CURRENT LITERATURE

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

General and Historical

Antia, N. H. Leprosy control by a people's program: "A new concept in technology transfer." Int. J. Health Serv. **17** (1987) 327–331.

Leprosy is a major health hazard in tropical countries as it also is in China. All programs for the control of this disease have been based on the cheap, effective, and low-toxicity antileprosy drug dapsone (DDS), available since the early 1950s. The emphasis has been on early detection and regularity of treatment, which has to be maintained for several years, if not a lifetime. Despite the availability of what might be rightly termed the "magic bullet," World Health Organization (WHO) figures demonstrate that leprosy has not been controlled in most countries and is generally on the increase. Blame has been ascribed to the patients for hiding the disease and for irregularity of treatment. Emphasis has now shifted to high-technology research to evolve more expensive and much more difficult multidrug regimens and an antileprosy vaccine.

China, isolated from the rest of the world and using only simple DDS therapy, but ensuring its use through its barefoot doctor approach, has shown a reduction of leprosy cases from 500,000 to 100,000 in the past three decades. The author suggests that the world, including WHO, should learn from the experience of China rather than try to impose its own low-effective and more expensive high-technology approach on this country.—Author's Abstract

Char, D. F. B. Hui Hoa Aloha—the Hansen's Disease Association. Hawaii Med. J. **47** (1988) 45.

This organization, as with so many other human efforts dealing with social changes, was born amid strife and turmoil and grew out of adversity.

In the late 1970s and early 1980s, Hawaii was embroiled in much controversy surrounding the event of the closure of Hale Mohalu in Pearl City, and the transfer of its patients to Leahi Hospital. Several young public health students who were joined in this protest movement recognized that there was a great need to gather together a group of people dedicated to being advocates expressing the concerns and needs of Hansen's disease (HD) patients in our state. It had to be a privately sponsored organization, divorced from public governmental funding, and able to recruit membership and support from the entire spectrum of our community. By spring of 1984, following the destruction by bulldozers of Hale Mohalu in Pearl City in September 1983, this band of young people got together with a number of HD patients and a few physicians, who were actively involved in providing patient care, to begin to discuss the need for establishing such an organization. In October 1984, following many meetings and discussions, this entity became officially incorporated.—Author's Abstract

Chen, P. C. Y. Human behavioural research applied to the leprosy control programme of Sarawak, Malaysia. Southeast Asian J. Trop. Med. Public Health **17** (1986) 421–426.

In 1984, in Sarawak, there were a total of 1099 recorded cases of leprosy for a population of 1.3 million. However, for each case recorded, it is estimated that two others remain undiagnosed as a consequence of the stigmatization associated with leprosy. For the 5-year period 1979–1983, an average of 29 new cases were detected each year of

which 8.6 (30%) were deformed due to the late stages at which it was being reported. To increase the case-finding rate, human behavioral research was applied to the leprosy control program so as to develop culture-specific health education packages aimed at self-diagnosis and self-referral in order to detect the large pool of undiagnosed cases hidden behind the veil of aversion, fear and ignorance. This was achieved through anthropological studies to identify how the various major ethnic groups perceived leprosy and their attitudes toward leprosy. Taking into account these findings, health education packages aimed at adults as well as children were developed for the Chinese as well as the non-Chinese, and consisted of newspaper articles, cartoon tape-slides, cartoon story books and posters.—Author's Summary

Chen, P. C. Y. and Sim, H. C. The development of culture-specific health education packages to increase case-finding of leprosy in Sarawak. Southeast Asian J. Trop. Med. Public Health **17** (1986) 427–432.

For any health education to succeed, the people's perception of the disease, their beliefs and cultural practices are of utmost importance since these have tremendous influence on their acceptance of new ideas. It is therefore essential to develop appropriate health education packages based on the understanding of the traditional and socio-cultural belief systems of the people. Thus on the basis of anthropological studies, health education packages were developed for the leprosy control program in Sarawak, aimed at both adults and children. Newspaper articles, cartoon tape-slides, cartoon story books as well as posters were developed for both Chinese as well as other groups such as Malays, Ibans, and Kayans. These were field tested and are now used in the Rejang Valley of Sarawak.—Authors' Summary

Kawuma, H. J. Buluba Leprosy Hospital, Uganda: a review of admissions, 1981–84. Lepr. Rev. **58** (1987) 257–262.

The current functions of Buluba Leprosy Hospital are outlined. An analysis of 2416 conditions necessitating the admission to the hospital of 1944 leprosy patients registered for treatment in the control area over a period of 4 years, 1981–1984, has been made and the relative frequency of the reasons for admission indicated. It is shown that over 40% of the workload of the hospital, for treatment, involved conditions not due to leprosy and could have been undertaken by the general health services of the area. The possibility of decreasing the number of admissions by improving the efficiency of the field projects is discussed. The indications are that the introduction of the WHO-recommended multidrug regimens will not significantly reduce the number of admissions to the hospital, other circumstances remaining unchanged.

In the future, the main functions of the hospital should be to treat the complications of leprosy and to provide adequate and appropriate leprosy training for the staff of the general hospitals and other health units. The need to elicit the help of various specialists in the fields of medicine and surgery is emphasized. It is suggested that in the longer term it might be possible to transfer more of the responsibilities for the care of leprosy patients to the general health staff, but that this transfer should be gradual and take into account implications possibly detrimental to the care of the patients.—Author's Summary

Law, A. S. Challenging the stigma: Hawaii's role in dispelling the myths of leprosy. Hawaii Med. J. **47** (1988) 75–80.

Hawaii has a unique opportunity to challenge the age-old stigma associated with leprosy. In addition to its educational and inspiring history, Hawaii has many persons with the disease who are willing to share their experiences in order to promote a better understanding of the disease and society's treatment of them, both past and present. One of the most important lessons to be learned from this history and these individuals is that prior to making any medical decisions, one must carefully consider the long-term social effects of those decisions that will persist after the disease is no longer a problem medically.—Author's Summary

Law, H. G. Kalaupapa as part of the National Park System. Hawaii Med. J. **47** (1988) 82–85.

Kalaupapa National Historical Park (Hawaii, U.S.A.) was established on 22 December 1980. Still in its formative years, Kalaupapa National Historical Park is dedicated to the past, the present, and the future. It is dedicated to preserving the memories and experiences of the past in order that valuable lessons might be learned from them. It is dedicated to providing a well-maintained community to ensure that the present residents of the Kalaupapa Settlement may live out their lives in this, their home. And, it is dedicated to the education of present and future generations of the general public with regard to a disease that has been shrouded in fear and ignorance for centuries. Although isolation of Hansen's disease patients is no longer necessary, approximately 90 patients have chosen to remain at Kalaupapa, the place they have come to regard as home. Their average age is 65 with approximately one third of the population over the age of 70.—Author's Abstract

Modlin, R. L. and Rea, T. H. Leprosy: new insight into an ancient disease. J. Am. Acad. Dermatol. **17** (1987) 1–13.

Patients with leprosy may be classified into two clinical and histopathologic categories. At one end of the spectrum, patients with tuberculoid leprosy have few skin lesions in which organisms can rarely be identified. At the other end of the spectrum, patients with lepromatous leprosy have numerous skin lesions containing myriad bacilli. Because immunologic resistance is associated with this spectrum, the study of leprosy provides a unique opportunity to gain insight into immunoregulatory mechanisms in man. In addition, serodiagnosis to identify early cases and prevention by vaccination are areas of active research. For patient care, a network of Regional Hansen's Disease Centers has been established under the sponsorship of the National Program for Hansen's Disease, Carville, Louisiana, U.S.A. Because the patients are often poor, their receipt of care and medication without cost helps to ameliorate at least one of the burdens imposed by this potentially devastating illness. The program's central office may be called at 800-642-2477.—Authors' Abstract

Valencia, L. B. Psycho-social and environmental factors in triad model for the management of control programme: focus on leprosy. Southeast Asian J. Trop. Med. Public Health **17** (1986) 442–450.

The study addresses the question of how the qualitative aspect of the interaction between the people involved in the leprosy control program affects the process of patients (P), service providers (SP), and satellite informants (SI) composed of community leaders in the delivery of basic leprosy control services in two highly leprosy-endemic villages in La Union Province, The Philippines. The interaction between P, SP and SI as an independent variable is imagined to be linked in a form of a triad, influenced by psychosocial and environmental variables. Data were gathered by conventional methods as interviews, historical research and use of rating scales as well as nonconventional methods as PUP, a locally developed standardized instrument which measures variables that determine a Filipino's adjustment to social situations, and photographic documentation. Statistical analysis was made on the independent variable and the dependent variable—an improved leprosy control program. It was observed that the stigmatization of Hansenites had deep historical roots with the policy of colonial administrations to isolate and segregate Hansenites. This stigma remains to the present and was observed to exist even among service providers: low knowledge levels of patients on the causes of the disease on the one hand, and service providers on the cure, particularly on the use of multiple drug therapy. The reorganization scheme of the Health Ministry also resulted in the slowdown of leprosy control activities thereby affecting delivery of services. Individual personality traits and other psychosocial factors of P, SP and SI further contributed to the lag in service delivery. In conclusion, it was established that the interaction of the triad and the influences of psychosocial and en-

vironmental factors do affect the delivery of services. Concrete recommendations were forwarded that seek to make patients take more active participation in the management of their illness and how the service providers and community leaders can be made to share in the burden. In addition, further education was proposed for both patients and service providers on the causes and treatment of leprosy.—Author's Summary

Chemotherapy

Cartel, J. L., Naudillon, Y., Remy, J. C. and Grosset, J. H. Contribution of relapses to total infection sources of leprosy in Guadeloupe. Lepr. Rev. **58** (1987) 339–348.

