

CURRENT LITERATURE

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

General and Historical

Baillie, R. A. and Baillie, E. E. Biblical leprosy as compared to present-day leprosy. *South. Med. J.* **75** (1982) 855–857.

The authors review biblical leprosy as it relates to modern concepts of the disease. The clinical descriptions of the disease as it appears today are somewhat dated. There is mention, for example, that there are three types of leprosy: tuberculoid, lepromatous, and mixed and that the disease is easily treated by chemotherapy. The authors feel that leprosy as referred to in Leviticus doubtless included modern leprosy, although others would disagree with this point of view. The point is well taken that there is a continuing movement by some to permanently change the name of the disease to Hansen's disease in an effort to reduce the stigma associated with the biblical term leprosy.—RCH

Furness, Melville A. Physiotherapy in leprosy. *Aust. J. Physiother.* **6** (1982) 9–12.

This is an extremely lucid and concise article by an established expert written for practitioners who would not normally be familiar with leprosy. It covers the whole spectrum of leprosy concerned with the etiology, prevention and correction of deformity. It is prefaced by a short introduction of relevant immunology which makes the remainder of the article clear to all. It has been written with an eye to the education of doctors, nurses and paramedical personnel and can be highly recommended both to the beginner and to the seasoned student of the disease.—J. C. Hargrave

Mas, A. C. and Vaquer, R. R. La asistencia a los enfermos en Mallorca durante el antiguo regimen. [Assistance to patients on Mallorca in ancient times.] *Rev. Leprol.* **13** (1982) 635–641. (in Spanish)

The endemic of leprosy on the island of Mallorca in the years between 1456 and 1719 is reported. The authorities insisted on the voluntary or mandatory isolation of patients, sometimes in very precarious conditions. These hospitals were never utilized for any other illnesses, since leprosy was considered to be a disease/punishment.—*(Adapted from Authors' Summary)*

Ramanathan, U. and Ramu G. Attitude of doctors to working in leprosy. *Lepr. India* **54** (1982) 695–699.

A study was conducted to assess the attitude of doctors to working in leprosy; 35 subjects were studied using a questionnaire to tap the various areas of leprosy work. The results indicated that although a majority of the doctors were interested in the speciality and considered that they had been trained well, there was evidence of inadequate knowledge in 33% of them. Fears of being socially stigmatized and facing poor job prospects while working in this field were also revealed. It is suggested that training in the undergraduate and post-graduate levels and improving job prospects would remove the disincentives which hamper antileprosy work.—Authors' Summary

Rees, R. J. W. An appraisal of medical research in the treatment and control of leprosy. *J. R. Soc. Arts* **130** (1982) 186–198.

In this talk given to the Royal Society of Arts in March 1981, the speaker outlined the progress made in the understanding of leprosy since L. Rogers gave the previous talk on leprosy to the Society in 1954. Transmission of *Mycobacterium leprae* in the foot pads of mice was a major advance. Immunodepressed mice have proved more sensitive for detection of small numbers of viable organisms. With these two mouse

models it has been shown that *M. leprae* multiplies extremely slowly and behaves in the same manner whatever the geographical source. More importantly, bacilli from lepromatous and tuberculoid leprosy patients behave similarly, indicating that the type of disease is determined by the host's capacity to control the disease and not by a difference in virulence.

The prophecy of eradication of leprosy as a result of dapsone chemotherapy has been unfulfilled. By the use of mouse models clinical relapses have been shown to be due to emergence of secondary drug resistance or to bacterial persistence. The animal models also allow bacteriological and pharmacological assessment of new antileprosy drugs.

Future prospects and priorities discussed include combined chemotherapy regimens to limit the emergence of further cases of drug resistance. A table indicates doses, costs and need for supervision for various drug combinations. A third animal model, the nine-banded armadillo, has made possible the production of large quantities of *M. leprae* for potential vaccine, skin test and research materials. The development of a vaccine from armadillo material is progressing. Cultivation of *M. leprae* *in vitro* is still a priority because the expense of animal models and the need for specialized facilities limits the number of laboratories in which certain aspects of leprosy may be studied. Recent work on the biochemistry of the organisms may indicate important growth requirements.—C. A. Brown (*From Trop. Dis. Bull.*)

Sansarricq, H. The Kellersberger Memorial Lecture, 1981: The general situation of leprosy in the world. *Ethiopian Med. J.* **20** (1982) 89–106.

The author, Chief Medical Officer of the Leprosy Division of Communicable Diseases of the WHO, discusses in this lecture given in May 1981 "... the magnitude of the leprosy problem from the human and public health point of view; the relative importance of leprosy compared with some other communicable diseases in tropical countries; the achievements of the current strategy for leprosy control; the problems recently arisen; the needs and prospects for improving the available strategy and tools

for reducing the leprosy problem in the future."

Although global morbidity for leprosy is low, he explains that leprosy is a serious problem because about 1400 million people are exposed to the risk of contracting the disease and a significant proportion of the patients face permanent and progressive physical and social disability. In reviewing the achievement of control programs he quotes results from four countries: Thailand, Burma, Upper Volta, and India. Prevalence has been reduced in well-organized and well-conducted programs based on dapsone monotherapy by up to 80% but in the same programs there is little evidence of a parallel decline in incidence although a steady decline in case-detection rates has been observed in the first three countries.

He refers to the evidence from several countries of the development of drug-resistant mutants, with the risk of relapse ranging from about 2% in Malaysia and Israel to 3% per annum in Ethiopia. Cases of primary resistance to dapsone have been reported in Ethiopia, India, Malaysia, The Philippines, and the U.S.A. He mentions the survival of *Mycobacterium leprae* in patients after at least ten years' dapsone therapy and the need for combined drug therapy to prevent the emergence of secondary dapsone resistance (but notes that *M. leprae* has been shown to persist even after therapy with rifampin alone or with dapsone). He concludes by summarizing what the WHO intends to do in collaboration with its member states in the next decade, including the improving of case detection, field application of more effective control methods, training of all health workers, involvement of national experts, collaboration with other agencies, and operational studies on vaccination "according to progress made in the development and field testing of leprosy vaccine".—D. W. FitzSimons (*From Trop. Dis. Bull.*)

Shepard, C. C. Leprosy today. (Editorial) *N. Engl. J. Med.* **307** (1982) 1640–1641.

The editorial provides a succinct (one and one-half pages) update and review of leprosy. Among a number of interesting points, the point is made that in mice the route of

administration of antigen controls the type of immune response to *Mycobacterium leprae*, interdermal administration leads to delayed hypersensitivity and intravenous

administration leads to immune tolerance. It may be, therefore, that the route of infection in human beings controls the immune response.—(From the editorial)

Chemotherapy

Almeida Neto, E. Estudo comparativo entre a atividade terapêutica da imida ftálica do ácido glutâmico e a atividade terapêutica da triamcinolona no tratamento da reação hansênica da hanseníase Virchowiana. [A comparative study between the therapeutic activity of thalidomide and the therapeutic activity of triamcinolone in the treatment of reactions in Virchowian hanseniasis.] Hansen. Int. **6** (1981) 114–121. (in Portuguese)

A study was made of 20 in-patients of the Hospital das Clínicas of the Faculdade de Medicina da Universidade de São Paulo in order to compare the short-term activities of the Brazilian-made thalidomide and of the triamcinolone in the therapy of the hansenic reaction of the virchowian hanseniasis (in the erythema nodosum and in the erythema multiforma syndromes as well). In this research it was observed that the therapeutic activities of both drugs present a perfect and undeniable equivalence and that their use has reduced the period of hospitalization to 8.3 days per each patient.—Author's Abstract

Baquillon, G., Ferracci, C., Van Loo, G. and Pattyn, S. R. Further results on dapsone-resistant leprosy in Bamako (Mali). Lepr. Rev. **54** (1983) 19–21.

Between 1979 and 1981 a yearly survey of dapsone resistance was performed among two groups of leprosy patients in Bamako. In the first group of patients the yearly incidence was 5.7%, 3%, and 4.1%, with a mean of 4.1% per year. In the second group the yearly incidence was 3.4%, 0.8%, and 2.8% with a mean of 2.3%. Our results confirm research carried out in Addis Ababa Ethiopia, where a yearly incidence of 3% was found.

The need for the use of combined therapy including bactericidal drugs is emphasized.—Authors' Summary

de Almeida-Filho, J. and de Souza, J. M. A simple urine test for sulfonamides. Bull. WHO **61** (1983) 167–168.

The lack of a simple and reliable test for sulfonamides has created a problem because of the increasing use of these drugs in the chemotherapy of malaria. This paper describes a modification of the Bratton-Marshall technique, for which the reagents are easily obtainable and which can be carried out in simply equipped primary health care laboratories.—Authors' Summary

Ji Bao-Hong. Methodology of therapeutic trials in leprosy. Chin. J. Clin. Dermatol. **12** (1983) 88–91. (in Chinese)

Present-day chemotherapy of leprosy appears to be inadequate. Thus therapeutic studies, using either newly developed drugs or existing drugs in the most advantageous way, are still an important component part in strengthening the leprosy control program. An accurate design of a clinical trial in studies of the treatment of leprosy is a fundamental prerequisite in precisely assessing the therapeutic results. Therefore, the criteria of case selection for clinical trials, the method of random allocation of patients, the numbers of patients to be recruited for clinical trials, the indicators in assessing progress after treatment are outlined.—Author's Abstract

Jin Liang-Jian. Qualitative quick simplified method in the determination of urinary DDS. Chin. J. Clin. Dermatol. **12** (1983) 87–88. (in Chinese)

A filter paper method for the qualitative determination of dapsone in urine is introduced. The indicator paper is prepared from filter paper with oxalic acid and sodium nitrite, and on it are dropped, successively, solutions of ammonium sulfamate and N-1-naphthyl-ethylene-diamine dihydrochloride. The procedure is simple, easily handled, and requires little time.—Author's Abstract

Kulkarni, V. M. and Seydel, J. K. Inhibitory activity and mode of action of diaminodiphenylsulfone in cell-free folate-synthesizing systems prepared from *Mycobacterium lufu* and *Mycobacterium leprae*. A comparison. *Chemotherapy* **29** (1983) 58–67.

Cell-free folate-synthesizing extracts have been isolated from *Escherichia coli*, *Mycobacterium lufu*, *Mycobacterium smegmatis* (ATCC 607) and *Mycobacterium leprae*, and the inhibitory power of diaminodiphenylsulfone (DDS) in such cell-free systems on the synthesis of dihydropteroic acid has been determined. *M. lufu* and *M. leprae* extracts show very similar high sensitivities against DDS. Mode-of-action studies seem to indicate that the observed high sensitivity of *M. lufu* and *M. leprae* as compared to *E. coli* can be solely attributed to a high affinity for the dihydropteroic acid synthetase. A dihydropteroic acid analog formation where DDS is incorporated instead of *p*-aminobenzoic acid—as has been observed in *E. coli*—could not be detected.—Authors' Abstract

Kumar, A. and Balakrishnan, S. Monitoring the regularity of self administration of dapsone by leprosy patients. *Lepr. India* **6** (1982) 664–670.

An operational study was undertaken a) to monitor and assess the regularity of dapsone (DDS) intake by leprosy patients, b) to find out the operational feasibility of methods used for monitoring DDS intake, and c) to study the factors influencing the regularity of drug intake. The self administration of DDS by 319 leprosy patients, attending six field clinics of our mobile treatment unit, was assessed by a) physical verification of DDS tablets and b) screening

their urine for DDS spot test (in the field itself) and by estimating DDS/creatinine ratio in urine (in biochemistry lab). As assessed by physical verification of DDS tablets, on an average one patient had missed 3.67 ± 3.96 tablets in a fortnight, and only 62% of patients took more than 75% of treatment. The spot test was found to be positive in 84.64% of the patients. Both methods of monitoring the regularity of DDS intake were found operationally very feasible and acceptable and had a good correlation with each other. The spot test was found very reliable as judged by the DDS/creatinine ratio. Both methods can be used on a mass scale in the National Leprosy Control Programme for this purpose.—Authors' Summary

Mester de Parajd, L., Balakrishnan, S., Saint-André, P. and Mester de Parajd, M. Deoxyfructo-serotonin: a new drug with anti-leprosy activity. *Ann. Microbiol. (Paris)* **133B** (1982) 427–432.

In the mouse foot pad, deoxyfructo-serotonin (DES) shows a definite inhibitory effect on the multiplication of *Mycobacterium leprae* in dapsone-sensitive as well as dapsone-resistant cases.

In clinical trials, based on seven cases treated with DES for an average period of six months, the beneficial effects of DES are observed after a few weeks of treatment in BB cases, and after a few months in LL cases. In addition to clear improvements in the appearance of the skin (regression and healing of nodules, almost complete disappearance of infiltration, etc.) one observes in the majority of cases a rapid improvement in the Bacteriologic and Morphological Indexes, the latter falling to 0%. In the course of these studies, no single suggestion of intolerance was detected.—Authors' Summary

Modlin, R. L., Hofman, F. M., Taylor, C. R. and Rea, T. H. T lymphocyte subsets in the skin lesions of patients with leprosy. *J. Am. Acad. Dermatol.* **8** (1983) 181–189.

Lymphocyte subsets in the tissues of 14 patients with leprosy were studied using monoclonal antibodies and a modified immunoperoxidase technique. Two immu-

nohistologic patterns were observed. In tuberculoid leprosy, helper-inducer cells were present among the aggregates of mononuclear phagocytes (epithelioid cells), but the suppressor-cytotoxic cells were predominantly in the lymphocytic mantle surrounding the epithelioid cell aggregates. In reversal reaction and lepromatous tissues, the helper-inducer and the suppressor-cytotoxic cells were both distributed among the mononuclear phagocytes (histiocytes). In tuberculoid specimens the Langerhans' cells of the epidermis were increased in number as compared to lepromatous and normal tissues. The technique used appears to be of value in studying some of the cellular components of the immune response *in situ*.—Authors' Summary

Sanders, S. W., Zone, J. J., Foltz, R. L., Tolman, K. G. and Rollins, D. E. Hemolytic anemia induced by dapsone transmitted through breast milk. *Ann. Intern. Med.* **96** (1982) 465–466.

