/l for *M. avium, M. intracellulare and M. kansasii* and $\geq$ 32 mg/l for *M. tuberculosis* and *M. fortuitum.* The ^{90}MICs were confirmed by culturing these test organisms with dapsone in the BACTEC 460 system. Reduction of the ^{90}MIC from 8 mg/l to 2 mg/l was observed by combining dapsone with either or both of the potentiators tested. The dapsone-potentiator combinations had no effect on the bacteria with ^{90}MICs of $\geq$ 32 mg/l. The clinical relevance of this drug combination against *M. avium* complex infections remains to be evaluated.—Authors' Abstract

Jenner, P. J. and Ellard, G. A. Isoniazid-related hepatotoxicity: a study of the effect of rifampicin administration on the metabolism of acetylisoniazid in man. Tubercle **70** (1989) 93–101.

It has been proposed that isoniazid-induced hepatotoxicity may be increased by

concomitant rifampin treatment and that this could be mediated by inducing the metabolism of the isoniazid metabolite monoacetylhydrazine to potent acylating agents capable of causing liver necrosis. To investigate this postulated mechanism we studied the kinetics of the metabolism of acetylisoniazid in a slow and a rapid acetylator prior to and after rifampin administration. Pretreatment with rifampin did not modify the metabolism of acetylisoniazid to any noteworthy extent nor did it increase the metabolism by non-acetylation routes of the monoacetylhydrazine liberated *in vivo* from acetylisoniazid.—Authors' Summary

Kolk, A. H. J., Evers, R., Groothuis, D. G., Gilis, H. and Kuijper, S. Production and characterization of monoclonal antibodies against specific serotypes of *Mycobacterium avium* and the *Mycobacterium avium-Mycobacterium intracellulare-Mycobacterium scrofulaceum* complex. Infect. Immun. **57** (1989) 2514–2521.

Serotype-specific and *Mycobacterium avium-M. intracellulare-M. scrofulaceum* complex (MAIS complex)-specific monoclonal antibodies (MAbs) were prepared. A series of MAbs were obtained, 5 specific for serotype 2, 3 specific for serotype 4, 8 against a strain of serotype 19, 2 specific for the MAIS complex, and 2 against a common glycolipid shared by all the mycobacteria tested so far. The serotype-specific and the MAIS-complex-specific MAbs reacted in immunofluorescence with intact mycobacteria and in enzyme-linked immunosorbent assay and immuno-thin-layer chromatography with lipid extracts of mycobacteria. The two MAbs against a common mycobacterial glycolipid reacted only in lipid enzyme-linked immunosorbent assay and immuno-thin-layer chromatography. All MAbs were directed against glycopeptidolipids (GPLs), except for four MAbs against proteins of serotype 19. The serotype- and MAIS-complex-specific epitopes on GPLs are exposed on the mycobacterial cell wall, in contrast with the common mycobacterial glycolipid, which is probably located inside the cell wall. The serotype-specific MAbs reacted with native as well as deacetylated GPLs, in contrast with the MAIS-complex-specific MAbs, which reacted only with native GPLs. The MAbs will be useful for the identification of MAIS complex and *M. avium* serotypes 2 and 4 and a strain of serotype 19, GPL analyses with immuno-thin-layer chromatography, and the localization of GPL epitopes in mycobacteria.—Authors' Abstract

McLeod, D. T., Pringe, D., Zingoni, T. and Mbengeranwa, O. L. Is thiacetazone necessary or useful in the intensive phase of anti-tuberculous chemotherapy? Cent. Afr. J. Med. **35** (1989) 313–316.

A retrospective study of 596 case notes of 1195 patients notified for tuberculosis during a 3-year period, in one district, was conducted. Drug reactions occurred in 75 patients (12.6%) and required discontinuation of therapy in 59 (10%). In 69 patients the skin was involved. Thiacetazone was by far the commonest drug implicated: two patients died with the Stevens-Johnson syndrome. This study suggests that in the all important first 2 months of antituberculous chemotherapy, thiacetazone, a therapeutically unnecessary agent, should be omitted since its inclusion results in an unacceptably high rate of side effects.—Authors' Summary

Poença, N. G. and Bernardes, M. F. [Treatment of discoid lupus erythematosus by thalidomide.] Am. Bras. Dermatol. **64** (1989) 141–142. (in Portuguese)

Results of the treatment of seven discoid lupus erythematosus patients with thalidomide are presented. In all of them an initial daily dose of 200 mg was administered. At the end of the fourth week of treatment it was possible to register a substantial improvement. Complete remission was observed in all cases between the fifth and the twelfth weeks. After suppression of the drug, five patients presented recurrence between 4 and 20 weeks. Two patients did not return for follow-up.—Authors' English Summary

Thompson, D. E. and Giurintano, D. J. A kinematic model of the flexor tendons of the hand. J. Biomech. **22** (1989) 327–334.

The multijoint model is a kinematic simulation of the long flexor tendons of the fingers. The tendons modeled are the flexor

pollicis longus, the flexor digitorum profundus, and the flexor digitorum superficialis. The simulated tendons are displayed on an Evans and Sutherland PS330 color graphics terminal attached to a display of articulated bones of the hand. As a user changes the position of the joints of the simulated hand, the simulation displays the new tendon path and the excursion of the tendon for the new position of the hand. The multijoint model is one component of a comprehensive model for use in a hand biomechanics computer workstation.—Authors' Abstract

Van Vooren, J. P., Farber, C. M., Noel, E., Mavroudakis, N., Turneer, M., De Bruyn, J., Legros, F. and Yernault, J. C. Local anti-P32 humoral response in tuberculous meningitis. Tubercle **70** (1989) 123–126.

We report five cases of severe pulmonary tuberculosis admitted to the hospital with a suspicion of meningeal involvement. The diagnosis of tuberculous meningitis was confirmed by standard bacteriological techniques in 2 of the 5 patients. Specific IgG class antibodies directed against the recently purified BCG antigen P32 were detected by a dot-immunoblotting technique in the serum and in the cerebrospinal fluid of each patient; however, a higher anti-P32 immunoglobulins/total immunoglobulins ratio was observed in the cerebrospinal fluid of patients with tuberculous meningitis than in their serum, while the reverse situation was observed in the other patients.—Authors' Summary

Wang, B., Cao, G., Wang, D., Wang, Y. and Yang, G. [Electron microscopic observation on spleen T lymphocyte in animal model of lepromatous leprosy.] Hua Hsi I Ko Ta Hsueh Hsueh Pao **19** (1988) 342–345. (in Chinese)

It has been known that BALB/c mice infected with *Mycobacterium lepraemurium* (MLM) had been used as models similar to human lepromatous leprosy, and there was reduction of IL-2 production in this mouse model. In order to investigate the cause of the reduction, we observed the T cells in the spleen of infected mice under transmission electron microscope. It was found that the MLM-infected mouse spleen T-lymphocyte had changed strikingly, including cytoplasmic membrane evened, mitochondria swollen significantly, spine shortened, rough endoplasmic reticulum expanded, perinuclear space increased, nucleus solidified, cytoplasmic membrane and organelles in some cells disappeared. It was found that there were some MLM in T-lymphocyte cytoplasm, and the damage of the cytoplasmic membrane was seen close to the presence of MLM. It was shown that MLM in the cytoplasm were completely surrounded by the cytoplasmic membrane-like material to form a vacuole, and the structure of MLM became incomplete. It seems that MLM might be phagocytized by the T lymphocytes.—Authors' English Abstract