In Guadeloupe between 1970 and 1984, the incidence of new cases of leprosy, analyzed through the computerization of data collected by the Leprosy Control Unit on OMSLEP record cards, showed a decline from 24 per 100,000 inhabitants in 1970 to 11 per 100,000 inhabitants in 1984 ($y = -1.44$). The decline was not significantly different in paucibacillary forms ($y = -0.94$) and in multibacillary forms ($y = -0.45$) but was much stronger among children below the age of 15 years ($y = -3.22$) than among adults ($y = -0.67$). During the same period, 117 relapses were noted among the annual mean pool of 624 multibacillary patients who had been receiving lifelong treatment with dapsone alone for more than 5 years. The average number of relapses was 7.8 per year and the mean relapse rate 1.2% per year. The relapses have not in general been due to discontinuation of treatment by the patients because all cases of relapse for which a mouse inoculation has been carried out since 1980 harbored dapsone-resistant *Mycobacterium leprae.* Prevention of relapses by chemotherapy of inactive multibacillary cases still under treatment with dapsone alone appears as a priority for the control of leprosy in Guadeloupe.—Authors' Summary

Chen, J., *et al.* [Treatment of multibacillary leprosy cases with B663, RFP and DDS for one year.] Chin. Lepr. J. **3** (1987) 89–91. (in Chinese)

All of the 47 cases of multibacillary leprosy treated with clofazimine (B663), rifampin (RFP), and dapsone (DDS) for 1 year showed clinical improvement. The bacterial index decreased on the average by 0.57+ (33.7%). There was little type 2 reaction and neuritis. The side effects of the therapy are pigmentation and ichthyosiform change of the skin. Toxicity to the liver is not obvious.—Authors' English Abstract

David, H. L., Rastogi, N., Clavel-Sérés, S. and Clément, F. Studies of clofazimine resistance in mycobacteria: is the inability to isolate drug-resistant mutants related to its mode of action? Zentralbl. Bakteriol. Mikrobiol. Hyg. [A] **266** (1987) 292–304.

This study showed that clofazimine was not radiomimetic, it was not a mutagenic compound, it was not an inducer of prophage-λ, and it did not eliminate plasmids from appropriate host bacteria. The drug caused an effective inhibition of the growth of *Mycobacterium aurum,* and also inhibited the growth cycle of the mycobacteriophage D_{29}. Cross resistance between clofazimine, streptomycin and rifampin could not be demonstrated. Drug-resistant mutants toward clofazimine could not be isolated, and it was found that the existing clofazimine-resistant strains of *M. tuberculosis* were rather susceptible organisms requiring clofazimine in their growth medium to maintain their drug resistance. Ultrastructural studies showed that clofazimine did not act by cell wall lysis, nor did it act on bacterial ribosomes. Higher concentrations of the drug resulted in bacterial plasmolysis. These findings are discussed in the light of its known properties and proposed mode of action.—Authors' Summary

Georgiev, G. D. and Kielstrup, R. W. Blister calendar packs for the implementation of multiple drug therapy in DANIDA-assisted leprosy control projects in India. Lepr. Rev. **58** (1987) 249–255.

A brief description is given of leprosy control projects in Orissa, Madhya Pradesh and Tamil Nadu, set up by the government of India and assisted by the Danish International Development Agency (DANIDA), as part of the Indian National Leprosy Eradication Programme. In view of the crucial importance of assuring the highest possible compliance to prescribed medication and regularity of clinic attendance over adequate periods of time, it was decided to use blister calendar packs for the dispensing of antileprosy drugs to patients with both paucibacillary and multibacillary forms of the disease. The projects cover a population of 12 million people with an estimated 130,000 leprosy patients. The packs are being manufactured by Pharmanova, Denmark, and over the next 4–5 years, approximately 1.7 million will be used in the four project areas.

The rationale for the use of blister calendar packs, the design requirements and the operational methodology are discussed in a separate publication. This paper is concerned with the description, structure and technical specification of the packs to be used in India, illustrated with diagrams and photographs. The operational benefits and cost-effectiveness of the use of such packs in leprosy control have still to be established, but the approach is worth consideration in view of the limited drugs available for leprosy and the paramount importance of regular drug supply and adequate treatment compliance.—Authors' Summary

Joseph, M. S. Photodermatitis provoked by dapsone: a case report. Lepr. Rev. **58** (1987) 425–428.

A 61-year-old patient with leprosy developed photodermatitis due to dapsone. The diagnosis was confirmed by clinical trial. This case report demonstrates one of the rare and probably unreported side effects of the most commonly used antileprosy drug dapsone.—Author's Summary

Mac-Moune Lai, F., Lai, K. N. and Chong, Y. W. Papillary necrosis associated with rifampicin therapy. Aust. N.Z. J. Med. **17** (1987) 68–70.

The authors report a patient who developed progressive renal failure following 13 months of rifampin therapy for renal tuberculosis. The renal function continued to deteriorate despite the discontinuation of rifampin. Renal pathology did not demonstrate any evidence of tuberculosis of the kidney but revealed the unique pathological finding of glomerulosclerosis, granulomatous interstitial nephritis, and extensive papillary necrosis.—(AS, Trop. Dis. Bull.)

Orege, P. A., Obura, M. and Nyawalo, J. O. Short-course multidrug therapy for leprosy patients in Western Kenya. Preliminary communication. Lepr. Rev. **58** (1987) 263–270.

A prospective study has been undertaken to evaluate how tolerable and effective short-course multidrug (MDT) chemotherapeutic regimens are, for both multibacillary and paucibacillary cases of leprosy, using WHO-recommended regimens. For paucibacillary cases, we have compared the WHO-recommended multidrug regimen and a modified multidrug regimen, consisting of rifampin 1500 mg at the outset and repeated after 3 months, together with dapsone 100 mg daily unsupervised. The WHO-recommended multidrug regimen for multibacillary cases of leprosy is given for 2 years, after which the cases are followed for 3 years. Paucibacillary cases on WHO-recommended and modified MDT will get active therapy for 6 months after which they will be followed for 18 months.

A total of 145 patients were admitted to the study, of whom 37 (25.5%) were multibacillary and 108 (75.5%) paucibacillary cases. Of the registered cases 93 (64.1%) are females and 52 (35.9%) are males. Within the period of study, a quite high clinical cure rate was noted among paucibacillary cases, in many instances from the second month onward. The default rate was low and no adverse effects associated with the use of either clofazimine or rifampin were noted. One female patient developed exfoliative dermatitis, thought to be due to dapsone,

which completely cleared once the use of this drug had been stopped, and another female patient had hypochromic anemia, calling for transfusion, also possibly related to dapsone. Contrary to reports from some other centers on continuing activity in paucibacillary cases even after the full course of WHO-recommended therapy, our preliminary experience in Kenya suggests that clinical cure can be achieved in much shorter periods than had hitherto been supposed.—Authors' Summary

Pattyn, S. R., Groenen, G., Bourland, J., Grillone, S., Janssens, L. and the Collaborative Study Group for the Treatment of Leprosy in Zaire and Rwanda. A controlled therapeutic trial in paucibacillary leprosy comparing a single dose of rifampicin followed by 1 year of daily dapsone with 10 weekly doses of rifampicin. Lepr. Rev. **58** (1987) 349–358.

Results of prospective therapeutic trials among paucibacillary leprosy patients conducted in 1980–1982 in Anjouan, Burundi, Rwanda and Zaire are presented. Regimens were (TrA) rifampin (RMP) 1500 mg single dose, supervised, followed by 1 year of dapsone 100 mg daily unsupervised; (TrB) RMP 900 mg once a week during 10 weeks and (B-com) RMP 600 mg once a week during 10 weeks. Regimens are evaluated in terms of cure rates and relapse rates based on the histopathology of skin biopsies. Among patients with less than three skin lesions TrA and TrB perform equally well (96–97% cure rate), in patients with three or more skin lesions TrB is superior (98% cure) to TrA regimen (89% cure). Treatment B-com is as effective as TrB. The importance of late cures is stressed. Relapse rates are comparable in all regimens with a mean of 2.84 per 100 patient years.—Authors' Summary

Samuel, N. M., Samuel, S. and Adiga, R. B. Primary dapsone resistance in multibacillary leprosy among Nepalese children. Singapore Med. J. **28** (1987) 28–30.

Between 1980 and 1983 newly diagnosed patients (i.e., LL and BL) at our clinics had skin biopsies taken. In patients with a bacterial index (BI) >2.5 the *Mycobacterium leprae* obtained from the biopsies were inoculated into Swiss albino and nude mice to detect *M. leprae* resistant to dapsone. In this communication, we report multibacillary leprosy in 11 Nepalese child patients. In all except one, the index cases were relapsed multibacillary patients. Nine patients were tested for dapsone sensitivity in the mouse foot pad test system and seven were shown to have primary dapsone resistance.—(*From* the Article)

Subcommittee on Clinical Trials of the Chemotherapy of Leprosy (THELEP) Scientific Working Group of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. Persisting *Mycobacterium leprae* among THELEP trial patients in Bamako and Chingleput. Lepr. Rev. **58** (1987) 325–337.