Dapsone (4,4'-diaminodiphenyl sulfone) is used to treat several dermatologic disorders including dermatitis herpetiformis. Due to the chronicity of dermatitis herpetiformis and its frequent onset from age 20 to 40 years, therapy with dapsone may coincide with pregnancy and lactation. We describe an infant who had significant serum concentrations of dapsone and its primary metabolite, monoacetyldapsone, after

ingesting breast milk containing dapsone. Both the mother and infant had compensated hemolytic anemia.—(*From the article*)

Santos, M. F. Q., Jr., Lombardi, C. and Belda, W. Talidomida: uma revisao da literatura. [Thalidomide: a review of the literature.] *Hansen. Int.* **6** (1981) 136–145. (in Portuguese)

This article provides an extensive revision of the specific literature about pharmacological, metabolic, and teratogenic aspects of thalidomide, with special emphasis to its therapeutic employment in dermatology, focusing its effects in the hansenic reaction.—Authors' Abstract

Seshadri, P. S. and Ravi, N. T. Treatment of sulphone resistant leprosy—a review of sixty one cases. *Lepr. India* **54** (1982) 639–647.

The clinical, bacteriological, and histological results of treating 61 proved cases of sulfone-resistant leprosy with various drugs, such as thiacetazone, clofazimine, and rifampin are reported. Clofazimine appears to be the most efficacious since 31 of the 33 patients who became negative or nearly negative were from groups receiving the drug. The constraints in the management of sulfone-resistant leprosy patients are discussed and the need for planned therapeutic trials is stressed.—Authors' Summary

Clinical Sciences

Appa Rao, A. V. N., Krishna, D. R., Ramanakar, T. V. and Prabhakar, M. C. "Jala Neti" a yoga technique for nasal comfort and hygiene in leprosy patients. *Lepr. India* **54** (1982) 691–694.

The technique "Jala Neti" as described in yoga is a general hygienic procedure to cleanse the nostrils effectively with normal saline. The above-mentioned technique was tried in three leprosy centers, namely Jamikunta, Huzurabad, and Warangal in Andhra Pradesh, India, and was found to be acceptable to patients of leprosy. The tech-

nique has been found to be superior to the conventional method recommended to cleanse the nostrils in leprosy patients.—Authors' Summary

Bernardi, C., Ferreira, J., del Pino, G., Bakos, L., Gerbase, A. C., Gervini, R. L. and Gutierrez, M. Leprosy classification for use in control programs. *Hansen. Int.* **6** (1981) 130–135.

Some classifications of leprosy currently in use are reviewed and the difficulties of their application in field work are analyzed.

While the scientific value of these classifications in order to identify precisely the clinical, bacteriological, histological, and immunological aspects of the disease is recognized, an alternative simplified classification is suggested, to be used in control programs. In this classification clinical forms that require the same public health action are put together. Thus, clinical forms are reduced to three basic groups.

The clinical and laboratory criteria which define each group are presented, as well as the correlation between this simplified classification and the classic one.—Authors' Abstract

Brazin, S. A. Leprosy (Hansen's disease). Symposium on Granulomatous Disorders of the Head and Neck. Otolaryngol. Clin. North Am. **15** (1982) 597–611.

The author begins with a general review of clinical leprosy. Specific manifestations in the ear, nose, and throat are then considered. Ninety-seven percent of lepromatous leprosy patients present with changes of the nasal mucosa, most commonly beginning at the anterior inferior turbinate. A number of patients have an impaired sense of smell. The statement is made that collapse of the nose occurs in 26% of the patients as a result of nasal cartilage or bone destruction. The most frequently affected portions of the facial nerve are the zygomatic branches leading to the lower eyelid. Ear deformities are seen in 30%–73% of patients with leprosy as diffuse infiltrations, discrete nodules, or gross ulcerations. The histopathology, differential diagnosis, and treatment are briefly reviewed.—(*Adapted from the article*)

Christiansen, J. V., Jensen, J. R., Søgård, H. and Thestrup-Pedersen, K. Leprosy in Vietnamese refugees: A case report. Acta Derm. Venerol. (Stockh.) **63** (1983) 81–83.

A 41-year-old Vietnamese refugee was found to have tuberculoid leprosy. Dapsone treatment cleared her skin lesion, but did not remove the paresthesia in the right ulnar nerve. Immunological investigations revealed a strongly positive lepromin test and a significant change in the ratio of T γ and T μ lymphocytes in peripheral blood. The

incidence of leprosy in Vietnamese refugees in Scandinavia is discussed.—Authors' Abstract

Cook, G. C. and Corachan, M. Hepatic structure and function in Papua New Guineans with leprosy. Trans. R. Soc. Trop. Med. Hyg. **76** (1982) 721–727.

Hepatic function, including plasma bromsulphthalein (BSP) clearance was studied on 20 Papua New Guineans with leprosy: 11 lepromatous (LL) (6 had erythema nodosum leprosum (ENL)) (group A), and 9 tuberculoid or borderline (BT or BB) (group B); 12 controls (group C) were also studied. Four of five with abnormal BSP results had significant complicating or additional factors (hepatic amyloidosis, pustular ENL, hepato-cellular carcinoma and a pyogenic abscess), compared with two of 15 with normal results (tuberculous osteitis and pyogenic osteomyelitis). In 9 (5 from group A, and 4 from group B) needle liver biopsy histology was assessed: foci of vacuolated phagocytes and histiocytes, and tuberculoid granulomata were the most frequent lesions; none had cirrhosis.

Leprosy is not associated with impaired hepato-cellular function unless a severe complication or coincident disease is concurrently present. In this limited study therapeutic agents were not associated with abnormal liver structure or function. When liver function is abnormal in leprosy, another cause (e.g., secondary amyloidosis, sepsis or malignancy) should be searched for.—Authors' Summary

Das, R., Goswami, A., Mitra, A. K. and Roy, I. S. Ocular complications in leprosy. J. Indian Med. Assoc. **74** (1980) 5–8.

One hundred fifty cases of leprosy with ocular complications were studied in West Bengal. It was found that despite the advent of sulfone therapy, the ocular damage was extensive and crippling. As many as 38% had uveal lesions. The lids and eyebrows were involved in 56%, cornea in 34%, lens in 46% and the globe in 16% of the cases. Blindness was extensive (65.3%), but those due to cataract were operated on with success. The major factor contributing to the damage was delay in diagnosis and treatment. The obvious remedy is to have reg-

ular examination and treatment of the eyes as soon as a case of leprosy is detected.—Authors' Summary

de Maar, E. W. J., Chaudhury, R. R., Kofi Ekue, J. M., Granata, F. and Walker, A. N. Management of clinical trials in developing countries. *J. Int. Med. Res.* **11** (1983) 1–5.

Clinical trials in developing countries require consideration of factors which are not routinely emphasized in trials in developing countries. Different genetic, nutritional or climatic conditions can lower body weights, or differences in metabolism may make other dosage recommendations necessary. The protocol for clinical trials in developing countries needs to be worked out with broad participation from the investigators from the local area. In cases of doubt about the logistical feasibility of a clinical trial in developing countries, a pilot study consisting of a trial run of the test procedures or a pilot study using an established drug, may identify pitfalls. Compliance, concomitant unauthorized medications, and diversion of the test drug for the other purposes may create problems. Ethical considerations, data collection and analysis, and eventual publication of results all pose potential problems in clinical trials in developing countries which may not be encountered in such trials in developed areas.—(From the article)

Finkelstein, S., Sima, A. A. F., Loughheed, W. M., Gentili, F. and Keystone, J. S. Pure neural tuberculoid leprosy simulating a peripheral nerve tumor. *Neurosurgery* **10** (1982) 771–774.

A 21-year-old man had developed a subcutaneous swelling of the right upper arm over two years. The clinical impression was that of a neurofibroma. Pathological examination showed that the lesion was tuberculoid leprosy. Pure neural tuberculoid leprosy, unassociated with skin changes, is exceedingly rare. The difficulties encountered in its diagnosis are discussed.—Authors' Summary

Fleury, R. N., Opromolla, D. V. A. and Tonello, C. S. Meningoencefalite por *Cryptococcus neoformans* como complicação

de insuficiência vascular arteriosclerótica em hanseníase virchowiana. [Meningoencephalitis due to *Cryptococcus neoformans* complicated by arteriosclerotic vascular insufficiency in virchowian hanseniasis.] *Hansen. Int.* **6** (1981) 146–152. (in Portuguese)

A 39-year-old white man, with advanced virchowian hanseniasis, died with signs of extensive meningeal involvement. His medical background showed repeated episodes of erythema nodosum hansenicum (ENH) in the last three years of his life, besides ischemic gangrene with amputation of the left leg and cerebral vascular ischemic attacks. The autopsy revealed an advanced stage of arteriosclerosis affecting mainly the brain and the distal segment of the aorta and its ramifications. A propagating thrombus was found along the left femoral and iliac arteries and in the terminal portion of the aorta extending to the renal arteries. Thrombosis was also found along the left femoral vein, left iliac vein, and distal segment of the inferior vena cava. The brain showed anemic infarction in organization and a generalized meningoencephalic involvement with granulomatous reaction caused by *Cryptococcus neoformans*. A possible relationship between erythema nodosum reactions and thrombosis phenomena was suggested. Torulosis was considered as a final occurrence and the proliferative vasculitis due to the granulomatous process in the subarachnoidal space has certainly aggravated the cerebral ischemia.—Authors' Summary

García, R. R., Fliess, E. L. and Pacin, A. Actividad de la creatinfosfoquinasa (CPK) sérica en pacientes hansenianos. [Creatinophosphokinase (CPK) activity in the sera of hanseniasis patients.] *Leprologia* **24** (1982) 69–71. (in Spanish)

Serum activities of creatine phosphokinase (CPK) were studied in hanseniasis patients of the lepromatous, borderline, and tuberculoid types, with and without reactions. Mean values did not differ significantly between hanseniasis patients and healthy subjects ($p > 0.5$) nor among the clinical forms ($p > 0.7$). The results indicate that muscle cells are not severely involved in the damage of reactional phenomena.—Authors' Summary

Gatti, J. C., Cardama, J. E., Ocampo, J. C., López, M. L. and Margariños, R. A. Dificultad clínica e histopatológica en el diagnóstico diferencial de la enfermedad de Hansen. [Clinical and histopathological difficulties in the differential diagnosis of Hansen's disease.] *Leprologia* **24** (1982) 7–38. (in Spanish)

A short introduction about the differential diagnosis of Hansen's disease considered by some authors is made. Following, we detail our own difficulties which were sometimes only clinical, such as leonine facies, loss of hair of the eyebrows and eyelashes, gynecomastia, ulnar claw hand, etc., and sometimes the type of infiltrate involving capillaries, glands, the arrector pili muscle, and the nerve fibers, and often stimulating the free zone between the epidermis and dermis.—Authors' Summary

Gimenez, M. F. and Tonelli, H. B. Compromiso orquiepididimario en la lepra dimorfa. [Orchiepididymitis in dimorphous leprosy.] *Leprologia* **24** (1982) 47–55. (in Spanish)

A case of dimorphous leprosy with orchiepididymitis is reported. A summary of this clinical form, the genitourinary system in leprosy, and a bibliographical review are presented. The references that are in agreement with our paper are referred; endorsing the fact that although exceptional, this involvement should be investigated.—Authors' Summary

Hameedullah, A., Lal, S. and Garg, B. R. Composite skin contact smears in multibacillary leprosy patients. *Lepr. India* **54** (1982) 605–612.

Composite skin contact smears technique was used in 20 multibacillary leprosy patients to find out the presence of AFB on their intact skin. One hundred twenty-one acid-fast bacilli (AFB) were found in 930 sq cm area of skin surface examined. Seventy-five AFB were solidly staining and 46 were granular. The bacilli were found in all the sites examined. Immunofluorescent staining showed *Mycobacterium leprae* in one out of four patients. The number of bacilli discharged from the intact skin seems adequate for the transmission of leprosy con-

sidering the large surface area of the skin and evidence in mouse experiments that multiplication of *M. leprae* can be obtained after inoculation of very small number of bacilli.—Authors' Summary

Kenzhebaev, A. Y., Kharatiyan, A. M., Bdovina, N. A. and Esbergenov, B. Radiotelemetric examination of gastric function in patients with leprosy. *Vestn. Dermatol. Venerol.* **5** (1982) 63–67. (in Russian)

Radiotelemetric examinations of gastric function were carried out in 56 patients with different types of leprosy. The rate and degree of disorders in the acid-producing function of the stomach in patients with leprosy were found to depend on the state of the leprosy process, duration of the diseases, complications, and sequelae. Typical changes (delayed response) in the excitability of the secretory apparatus of the stomach are noted.—(From Trop. Dis. Bull.)

Kruyt, J. A., Klokke, A. H., Roenhorst, H. W. and The, T. H. Leprosy, borderline-lepromatous, and cytomegalovirus infection. *Netherlands Society Proceedings. Br. J. Dermatol.* **108** (1983) 113–114.

A 53-year-old male Indonesian had been living in The Netherlands almost continuously for 30 years. He had had a white spot on his right cheek in 1951. In 1980, after a coronary bypass operation, the patient noted red elevated spots on his face which spread to the trunk. Peripheral nerves were not enlarged and the only area of loss of sensation was on the lateral aspect of the left lower leg. The patient showed an elevated titer of antibodies to cytomegalovirus. The patient showed a depressed cell-mediated immunity as measured by low responsiveness against ConA in *in vitro* lymphocyte blast transformation studies. It seemed possible that a lepromatous infection, possibly acquired more than 30 years earlier, was activated because of a cytomegalovirus infection. The cytomegalovirus infection could be primary, or could be by blood transfusion or reactivation of a latent cytomegalovirus infection during the coronary bypass operation.—(From the article)

Kumar, B., Kaur, S., Kataria, S. and Roy, S. N. Concomitant occurrence of leprosy and tuberculosis—a clinical, bacteriological and radiological evaluation. *Lepr. India* **54** (1982) 671–676.

One hundred seventeen consecutive patients of leprosy were bacteriologically and radiologically investigated for evidence of concomitant tuberculosis anywhere in the body. Out of the total, only nine patients (7.7%) showed evidence of active tuberculosis, bacteriologically and/or radiologically. Three patients had sputum positive for acid-fast bacilli; two out of these were radiologically negative, while one had evidence of pulmonary tuberculosis. From seven patients with radiological evidence of tuberculosis, tubercle bacilli could be grown in only one. Tuberculosis was found to occur throughout the leprosy spectrum. It is important to recognize the presence of tuberculosis in leprosy patients so that proper therapeutic measures may be taken to avoid monotherapy of tuberculosis.—Authors' Summary

Lewis, S. Reproducibility of sensory testing and voluntary muscle testing in evaluating the treatment of acute neuritis in leprosy patients. *Lepr. Rev.* **54** (1983) 23–30.