The availability of approximately 75% of the anticipated results with respect to persisting *Mycobacterium leprae* from the THELEP controlled clinical trials in Bamako and Chingleput has made possible an interim analysis. Persisting *M. leprae* were detected in 43 skin-biopsy specimens obtained from 39 patients, among a total of 468 specimens obtained at intervals of 3, 12 and 24 months from 199 patients during treatment with five combined drug regimens. The proportion of specimens in which persisting organisms were discovered appeared not to vary with regimen or duration of treatment. The regimen consisting of a single large initial dose of rifampin plus daily dapsone was not shown to be less effective, in terms of the proportion of specimens in which persisters were detected, than regimens consisting of rifampin, dapsone and clofazimine or prothionamide, each drug administered daily. The average number of persisting *M. leprae* per patient was calculated to lie in the range 50,000–250,000 at each of the intervals. The results of these trials lend strong support to the multidrug regimen recommended for treatment of multibacillary leprosy by the World Health Organization Study Group on Chemotherapy of Leprosy for Control Programmes.—Authors' Summary

Tao, M., *et al.* [Effect of MDT regimen on bacillus index for 2 years in 317 multibacillary leprosy patients.] Chin. Lepr. J. **3** (1987) 99–101. (in Chinese)

The authors report the results of bacteriological examinations of the skin in 317 cases of multibacillary leprosy treated with a multidrug therapy (MDT) regimen containing rifampin (RFP), clofazimine (B663) and dapsone (DDS) for 2 years which showed that the bacterial index (BI) decreased by 0.76 on the average every year and no rise again in the BI was seen. The MDT regimen was also effective in newly found, relapsed and DDS-resistant cases.—Authors' English Abstract

Wang, Z., *et al.* [Clinical effect of multidrug therapy regimen.] Chin. Lepr. J. **3** (1987) 87–88. (in Chinese)

Thirty cases of multibacillary leprosy have been treated with dapsone (DDS), rifampin (RFP or RFD) and prothionamide (PTH) for 3 years, and the clinically effective rate among them is 68.9% in the sixth month and 100% in the twelfth month. All of the skin lesions and neural signs subsided by the end of the second year. The morphological index decreased by 67.2% on the average in the third month and to zero in the twelfth month. The bacterial index decreased on the average by 22.2% in the first year, by 46.5% in the second year, and by 66.8% with 12 cases being negative by the end of the third year. Bacteriological negativity under the multidrug therapy regimen seems to come more rapidly. Toxicity to the liver is less and slighter. PTH is more sufficient in supply, is less expensive, and produces less pigmentation; therefore patients are more willing to take it.—Authors' English Abstract

Zeis, B. M. and Anderson, R. Clofazimine-mediated stimulation of prostaglandin synthesis and free radical production as novel mechanisms of drug-induced immunosuppression. Int. J. Immunopharmacol. **8** (1986) 731–739.

The effects of clofazimine (3-(*p*-chloroanilino)-10-(*p*-chlorophenyl)-2, 10-dihydro-2-(isopropylimino)-phenazine) at concentrations of 0.625–20 μg/ml on the mitogen-induced transformation, luminol-enhanced chemiluminescence, arachidonic acid metabolism and sulphydryl content of human mononuclear leukocytes (MNL) were investigated *in vitro*. The drug at all concentrations tested decreased MNL sulphydryl content and inhibited mitogen-induced transformation. Clofazimine increased the spontaneous luminol-enhanced chemiluminescence and activated the arachidonic acid cascade in MNL. The anti-oxidants ascorbic acid and cysteine and the prostaglandin (PG) synthesis inhibitor indomethacin were used individually and in combination to identify the primary mediators of the anti-proliferative effects of clofazimine on MNL. Combinations of an anti-oxidant with a PG synthesis inhibitor completely protected MNL from clofazimine-mediated inhibition of mitogen-induced transformation. These results show that the anti-proliferative activity of clofazimine is related to both the pro-oxidative and PG synthesis enhancing effects of the drug on MNL.—Authors' Abstract

Zeis, B. M., Anderson, R. and O'Sullivan, J. F. The effect of ten phenazine-derivatives in comparison to clofazimine on the production of prostaglandin E_2 by polymorphonuclear leucocytes. Lepr. Rev. **58** (1987) 383–388.

The antileprosy drug clofazimine (B663) apart from its antimycobacterial effects has been shown to stimulate the production of prostaglandin E_2 (PGE_2) by polymorphonuclear leukocytes (PMNL). To separate these two activities on a molecular basis a limited number of 10 phenazine-derivatives was investigated for their effects on prostaglandin synthesis. It was found that the *p*-chlorophenyl- and *p*-chloroanilino-groups in position 10 and 3 of the phenazine molecule, respectively, were indispensable for stimulation of PGE_2 production by PMNL; whereas modifications of the imino-isopropyl-group in position 2 did not affect this activity but as shown previously decreased the antimycobacterial effects of the agents against murine tuberculosis.—Authors' Summary

Clinical Sciences

Arora, S. K. and Mukhija, R. D. Pure neural leprosy in a child: a case report. Indian J. Lepr. **59** (1987) 223–224.

Pure neural leprosy developing in a 3½-year-old female child is reported.—Authors' Abstract

Atkin, S. L., Welbury, R. R., Stanfield, E., Beavis, D., Iwais, B. and Dick, W. C. Clinical and laboratory studies of inflammatory polyarthritis in patients with leprosy in Papua New Guinea. Ann. Rheum. Dis. **46** (1987) 688–690.

The results of a combined clinical and laboratory study in 55 patients throughout the leprosy spectrum are reported. Thirty-one of these patients suffered from an inflammatory peripheral polyarthritis which has not been previously described and which was unassociated with the characteristics of erythema nodosum leprosum reactions or with Charcot's joints. α_2 Macroglobulin was raised significantly only in those patients with leprosy and arthritis.—Authors' Summary

Azulay, R. D. Autoaggressive hanseniasis. J. Am. Acad. Dermatol. **17** (1987) 1042–1046.

I have given the name *autoaggressive hanseniasis* to a syndrome with immunopathologic and clinical pictures resembling autoaggressive systemic diseases observed in some cases of lepromatous and borderline hanseniasis. It is probably caused by B-cell stimulation by antigenic complex of *Mycobacterium leprae* plus autologous tissue, along with a dysfunction of the T-suppressor lymphocytes.—Author's Abstract

Bombach, B. and Reichart, P. Periodontal findings in patients with leprosy. Lepr. Rev. **58** (1987) 279–289.

The periodontal status of 110 patients with leprosy and 34 healthy controls was studied using periodontal indices. Comparison of the different periodontal indices between controls and patients showed significantly higher values for some of these indices in the latter group. Limitation of oral hygiene due to deformation or mutilation of fingers and hands had no statistically significant correlation to the periodontal findings. Indices for plaque and calculus, factors contributing to the degree of gingival and periodontal inflammation, were higher in the group of patients even if the same degree of inflammation was present in both groups. A probable influence of the antileprosy therapy may be considered. Comparably low values for the gingival index and the sulcus fluid rate for those patients treated with clofazimine may indicate an anti-inflammatory effect of this specific therapy at the gingivo-periodontal complex. Poor oral hygiene due to lack of motivation and/or a generally reduced status of health in leprosy patients must be considered as one of the main causes of periodontal disease.—Authors' Summary

Castells, A., Terencio, J., Ramirez, A., Sundal, E. and Bolla, K. Thymopentin treatment in patients with chemotherapy-resistant lepromatous leprosy. Surv. Immunol. Res. **4** Suppl. 1 (1985) 63–69.

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*; it is chiefly involving the skin and peripheral nerves. In lepromatous leprosy there are widespread loose infiltrates with *M. leprae* multiplying extensively in the skin macrophages and Schwann cells of peripheral nerves. Such patients reveal a decrease of circulating T-helper cells, which is still more pronounced in the cutaneous lesions. Due to the ever-increasing bacterial resistance to classical dapsone and combined chemotherapy as well, an immunomodulatory approach seemed reasonable: Eight patients with long-lasting (5–40 years) disease who had become resistant to combined chemotherapy were treated with thymopentin, 50 mg s.c., 3 times weekly for 5 weeks and thereafter combined with dapsone and clofazimine for 5 months. During the trial a statistically significant increase in E-rosette-forming cells ($p < 0.05$) was observed, along with a steady improvement of the bacterial status of the nasal mucus. Although the skin lesions did not disappear within the obser-

vation period of the study, it is important to realize that long-term improvement of such lesions is always initiated by clearance of bacilli from the nasal mucus, hence, thymopentin treatment appears to be a promising approach to chemotherapy-resistant lepromatous leprosy.—Authors' Summary

Correa, P., Bah, M. D., Ngom, A., Traore, M., Moreau, J. C. and Kandji, T. [Leprosy and pregnancy.] Afr. Med. **25** (1986) 191–196. (in French)

Following an account of the part played by the Service National des Grandes Endémies in Senegal, the authors describe a study they carried out based on the village of Peycouck in the Thiès region. They record the incidence of leprosy in a population of 1047, the impact of this disease on fertility, the abortion rate, and their experience in the management of 113 female leprosy patients who had 96 pregnancies without treatment and 479 with. Details are given of chemotherapy during pregnancy, parturition, the condition of babies in the neonatal period and the state of the placenta. (One placenta was examined histopathologically but did not reveal a granuloma or bacilli.) A final section deals with the further development of children born to leprous mothers, including a review of some of the literature. The authors conclude that women with leprosy, if correctly treated and supervised, have normal pregnancies and that their children develop normally, but that it is particularly important to pay attention to the social aspects for both mother and child.—(A. C. McDougall, Trop. Dis. Bull.)

Dann, F. J. A clinician's experience in managing patients with Hansen's disease. Hawaii Med. J. **47** (1988) 68–70.

Patients with Hansen's disease (HD) in Hawaii are now being treated in the private offices of physicians experienced in HD. The Hawaii Hansen's Disease Community Program (HDCP) coordinates ancillary medical services, but there is no "HD clinic" or central locale for the vast majority of HD victims who are now outpatients. Fourteen years ago we saw our first case of HD, and began accumulating patients as interest and skill in management increased. There are now about 50 patients with HD in our practice. This report includes practical information on making the diagnosis and informing the patient, about controling reactional states, and about general management of the patient with Hansen's disease.—Author's Abstract

Gnanadoss, A. S. and Rajendran, N. Ocular lesions in Hansen's (leprosy). Indian J. Ophthalmol. **34** (1986) 19–23.

In 250 Hansen's cases assessed, ocular lesions were seen in 59.2% of cases. The cornea was more frequently involved (25.2%). Excluding lagophthalmos, most of the lesions were seen in lepromatous cases of long duration. Unless systemic treatment is instituted early, this does not prevent the development of ocular lesions. The posterior segment was uninvolved. Ocular tension and refractive status were that of a normal population. Operations were attended with good results. Visual loss, which was seen in 4.8% of cases, was due either to corneal or to uveal lesions.—Authors' Summary

He, H. [Acid-base and gas assay in the blood of leprosy cases.] Chin. Lepr. J. **3** (1987) 102–103. (in Chinese)

The authors report the results of analysis of acid-base and gases in the blood of leprosy patients which show that there is no significant difference between patients with various forms of the disease. The value of pO_2 in the blood of all leprosy patients is lower than that in healthy people, which might be due to pathological changes in the nose. The value of pCO_2 in the blood of multibacillary and paucibacillary leprosy patients is significantly different and its cause is not known yet.—Author's English Abstract

He, H., *et al.* [Determination of SIgA in the tears of leprosy patients by radioimmunoassay.] Chin. Lepr. J. **3** (1987) 101–102. (in Chinese)

The content of secretory IgA (SIgA) in the tears of 49 leprosy patients and 33 healthy controls was determined with radioimmunoassay. The average level of SIgA in the

tears of the healthy control group was 46.12 ± 11.20 μg/ml, and 28.18 ± 9.2 μg/ml in that of LL patients and 29.55 ± 8.8 μg/ml in TT cases. The difference between healthy people and leprosy patients is significant statistically. Because SIgA in the tears of leprosy patients is significantly less than that in healthy people, local resistance to infection in the eyes of the patients is lower so that the eyes are more liable to be affected by infection.—Authors' English Abstract

Hodges, E. J., Ostler, H. B., Courtright, P. and Gelber, R. H. Keratoconjunctivitis sicca in leprosy. Lepr. Rev. **58** (1987) 413–417.

Our studies indicate that the patient with leprosy is at risk for developing keratoconjunctivitis sicca. The cause of keratoconjunctivitis sicca in our patients suggests that the aqueous layer of the tear film may be decreased as a result of a decrease in secretion of tears from the accessory lacrimal gland of the conjunctiva although it could also be decreased due to a diseased afferent arc to the lacrimal gland or to a diseased lacrimal gland both resulting in decreased aqueous production. In addition, the stability of the precorneal tear film is probably affected due to a decrease in corneal sensation and to lagophthalmos both of which result in decreased blinking, as well as failure of the lid to resurface the tears because of irregularity of the conjunctiva or cornea.

Our results suggest that patients with leprosy should be followed closely for keratoconjunctivitis sicca and that treatment directed toward this problem should be initiated early.—Authors' Summary

Kar, H. K., Saxena, A. K., Jain, R. K. and Sharma, A. K. Type 1 (reversal) lepra reaction in borderline leprosy with unusual clinical presentation—a case report. Indian J. Lepr. **59** (1987) 219–222.

A male 26-year-old patient with BB type leprosy was encountered with a typical clinical presentation of up-grading (reversal) type 1 lepra reaction. These included the sudden appearance of tender, erythematous nodular eruptions mimicking ENL, severe constitutional symptoms like high-grade fever, malaise, vomiting, epistaxis, joint pain and tenosynovitis simulating type 2 lepra reaction. To the best of our knowledge, this may be the first such case in our hand.—Authors' Abstract

Kumar, A., Sirumban, P., Durgambal, K. and Kalaivani, S. Operational efficiency of leprosy clinics: a time-motion study. Lepr. Rev. **58** (1987) 239–247.

A time-motion study was undertaken to estimate the time spent by leprosy patients in waiting as well as in utilization of various medical care services at monthly mobile leprosy clinics. On an average (mean ± SE), a patient spent 48 ± 2.6, 42 ± 4.8 and 104 ± 4.2 min each time at rural, urban and referral leprosy hospital clinics, respectively. More than 90% of this time was spent in waiting in queues for various clinic services. Based on the observations, the reorganization of a leprosy clinic to improve its operational efficiency is discussed in this communication.—Authors' Summary

Kunz, K. Relapse in Hansen's disease. Hawaii Med. J. **47** (1988) 70–75.

Both Hansen's disease (HD) relapse and an increasing prevalence of dapsone-resistant *Mycobacterium leprae* are recognized worldwide and have necessitated major changes in HD treatment and control efforts. Hawaii's HD problems are representative of those encountered elsewhere. We physicians remain essential to the task of patient care and interruption of disease transmission. The complexity of social factors involving patients, as well as the complexity of antileprosy drug regimens, are challenges for each of us who are HD caregivers, and for Hawaii's HD control programs.—Author's Abstract

Lagueny, A., Rommel, A., Vignolly, B., Taieb, A., Vendeaud-Busquet, M., Doutre, M. S. and Julien, J. Thalidomide neuropathy: an electrophysiologic study. Muscle Nerve **9** (1986) 837–844.

Thalidomide is effective in the treatment of such disabling dermatologic diseases as aphthosis, discoid lupus erythematosus, and

prurigo nodularis, in which other drugs fail. However, its use can induce neuropathy, necessitating caution in its administration. It was found in this electrophysiologic study of 13 patients that the data best revealing neuropathy, even when clinical abnormalities were not apparent, were reduction of sensory nerve action potential amplitude on the sural nerve, increase of somatosensory evoked potential latency following sural nerve stimulation, and reduction of sensory action potential amplitude on stimulating the median nerve at the wrist. In two patients, electrophysiologic abnormalities had increased after withdrawal, suggesting a prolonged action of thalidomide. Timely reduction of dosage, after detection of changes indicating the onset of side effects, could reduce the risk of the sometimes rapid emergence of clinical symptoms.—Authors' Abstract

Nigam, P., Mukhija, R. D., Gupta, A. K., Dayal, S. G. and Goyal, B. M. Gonadal involvement in leprosy—study of gynaecomastia, testicular and epididymal involvement and therapeutic efficacy of indigenous drugs. Hansenol. Int. **9** (1984) 10–20.

Sixty male patients with leprosy (mean age = 27.2 ± 5.04 years) selected at random, were studied for gonadal involvement and the therapeutic efficacy of two indigenous drugs. Of these 34 were married, with the mean duration of illness 4.17 ± 3.27 years. Only those with lepromatous and dimorphous leprosy developed testicular and epididymal changes. Testicular pain and/or swelling (lepromatous = 62.5%, dimorphous = 30%) was the commonest presenting feature. Altered sexual function was observed in 34 (56.6%) cases, while 11 patients revealed altered sexual hair pattern and nine gynecomastia. Reduced testicular size associated with soft feel was present in 25% of cases with no testicular sensation in 8 (13.3%) and impaired testicular sensation in 9 (15%) patients. Spermograms revealed azoospermia in 19 (35%) and oligospermia in 16 (26.6%) patients. Histopathological findings of testicle biopsy revealed evidence of leprous pathology irrespective of testicular size, semen picture and clinical manifestations. Histopathological changes showed marked variation and so did not enable categorizing them into vascular, interstitial and obliterative phases. These changes were believed to be due to the altered gonadal state in leprosy. The therapeutic efficacy of the indigenous preparations, Speman and Tentex forte (Himalaya), was evaluated subjectively as well as objectively in 34 patients; 82.3% of cases showed subjective improvement while objective improvement in the spermogram was noted in 87.5% of the cases with oligospermia. The drugs have no side effects and were well tolerated.—Authors' Abstract

Olivier, H. R. Psychiatric aspects of Hansen's disease (leprosy). J. Clin. Psychiatry **48** (1987) 477–479.

Hansen's disease or leprosy is a major worldwide public health problem that has profound psychological effects on its victims. This paper is the first systematic study of psychiatric patients with Hansen's disease in 30 years and the first to use current diagnostic criteria. Because the incidence of Hansen's disease appears to be rising, the implications of psychiatric diagnosis in Hansen's disease patients and treatment considerations for the future are discussed.—Author's Abstract

Olivier, H. R. Sixty years of psychiatry at Carville. South. Med. J. **80** (1987) 1498–1504.

The hospital now known as the Gillis W. Long Hansen's Disease Center is the only hospital in the United States solely treating Hansen's disease (leprosy). From the time of its establishment in 1894 until 1923, the psychiatric patients presented treatment and management problems that remained unaddressed. Since 1923, however, psychiatric consultants have provided care and treatment for this segment of the Carville population. This paper presents the findings of three of these consultants for the period 1923 to 1985, and outlines similarities and differences in the diagnoses, treatments, and disposition of patients, as well as indications for future investigations.—Author's Abstract

Rao, K. N., Saha, K. and Chakrabarty, A. K. Undernutrition and lepromatous leprosy. III: Micronutrients and their transport proteins. Hum. Nutr. Clin. Nutr. **41C** (1987) 127–134.