Based on methods discussed at a neuritis workshop held in Karigiri in South India in 1980, this study describes attempts to standardize sensory testing and voluntary muscle testing in a group of 20 patients with tuberculoid leprosy. Patients were assessed by the same observer on two occasions at intervals of two weeks. The results confirm that accurate methods for assessing the treatment of neuritis in leprosy remain elusive. In this group of patients, however, and under the conditions described, it appears that greater reliance can be placed on sensory testing, particularly fine touch, than on voluntary muscle testing.—Author's Summary

Manzur, J. Skin diseases in Addis Ababa: A preliminary review. *Ethiop. Med. J.* **19** (1981) 123–134.

The pattern of skin diseases in 1000 consecutive new patients seen in several dermatological clinics between 13 August and

22 November 1980 in Addis Ababa, Ethiopia, is presented. In addition to the common diseases of temperate climates, a number of tropical dermatoses were found. More than 50% of patients were in the age group 15–34 years. There was no statistical difference between the sexes with regard to skin diseases. Infectious diseases were the most frequent (37.8%). Hyperpigmentation of the face (7.5%) was the most frequently observed single disease, followed by acne vulgaris, contact eczema, and scabies. Out of every five patients, one classified under the eczema group. High detection of leprosy was another important finding: 26 new cases in only three months. Borderline tuberculoid and borderline lepromatous leprosy were the types most often seen.

Similar studies and evaluation (preferably made by a dermatologist) in Addis Ababa, in Shoa, and in other administrative regions in Ethiopia, would be useful in determining the incidence of skin diseases in the nation.—Author's Abstract

Mishner, H. S. and McTighe, A. H. A case report of lepromatous leprosy. *Md. State Med. J.* **31** (1982) 53–54.

A Chinese man was admitted to the Maryland General Hospital in Baltimore, Maryland, U.S.A., with biopsy-proven leprosy. Although leprosy is rare outside certain endemic foci in the United States, we believe it should be thought of in the differential diagnosis of cutaneous nodules with anesthesia. This discussion reviews the pathology of leprosy and its diagnosis.—(From the article)

Nagar, K. S., Laha, N. N., Sethi, N. C. and Mehta, R. S. A study of palmar dermatoglyphics in leprosy. *J. Assoc. Physicians India* **29** (1981) 841–847.

Palmar dermatoglyphics were studied in 50 cases of leprosy, 25 males and 25 females. Fifty normals were studied as controls, comprising 25 males and 25 females. Three parameters were considered for the study. In males, ridge count from the tri-radial point to point of core showed significant differences in right palm digit I, left palm digits I, II, III and IV, from normals. In females, the same parameter revealed statistically significant differences in the right

palm digit II only. In males, metrics analyses of palms showed that the interval from the axial triradius to a vertical dropped from triradius a on the right side and the intertriradial interval c-d on left side were having significant differences from normals. In females, the same parameter showed statistically significant differences in the intertriradial intervals b-c on both sides, and c-d on the left side. Mean values of the atd angle revealed statistically insignificant differences from normals in both sexes.—Authors' Summary

Prabhu, S. R. and Daftary, D. K. Atrophic lesions of the tongue in leprosy patients. *Trop. Dent. J.* **5** (1982) 75–85.

“Out of the 700 leprosy patients [in Bombay] examined for oro-facial lesions, 59 showed papillary atrophy of the tongue”—(From *Trop. Dis. Bull.*)

Prasad, S. B. Calcification in ulnar nerve abscess in a patient with leprosy—a case report. *Lepr. India* **54** (1982) 809–812.

A patient attended the Surgical Department of Darbhanga Medical College, Laheriasarai, India, with the complaint of loss of sensation in the left little and ring fingers and mild incoordination of the left hand for the last nine months. On examination there was hard swelling which was firm, painless, fusiform, about 4 cm in diameter situated in the subcutaneous tissue two inches proximal to the medial epicondyle of the left elbow. The mass was immobile axially, but freely mobile mediolaterally, and on percussion of the mass paraesthesia in the distribution of ulnar nerve was detected. Moreover, there was a mild decrease in two points discrimination in the tactile surfaces of the little finger and ulnar border of the ring finger. A large number of investigations for the diagnosis of the case were undertaken but the diagnosis was not clear. Only after the histological examination from the swelling was it revealed that the patient was suffering from leprosy. There were no signs in the skin, and it was a case of pure neural type.—(From the article)

Ramos-Caro, F. A. Histoid lepromas. *Cutis* **30** (1982) 108–131.

Histoid lepromas are nodular lesions which usually arise in patients with lepromatous leprosy who have been on sulfones for many years. It is postulated that they are produced by sulfone-resistant, acid-fast mutant organisms. Here, two patients with this condition are presented and the pertinent literature is reviewed.—Author's Abstract

Raval, S. N., Sengupta, U., Ramu, G., Prabhune, P. V. and Desikan, K. V. A study of continuous bacillaemia in borderline and lepromatous type of leprosy. *Lepr. India* **54** (1982) 623–633.

The present work has established beyond doubt that bacilleamia occurs practically in all cases of borderline and lepromatous leprosy. The number of bacilli in the blood is significantly high, to the tune of 4000 bacilli per ml. Even so, it does not produce any adverse symptoms of septicemia. Special emphasis was laid in the present study for determining the continuity or otherwise of bacilleamia. Some of the patients had continuous bacilleamia according to the criteria fixed in the present study. It was also found that the number of bacilli discharged into the blood bears no relationship with the bacillary load in the body as assessed by skin and nasal smears.—Authors' Summary

Reichart, P. E., Srisuwan, S. and Metah, D. Lesions of the facial and trigeminal nerve in leprosy. An evaluation of 43 cases. *Int. J. Oral Surg.* **11** (1982) 14–20.

Facial and trigeminal nerve involvement was studied in 43 leprosy patients 5.7% of the 750 Thai national in-patients of a leprosy rehabilitation center. Involvement of the facial nerve occurred late in the disease and had an average duration of 12.1 years. The zygomatic branches of this nerve were the most frequently affected. Hypesthesia and anesthesia were most often observed in the maxillary divisions. Periorbital surgical procedures to prevent severe ocular complications are evaluated and discussed.—Authors' Abstract

Ruan Xi-Yuan, et al. A preliminary study of dermatoglyphics in patients with leprosy. *Chin. J. Clin. Dermatol.* **12** (1983) 30–32. (in Chinese)

A statistical analysis of dermatoglyphic patterns of finger tips and palms was obtained from 62 patients with multibacillary leprosy and a control group of 750 persons without leprosy.

The preliminary study reveals that there is a noticeable difference in dermatoglyphic patterns between the two groups with respect to the following: a) There were less whorls on finger tips seen in the leprosy group; b) Loops on finger tips are more common in male patients and arches are more common in female patients; c) The total ridge count of patients with leprosy was also significantly less than the controls; d) Among palmar flexions creases, the single radial base crease (Simian crease) is more common in patients with leprosy than their respective controls.

This study suggests that certain factors about dermatoglyphic patterns may be correlated with the hereditary susceptibility to leprosy. However, it is felt that this study should not be considered conclusive, since it was done only on a small number of patients with leprosy. More work in this respect is needed.—(*From Authors' Abstract*)

Sarno, E. N., Azulay, D. R., Vieira, L. M. M., Quadra, A. A., Barbosa, I. S. and Azulay, R. D. Prevalência do antígeno Austrália (HbsAg) em pacientes hansenianos. [Prevalence of Australia antigen (HBsAg) in hanseniasis patients.] *AMB* **126** (1980) 391–392. (in Portuguese)

The serum from 153 patients with various clinical forms of hanseniasis were studied to observe the prevalence of Australia antigen in this population. We compared the results of this group with control groups constituted by hospitalized patients and a normal group constituted by people who worked in the hospital. In the group of virchowian and borderline hanseniasis we found two positive cases (1.55%) in 129 studied, in the tuberculoid and indeterminate forms (24 cases) the results were negative. The highest prevalence (2.0%) was found in the control group of hospitalized patients (6/300).—*Authors' Summary*

Sasaki, N. and Kawatsu, K. Problems of malignant tumor complications in leprosy. I. An increase in the incidence of

malignant tumor complication. *Jpn. J. Lepr.* **51** (1982) 85–95.

Through investigations of the autopsies made at the National Leprosarium Tama-Zensho-en in the past 25 years, a remarkable increase with the lapse of time was confirmed in the incidence of malignant tumor (MT) complications of leprosy patients.

Through observation of the MT complications by the difference of sex, age, and disease type, the incidence was especially high among the males in lepromatous patients. On comparison with tuberculoid patients, the frequency of MT complications among lepromatous patients became especially remarkable in the latter period (1976–1979).

Among the various MT complications, the predominance was cancer of the digestive system, especially the stomach followed by liver and esophagus. As to the MTs other than the digestive system, an increase was observed in the incidence of lung cancer. Noteworthy were complications of malignant lymphoma and skin cancer.

On the other hand, out of the total of 1136 leprosy patients who died in the whole national leprosaria during the recent eight-year period 1971–1978, excluding autopsy cases, MT complications were found in 17.3% which was almost the same as that of the general population.—(*From the article*)

Sheskin, J. Lepromatosis difusa de Lucio-Alvarado-Latapi con fenomeno de Lucio. Primer caso en el cercano oriente. [Diffuse lepromatosis of Lucio-Alvarado-Latapi with Lucio phenomenon. First case in the Near East.] *Rev. Leprol.* **13** (1982) 651–656. (in Spanish)

A case of diffuse lepromatosis of Lucio-Alvarado-Latapi, with a necrotic leprosy reaction (Lucio phenomenon) is reported. It is the first case reported in the geographic area of the author.—(*Adapted from Author's summary*)

Takizawa, H., Kobayashi, S., Miura, M. and Fukuda, M. Glucose-6-phosphate dehydrogenase in Hansen's disease patients receiving sulfones or sulfamethoxypyridazine. *Jpn. J. Lepr.* **51** (1982) 65–67. (in Japanese)

Two hundred eighty-one patients receiving sulfones (DDS, Protogen, or Promin) or sulfamethoxypyridazine were examined by a dichlorophenol indophenol (DPIP) test for glucose-6-phosphate dehydrogenase (G6PD).

The blood samples of 230 cases decolorized the dye within 80 min; while the residual 51 samples required 80 min or more. A quantitative UV test for G6PD was performed on 48 of these 51 patients.

The results of the UV test showed that all of the patients had G6PD values between 120 mU and 240 mU per 10^9 red blood cells except one male patient (114.4 mU). His red blood cell count and hemoglobin index were within normal range, and Heinz bodies were not formed in his red blood cells although he was receiving 50 mg of DDS every day.—(From Authors' Summary)

Immuno-Pathology

Bottasso, O. A., Corona, C. J. J. and Morini, J. C. Mecanismos probables de inmunosupresion en lepra. [Probable mechanisms of immunosuppression in leprosy.] *Leprologia* **24** (1982) 65–67. (in Spanish)

The clinical characteristics of leprosy and especially the immunological ones, their modifications with therapy and the type of reaction of the people who live together are reviewed.

Then a review of the experimental facts realized by different authors is made in order to finish postulating that some mechanisms of immunosuppression are produced in Hansen's disease and that they should play an important function in the pathophysiology of the disease.—Authors' Summary

Das, P. K., Ibrahim, A. A., Binkhuysen, F., Hue, P. T., Qui, T. H., Rangarajan, R. and Ruitenbergh, E. J. The use of subcellular components of BCG for studying host-mycobacterium interaction in relation to leprosy. *Ann. Immunol. (Paris)* **133D** (1982) 41–59.

Mycobacterium bovis-BCG was sonified and centrifuged at 90,000 *g* for 2 hr to obtain pellet (P90) and supernatant (S90), and bacilli broken by chilled X-press were fractionated into cell wall (CW), plasma membrane and cytosol. Rabbits were immunized with P90, S90 and whole sonified-broken BCG. The antigenic make-up of these sub-

cellular components was analyzed by cross-immunoelectrophoresis using these antisera. These subcellular preparations were also used for detecting circulating antibodies in the sera of 45 leprosy patients by Ouchterlony's technique and immunoelectrophoresis. Although there were many antigenic determinants common to more than one fraction, some components were found in only one fraction. Furthermore, different leprosy patients showed different patterns of antibody response to the antigens in the different fractions.

In addition, these fractions were also used to assess cell-mediated immunity in mice sensitized with lyophilized whole BCG as well as with irradiated mycobacterium. It was found that BCG, intraperitoneally injected, engendered different specifically antigen-sensitized populations of lymphocytes in the spleen and lymph node. Moreover, a certain degree of antigenic crossreactivity was observed between BCG and *M. leprae*, possibly at the T cell level. *In vitro* experiments suggested that the CW stimulated B cells, indicating a mitogenic activity leading to polyclonal activation. Finally, *in vitro* priming experiments established that these subcellular fractions could sensitize human peripheral lymphocytes, and upon secondary culture all primed cells were able to respond to homologous preparations but not always to heterologous preparations, thus offering a means to distinguish antigens of interest from those antigenically less complicated fractions at the T cell level.—Authors' Summary

de la Cruz, F., Diaz, J. W. and Goncharonko, I. Estudio de la asociación entre los antígenos del sistema HLA y la enfermedad de Hansen. Estudios familiares. [Study of the association between the antigens of the HLA system and Hansen's disease. Family studies.] *Rev. Cub. Med. Trop.* **34** (1982) 26–33. (in Spanish)

Results on the study of the distribution of HLA antigens within ten families, where at least one of their members was affected by Hansen's disease, are offered. The existence of variable degrees of familial haplotypes and disease association allow one to suppose the possible existence of one or more factors relating Hansen's disease and HLA region antigens.—(Translation of Authors' abstract)

Finiasz, M. R., Arias, D. A., Valdez, R., Estevez, M. E. and Sen, L. Subpoblaciones linfoides T y B en enfermos con lepra. [Subpopulations of T and B lymphocytes in leprosy patients.] *Medicina (B. Aires)* **41** Suppl. (1981) 131–136. (in Spanish)

The results obtained by various authors regarding the lymphocyte populations of leprosy patients are controversial. The aim of this study was to determine the number of T and B lymphocytes in peripheral blood of patients with lepromatous leprosy (LL) and in patients with tuberculoid leprosy (LT) using a battery of membrane markers. The absolute lymphocyte number and the following membrane markers were determined: E rosettes, mouse red blood cell rosettes, *Saccharomyces cerevisiae* plus complement rosettes and membrane bound immunoglobulins. Our results indicate that: leprosy patients were lymphopenic; the thymic dependent population was decreased in both polar forms of leprosy with respect to normal controls (N). B lymphocytes with C3 receptors and those with surface immunoglobulins were not altered. The B subset expressing mouse erythrocyte receptors was decreased while LT had the same number of null lymphocytes as normal subjects. The decrease in the T cell population contributed to lymphopenia in leprosy patients. The reduced levels of circulating T cells might reflect altered lymphocyte traffic occurring as a result of the infection. The

use of monoclonal antibodies to identify human T cell subsets will provide a new tool for the analysis of T subpopulations in leprosy patients. Future functional knowledge of the B cell subset with mouse erythrocyte receptors, that we found decreased in the lepromatous polar form of leprosy, should contribute to a better understanding of the disease.—Authors' Summary

Fleming, B. and Rook, G. A. W. T-cell-dependent polyclonal activation by soluble mycobacterial extracts of B cells in peripheral blood mononuclear cell populations from leprosy patients and normal donors. *Immunology* **47** (1982) 589–595.