The present report is a continuation of our earlier studies on the complex interaction between undernutrition and leprosy. Serum levels of vitamins A and E, zinc and iron were determined in healthy control subjects and lepromatous leprosy patients belonging to an eastern state of India. Results indicated a significant lowering in the two above-mentioned fat-soluble vitamins and also a remarkable hypozincemia in the patient group. However, serum iron levels were found to be comparable in both the groups. Also concentrations of vitamin A transport proteins such as retinol binding protein and prealbumin in sera of the lepromatous patients were significantly decreased in comparison with the control subjects. Of the two zinc-binding proteins, i.e., serum albumin and α-2 macroglobulin, only the former was significantly reduced in the patient group. Surprisingly, although serum iron, transferrin and ferritin levels were similar in both the patient and control groups, the hemoglobin levels were significantly reduced in the lepromatous patients. The implications of these findings have been discussed. This is the first report describing the serum ferritin levels in lepromatous patients.—Authors' Abstract

Sayer, J., Gent, R. and Jesudasan, K. Are bacterial counts on slit-skin smears in leprosy affected by preparing slides under field conditions? Lepr. Rev. **58** (1987) 271–278.

A study was undertaken to look at two of the factors which may have an effect on the bacterial index (BI) of slit-skin smears collected in the field. The effect of sunlight during air-drying of the smears was examined by comparing smears dried in sunlight with those dried in darkness or in the shade. The results showed no significant difference in the BI readings of the slides from the three different groups.

A second set of slit-skin smears was used to investigate whether staining would be affected by delaying the staining of the fixed smears by intervals of 1 week and 3 weeks. The readings from these various groups also showed no significant difference. However, there was a trend toward lower readings in the slides that had been stored for longer periods.

The relevance of these findings for leprosy field workers is discussed.—Authors' Summary

Sehgal, V. N. and Srivastava, G. Indeterminate leprosy. A passing phase in the evolution of leprosy. Lepr. Rev. **58** (1987) 291–299.

The diagnosis of leprosy at an early stage, when the signs and symptoms are still equivocal, is a matter of continuing difficulty to the clinician. This is the case in indeterminate leprosy. The physician's dilemma is further compounded by the different schools of thought regarding the clinical features and treatment practice of this form of leprosy. This paper reviews the subject of indeterminate leprosy and attempts to shed some light on a controversial entity.—Authors' Summary

Sroat, D. A. Ocular leprosy. Hawaii Med. J. **47** (1988) 66–67.

One can expect that, in Hawaii, most general physicians and dermatologists will have among their patients at least several who have HD. During the ongoing care of these patients, attention should be directed to their eyes. The history and examination should seek to elicit evidence of past and present episodes of unusual ocular inflammation and the presence of weakness of eyelid closure. Any of these findings call for an ophthalmological consultation. The ophthalmologist must be an important member of the therapeutic team for the leprosy patient because the loss of sight combined with the loss of the sensation of touch from leprotic peripheral nerve damage combine to produce a profound disability in these patients.—Author's Conclusion

Stingl, P. [Differential diagnosis of leprosy in developing countries—skin and oral cavity.] Z. Hautkr. **62** (1987) 227–231. (in German)

There are some skin diseases which are frequently mistaken for leprosy and in consequence, often treated like it for a long period of time. The rate of false diagnoses is especially high in leprosy control programs of developing countries. However, a wrong diagnosis of leprosy can mean psychological disaster to the patient because of the stigma still attached to leprosy. According to the literature and our own observations in Sierra Leone, Ethiopia, and the Sudan, we present data on the differential diagnosis of leprosy concerning the skin and oral cavity.—Author's English Summary

Wang, Q. [Analysis of 71 cases of relapsed leprosy in Lufeng County, Guangdong.] Chin. Lepr. J. **3** (1987) 84–86. (in Chinese)

Seventy-one cases among 2583 cured leprosy patients have relapsed (2.75%), of which 29 came from 365 multibacillary (MB) leprosy cases (7.93%) and 42 from 2218 paucibacillary (PB) cases (1.89%). The longer the time elapsing within 5 years after being cured, the more relapsed cases there were. Relapsed cases of MB leprosy are more than those of PB cases, and proportions of relapsed ones to newly found cases and to active ones are increasing. Patients whose treatment duration was less than 5 years and whose time after recovery is less than 5 years relapsed more frequently.—Author's English Abstract

Wang, Y. [Analysis of leprosy case finding in a dermatology outpatient department in the last ten years.] Chin. Lepr. J. **3** (1987) 80–81. (in Chinese)

Patients with various skin diseases consulted at the Outpatient Department of Qingdao Skin Hospital a total of 653,929 times during the period of 1977 to 1986. From among them 192 cases of leprosy were discovered. The author points out that outpatient examination in the Skin Department has already become an important measure of case finding as early as possible in the leprosy control campaign, because the proportion of the patients found by this means to all of the newly found cases has gradually increased. The indeterminate form is more frequently recognized and the duration of their disease shortened; 77 cases of them were reported by different medical units, accounting for 40%, which fully showed the importance of incorporating medicine in the leprosy control program.—Author's English Abstract

Immuno-Pathology

Agius, G., Baillargeau, E., Ranger, S., Castets, M., Millan, J. and Samb, A. [Titrations of anti-BCG antibodies in healthy Africans and Africans with leprosy.] Acta Leprol. (Genève) **5** (1987) 207–218. (in French)

An immunoperoxidase reaction was used for the titration of immunoglobulins G and M antibodies to BCG in 171 leprosy patients from Dakar. The results show mean titers decreasing from lepromatous to tuberculoid cases. The antibody profiles of some clinical forms such as reversal reactions and erythema nodosum leprosum are discussed. This test in association with the Mitsuda reaction, bacteriology and histology should allow an easier classification of the borderline forms. The main advantages of the technique are simplicity, speed, low cost and the easy availability of the BCG. These qualities are essential in endemic zones.—Authors' English Summary

Barros, U., Ladiwala, U., Birdi, T. J. and Antia, N. H. Localization and retention of mycobacterial antigen in lymph nodes of leprosy patients. Br. J. Exp. Pathol. **68** (1987) 733–741.

Although leprosy, a chronic disease caused by *Mycobacterium leprae,* primarily affects skin and peripheral nerves, pathological changes and granulomas have been observed in lymph nodes which are: a) present in tuberculoid lymph nodes in the absence of acid-fast bacilli and b) persistent in lepromatous patients even after prolonged

treatment. We detected substantial amounts of mycobacterial antigen in 16 leprous lymph nodes using anti-BCG by the peroxidase anti-peroxidase method. The load and distribution of antigen varied along the spectrum and with the duration of treatment. Tuberculoid and long-term-treated lepromatous lymph nodes had a similar distribution of antigen in clusters of cells giving a "speckled" appearance. The untreated lepromatous had a "diffuse" staining of antigen in foamy histiocytes; whereas lepromatous lesions with a lower bacillary load had a mixed pattern of "diffuse" and "speckled." Antigen was also detected in a number of plasma cells along the spectrum but predominantly in lepromatous lymph nodes. Our observations indicate that: a) antigen exists in lymph nodes despite prolonged chemotherapy which may be responsible for the persistent granuloma and b) antigen is not confined to any particular anatomical compartment of the lymph node.—Authors' Summary

Behra, R. N., Sen, P. C., Sharma, B. N. and Rajendran, P. Cell-mediated immunity in tuberculoid leprosy—a study of T lymphocyte population by "E" rosette technique. Indian J. Public Health **30** (1986) 85–90.

The T-lymphocyte population was estimated in 22 cases of tuberculoid leprosy patients and 20 healthy individuals. Significant reduction in the percentage of rosette-forming T lymphocytes was observed in tuberculoid leprosy patients as compared to corresponding controls and the difference between them was statistically significant. The values of T-cell percentage were found to be independent of duration of disease and treatment. Among the absolute T-cell count and absolute lymphocyte count only the former was found to be significantly reduced. The difference in T-cell percentage of treated and untreated cases was statistically insignificant.—Authors' Summary

Bonfa, E., Llovet, R., Scheinberg, M., De Souza, J. M. and Elkon, K. B. Comparison between autoantibodies in malaria and leprosy with lupus. Clin. Exp. Immunol. **70** (1987) 529–537.

Sera from 16 patients with falciparum malaria, 16 patients with vivax malaria and 31 patients with leprosy were tested for autoantibodies to intracellular proteins and nucleic acids. Precipitating antibodies to soluble protein extracts were not detected in any serum. Sera from malaria patients showed prominent immunofluorescence staining of the HEP2 nuclear membrane as well as frequent 75% (24/32) and intense Western blot reactivity. In contrast, only 20% and 36% of patients with leprosy had positive immunofluorescence or positive immunoblots respectively, and reactivity was weak in most cases. Neither the malaria nor leprosy sera contained autoantibodies with specificities similar to the characteristic lupus autoantibodies such as double-stranded DNA (dsDNA), Ro/SSA, La/SSB, Sm, RNP and P proteins. Low levels of antibodies to single-stranded (ssDNA) were however found in 11 (34%) malaria sera and in seven (23%) leprosy sera. Thirteen percent of patients with leprosy had anti-histone antibodies. These findings demonstrate considerable differences in the capacity of infectious agents to induce autoantibodies and also the infrequency with which autoantibodies characteristic of idiopathic systemic lupus erythematosus are induced.—Authors' Summary

Campbell, P. B., Tolson, T. A., Yoder, L., Loesch, J. and Krahenbuhl, J. L. Lesional modulation of peripheral monocyte leucotactic responsiveness in leprosy. Clin. Exp. Immunol. **70** (1987) 289–297.

Because the accumulation and activation of mononuclear phagocytes are critical to the host response to intracellular microbial pathogens, we evaluated mechanisms of peripheral monocyte leukotactic regulation in leprosy. Plasma from 53 of 67 patients was found to inhibit the locomotion of normal human monocytes. Neither the prevalence nor the magnitude of plasma leukotactic inhibitory activity correlated with disease histology or duration, type or duration of chemotherapy, or history of erythema nodosum leprosum. Plasma leukotactic inhibitory activity resided principally in a non-immunoglobulin, cell-directed inhibitor of 230,000 daltons molecular weight. Fractionation of plasma from patients with lep-

romatous leprosy revealed an additional, immunoglobulin-containing inhibitor of approximately 400,000 daltons weight, possibly an IgG-IgA immune complex. Production of leukotactic inhibitors by unstimulated and concanavalin A-stimulated peripheral mononuclear cells was normal; however, cutaneous explants from these patients spontaneously produced the 230,000 dalton leukotactic inhibitor *in vitro*. The ability of the lesions of leprosy to impede monocyte traffic may be an important pathogenetic mechanism.—Authors' Summary

Chaudhury, S., Hazra, S., Chatterjee, B. C., Dey, S. K., Chaudhury, S. N. and Das, P. Immunostimulation with an allied mycobacterium and DDS chemotherapy in lepromatous leprosy. Indian J. Dermatol. **30** (1985) 3–10.

Short-term combined immunostimulation with an allied mycobacterium and chemotherapy in lepromatous cases resulted in better clinical and bacteriological improvement in comparison to that with chemotherapy alone. Lepromin conversion occurred in four cases (33.3%) but typical delayed hypersensitivity granuloma was not formed. Correlation with *in vitro* immunological parameters was observed in 2 of the 4 lepromin-converted cases only.—Authors' Abstract

Dandekar, S. R., Shah, D. H., Naik, S. S. and Ganapathi, R. Serodiagnosis of leprosy with PGL-I using ELISA technique. Indian J. Med. Res. **85** (1987) 597–603.

A total of 208 sera from 55 normal volunteers, 92 patients of leprosy (LL = 41, BL = 11, BB = 18, BT = 20 and TT = 2) and 61 family contacts of these patients with no clinical evidence of disease were evaluated for detection of antibodies to phenolic glycolipid-I (PGL-I), specific for *Mycobacterium leprae*, using solid-phase ELISA technique. The antigen was used in deacylated form and the sera were tested at 1:100 dilution. The horseradish peroxidase conjugated rabbit antihuman gammaglobulin used was prepared by two-step periodate method. The PGL-I reactivity was expressed as a ratio (optical density at 492 nm obtained with PGL-I-coated wells/water-coated wells). PGL-I reactivity ratio in 41 lepromatous leprosy (LL) patients was significantly higher (1.54 ± 0.68 S.D.) as compared to that of healthy controls (0.99 ± 0.11 S.D.). The reactivity of the antibody of PGL-I decreased after treatment. Among the various types of leprosy examined the reactivity to PGL-I was LL > BL > BB > BT > TT.—Authors' Abstract

Douglas, J. T. Progress in the serology of leprosy at the University of Hawaii. Hawaii Med. J. **47** (1988) 62–65.

Serology in leprosy holds the promise of providing quantitative markers to aid in our understanding of interactions between *Mycobacterium leprae* and its hosts. The markers referred to are the antibody classes, or isotypes, of the host and the antigens of *M. leprae*. The key to the application of these markers has been the development of sensitive and specific immunoassays based on accurate clinical and epidemiological information. Since 1980 we have been developing assays and using serology to study markers for early detection of leprosy prior to clinical onset of disease. We have also examined the influence of chemotherapy on antibody levels during treatment. In this article we describe our serological research of leprosy in Hawaii, the Federated States of Micronesia, and The Philippines.—Author's Abstract

Ehrenberg, J. P. and Gebre, N. Analysis of the antigenic profile of *Mycobacterium leprae*: cross-reactive and unique specificities of human and rabbit antibodies. Scand. J. Immunol. **6** (1987) 673–681.

Thirty-two mycobacterial components were detected by antibodies contained in leprosy patients' sera across the clinical spectrum and rabbit anti-*Mycobacterium leprae* hyperimmune sera by Western blot analysis of armadillo-derived *M. leprae* antigen preparations. Sera of borderline tuberculoid patients were found to contain antibodies recognizing 18 *M. leprae* components. While the reactivity of the sera on the lepromatous pole seemed to be distributed over the entire molecular weight range, most of the reactivity in the borderline tuberculoid patients was directed at higher molecular weight components

(>70,000). Identification of a series of previously unrecognized *M. leprae* components offers new possibilities in regard to the potential use of these antigens as targets for immunodiagnosis. Antibodies contained in the rabbit anti-*M. leprae* sera reacted with 19 *M. leprae* components. Antigens migrating at 64,000, 38,000, and 22,000 were detected by the rabbit sera only. Evidence of extensive crossreactivity between *M. leprae* and BCG organisms emphasizes the need to use well-characterized antibody probes to determine the specificity of select mycobacterial antigens. The potential usefulness of rabbit monospecific hyperimmune sera to select *M. leprae* fractions in immunodiagnosis, in immune regulation studies, or as a tool to screen for mycobacterial products in phage lysates of *Escherichia coli* is discussed. Select *M. leprae* components were partially purified and their recovery assessed through SDS-PAGE analysis of Coomassie blue-stained gels.—Authors' Abstract

Fliess, E. L., Franceschini, G. and Ortiz, M. C. *In vitro* effect of *Mycobacterium leprae* suspensions on the polymorphonuclear neutrophil function of hanseniasis patients to *Candida albicans* and *Candida pseudotropicalis.* Hansenol. Int. **9** (1984) 3–9.

The *in vitro* effect of *Mycobacterium leprae* suspensions on the ability of neutrophils to phagocytose and fill *Candida albicans* and *C. pseudotropicalis* was studied in 45 patients with Hansen's disease (HD) and in 15 healthy controls. Our results show no significant differences between the different studied groups, both for the phagocytosis and for the lysis of yeasts. There were no significant changes in the mean values of these functions after previous or simultaneous incubation with *M. leprae* suspensions. Those observations confirmed that there are no alterations in the enzymatic battery of neutrophils in HD patients and that the *M. leprae* presence does not exert a stimulating effect on this *in vitro* model.—Authors' Abstract

Frehel, C. and Rastogi, N. *Mycobacterium leprae* surface components intervene in the early phagosome-lysosome fusion inhibition event. Infect. Immun. **55** (1987) 2916–2921.

Bone-marrow-derived culture macrophages were infected with *Mycobacterium leprae.* The bacteria were either used as freshly isolated organisms or incubated with *M. leprae* antiserum (1:5) for 30 min prior to phagocytosis. Immediately after inoculation (1 to 4 hr) and at 1 to 8 days later, macrophages were stained for acid phosphatase activity to assess fusions between phagosomes and lysosomes. Inhibition of fusions was essentially apparent as an early event, which was partially reversed by antiserum treatment of the bacteria, suggesting a role for *M. leprae* immunogenic surface components in this early phenomenon. Later incubation times (1 to 8 days) did not show any considerable difference between antiserum-treated and nontreated bacteria. The formation of an electron-transparent zone around phagocytized bacteria and its role in phagosome-lysosome fusion was investigated, and a direct relationship could not be established.—Authors' Abstract

Gaylord, H. and Brennan, P. J. Leprosy and the leprosy bacillus: recent developments in characterization of antigens and immunology of the disease. Ann. Rev. Microbiol. **41** (1987) 645–675.

Current understanding of the basic immunology of leprosy, and particularly of the immunologic nonresponsiveness exhibited at the lepromatous end of the disease spectrum, has not yet reached a satisfactory level. While it is clear that specifically immune T lymphocytes are required to successfully amplify the bacteriocidal activity of mononuclear phagocytes, there is a spectrum of possible explanations for why T cells fail to do this in some cases. A complete lack of T-cell clones reactive toward *Mycobacterium leprae* represents one possibility, but this would require further explanation. Alternatively, *M. leprae*-reactive clones may be expanded normally, but may be functionally inhibited from operating, i.e., suppressed. That some form of suppression exists seems indisputable: If other mycobacteria such as BCG share T-cell epitopes with *M. leprae,* as is undoubtedly the case, and if the lepromatous patient responds well to BCG, then either a) the patient's positive

response to BCG is based on a different set of determinants or b) the response to these determinants is actively suppressed when the patient is challenged with *M. leprae*. While a) has not been rigorously excluded, it seems unlikely. Accepting b), is suppression mediated by T cells? In the absence of an experimental system allowing adoptive cell transfer, it could be argued that identification of a T-cell clone with suppressive activity is only part of the normal regulatory network and is not pathological.

The above remarks should not obscure the fact that a search for T-cell-based regulatory schemes will in fact continue, based on T-cell lines and clones and making use of the recombinant protein products of *M. leprae*. The thrust will be to determine which specific or crossreactive determinants lead most often to effective T-cell immunity, and which determinants induce suppressive effects. This would refine both immunization and therapeutic schemes based on BCG crossreactivity and would help in the development of anti-idiotypic probes to assess the presence of antigen-specific clones in lesions.