Soluble extracts of ultrasonically disrupted mycobacteria (including *Mycobacterium leprae*) cause strong T cell-dependent, Cyclosporin A-sensitive, polyclonal B cell activation, in human peripheral blood mononuclear cell preparations. It is not enhanced by cortisol.

Cells from cases of lepromatous leprosy show no polyclonal B cell activation in the presence of extracts of *M. leprae*, although they respond normally to other mycobacterial species.

The polyclonal B cell activation response to the *M. leprae* extract, of a small group of normal leprosy contacts, was reduced relative to that of non-contacts.—Authors' Summary

Fliess, E. L., Comesaña, G., Carrara, R. C. and España, A. Fagocitosis y lisis de *Candida albicans* y *Candida pseudotropicalis* por polimorfonucleares neutrófilos de pacientes hansenianos. [Phagocytosis and lysis of *Candida albicans* and *Candida pseudotropicalis* by polymorphonuclear leukocytes of hanseniasis patients.] *Hansen. Int.* **6** (1981) 109–113. (in Spanish)

The phagocytosis and lysis of *Candida albicans* and *C. pseudotropicalis* by human neutrophils were examined in 43 hanseniasis patients (19 quiescent virchowians, 12 reactional virchowians and 12 tuberculoid patients) and 15 healthy subjects. The purpose of this study was to determine whether neutrophils from hanseniasis patients were altered in their enzyme systems myeloperoxidase-dependent (tested by lysis of *C. albicans*) and myeloperoxidase-independent

(tested by lysis of *C. pseudotropicalis*). The results indicate that polymorphonuclear neutrophils of hanseniasis patients had a similar candidacidal activity as that of human normal neutrophils ($p > 0.2$) in their myeloperoxidase-dependent and myeloperoxidase-independent systems. The enzymatic system activity is also similar in all the clinical forms of hanseniasis ($p > 0.3$).—Authors' Abstract

Gilbert, E., Cubria, J. L., Gratacos, R., Castro, J., Monfort, J., Castel, T. and Lecha, M. Lepra de Lucio. [Lucio leprosy.] *Med. Cutan. Iber. Lat. Am.* **10** (1982) 41–46. (in Portuguese)

A case of diffuse lepromatous leprosy with lepra reaction type II—Lucio's phenomenon—in a 24-year-old male patient is reported.

The histological examination of the necrotic lesions and of the apparently normal skin showed the presence of dense perivascular and perianexial lymphohistiocytic infiltrates with great quantities of bacilli. The first biopsy did not show a picture of leukocytoclastic vasculitis but only areas of necrosis.

The immunofluorescence studies revealed, on direct examination, complement deposits on vessel walls. The complement levels in blood were lowered and circulating immune complexes were also detected.

These data confirm the opinion that Lucio's phenomenon is caused by circulating immune complexes fixed on dermal vessel walls causing skin necrotic lesions.—Authors' Summary

Giménez, M. M., de Sorrentino, A. H. and Sorrentino, A. P. Perfil inmunológico en pacientes de lepra lepromatosa; nuestra experiencia. [Immunological profile in lepromatous leprosy patients; our experience.] *Leprológia* **24** (1982) 57–63. (in Spanish)

The authors realize an immunological profile in 54 lepromatous leprosy patients and divide them in four groups: lepromatous leprosy type with clinical healing and negative bacteriology (27); evolutive leprosy in periodic reaction (13); evolutive leprosy in reactional state (3); and patients

without treatment (6). The results are compared with 55 healthy controls.

There is a diminution of circulating T lymphocytes in all of the patients; the B lymphocytes are within the upper normal values and the IgA presents significant increases in respect to the controls. In the different groups, the T lymphocytes were within the normal values in the first; little decreased in those with periodic reaction; and significantly decreased in patients with no reactional state and virgin of treatment.

The values of B lymphocytes did not present any variation. The IgG was within the upper normal values in all groups; the IgA was significantly increased in the healthy, periodic reaction and virgin of treatment groups.

IgM showed a great increase in the evolutive form with periodic reaction and virgin of treatment. These findings are discussed.—(Adapted from the Authors' Summary)

Jaswaney, V. L., Nadkarni, J. S. and Rao, S. S. Serum-mediated suppression of E-RFC levels in leprosy and reversal by fetal calf serum. *Indian J. Exp. Biol.* **20** (1982) 731–733.

A significant decrease in the erythrocyte rosette forming cell (E-RFC) levels in the peripheral blood lymphocytes (PBL) of lepromatous leprosy (LL) patients was observed and it was shown that the same could be brought to normal levels upon incubation for 18–24 hr in medium containing 20% fetal calf serum (FCS). E-RFC levels of PBL from normal donors were reduced significantly upon incubation in sera from LL patients, but not when sera from tuberculoid leprosy (TT) or normal AB donors are used. The results suggest that the decreased E-RFC levels found in LL patients are due to serum factor(s) which specifically interact with a subset of T lymphocytes.—Authors' Summary

Lad, S. J. and Mahadevan, P. R. Adherence of *Mycobacterium leprae* to macrophage as an indicator of pathogen induced membrane changes. *Indian J. Med. Res.* **76** (1982) 804–813.

The phenomenon of adherence was studied using *Mycobacterium leprae* and its host

cell—the macrophages. Macrophages were found to possess receptors for the carbohydrate moiety present on the cell wall of *M. leprae*. The level of adherence was reduced in the active state of the disease, but was restored on effective treatment of the patient and by trypsin treatment of macrophages, *in vitro*. The role of carbohydrates in this binding was demonstrated by competitive inhibition studies using simple sugars. The overall competitive inhibition pattern showed the high specificity of this interaction among acid-fast bacteria. The altered membrane structure of the macrophage with respect to its receptors for carbohydrates may imply an impairment in the recognition of the pathogen.—Authors' Summary

Lyberg, T., Closs, O. and Prydz, H. Effect of purified protein derivative and sonicates of *Mycobacterium leprae* and *Mycobacterium bovis* BCG on thromboplastin response in human monocytes *in vitro*. Infect. Immun. **38** (1982) 855–859.

Human monocytes isolated from peripheral blood responded with increased thromboplastin expression upon stimulation *in vitro* with three mycobacterial antigens: tuberculin purified protein derivative, and sonicates of *Mycobacterium bovis* BCG and *M. leprae*. The stimulating principle of mycobacteria is probably a cell wall constituent since crude extracts of cell walls were 2.5–25 times more potent in stimulating thromboplastin synthesis than were whole sonicates. This thromboplastin response was inhibited by inhibitors of RNA and protein synthesis, dexamethasone, and agents that caused elevation of intracellular cyclic AMP. The presence of lymphocytes did not enhance the monocyte thromboplastin response significantly during the first 24 hr of incubation. For *M. bovis* BCG and *M. leprae* sonicates, the thromboplastin response correlated with general activating effects measured by determining the release of lysozyme and β -glucuronidase. The role of thromboplastin in chronic inflammatory reactions is discussed.—Authors' Summary

Mackay, I. G., Sengupta, U., Ghei, S. K., Sinha, S. and Ramu, G. Immune status of subsided cases of tuberculoid (TT) and

borderline tuberculoid (BT) leprosy. Lepr. India **54** (1982) 653–663.

A comparative study of lepromin reactions (early and late), *Mycobacterium leprae* induced lymphocyte blastogenesis, percent T cell number in peripheral blood, and immunoglobulin (IgG, IgA and IgM) levels has been made in TT-active, TT-subsided, BT-active and BT-subsided leprosy cases. No significant difference has been noted among these groups in the above-mentioned investigations except in subsided BT cases where 9 out of 11 cases failed to evoke any late skin reaction to Dharmendra antigen. In addition, BT subsided cases also showed significantly raised levels of IgG. The significance of these findings with respect to their immunity and reinfection has been discussed.—Authors' Summary

Manimakalai, Bhatia, V. N., Balakrishnan, S. and Shanmugham, N. E-rosettes in leprosy patients. Lepr. India **54** (1982) 685–690.

Early and total E-rosettes counts were made in the leprosy patients of different clinical types classified histologically and compared with those of healthy controls. The T cell population in LL cases were found to be significantly lower than in other types of leprosy cases and controls. The study of the E-rosette formation at different times of incubation indicated that any point of observation could be used for comparison. However, early (1 hr–2 hr) counts help to distinguish the LL cases from other types of leprosy. A good correlation was noticed between the percentage of rosettes and the lepromin test.—Authors' Summary

Modlin, R. L., Hofman, F. M., Meyer, P. R., Sharma, O. P., Taylor, C. R. and Rea, T. H. *In situ* demonstration of T lymphocyte subsets in granulomatous inflammation: leprosy, rhinoscleroma and sarcoidosis. Clin. Exp. Immunol. **51** (1983) 430–438.

T lymphocyte subpopulations in frozen tissue sections of four granulomatous conditions (5 patients with tuberculoid leprosy, 5 with lepromatous leprosy, 7 with sarcoidosis, and 4 with rhinoscleroma) were studied using monoclonal antibodies and a

modified immunoperoxidase technique. Two immunohistological patterns were observed. In tuberculoid leprosy and sarcoidosis, lymphocytes expressing the helper/inducer phenotype were present within the aggregates of mononuclear phagocytes (epithelioid cells); however, cells with the suppressor/cytotoxic phenotype were predominantly in the lymphocytic mantle surrounding each granuloma. In lepromatous leprosy and rhinoscleroma the helper/inducer T cells and suppressor/cytotoxic T cells were both diffusely distributed among the mononuclear phagocytes (histiocytes) without any discernible mantle. The segregation of the helper/inducer and suppressor/cytotoxic phenotypic subsets was associated with an epithelioid cell differentiation of mononuclear phagocytic cells, bacterial elimination, and a delayed-type hypersensitivity response. The intimate admixture of helper/inducer and suppressor/cytotoxic subsets was associated with undifferentiated mononuclear phagocytes, bacterial proliferation, and the absence of a delayed-type hypersensitivity response. Thus the different distributions of T cell subpopulations in granulomas may be associated with differences in the host's immune response in several forms of granulomatous reactions.—Authors' Summary

Mshana, R. N., Haregewoin, A. and Beleh, A. Thymus-dependent lymphocytes in leprosy. II. Effect of chemotherapy on T-lymphocyte subpopulations. *J. Clin. Immunol.* 2 (1982) 69–74.

The basis of the immunological unresponsiveness seen in leprosy patients is unknown. Untreated lepromatous leprosy patients display an unspecific cellular anergy which disappears with treatment, leaving an anergy specific for *Mycobacterium leprae*. These patients suffer from a complication, erythema nodosum leprosum, characterized by a recurrent eruption of tender skin nodules disappearing in two to three days. These nodules show a histological picture reminiscent of an Arthus reaction. Erythema nodosum leprosum can occur in untreated patients but it is more frequent in those receiving effective chemotherapy, and this has been thought to be due to massive release of antigens from the bacilli. By using

monoclonal antibodies detecting different subpopulations of human peripheral blood T lymphocytes, we have shown that both borderline lepromatous and lepromatous leprosy patients had increased circulating suppressor cells ($p < 0.001$) while the total number of T cells was within the normal range. The suppressor-cell population decreased with the duration of treatment, the change being evident at as early as 21 days. Five patients developed erythema nodosum leprosum during the study period. In all these patients the number of suppressor cells was decreased prior to the complication, increasing to original values with clinical recovery from this syndrome. There was no significant effect on T lymphocyte subpopulations during chemotherapy of borderline tuberculoid leprosy patients. It seems that antileprosy chemotherapy precipitates erythema nodosum leprosum by interfering with immunoregulatory T cells.—Authors' Abstract

Mshana, R. N., Humber, D. P., Beleh, A. and Harboe, M. Immunohistological studies of skin biopsies from patients with lepromatous leprosy. *J. Clin. Immunol.* 3 (1983) 22–29.

Forty-six skin biopsies from lepromatous leprosy patients were examined for immunoglobulin and complement deposits as well as mycobacterial antigens. Rabbit anti-human immunoglobulin, rabbit anti-human C3, and rabbit anti-*Mycobacterium bovis* (BCG) were used as the primary antigen-detecting antibodies in a peroxidase anti-peroxidase technique. Of the 26 biopsies from active erythema nodosum leprosum lesions, six were positive for immunoglobulin or complement deposits. These deposits were found in the dermoepidermal junction, within the foamy cells, and, in one patient, around a blood vessel. Five of 20 patients with lepromatous leprosy without erythema nodosum leprosum showed similar deposits in the dermo-epidermal junction and within foamy cells. None of these patients had these deposits around blood vessels. Mycobacterial antigens were seen in all biopsies studied. The presence of acute inflammatory infiltrates did not correlate with the presence or absence of immunoglobulin or complement deposits. It is felt

that immunoglobulin or complement deposits are not a constant feature of early erythema nodosum leprosum lesions and that these deposits may be secondary rather than primary in these lesions.—Authors' Abstract

Narayanan, R. B., Bhutani, L. K., Sharma, A. K. and Nath, I. T cell subsets in leprosy lesions: *in situ* characterization using monoclonal antibodies. Clin. Exp. Immunol. **51** (1983) 421–429.

Cryostat sections of dermal lesions from 30 untreated leprosy patients were studied by indirect immunofluorescence using monoclonal antibodies defining T cell subsets and Ia like antigens. Most lymphocytes in leprosy lesions were positive for OKT3 and Ia like antigens indicating thereby the presence of activated T cells. Maximal numbers of these cells were seen in localized paucibacillary tuberculoid leprosy lesions in close association with epithelioid cells. A decline in their numbers was observed over the leprosy spectrum with a marked reduction in disseminated, multibacillary, lepromatous leprosy where only scattered OKT3⁺ cells were visualized. OKT4 and OKT8 positive cells defining T cell subsets were frequently found within the OKT3⁺ lymphocytes throughout the leprosy spectrum. The ratio of OKT4⁺/OKT8⁺ cells ranged from 1.2 to 5.0 in tuberculoid and from 0.2 to 1.0 in lepromatous lesions. Macrophages in the granulomas stained intensely with anti-Ia antisera. Ia like antigens were expressed to the same degree on macrophages with or without intracellular acid-fast bacilli.—Authors' Summary

Nye, P. M., Price, J. E., Revankar, C. R., Rook, G. A. W. and Stanford, J. L. The demonstration of two types of suppressor mechanism in leprosy patients and their contacts by quadruple skin-testing with mycobacterial reagent mixtures. Lepr. Rev. **54** (1983) 9–18.

A previous study in Nepal involving skin testing simultaneously with four different mycobacterial reagents (three of them mixtures) revealed that the addition, in the same skin test site, of pooled reagents from fast-growing mycobacteria locally suppressed the

response to pooled slow growers. This finding has been confirmed in Bombay. It has also been shown that the addition of reagents prepared from certain fast-growing species to that prepared from slow growers in one skin test site will suppress the response to the same slow-grower reagent injected alone in the other arm. This type of suppression probably requires recognition of species-specific antigens of the fast-growing species concerned. The importance of the observations in relation to leprosy and possible mechanisms underlying them are discussed.—Authors' Summary

Opromolla, D. V. A., Arruda, M. S. P., Ura, S., Pernambuco, J. C. A., Dastazini, I., Fleury, R. N., Tolentino, M. M., Tonello, C. J. S. and Arruda, O. S. Aspectos evolutivos de reação de Rubino. [Evolutionary aspects of the Rubino reaction.] Med. Cutan. Iber. Lat. Am. **10** (1982) 9–14. (in Portuguese)

The Rubino reaction was studied in 178 leprosy patients to correlate its positivity, clinical form, ENL, and time and activity of the disease. The patients studied were classified according to the criteria established by the 1953 Madrid Congress.

The results show that the tuberculoid patients presented negative Rubino reactions regardless of any of the parameters studied. The borderline patients showed 9% positive Rubino reaction not related to any of the observed parameters studied.

The lepromatous patients showed a significant difference of positivity to the Rubino reaction when grouped as to the disease's active or non-active status. Active lepromatous patients showed 55% positivity to the Rubino reaction; whereas patients considered clinically inactive showed only 6% positivity.

The fact that the Rubino reaction is negative in the majority of patients who are clinically cured would indicate that this test could be included as part of the criteria used in determining which clinically cured lepromatous patients can discontinue medication without risking a relapse.—Authors' Summary

Ramos-Zepeda, R., Franco-Gamboa, E., Gonzalez-Mendoza, A., Rubio, J. B. and

Mariat, F. Phagocytose de *Candida albicans* par des leucocytes polynucléaires obtenus de malades atteints de lèpre lépromateuse nodulaire. [Phagocytosis of *Candida albicans* by polymorphonuclear leukocytes from patients with nodular lepromatous leprosy.] Bull. Soc. Pathol. Exot. Filiales **75** (1982) 476–483. (in French)

Patients suffering from nodular lepromatous leprosy are deficient in cellular immunity but may not be more susceptible to other infections. Therefore it is possible that other defense mechanisms are operational in dealing with other infectious agents these patients may be exposed to. In this report, the phagocytic and fungicidal activity of polymorphonuclear (PMN) cells against *Candida albicans* was examined using PMN from 20 nodular lepromatous patients and from 20 healthy subjects (controls). The method used was that of PMN adherence to glass.

The phagocytic activity was evaluated after 15 min and 45 min. We observed that there was phagocytosis by 94% of the PMN from patients and by 95% of the PMN from the controls. The phagocytic index of the yeasts ingested by the PMN were 4.47 and 4.10 for, respectively, patients and controls.

The frequencies of yeasts killed by PMN from patients and controls were, respectively, 29.6% and 29.4%. The results indicated that PMN from patients and healthy controls had the same capacity to phagocytize and to destroy yeasts of *C. albicans*.—Authors' Summary

Rea, T. H. and Yoshida, T. Serum macrophage migration inhibition activity in patients with leprosy. J. Invest. Dermatol. **79** (1982) 336–339.

We have found that 26 of 54 (48%) untreated patients with leprosy had serum migration inhibitory activity, and that this was present in tuberculoid, borderline, and lepromatous forms of the disease. Patients with active reactional states, i.e., reversal reactions, Lucio's reaction, or erythema nodosum leprosum, were particularly apt to have this inhibitory activity. The prevalence of inhibitory activity did not vary significantly with treatment, dinitrochlorobenzene responsiveness, tuberculin responsiveness, or

serum lysozyme levels.—Authors' Summary

Saha, K., Sharma, V., Chakrabarty, A. K. and Sehgal, V. N. Breakdown product of factor B as an index of complement activation in lepromatous leprosy and its relation with bacillary load. Scand. J. Immunol. **17** (1983) 37–43.

Serum complement profiles studied in 50 lepromatous leprosy patients with various bacillary loads demonstrated significantly decreased C3 levels in patients with high Bacteriologic Index (2+ to 4+) as compared with those with lesser bacterial load. In contrast, mean serum levels of C1q and C4 components remained unchanged. The concentration of factor B breakdown product (Ba) and its ratio to factor B increased with the bacterial density and more so in patients with erythema nodosum leprosum. A significant negative correlation was found between serum C3 and Ba levels in most lepromatous patients. Analysis of the data suggested the alternative pathway as the possible mechanism of complement activation in lepromatous leprosy.—Authors' Abstract

Turk, J. L. Dissociation between allergy and immunity in mycobacterial infections. Lepr. Rev. **54** (1983) 1–8.

The relationship between delayed hypersensitivity and granulomatous hypersensitivity to host resistance in mycobacterial infections has been discussed. The grounds for a dissociation between allergic reactions and resistance to infections is reviewed firstly in tuberculosis and then in leprosy. Evidence from clinical observations is compared with data from animal experiments, particularly in mice infected with *Mycobacterium lepraemurium*. Further comparison is made of the use of sonicated bacterial extracts versus autoclaved whole organisms. The relevance of the discussion to the assessment of the efficacy of the various 'leprosy vaccines,' now being tested, is considered.—Author's Summary

Van Voorhis, W. C., Kaplan, G., Sarno, E. N., Horwitz, M. A., Steinman, R. M., Levis, W. R., Nogueira, N., Hair, L. S., Gattas, C. R., Arrick, B. A. and Cohn, Z.

A. The cutaneous infiltrates of leprosy. Cellular characteristics and the predominant T cell phenotypes. *N. Engl. J. Med.* **307** (1982) 1593–1597.

We report on the characteristics of cells in the cutaneous lesions and blood of 21 patients with lepromatous, tuberculoid, and intermediate forms of leprosy. A large proportion of the infiltrates in lepromatous lesions consist of macrophages heavily parasitized with *Mycobacterium leprae*. The T cells in the lesions are devoid of OKT4/Leu 3a-positive (helper) cells and consist almost exclusively of OKT8/Leu 2a-positive (suppressor) populations. In contrast, the tuberculoid infiltrates contain well-organized epithelioid and giant-cell granulomas and only remnants of bacilli, and the predominant T cell is from the OKT4/Leu 3a-positive subset. In both tuberculoid and lepromatous infiltrates, T cells and macrophages expressed HLA-DR antigen. No marked alteration in the distribution of blood T cell phenotypes was noted. We conclude that there is a marked difference between T cell subsets in lepromatous and tuberculoid infiltrates, which may influence the microbicidal activity of macrophages in the lesions.—Authors' Abstract

Vazquez-Escobosa, C., Gomez-Estrada, H., Gonzalez-Mendoza, A. and Barba-Rubio, J. Complejos inmunitarios circulantes en pacientes con lepra lepromatosa nodular. [Circulating immune complexes in patients with nodular lepromatous leprosy.] *Arch. Invest. Med. (Mex.)* **13** (1982) 181–183. (in Spanish)

The chronic infection caused by *Mycobacterium leprae* leads to the formation of circulating immune complexes (CIC). Because the presence and the composition of the CIC may have an important function in the pathogenesis of the lesions of the patients with leprosy, it seemed interesting to investigate the characteristics of the CIC in patients with nodular lepromatous leprosy.

We studied 20 patients with nodular lepromatous leprosy, 17 males and 3 females between the ages of 35 and 48 with the diagnosis of nodular lepromatous leprosy without reaction. The patients had received little treatment with dapsone, from 1–3 years in duration, and had demonstrable bacilli in skin biopsies. The CIC were investigated by the method of phagocytosis and immunofluorescence of Hurd, Andreis and Ziff. This is based on the phagocytosis of CIC by the neutrophils of the patients and demonstration of them with an immunofluorescent reaction. As controls we studied 30 healthy subjects with characteristics similar to those of the patients.

The CIC were very abundant, as demonstrated in the cytoplasm of the neutrophils of the patients with nodular lepromatous leprosy, and they consisted of IgG, but gave negative results for IgA, IgM, and C3. The controls all showed negative results.

These results demonstrate that, in the absence of lepra reaction, patients with nodular lepromatous leprosy have large quantities of CIC consisting of IgG.—(Translated from the article)

Microbiology

Das, P. K. and Tulp, A. Use of a unit gravity sedimentation chamber for the purification of *Mycobacterium leprae*. *Ann. Microbiol. (Paris)* **133B** (1982) 389–400.

The present paper summarizes results concerning a mild isolation method of *Mycobacterium lepraemurium* and *M. bovis* BCG from host tissues, and describes the application of such a method in purifying

M. leprae (Ml) from either infected armadillo tissues or human skin biopsies. This isolation method consists of homogenization, two-phase partition in dextranpolyethylene glycol and finally sedimentation in sucrose gradient using a unit gravity chamber. Such a purified Ml preparation appears to be devoid of host-tissue contaminants as examined by light and electron microscopy as well as by a radioimmuno spot test. The

results indicate that the present method is mild enough to allow the purification of M1 from infected host tissues with *in vivo* conservation of antigenicity and viability of the bacilli.—Authors' Summary

Delville, J., Spina, A., Rajjan, W. and Co-cito, C. Modification of the kinetics of growth of *Mycobacterium leprae* by a group of corynebacteria. *Fems Microbiol. Lett.* **15** (1982) 253–256.

The authors compared the growth of *Mycobacterium leprae* in the presence and absence of leprosy-derived corynebacteria in the mouse foot pad. The mice received different amounts of either live or inactivated leprosy-derived corynebacteria subcutaneously, intraperitoneally, or intravenously. They were then challenged by inoculations of *M. leprae* into the foot pads. Counting of acid-fast bacteria in the mouse foot pads was conducted monthly over a six-month period. If leprosy-derived corynebacteria were injected into the same foot pad, the total number of acid-fast bacilli was increased 14-fold over controls after 90 days. The introduction of leprosy-derived corynebacteria by other routes was ineffective. Killed leprosy-derived corynebacteria, injected locally, completely abolished the growth of *M. leprae* in the same foot pads. The results may provide support for the hypothesis that leprosy-derived corynebacteria may be involved in the pathogenesis of leprosy. The other possible application of these findings is the exploitation of the vaccine-like effect displayed by large amounts of inactivated leprosy-derived corynebacteria.—(Adapted from the article)

Imaeda, T., Barksdale, L. and Kirchheimer, W. F. Deoxyribonucleic acid of *Mycobacterium lepraemurium*: Its genome size, base ratio, and homology with those of other mycobacteria. *Int. J. Syst. Bacteriol.* **32** (1982) 456–458.

Deoxyribonucleic acid of *Mycobacterium lepraemurium* grown in mice was isolated and analyzed spectrophotometrically. The genome molecular weight and guanine-plus-cytosine content of this *M. lepraemurium* deoxyribonucleic acid were 1.8×10^9 and 65.5 mol%, respectively. Among selected strains of mycobacterial species, four strains

of *M. avium* showed the highest degree of deoxyribonucleic acid homology (74.2% to 92.9%) with *M. lepraemurium*, suggesting a close genetic relatedness.—Authors' Summary

Katoch, V. M., Wayne, L. G. and Diaz, G. A. Characterization of catalase by micro-immunoprecipitation in tissue-derived cells of *Mycobacterium lepraemurium* TMC 1701. *Int. J. Syst. Bacteriol.* **32** (1982) 416–418.

Cell-free extracts of tissue-derived cells of *Mycobacterium lepraemurium* TMC 1701 have been found to have mycobacterial catalase which is of the T type. Immunological distance measurements of this catalase against three reference mycobacterial systems, as determined by a micro-immunoprecipitation technique, showed that catalase from *M. lepraemurium* TMC 1701 is most closely related to that of *M. avium* but is still distinct from it. In this respect, this strain is uniquely positioned between *M. tuberculosis* and *M. avium*.—Authors' Summary

Nakamura, M. Enhanced growth of *Mycobacterium lepraemurium* in cell-free liquid medium with DL-aspartic acid. *Kurume Med. J.* **28** (1981) 315–318.

During experiments on the effects of amino acids on the growth of *Mycobacterium lepraemurium*, it was found that DL-aspartic acid markedly stimulates the growth of the bacilli in cell-free liquid medium. When DL-aspartic acid was added at a final concentration of 0.01% or 0.02% to ND-5 or ND medium containing dextran and liposome, markedly stimulated and prolonged growth of bacilli was observed. The possibility of producing continuous growth of *M. lepraemurium* by using DL-aspartic acid is suggested.—Author's Summary

Nakamura, M. Stimulation effect of dextran on *in vitro* growth of *Mycobacterium lepraemurium*. *Jpn. J. Lepr.* **51** (1982) 81–84. (in Japanese)

In a previous paper, it was reported that the growth of *Mycobacterium lepraemurium* was significantly stimulated by soluble starch. In the present paper, effects of com-

pounds related to soluble starch on the growth of *M. lepraemurium* were investigated. The results obtained indicate that dextran remarkably stimulated the growth of *M. lepraemurium* more than soluble starch. The optimal concentration of dextran was 0.2%. Dextran having molecular weights (MW) 100,000~200,000 was better than those of MW 60,000 and over 200,000; α -, β - and γ -cyclodextrin had the same effect as dextran. Dextrin and maltose were not effective.—Author's Summary

Ridell, M. Ribosomal antigens of *Mycobacterium leprae*. Ann. Microbiol. (Paris) **133B** (1982) 401–406.