Experimentation with patient cells *in vitro* is marked by a distressing amount of variability, some of which reflects a real heterogeneity of individual cases. However, there appears to be a strong component of nonspecific suppression, some of which may be traceable to the lipoarabinomannan. Various forms of lepromin or soluble extracts of *M. leprae* may contain differing amounts of LAM, and this may contribute to variable responses *in vitro*. Given the number of complex and lipophilic products in mycobacteria, some of which can intercalate into membrane bilayers, much of the immunologic disturbance in leprosy may be pharmacologic. Cloned T-cell systems may allow an improved understanding of these nonspecific as well as specific effects, and use of recombinant DNA systems may be the only way to eliminate some of these products while leaving protein relatively intact.—(*From* the article)

Kale, V., Mandock, O., Ibegbu, C. and Navalkar, R. G. Studies on the antigenic specificity of *Mycobacterium leprae*. III. Further studies on immunological characterization. Zentrabl. Bakteriol. Mikrobiol. Hyg. [A] **265** (1987) 20–32.

The ability of the various protein antigens of *Mycobacterium leprae* to induce as well as detect delayed type hypersensitivity has been confirmed by studies in mice. Additionally, one of the fractions obtained from untreated *M. leprae* has been shown to possess specificity to the organism through immuno-analysis, thus confirming previous observations on skin reactivity in guinea pigs. SDS-PAG electrophoresis has shown that this fraction contains a single antigen. A suggestion has been made that this single protein could be a target antigen for early diagnosis of leprosy, specifically in contacts of leprosy patients. It could also assist in detecting a latent infection. Additional studies, using different parameters, should lead to further confirmation of its specificity. It has also been suggested that such *M. leprae*-specific protein antigens could play an important role in the immune response of leprosy patients. They could also have a significant impact as possible immuno-protective agents, either by themselves or in combination with other immuno-potentiating agents.—Authors' Abstract

Kaplan, G., Nusrat, A., Sarno, E. N., Job, C. K., McElrath, J., Porto, J. A., Nathan, C. F. and Cohn, Z. A. Cellular responses to the intradermal injection of recombinant human γ-interferon in lepromatous leprosy patients. Am. J. Pathol. **128** (1987) 345–353.

The local response to a single intradermal injection of 10 μg recombinant γ-interferon (rIFNγ) has been studied in 17 patients with lepromatous leprosy. Of these, two patients additionally received two intradermal injections of 10 μg rIFNγ at another site. The results were compared with those of three patients who received three injections of the same dose at a single site in an earlier study. One to 7 days after lymphokine administration 4-mm punch biopsies were obtained and examined for cellular alterations in the dermis and epidermis. This allowed a kinetic analysis of mononuclear cell infiltration, keratinocyte proliferation and differentiation, and Langerhans' cell redistribution. At 24 hr, the migration of large

numbers of helper T cells and monocytes was already prominent and associated with induration. Mononuclear cell accumulation peaked at 72 hr but then persisted for 5–7 days. Only small numbers (one-third or less of total T cells) of suppressor/cytotoxic T cells were present at any time, and granulocytes were absent. Two daily injections of rIFNγ led to a more intense accumulation of cells. Ten μg of rIFNγ resulted in enhanced keratinocyte proliferation, Ia expression, and thickening of the epidermis. At 24–48 hr, major histocompatibility Class II (Ia) antigen was first noted on the dividing cells of the basal layer. By 72–96 hr, the entire epidermis exhibited strong expression of Ia antigen on cell surfaces. Repeated doses of lymphokine accentuated these changes and resulted in a more prompt keratinization and sloughing of this layer. Whereas a single dose of rIFNγ resulted in the upward movement of T6+ Langerhans' cells (LCs) in the epidermis, two injections led to a 50% reduction in their numbers and three doses were associated with an almost total loss of detectable T6+ LCs from the epidermis. These are probably sloughed along with keratinocytes. In contrast to the situation with a delayed immune response in the skin (purified protein derivative), no LCs accumulated in the dermis in association with helper T cells.—Authors' Abstract

Kardjito, T., Beck, J. S., Grange, J. M. and Stanford, J. L. A comparison of the responsiveness to four new tuberculins among Indonesian patients with pulmonary tuberculosis and healthy subjects. Eur. J. Respir. Dis. **69** (1986) 142–145.

Multiple skin testing with reagents (new tuberculins) prepared from different mycobacterial species places individuals in three categories: those reacting to all reagents (Category 1), those reacting to none (Category 2), and those reacting to some but not all (Category 3). This pattern of reactivity led to the postulate that Category 3 individuals respond only to those antigens that are unique to each individual species, while Category 1 individuals respond to antigens common to all mycobacteria, although a few of the latter may be responding independently to the specific antigens of all the reagents used. The percentage of patients with tuberculosis responding to all of four new tuberculins was much lower than among healthy subjects—a pattern of reactivity observed previously in leprosy. These findings strongly suggest that patients with mycobacterial diseases fail to respond to shared mycobacterial antigens.—(AS, Trop. Dis. Bull.)

Kaufmann, S. H. E. Towards new leprosy and tuberculosis vaccines. Microbiol. Sci. **4** (1987) 324–328.

Leprosy and tuberculosis are chronic infectious diseases causing major global health problems, for which no effective control by vaccination has been achieved. Recent advances in biotechnology may facilitate the design of a new vaccine generation. In this paper the need for, and the potential of, leprosy and tuberculosis vaccines are discussed.—Author's Abstract

Lamb, J. R., Ivanyi, J., Rees, A. D. M., Rothbard, J. B., Howland, K., Young, R. A. and Young, D. B. Mapping T cell epitopes using recombinant antigens and synthetic peptides. EMBO J. **6** (1987) 1245–1249.

Two complementary approaches were used to determine the epitope specificity of clonal and polyclonal human T lymphocytes reactive with the 65 kD antigen of *Mycobacterium leprae*. A recombinant DNA sublibrary constructed from portions of the 65 kD gene was used to map T-cell determinants within amino-acid sequence 101–146 and 409–526. Independently, potential T-cell epitopes within the protein were predicted based on an empirical analysis of specific patterns in the amino-acid sequence. Of six peptides that were predicted and subsequently synthesized, two (112–132 and 437–459) were shown to contain human T-cell epitopes. This corroborated and refined the results obtained using the recombinant DNA sublibrary. Both of these regions are identical in *M. leprae* and *M. tuberculosis* and are distinct from the known B-cell epitopes of the 65 kD protein. This combination of recombinant DNA technology and peptide chemistry may prove

valuable in analysis of the cellular immune response to infectious agents.—Authors' Abstract

Launois, P., Shankar, P., Wallach, D., Flageul, B., Cottenot, F. and Bach, M.-A. *Mycobacterium leprae*-reactive T-cell clones isolated from polar lepromatous and tuberculoid leprosy patients. Ann. Inst. Pasteur Immunol. **138** (1987) 723–735.

T-cell clones capable of mounting a proliferative response to *Mycobacterium leprae* were obtained in 3 leprosy patients (2 polar lepromatous and 1 polar tuberculoid) either from *M. leprae*-activated or from protein-purified derivative-activated polyclonal T lymphoblasts. All these clones expressed the CD4 surface marker. Some of them proliferated to the antigen only in the presence of interleukin-2. A majority expressed crossreactive responses to other mycobacteria. Clones obtained from the lepromatous patients did not differ in any of these features from those obtained from the tuberculoid patient. *M. leprae*-reactive clones obtained from one lepromatous patient displayed strong antigen-specific cytotoxicity toward autologous antigen-coated target cells. This phenomenon was not observed for any clone of the other lepromatous patient and was seen only for one clone in the tuberculoid patient.—Authors' Summary

Levis, W. R., Meeker, H. C., Schuller-Levis, G., Sersen, E., Brennan, P. J. and Fried, P. Mycobacterial carbohydrate antigens for serological testing of patients with leprosy. J. Infect. Dis. **156** (1987) 763–769.

To determine whether quantitation of antibodies to mycobacterial carbohydrate determinants would be valuable in serodiagnosis and monitoring of leprosy, we tested serum IgM antibody to *Mycobacterium leprae* phenolic glycolipid-I and IgM and IgG antibodies to *M. tuberculosis* and *M. leprae* lipoarabinomannan (LAM) by enzyme-linked immunosorbent assay. Seventy-one percent of patients with paucibacillary disease and 85.5% of patients with multibacillary disease were positive for at least one of the three antibodies. The 15% of antibody-negative patients with multibacillary disease were mostly long-term treated patients, with inactive disease by biopsy. There was excellent agreement between *M. tuberculosis* LAM and *M. leprae* LAM in detection of antibodies. Bacillary index and levels of both IgG and IgM antibodies to LAM were positively correlated when all patients were analyzed. When patients with a history of erythema nodosum leprosum (ENL) were analyzed separately, there was no correlation between IgM or IgG antibody to LAM and bacillary index, a result suggesting a possible role for LAM in the pathogenesis of ENL.—Authors' Abstract

Mandock, O., Ibegbu, C., Kale, V. and Navalkar, R. G. Studies on the antigenic specificity of *Mycobacterium leprae*. II. Immunological characterization. Zentrabl. Bakteriol. Mikrobiol. Hyg. [A] **265** (1987) 12–19.

Antigens from untreated and autoclaved *Mycobacterium leprae* obtained through chromatofocusing were tested for their ability to both induce as well as elicit skin reactivity in guinea pigs sensitized either with homologous and heterologous mycobacteria or with the fractions derived from autoclaved *M. leprae*. In former studies, of the several antigen-positive fractions, one showed specific activity and the remaining others cross-reactivity, as indicated by studies of hypersensitivity. The fraction exhibiting specificity contained only one antigen; whereas the other fractions contained more than one antigen. Because of the technique employed, all the fractions contained antigens that were proteinic in nature. In the latter studies, the antigens obtained from autoclaved *M. leprae* were shown to possess sensitizing capabilities, in addition to induction properties. Two fractions from untreated *M. leprae* had antigens that were heat-labile; whereas the remaining fractions contained heat-stable antigens.—Authors' Abstract

Marolia, J. and Mahadevan, P. R. Superoxide production from macrophages of leprosy patients after stimulation with *Mycobacterium leprae*. J. Biosci. **12** (1987) 273–279.