The β -antigen of *Mycobacterium leprae* has been identified by immunodiffusion utilizing leprosy sera as a source of antibodies. This antigen has also been demonstrated in a large number of mycobacterial species as well as several *Rhodococcus* strains and a small number of *Nocardia* strains, but not in any other corynebacteria studied. The β -antigen is structurally located on the ribosomes and is present on both ribosomal subunits, i.e., in the 30S and 50S as well as in the 16S core particle. It has therefore been concluded that the β -antigen consists of RNA and/or ribosomal proteins. The β -antigen is probably an antigen of the *M. leprae* 16S core particle and provokes antibody production in patients with leprosy. The β -antigen seems to correspond to antigen 5 of *M. leprae* and antigen 1 of *M. smegmatis* as defined by crossed immunoelectrophoresis. It is likely that many ribosomal antigens of *M. leprae* are common to other mycobacteria.—(Adapted from the article)

Silva, M. T., Macedo, P. M., Costa, M. H. L., Goncalves, H., Torgal, J. and David, H. L. Ultrastructural alterations of *Mycobacterium leprae* in skin biopsies of untreated and treated lepromatous patients. Ann. Microbiol. (Paris) **133B** (1982) 75–92.

Mycobacterium leprae cells under a process of progressive disaggregation are present in the skin of both treated and untreated patients.

The ultrastructural alterations observed during the degenerative process seem to be

qualitatively similar in treated and untreated patients.

The proportion of altered *M. leprae* cells increases during the treatment, mainly with rifampin and rifampin + clofazimine + diaminodiphenyl sulfone.

The cell wall of *M. leprae* is the last bacterial structure to disappear during the degenerative process.—(From Trop. Dis. Bull.)

Veeraraghavan, N. Method of cultivation of *M. leprae*. Curr. Sci. **52** (1983) 60–63.

The composition of medium V (Veeraraghavan) used for the cultivation of *Mycobacterium leprae* is given. The details of the method employed for the isolation of *M. leprae* from the skin scrapings of lepromatous patients, the cultivation of these isolates, as well as the armadillo strain of *M. leprae* *in vitro* in the synthetic medium are described.—Author's Abstract

Wheeler, P. R., Bharadwaj, V. P. and Gregory, D. *N*-Acetyl- β -glucosaminidase, β -glucuronidase and acid phosphatase in *Mycobacterium leprae*. J. Gen. Microbiol. **128** (1982) 1063–1071.

N-Acetyl- β -glucosaminidase, β -glucuronidase and acid phosphatase activities were detected in cell-free extracts of *Mycobacterium leprae* (from armadillo liver). Extracts of bacteria which had been treated with 7-diazonaphthalene-1,3-disulphonic acid to inactivate surface enzymes retained 30%–45% of the activity of the glycosidases and 15% of the activity of the acid phosphatase. When intact bacteria were treated with 1M NaOH, the corresponding activity in the extracts was 4%–9% for the glycosidases and 7% for the acid phosphatase. Inhibition studies with lactones and the use of concanavalin A-agarose showed differences between the glycosidases in extracts of *M. leprae* and those of armadillo liver. Inhibition studies with vanadate using extracts from NaOH-treated bacteria and extracts of armadillo liver showed differences between the acid phosphatases. Enzymes removed from the surface of *M. leprae* could have been adsorbed to the surface from host tissue (i.e., lysosomal enzymes) or they could have been extracellular enzymes or associated with the bacterial membrane.—(From Trop. Dis. Bull.)

Young, D. B. Mycobacterial lipids in infected tissue samples. *Ann. Microbiol. (Paris)* **133B** (1982) 53–58.

Mycobacteria synthesize characteristic lipids which can readily be distinguished from those synthesized by the host cells which they infect during pathogenesis. This fact can be exploited to provide information about mycobacteria growing in infected tissue samples:

(a) qualitative analysis of lipid extracts from lepromatous leprosy skin biopsies reveals the presence of several mycobacterial

lipids including *Mycobacterium leprae*-specific glycolipid, phthiocerol dimycocertate and mycolic acids;

(b) quantitative analysis shows that the amount of mycobacterial lipids present in lepromatous lesions is much greater than that expected on the basis of the number of acid-fast bacilli present; and

(c) incorporation of ^{14}C -acetate into cell wall mycolic acids can be used to monitor the growth of intracellular mycobacteria.—(*From Trop. Dis. Bull.*)

Experimental Infections

Bhat, K. R. and Vaidya, M. C. Quantitative analysis of the sequence of nerve damage in experimental leprosy. *Lepr. India* **54** (1982) 613–622.

It is now accepted that the *Mycobacterium leprae* infection in normal and immunosuppressed mice involves their peripheral nerves as well. In our study on sciatic nerves of immunosuppressed mice with *M. leprae* infection, an early segmental demyelination and late axonal degeneration were observed. In the present study, an attempt to correlate the relationship between the axon thickness and internodal lengths with the sequence of nerve damage is made.—(*From the article*)

Ha, D. K. K., Gardner, I. D. and Lawton, J. W. M. Macrophage function in *Mycobacterium lepraemurium* infection: Morphological and functional changes of peritoneal and splenic macrophages *in vitro*. *Infect. Immun.* **39** (1983) 353–361.

Morphological and functional changes in peritoneal macrophages (PM) and splenic macrophages (SM) from mice infected with *Mycobacterium lepraemurium* were investigated. A decrease in the number but an increase in size of PM were observed during the infection. PM were vacuolated, and a small proportion of them were observed in cell division. They demonstrated greater ability to adhere and spread *in vitro*, enhanced phagocytosis of immunoglobulin G

(IgG) and IgM erythrocytes, and greater phagocytosis and killing *Candida* sp., when compared with normal resident PM. In contrast, parasitized SM demonstrated significantly reduced phagocytic ability; whereas heavily parasitized SM neither spread nor phagocytosed *Candida* sp. The random migration and chemotactic responsiveness of PM from infected animals were also enhanced. These results indicated the persistent activation of PM but the suppression of some activities of SM during *M. lepraemurium* infection.—Authors' Summary

Hoffenbach, A., Lagrange, P. H. and Bach, M.-A. Deficit of interleukin 2 production associated with impaired T-cell proliferative responses in *Mycobacterium lepraemurium* infection. *Infect. Immun.* **39** (1983) 109–116.

C57BL/6 and BALB/c mice were infected intravenously with 10^7 *Mycobacterium lepraemurium* (MLM). At various times after infection, spleen cells were tested for their capacity to proliferate *in vitro* in response to concanavalin A (ConA) and to allogeneic cells. The generation of alloreactive cytotoxic T lymphocytes was also studied. The mitogen- and allogeneic-cell-induced blastogenesis of splenocytes from MLM-infected C57BL/6 and BALB/c mice was shown to be depressed during infection. The maximal decrease occurred six months after infection. Conversely, no reduction in the

ability to generate alloreactive cytotoxic T lymphocytes was observed even after six months of infection. At the same time, interleukin 2 (IL2) activity generated by ConA stimulation of infected splenocytes was measured in both strains. IL2 activity in the ConA-stimulated culture supernatants was decreased as early as one month after MLM inoculation as compared with supernatants from age-matched control mice. Thus, IL2 production by infected-mouse spleen cells was shown to decline earlier than their proliferative responses to ConA and to allogeneic cells. ConA-induced T-cell blasts from infected mice showed a reduced ability to proliferate when incubated with an IL2-containing reference supernatant from ConA-stimulated normal spleen cells. These data suggest that a defect in IL2 production and utilization might contribute to the impairment of T cell-mediated immunity observed in MLM-infected mice.—Authors' Summary

Ishaque, M. Pathogénicité chez le rat de *Mycobacterium lepraemurium* cultivé *in vitro*. [Pathogenicity of *in vitro* cultivated *Mycobacterium lepraemurium* in rats.] Rev. Can. Biol. **41** (1982) 197–200. (in French)

The pathogenicity in Sprague-Dawley rats of *Mycobacterium lepraemurium* cultivated on egg-yolk medium was investigated. The results show that *in vitro* grown cultures provoked huge subcutaneous lepromata in rats similar to those produced by the *in vivo* grown *M. lepraemurium*. The acid-fast bacilli isolated from lepromata of rats infected with the *in vitro* or *in vivo* grown cultures were microscopically and histopathologically identical to each other.—Author's Abstract

Izaki, S., Isozaki, Y., Satoh, M., Hibino, T., Kon, S. and Izaki, M. Comparative study with two polar types of murine leprosy: An involvement of plasminogen activator and its possible regulating factor in the granulomatous tissue reaction. J. Invest. Dermatol. **80** (1983) 81–85.

Enzymatic activities in a saline-extractable fraction from two polar types of murine lepromas were investigated using pyroglutamyl-glycyl-arginine-*p*-nitroanilide and

plasminogen-rich, as well as plasminogen-free, fibrin plates. An inhibitor activity for urokinase was also measured. C57BL/6NJcl (immunologically high responder strain) mice inoculated with 2×10^8 *Mycobacterium lepraemurium* developed a localized lepromatous lesion after four weeks. The tissue extracts obtained after 4–6 weeks exhibited inhibition for urokinase (8.8 IU/mg protein), but no enzymatic activity. After 8–11 weeks, when the lepromas showed an ulcerative change, prominent peptide hydrolytic activity (84.8 nmol/mg protein/min) was demonstrated. The fibrin plate assay confirmed that plasminogen activator is predominantly involved (26.4 IU/mg protein). The proteolytic activation was apparently correlated with discharge of purulent materials containing the bacilli and subsequent limitation of leproma development. However, similar modulation of the fibrinolytic enzyme-inhibitor system was not shown in CBA/N mice (immunologically low responders). The tissue extracts showed a low level of urokinase inhibitor activity (1.9 IU/mg protein), but no peptidolytic or plasminogen activator activity. Consequently, lepromas were developed progressively until 25 weeks after infection and dissemination from the lepromatous lesion took place thereafter.

In comparison with histologic findings, which revealed accumulation of lymphocytes and mononuclear cells in the peripheral zone of lepromatous lesions in the C57BL/6NJcl, but not in the CBA/N mice, a controlling mechanism of plasminogen activator in tissue is assumed to be involved in the development of the granulomatous tissue reaction.—Author's Abstract

Lancaster, R. D., Hilson, G. R. F., McDougall, A. C. and Colston, M. J. *Mycobacterium leprae* infection in nude mice: Bacteriological and histological responses to primary infection and large inocula. Infect. Immun. **39** (1983) 865–872.

Previous studies have demonstrated that congenitally athymic, nude mice are highly susceptible to infection with *Mycobacterium leprae*. In this study, we showed that foot pad inoculation of nude mice with different inoculum sizes of *M. leprae* resulted in exponential growth of bacilli until bacil-

lary numbers reached approximately 10^{10} bacilli per foot pad. There was dissemination of the infection from approximately ten months after inoculation. When nude mice were compared with thymectomized and irradiated mice and normal intact mice for the ability to detect growth from large inocula of low viability, nude mice were the most sensitive, permitting the detection of 10^2 viable *M. leprae* among 10^7 irradiation-killed organisms. There was widespread dissemination of the infection throughout the reticuloendothelial system and the tissues of the cooler body sites from approximately ten months after inoculation. Histologically, the lesions resembled those seen in lepromatous leprosy, although the bacillary load appeared larger and was similar to that seen in heavily infected tissues of the nine-banded armadillo. An unusual feature was the presence of numerous foci of neutrophil polymorphs in the foot pads and liver of infected nude mice.—Authors' Summary

Matsuoka, M. and Kawaguchi, Y. Observations on the host reaction to the cultivated *Mycobacterium lepraemurium* in the spread subcutaneous tissue preparations of mice. *Jpn. J. Lepr.* **51** (1982) 93–106.

Cultivated murine leprosy bacilli from rough colonies (HO-R) and smooth colony variant (HO-S) were subcutaneously inoculated into mice of inbred strains (C3H, C57BL/6, BALB/c and DDD). Growth patterns of the bacilli of each strain and cellular reactions of host in subcutaneous tissue at the inoculation site were examined by means of the spread tissue preparation technique.

There were no remarkable differences in cellular reactions at the inoculation site among these inbred strains of mice infected with HO-R bacilli two days and one week after the infection. An acute inflammatory reaction with accumulation of many polymorphonuclears was observed at two days. At one week, it had disappeared and monocytes and macrophages were dominant. A vigorous granulomatous reaction consisted of polymorphonuclears and lymphocytes developed in C57BL/6, BALB/c and DDD mice at eight weeks. In the course of the following weeks the cellular reaction was augmented in C57BL/6 and BALB/c mice

and further local spread of the infection was arrested. On the other hand, in DDD mice the diminution of cellular reaction occurred at eight weeks and bacilli increased in number. In contrast, no signs of host reactions were observed in C3H mice and many murine leprosy cells were observed at the inoculation site.

C57BL/6 and BALB/c mice infected with HO-S bacilli showed essentially the same host reaction as those observed in the experiment with HO-R bacilli. The diminution of cellular reaction observed in the DDD mice infected with HO-R bacilli could not be found in those infected with HO-S bacilli and the multiplication of the bacilli was not seen. In C3H mice infected with HO-S bacilli no specific host reaction was found until five weeks, but cellular reactions happened at seven to eight weeks which were never observed in C3H mice infected with HO-R or H-M bacilli. The bacilli decreased in number from the eighth to the tenth week but bacillary multiplication was gradually recovered at 15 weeks. The multiplication of HO-S bacilli was very slow even in C3H mice throughout the observation period.

In this study, we found that slower development of mouse leprosy with HO-S bacilli in C3H mice is due to their poor ability to multiply *in vivo* and the inexplicable host reaction.

The mouse strain differences in response to cultivated *Mycobacterium lepraemurium* were also discussed on the basis of cell-mediated immunity in the host.—Authors' Summary

Stach, J.-L., Fumoux, F., Strobel, M., Barret, A. and Michelson, M. Augmentation de l'activité dismutasique dans les leucocytes spléniques de souris sensibles au BCG et à *Mycobacterium lepraemurium*. [Enhancement of dismutase activity in the splenic leukocytes of mice sensitive to BCG and *Mycobacterium lepraemurium*.] *C. R. Seances Acad. Sci. [III]* **293** (1981) 575–578. (in French)

A marked enhancement of superoxide dismutase activity was evidenced when mice susceptible to BCG and *Mycobacterium lepraemurium* were infected. Such increases were not found in nonsusceptible mice. This seems related to a genetic factor of the breed of mice studied.—Authors' Abstract

Venkataramaniah, H. N., Harikrishnan, S., Balakrishnan, S. and Bhatia, V. N. Mouse foot-pad growth patterns of *M. leprae* in relation to Morphological Index. *Lepr. India* **54** (1982) 634-638.

Growth patterns of *Mycobacterium lep-*

rae from leprosy patients with low, high and intermediate Morphological Index have been compared in mouse foot pads. No significant differences were observed.—Authors' Summary

Epidemiology and Prevention

Alemayehu, A. and Naafs, B. The age at onset of overt leprosy patients presenting at the Addis Ababa Leprosy Hospital. *Ethiop. Med. J.* **20** (1982) 117-123.

The age at onset of leprosy between 1965 and 1978 in Ethiopia was analyzed in relation to the type of leprosy and endemicity. The peak in the age at onset was found to be between 15 and 20 years of age in all classifications. The age at onset was earlier in areas with high endemicity than in those with low endemicity. This fact may indicate an inexpensive way of defining areas of high and low prevalence.—Authors' Abstract

Das, M. L., Dutta, S. and Tripathy, S. R. Leprosy—a major community health problem in pediatric age group. *Indian J. Dermatol.* **17** (1982) 5-10.

Eleven years' prospective study in West Bengal and Bihar in India on children below 14 years of age showed 358 cases of leprosy which constituted 33.20% of total leprosy patients (1079) encountered during 1971-1981.

Although the present study reflected a declining trend of leprosy in children during recent years, its prevalence rate was 2.7 per 1000 population of Adra division.

Girls were more affected than boys (1.2:1). Leprosy assumed a major health problem status in school children since 73.6% of the affected children belonged to the age group of 6-14 years. Nonlepromatous leprosy was the chief clinical variety (84.9%). The aspect of contact tracing and source of infection is discussed.—Authors' Abstract

De Muynck, A. Epidemiologic patterns of leprosy in Vallegrande, Bolivia. *Lepr. Rev.* **54** (1983) 51-59.

The Andean province of Vallegrande (6412 km²; 33,532 inhabitants, of which

99% are mestizos of Indian-Caucasian descent) has been an endemic area of leprosy for centuries. In 1977 the National Center for Tropical Diseases (CENETROP) integrated the existing leprosy control activities in a comprehensive basic health service. The clinical status of all known cases was assessed, and an important effort at case finding was carried out by the basic health teams and the mobile leprosy control team. The overall prevalence rate on 31 July 1980 was 9.4 per thousand. The leprosy problem was mainly one of adults; the prevalence rate in males being 60% higher than in females. The proportion of lepromatous and borderline forms was 47%. The epidemiological patterns of leprosy in Vallegrande Province are consistent with those generally found in Latin America.—Author's Summary

Fekete, E. and Tedla, T. Leprosy in 18-month-old children, Bichena District, Gojjam Administrative Region, Ethiopia. *Lepr. Rev.* **54** (1983) 61-63.

In a mass survey of leprosy in Bichena District, Ethiopia, where a total of 814 new cases were detected, two cases of borderline-tuberculoid (BT) leprosy were discovered in children aged 18 months. Although incubation periods of less than two years are generally considered extremely rare, this finding emphasizes that young children under 2 years of age should not be excluded from leprosy surveys in endemic regions.—Authors' Summary

Hudson, T. and Genessi, J. Hansen's disease in the United States. *Soc. Sci. Med.* **16** (1982) 997-1004.

This article offers a general overview of Hansen's disease (leprosy) and examines in some detail the spatial characteristics and

demographic profiles of known sufferers. Over the years the pejorative labels attached to the disease and the societal and psychological attitudes which produce and accompany them have stigmatized leprosy sufferers. Unfortunately this stigma has often preempted rational understanding and treatment. Contrary to popular belief, leprosy, caused by the bacteriological agent *Mycobacterium leprae*, is relatively non-contagious and can be rendered completely non-contagious by chemotherapy. Incidence rates in the United States are extremely low (0.08 per 100,000 in 1979), but have shown a slight if erratic increase since 1942. Most of this can be attributed to increases in the number of foreign born cases; a result of immigration from areas of higher incidence (e.g., Southeast Asia, Latin America). Six states, California, Texas, Hawaii, New York, Florida, and Louisiana, accounted for over 80% of the 1432 cases reported in the United States between 1967 and 1976.—Authors' Abstract

Krishnamoorthy, K. V., Kumar, K. S. A. and Venkatesam, B. A review of five years leprosy work in an urban area Rayadurg. *Lepr. India* **54** (1982) 700–715.

The present study includes the analysis of 240 leprosy cases detected during five years from 1977 to 1981 at Rayadurg, a municipal town in Anantapur District of Andhra Pradesh, India. Various aspects such as age, sex, deformity, educational, economic, caste, and occupational details are brought out. The strategy used in leprosy control and the results obtained are dealt with. The prevalence rate of leprosy in this area is estimated to be 8.4 per 1000.—Authors' Summary

Lal, S., Mahalingam, C. and Garg, B. R. Epidemiology of leprosy in rural population of Pondicherry. *Lepr. India* **54** (1982) 677–684.

A village having a population of 2000 in 350 families and coming under the Villianur Commune of the Union Territory of Pondicherry, India, was subjected to a total population survey. The population examined was 92.2%. A total of 138 cases of leprosy were found in 94 families, making a prevalence rate of 6.9%. There were single cases in 61 families and two to four cases in 33

families. Child rate for leprosy was 37%. The male-to-female ratio showed no sex predilection. The maximum percentage (30.4%) of cases belonged to maculoanesthetic type, followed by tuberculoid (27.5%), indeterminate (19.6%), borderline (14.5%), polyneuritic (6.5%) and lepromatous (1.5%) types. Nerve involvement was more frequent in multiple skin lesion cases than in single lesion cases.—Authors' Summary

Lyons, N. F. and Ellis, B. P. B. Leprosy in Zimbabwe. *Lepr. Rev.* **54** (1983) 45–50.

In Zimbabwe, as in many countries in Africa, leprosy is an endemic disease. The known incidence is approximately 2 cases per 1000 population and 350 new cases are seen annually. Many factors have influenced the spread of the disease including the recent bush war but progress in control measures is being made.—Authors' Summary

Risso, H. I. Epidemiologia de la lepra en el Chaco. [The epidemiology of leprosy in Chaco.] *Leprolgia* **24** (1982) 39–45. (in Spanish)

Based upon the data obtained in these different epidemiologic studies, the author concludes that the endemic of leprosy still represents a serious problem of public health. However, there are indications that show with optimism the immediate future of it.

- a) The decrease of the rate of prevalency in the students of Resistencia.
- b) The increase of the number of sources of contagion that became negative.
- c) The systematic control of the "womb of endemy," the intermediate form of leprosy.—Author's Summary

Saikawa, K. Study on prevention of leprosy. I. BCG vaccination trial for leprosy contact children in Okinawa. *Jpn. J. Lepr.* **51** (1982) 75–80. (in Japanese)

BCG has been used as a vaccine for leprosy in contact children (under 14 years of age) from 1963 to 1976 in Okinawa in order to prevent leprosy.

The total number of BCG-vaccinated children was 951. They were examined after 3, 6, 8, 10, and 13 years to follow up on the

possible onset of leprosy. Ten contact children among 534 had developed leprosy by the sixth year of examination for an incidence rate of 18.7%. No leprosy cases have been detected at the 3, 8, 10, or 13 years' examinations. The incidence rate by contact tracing examination for BCG unvaccinated contact children in the same period and at the same place was 20.6%.

No special difference was observed in leprosy incidence rates between the two groups. The incidence rate in this BCG trial in Okinawa was higher than other trials in foreign countries because the lepromatous ratio in Okinawa was higher than other places and index cases with whom children were in contact were mainly of the lepromatous type. Moreover, children had had contact with lepromatous index cases before they were vaccinated with BCG, and they already might have been infected with leprosy bacilli.

So it seems that no noticeable effect was observed in this BCG trial in Okinawa.—*(Adapted from Author's Summary)*

Soni, S. and Ingle, P. Comparison of slum survey, school survey and health education as methods of detection of leprosy cases in urban area. *Lepr. India* **54** (1982) 716–720.

The present study includes the analysis of different methods of survey adopted by the Shram Mandir Trust in its urban leprosy control unit of Baroda. The results are obtained from the work of the Trust of the last decade (i.e., from 1972 to 1982). It reveals that slum survey (1.90/1000) has better results as compared to school survey (0.29/1000); 91 cases were detected in one year from 1 April 1981 to 31 March 1982; 38 were through slum survey (41.76%) and 37 were through health education (40.66%). (School survey was not carried out.) Thus health education has a very important place in case detection.—*Authors' Summary*

Srinivasan, H. Changes in epidemiology of deformity in leprosy in a rural area in South India. *Indian J. Med. Res.* **76** (1982) 795–803.

The epidemiology of deformity due to leprosy was studied in 15 villages with a population of 1381 leprosy patients, 97% of

whom were examined. The same villages had been surveyed 14 years earlier (1966). Comparison of the data of these two studies showed that while the general epidemiological characteristics had not changed much, the crude deformity rate had decreased by about 50%. This reduction was due to a gross reduction in the deformity rate in the male patients in 1980, which could not be explained by over-representation of variables known to be associated with low deformity rates. Nerve trunk involvement in the male patients in 1980 was similar to that in 1966, but for some reason the nerves seemed to be getting damaged less often in 1980. Among those with deformities, feet were found to be involved much less often in 1980 compared to 1966. The study thus indicates that secular changes, i.e., changes with passage of time, do occur in leprosy and these changes can be detected only by repeat surveys carried out in the same area.—*Author's Summary*

Tornero, N., Asseis, E. A., Magalhães, L. B., Priscinotti, T., Barth, Y. L. and Casagrande, N. A. Alguns aspectos sobre a hanseníase no região de Londrina, Paraná, 1968–1978. 2. Características específicas. [Some aspects of hanseniasis in the region of Londrina, Parana, 1968–1978. 2. Specific characteristics.] *Hansen. Int.* **6** (1981) 122–129. (in Portuguese)

Following a previous work, this one intends to add new data on the occurrence of hanseniasis in the Public Health District of Londrina, in the state of Parana, Brazil. In this study, it was observed that an increasing percentage of patients were coming from the urban area of the nearby towns and one of the aspects stressed in this research was the great importance of the V and D forms in the dissemination of the disease, since they affect mostly male individuals. Once this area is characterized by a high endemicity, a new sanitary policy should be put into practice comprising aspects of control and search for cases. In addition, it should develop a special program of case detection among the students carried out by large scale medical examinations and through extensive observation of contacts of the bacilloscopic positive patients, mainly in the household contacts.—*Authors' Abstract*

Rehabilitation

Brandsma, J. W., Nugteren, W. A. H., Andersen, J. B. and Naafs, B. Functional changes of the ulnar nerve in leprosy patients following neurolysis. *Lepr. Rev.* **54** (1983) 31–38.

A functional follow up of ulnar neurolysis is presented. Functional changes have been related to the indication for neurolysis. Motor function of 52% of the nerves was improved in the group in which neurolysis was performed to facilitate nerve recovery. The rate of functional improvement appears also to depend on the duration of the recorded nerve damage and the classification of leprosy. Functional changes in the operated nerve have been compared with the non-operated nerve in cases of bilateral ulnar nerve involvement.—Authors' Summary

Fritschi, E. P. Teaching foot care. *Lepr. Rev.* **54** (1983) 65–68.

A new approach is being made to the teaching of foot care. The learning of the group is in the context of the team involved. The emphasis is on a practical and participative approach.—Author's Summary

Joseph, B., Joshua, S. and Fritschi, E. P. The moulded double-rocker plaster shoe in the field treatment of plantar ulcer. *Lepr. Rev.* **54** (1983) 39–44.

The present study has shown that the moulded double rocker plaster shoe offers a very feasible method of treatment of the simple plantar ulcer under field conditions. It is effective, inexpensive, socially acceptable and it can be applied, and the patient sent home, on the same day. There are no significant complications which have been noted either during or subsequent to this trial.—Authors' Summary

Lin De-Pao, et al. Transposition of post-tibial muscles and fasciae for correcting leprosy patient's drop foot. *Chin. J. Clin. Dermatol.* **12** (1983) 13–14. (in Chinese)

This article introduces the plastic operation for correcting leprosy patient's drop foot by means of transposition of posterior tibial muscles and fasciae and reports the results of this operation in 25 cases. The transposed posterior tibial muscle is thrust through a subcutaneous tunnel or interosseous membrane to the front of the tibia and is sutured with the fascia of the pretibial extensor muscles. Splints are then applied to fix the transposed muscle in position. Results of the operation were excellent in 10 feet, good in 11 feet, fair in 4 feet and ineffective in 1 foot. The operation is easily done, and is capable of correcting drop foot and recovering extensor function of the toes in some cases.—(From Authors' Abstract)

Other Mycobacterial Diseases and Related Entities

Buechner, S. A., Winkelmann, R. K. and Banks, P. M. Identification of T-cell subpopulations in granuloma annulare. *Arch. Dermatol.* **119** (1983) 125–128.

Granuloma annulare is a lymphohistiocytic process of unknown cause characterized by necrobiotic dermal papules. Acetone-fixed frozen sections of eight granuloma annulare lesions were studied for the presence of T cell subsets, using monoclonal antibodies to T cell surface antigens. The palisading and perivascular lymphocytic

infiltrate shows that most of the mononuclear cells are reactive with Leu 1 antibody, which characterizes peripheral T cells and activated T cells. Numerous cells were reactive with Leu 3a antibody, which identifies the helper-inducer T cell subset. Some cells were positive with Leu 2a antibody, which detects suppressor-cytotoxic cell populations. Masses of histiocytes were identified infiltrating between the collagen fibers and surrounding the central necrobiosis area; the histiocytes showed a very strong diffuse acid phosphatase and non-specific esterase activity. These findings

suggest that a cell-mediated immune response may be the dominant pathogenic event in granuloma annulare.—Authors' Summary

Chaparas, S. D. L'immunité dans la tuberculose. [Immunity in tuberculosis.] Bull. WHO **60** (1982) 827–844. (in French)

La tuberculose reste une des maladies les plus fréquentes et les plus graves dans le monde. Les réponses immunitaires variées et parfois intenses suscitées par *Mycobacterium tuberculosis* ne sont pas seulement responsables de l'immunité, elles peuvent aussi entraîner des lésions tissulaires considérables et des métastases. Pendant de nombreuses années, l'immunité cellulaire et humorale induite par *M. tuberculosis* a constitué un précieux modèle; cependant, de nombreuses questions concernant la pathogénicité de ce microorganisme et la protection contre la tuberculose restent sans réponse. Dans la présente étude, divers aspects de l'immunité antituberculeuse, ainsi que de la pathogénie et du diagnostic de la tuberculose, sont examinés à la lumière des connaissances actuelles en immunologie.—Author's Summary

Goode, D. Bacteriophage typing of strains of *Mycobacterium tuberculosis* from Nepal. Tubercle **64** (1983) 15–21.

One hundred strains of *Mycobacterium tuberculosis* isolated from cases of pulmonary tuberculosis in Nepalese villagers were typed with the World Health Organization set of bacteriophages. The number of strains in the three major phage types A, I, and B were 19, 53, and 28, respectively. This distribution is significantly different from those described in other geographical regions. In particular there was a relatively low incidence of type A strains and, in common with South India, there was a high proportion of type I strains. All the strains in this study were resistant to 5-Furan-2 carbonic acid hydrazine and 34 were highly resistant to isoniazid. Representative strains of the three phage types, including four isoniazid-resistant type I strains, did not differ in their virulence in the guinea pig; thus the type I strains found in Nepal may not be of the same origin as those of this phage type from

India, which are usually attenuated in the guinea pig. This study provides further evidence for the existence of geographical differences in the types of tubercle bacilli.—Author's Summary

Harboe, M. Antigens of PPD, old tuberculin, and autoclaved *Mycobacterium bovis* BCG studied by crossed immunoelectrophoresis. Am. Rev. Respir. Dis. **124** (1981) 80–87.

The effect of heat on mycobacterial antigens was studied by crossed immunoelectrophoresis in a system permitting identification and analysis of about 30 distinct components in *Mycobacterium bovis* BCG. By heating BCG concentrated culture fluid and BCG sonicates to 120°C for 15 min, most antigens detectable by reaction with rabbit anti-BCG antibodies were destroyed. The BCG antigens 60, 63, 82, and 89 still gave strong precipitate lines, antigens 1B and 23 gave weak but distinct precipitate lines; whereas BCG antigens 27, 71, and 84 did not precipitate but retained some of their ability to combine with anti-BCG antibodies. Tuberculin PPD preparations showed a varying antigen content, the most prominent component corresponding to BCG antigen 60, and six additional components being detected in PPD RT33. The polysaccharide antigen responsible for the prominent peak of BCG antigen 89 was not detected in PPD RT23 or PPD RT33. Only five distinct antigenic components were detected in old tuberculin. They corresponded to the components remaining in autoclaved BCG, with 60 and 89 being the only prominent peaks in direct precipitation tests. The relevance of these findings concerning purification of mycobacterial antigens and the importance of individual antigenic components for induction of delayed hypersensitivity is discussed.—Author's Summary

Immunological research in tuberculosis: Memorandum from a WHO meeting. Bull. WHO **60** (1982) 723–727.

This memorandum discusses the application of modern immunological techniques to various problem areas in tuberculosis. The recent isolation of highly purified mycobacterial antigens will have important application in providing specific

skin-test reagents for diagnosis, classification, and epidemiological investigations, and agents for use as immunogens and adjuvants. The development of monoclonal antibodies obtained by immunization of susceptible animals with partially purified antigens is considered a most promising approach to the identification and isolation of antigens.

In vitro studies of the mechanisms of immunity and the effects of immunization in tuberculosis are needed. Several methods have been proposed recently which require further validation, e.g., through correlation of *in vivo* resistance with results *in vitro*, and comparison of different antigens in the *in vitro* tests.

The specific antigens as well as the *in vitro* tests of tuberculosis immunity would be readily applicable in clinical investigations of immunological parameters and the effects of immunization. New serological tests using purified antigens would also be of value in this regard. *In vitro* tests for cell-mediated immunity could be used to study the effect of various BCG vaccines in different populations, in order to investigate the role of genetic and environmental factors in determining the response to immunization. Specific antigens and serological tests should prove useful in the diagnosis of different forms of extrapulmonary disease, especially in children. A test that could distinguish between infection with *Mycobacterium tuberculosis* and sensitivity induced by BCG immunization or environmental mycobacteria would be very useful both in diagnosis and in epidemiological studies. Investigations are needed on the mechanisms of endogenous reactivation of disease and the breakdown of apparently quiescent disease, in order to try to identify high-risk groups. — (From the Memorandum)

Kardjito, R. and Grange, J. M. Diagnosis of active tuberculosis by immunological methods. 2. Qualitative differences in the dermal response to tuberculin in patients with active pulmonary disease and healthy tuberculin-positive individuals. *Tubercle* **63** (1982) 275–278.

The tuberculin reactivity of 107 patients with active pulmonary tuberculosis and 143

healthy age-matched control subjects were compared. At 48 hr 96% of patients and 76% of control subjects were positive reactors. The diameters of the reactions were of similar size. At 24 hr 93% of patients and 65% of controls were positive; the reactions tended to be larger in the patient group but the difference was of no diagnostic value. The greatest discrimination was apparent at 6–8 hr when 72% of patients and only 3.5% of control subjects reacted. Although probably an Arthus reaction, this early response did not correlate significantly with antibody levels measured by enzyme-linked immunosorbent assay. Accordingly the two tests, to some extent, complemented each other diagnostically. — Authors' Summary

Kardjito, T., Handoyo, I. and Grange, J. M. Diagnosis of active tuberculosis by immunological methods. 1. The effect of tuberculin reactivity and previous BCG vaccination on the antibody levels determined by ELISA. *Tubercle* **63** (1982) 269–274.

Enzyme-linked immunosorbent assay (ELISA) was used to compare the levels of antibody to *Mycobacterium tuberculosis* in the IgG, IgM, and IgA classes in 107 patients with active pulmonary tuberculosis, 109 healthy tuberculin-positive, and 34 healthy tuberculin-negative individuals and to assess the effect of previous BCG vaccination on these levels. Tuberculin-positive control subjects had higher levels of antibody than tuberculin-negative controls in the IgG class only. As the IgG class was the most discriminative from the diagnostic point of view, this phenomenon reduced the usefulness of the test. While 77% of patients had amounts of antibody above the level which included 97.5% of tuberculin-negative control subjects, only 62% of patients had such elevated levels when compared with the tuberculin-positive controls. The discriminatory power of the test was increased from 62% to 75% by assaying antibodies in both the IgG and IgA classes, but only two further patients were found to be positive when IgM antibody levels were also assayed. Previous BCG vaccination had no significant effect on the antibody levels. — Authors' Summary

Kathipari, K., Seth, V., Sinclair, S., Arora, N. K. and Kukreja, N. Cell mediated immune response after BCG as a determinant of optimum age of vaccination. *Indian J. Med. Res.* **76** (1982) 508-511.

A total of 120 newborns of full term gestation with normal birth weight were investigated for cell-mediated immune response (CMIR) in two groups. BCG was given at birth in group A and at the age of three months in group B. Mantoux and leukocyte migration inhibition test positivity was comparable in the two groups. With the use of both the tests, CMIR could be induced in a comparable proportion of cases, in groups A (78.2%) and B (72.5%). It is therefore considered that newborns are capable of evoking CMIR at birth and the practice of giving BCG at birth may be continued.—Authors' Summary

Mouldsdaile, M. T., Harper, J. M. and Thatcher, G. N. Infection by *Mycobacterium haemophilum*, a metabolically fastidious acid-fast bacillus. *Tubercle* **64** (1983) 29-36.

A case of infection with *Mycobacterium haemophilum*, an unusual iron or hemin-dependent mycobacterium is described. Cultural requirements, biochemical reactions, and drug sensitivities are discussed and compared with other recent isolations of *M. haemophilum* and similar unusual mycobacteria.—Authors' Summary

Murzy de Souza, G. R., Sant'Anna, C. C., Lapa e Silva, J. R., Mano, D. B. and Bethlem, N. M. Intradermal BCG vaccination complications—analysis of 51 cases. *Tubercle* **64** (1983) 23-27.

The authors describe 51 cases of local complications due to intradermal BCG vaccination which occurred among 117,533 children between 1974 and 1979, in the city of Niteroi (Rio de Janeiro State), Brazil.

The ages ranged from 0 to 16 years and the lesions observed were abscesses, enlargement of regional lymph nodes, chronic ulceration, and ulceration associated with enlarged lymph nodes.

The patients were treated with isoniazid, except two who required surgical drainage, with favorable results in all cases.—Authors' Summary

Osborn, T. W. Changes in BCG strains. *Tubercle* **64** (1983) 1-13.

BCG originated from a virulent bovine strain of the tubercle bacillus after prolonged serial subculture on a potato medium. Since attenuation was achieved, the BCG strain has been distributed to a large number of centers where BCG vaccine is produced. Many of these production laboratories have maintained their BCG lines by continuing serial transfers, but have employed a variety of media for this purpose, and have produced BCG vaccine by a variety of techniques. Distinct differences have developed between some of the daughter strains of BCG, but the mechanism through which these changes have occurred has not been clear.

In recent years methods have been developed which have enabled changes taking place within some BCG strains during experimental serial subculture to be monitored. In this survey the relationship of the changes observed to the different techniques employed for the maintenance of BCG lines and for the preparation of vaccine is considered. It is suggested that selection of minority populations within BCG strains noted during experimental studies may provide an analogy with the mechanism through which the original attenuation of the virulent bovine strain was brought about. The relevance of small-scale laboratory investigations to full-scale production procedures is also discussed, and finally some additional measures that might be taken to minimize changes in BCG strains are proposed.—Author's Summary

Seth, V., Kukreja, N., Sundaram, K. R. and Seth, S. D. Waning of cell mediated immune response in preschool children given BCG at birth. *Indian J. Med. Res.* **76** (1982) 710-715.

A total of 108 preschool children given BCG within the first week of life were tested for cell mediated immune response (CMIR) in relation to age (1-6 yr) and nutritional status. Mantoux test (5 TU PPD) and leukocyte migration inhibition test (LMIT) were used as parameters of CMIR. Mantoux positivity was 32.4% in comparison to LMIT positivity of 50.0%. In the absence of a positive skin response, CMIR could be elicited

by LMIT in 36.1% of cases, indicating that an absent skin response does not mean absent CMIR. By the use of both Mantoux test and LMIT, CMIR could be elicited in 65.0% to 73.3% of cases. Maximum waning of CMIR occurred in the first three years. Malnourished children seemed to be at a disadvantage with regard to retention of CMIR. There seems to be a need for planning a vaccination schedule in relation to the nutritional status of the children on the basis of a study of immune mechanisms after BCG in a larger sample of malnourished children.—Authors' Summary

Soo Duk Lim, Choong Rim Haw, Nack In Kim and Fusaro, R. M. Abnormalities of T-cell subsets in Behçet's syndrome. *Arch. Dermatol.* **119** (1983) 307–310.

T cells and T cell subsets were determined in the peripheral blood of 12 patients with Behçet's syndrome and 30 normal healthy control subjects. When compared with the control group, the mean percentage of T cells for the group with Behçet's syndrome was significantly decreased (73% vs. 61%). The mean percentage of T μ (helper) cells for the group with Behçet's syndrome (26%) was also significantly decreased from the mean value of the control group (42%). There was a concomitant significant increase of T γ (suppressor) cells of the group with Behçet's syndrome (19%) over the mean value of the control group (10%). These results clearly indicated that there were alterations of T cells and T cell subsets in this disease.—Authors' Summary

Stanford, J. L., Shield, M. J. and Rook, G. A. W. An investigation of a range of new tuberculins. I. The effects of ageing, place of domicile, BCG immunisation and tuberculosis. *Bull. Int. Union Tuberc.* **56** (1982) 28–34.

Skin-test antigens were prepared from a wide variety of mycobacterial species and used to test subjects in East Africa, Burma, and Libya. In schoolchildren aged 6–10 and 11–18 years there was considerable variation in response to the different antigens, but increasing age led to more frequent reactions irrespective of the BCG status of the individuals. It appeared that it was irrelevant how tuberculin positivity was pro-

duced. Thus, subjects who developed tuberculin positivity spontaneously gave similar reactions to those whose tuberculin positivity had been brought about by BCG vaccination.

It was further shown that differences existed in the incidence of reactions to the antigens dependent on the area in which the subjects lived. In general, subjects in Burma were more likely to give reactions than those in East Africa or Libya. This may reflect the relative abundance of the mycobacteria in the environment.

There was also a variation in the effect of active tuberculosis on the incidence of reactions. Where the level of positivity is high in the susceptible tuberculin-negative population, tuberculosis has little effect or produces a depression. Conversely, where the level of positivity is low in the tuberculin-negative group, tuberculosis produces an increase in the incidence of positive reactions. This may be due to trapping of T lymphocytes in lymph nodes, or the activation of a suppressor system.—P. A. Jenkins (*From Trop. Dis. Bull.*)

Sutherland, I., Švandová, E. and Radhakrishna, S. The development of clinical tuberculosis following infection with tubercle bacilli. 1. A theoretical model for the development of clinical tuberculosis following infection, linking from data on the risk of tuberculous infection and the incidence of clinical tuberculosis in The Netherlands. *Tubercle* **63** (1982) 255–268.

Information on the risk of tuberculous infection in The Netherlands has been linked with information on the incidence of tuberculosis, in an attempt to estimate the risks of developing the disease following infection or reinfection. It was postulated that: a) those with a recent primary infection had a characteristic risk of developing progressive primary tuberculosis; b) those with a distant (i.e., not recent) primary infection and a recent reinfection had a characteristic risk of developing exogenous tuberculosis; and c) those with a distant primary infection but no recent reinfection had a characteristic risk of developing endogenous tuberculosis.

The information on the risk of tuberculous infection was used to estimate the size

of the population in each of these infection classes for different age groups and calendar years in The Netherlands. Using multiple regression to link these population figures with the information on tuberculosis incidence in the same age group and calendar year, it was possible to estimate the above risks of developing tuberculosis.

For Netherlands males aged 15–69 years during the period 1951–1970, the three risks of developing pulmonary tuberculosis were estimated to be: a) 5.06% annually (for five years) following primary infection; b) 1.91% annually (for five years) following reinfection; c) 0.0253% annually, after the first five years following primary infection, in the absence of reinfection. The corresponding (and significantly different) estimated annual risks of development of pulmonary tuberculosis for females were 5.85%, 1.10%, and 0.0020%, respectively.

From these risks, it may be estimated that the degree of protection conferred by a distant primary infection, against pulmonary tuberculosis arising from a recent reinfection, was 63% for males and 81% for females. The estimated relative proportions of cases of progressive primary, exogenous, and endogenous tuberculosis varied considerably with age and calendar year. Progressive primary tuberculosis was dominant at the younger ages; exogenous and endogenous tuberculosis at older ages. At these older ages, the great majority of cases in The Netherlands in the early 1950s appeared to be exogenous in origin, but by 1970, with the decrease in the risk of infection, the exogenous contribution had dwindled substantially, especially among males.—Authors' Summary