The macrophages from peripheral blood of normal healthy individuals respond to live or killed *Mycobacterium leprae* by pro-

ducing superoxide. On the other hand, the macrophages from bacteriologically positive (B+LL) or long-term-treated bacteriologically negative (B−LL) and tuberculoid leprosy patients are unable to produce superoxide when stimulated with live *M. leprae*. While killed *M. leprae* induce superoxide with the cells from tuberculoid and B(−)LL patients, cells from B(+)LL patients fail to respond. The deficiency in B(−)LL patients to produce superoxide appears to be specific with *M. leprae* and the defect can be counteracted by the addition of colchicine. These observations indicate a preexisting membrane disposition which does not favor superoxide production. A similar situation is seen in the cells from tuberculoid leprosy patients. Thus it appears that both cured and active lepromatous leprosy patients have defective macrophages, unable to respond to live *M. leprae* to produce superoxide anion, in contrast to the situation with the cells from normal healthy individuals.—Authors' Abstract

Mukherjee, A. and Meyers, W. M. Endothelial cell bacillation in lepromatous leprosy: a case report. Lepr. Rev. **58** (1987) 419–424.

We report observations on a biopsy specimen of skin from a lepromatous leprosy patient with heavy bacillation of vascular endothelial cells. The staining properties of the bacilli in the endothelial cells when compared to those in the surrounding macrophages suggest that endothelial cells may be preferential sites for growth of *Mycobacterium leprae*.—Authors' Summary

Munno, I., Pellegrino, N. M., Fumo, G., Barbieri, G., Polimeno, G., de Filippis, V. and Jirillo, E. Effects of a synthetic extract (thymopentin) on the immune system of lepromatous leprosy patients. Cytobios **52** (1987) 167–173.

Twenty-three patients with lepromatous leprosy (LL) not in reactional phase and bacteriologically negative were evaluated for their immune status (T-cell frequency and interferon γ production). In six patients with deficits of both immune parameters, a synthetic thymic extract (TP-5) was administered. At the end of the treatment, a full recovery of immune dysfunction was observed. In light of these results, the efficacy of TP-5 as an immunomodulating agent in LL patients is discussed.—Authors' Abstract

Munro, C. S., Campbell, D. A., Collings, L. A. and Poulter, L. W. Monoclonal antibodies distinguish macrophages and epithelioid cells in sarcoidosis and leprosy. Clin. Exp. Immunol. **68** (1987) 282–287.

Existing antimacrophage monoclonal antibodies are unable to differentiate between macrophages and epithelioid cells. In search of more precise reagents, [the authors] have applied recently developed antibodies to lesions of sarcoidosis and leprosy. UCHM1 and Leu-M3 stained both granulomas and surrounding histiocytes. However, in lesions with epithelioid granulomas there was a clear distinction between cells identified by RFD9 (epithelioid and giant cells) and RFD7 (macrophages in the surrounding mantle and normal tissue); whereas macrophages in the non-hypersensitivity granulomas of lepromatous leprosy were labeled by both the latter antibodies. In lung biopsies, alveolar macrophages were also labeled by both RFD7 and RFD9. These reagents may be useful for studying pathogenic mechanisms in granuloma formation.—(AS, Trop. Dis. Bull.)

Noordeen, S. K. BCG vaccination in leprosy. Develop. Biol. Standard. **58** (1986) 287–292.

The results from the four major trials on BCG indicate that the rate of protection varied widely in the four situations. The possible explanations are:

i) Differing epidemiological situations providing different degrees of exposure to *Mycobacterium leprae* including the possibility of "reinfection" or "super infection" being different in different areas.

ii) Differing strains of *M. leprae*.

iii) Differing prevalence of environmental mycobacteria and *M. tuberculosis*.

iv) Differing immuno-genetic character of the population.

v) Other differing environmental factors.

Even though the trials have failed to provide a consistent answer on the efficacy of BCG in preventing leprosy, the field studies by themselves have enabled the identifica-

tion of the various problems involved in the undertaking of vaccine trials in leprosy, and this is particularly relevant for the killed *M. leprae* vaccine which is under development in the Immunology of Leprosy (IMMLEP) component of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.—(*From* the article)

Pinto, M. R. M., Eriyagama, N. B. and Pemajayantha, V. Immunological effects of lepromin testing in Sri Lankan population groups. II. Effect of reactivity to a soluble protein antigen of *Mycobacterium leprae.* Lepr. Rev. **58** (1987) 227–232.

Reactivity to the soluble protein antigen (SPA) of *Mycobacterium leprae* is altered in a small but measurable way following the lepromin test when the retest with SPA is done 1 month after the lepromin test. The alteration resembles that shown by Fernandez reactivity in Sri Lanka after repeated lepromin testing, with nonreactors showing increases and reactors showing decreases of reaction size. The change observed is seen in greater numbers in the reactors. Sex and BCG vaccination status does not seem to effect the result of the post-lepromin SPA test. Of the three reactivities to antigens of *M. leprae* (SPA, Fernandez and Mitsuda), the factor that seems to influence the behavior of post-lepromin SPA reactivity most is the reactivity status (reactor/nonreactor) of the SPA pre-lepromin test.—Authors' Summary

Pinto, M. R. M., Eriyagama, N. B. and Pemajayantha, V. Studies of reactivity of some Sri Lankan population groups to antigens of *Mycobacterium leprae.* II. Reactivity to a soluble protein antigen. Lepr. Rev. **58** (1987) 219–226.

This paper reports a survey of reactivity to a soluble protein antigen (SPA) of *Mycobacterium leprae,* in two adult population groups in Sri Lanka, from two localities with widely differing geographical characteristics and levels of nonspecific mycobacterial sensitization. The patterns of reactions observed in the populations were bimodal with distinct "reactor" and "nonreactor" components. It was decided that the reactor and nonreactor ("positive" and "negative" respectively) could be best demarcated in both areas at a reaction size of 5 mm. The mode of reactors with SPA was at 11–12 mm.

Reactivity to SPA was found to show no statistically significant changes with age, sex, race or BCG vaccination status, while there was a possibility of differences with geographical locality. The patterns of reactivity shown by SPA and the Fernandez reaction were different in both areas. A likely reason for this difference was thought to be the possibility that the antigens available for eliciting the reactions in both were probably different—lepromin being whole *M. leprae,* and SPA, disrupted *M. leprae.*—Authors' Summary

Pinto, M. R. M., Eriyagama, N. B. and Pemajayantha, V. Studies of reactivity of some Sri Lankan population groups to antigens of *Mycobacterium leprae.* III. The post-lepromin test scar in healthy populations in Sri Lanka. Lepr. Rev. **58** (1987) 377–382.

The occurrence of the post-lepromin scar was investigated in two general population groups, in two geographically different areas, in whom reactivity to lepromin A and SPA of *M. leprae* were also studied earlier. The incidence of the scar was more or less similar to that reported in a patient group in Burma. The incidence of scar was not related to age, sex, race or geographic area (even though examination for the scar was carried out in 3 months at one area and 7 months at the other). The occurrence of the scar increased with BCG vaccination, and was directly related to Mitsuda, Fernandez and SPA reactivity—being most correlated to Mitsuda reactivity and least to SPA reactivity.—Authors' Summary

Praputpittaya, K. and Ivanyi, J. Study of idiotypes expressed by monoclonal antibodies to the 35 kD and 12 kD antigens of *Mycobacterium leprae.* Clin. Exp. Immunol. **70** (1987) 298–306.

Rabbit antisera were raised against four monoclonal antibodies (MoAb) binding with the 35 kD protein and four MoAb binding with the 12 kD protein antigen of *Myco-*

bacterium leprae. Antisera showed idiotype (Id) specificity following cross-absorption with normal mouse globulin. One Id on a single MoAb and another Id shared between three MoAb were identified for each group. Functional studies were carried out with the Rb04 anti [anti-35 kD] specificity. The expression of this Id and paratope in antigen-immunized mice was associated with Igh alleles. Inoculation of mice with anti-Id Rb04 induced an "Ab3" serum response of corresponding Id specificity only when the anti-Id was given in emulsion with incomplete Freund's adjuvant (IFA). Conversely, prior injection of soluble anti-Id inhibited the subsequent Ab3 response to Rb04/IFA. Moreover, the suppressive effect of soluble anti-Id was abrogated by prior injection of 50 mg/kg cyclophosphamide. These results indicate that regulatory mechanisms similar to those involved in antigenic stimulation may explain the stimulatory or suppressive potency of anti-Id antibodies. Finally, the Ab3 responses to the two tested anti-Ids did not contain any antigen-binding activity.—Authors' Summary

Rada, E., Trujillo, D., Castellanos, P. L. and Convit, J. Gamma interferon production induced by antigens in patients with leprosy and American cutaneous leishmaniasis. Am. J. Trop. Med. Hyg. **37** (1987) 520–524.

In this study, we measured gamma interferon production in mononuclear cell cultures from patients with diverse forms of leprosy and American cutaneous leishmaniasis. We studied patients with lepromatous, borderline lepromatous, borderline, and borderline tuberculoid forms of leprosy, as well as a Mitsuda-negative contact. In leishmaniasis we studied patients with localized cutaneous, mucocutaneous, and diffuse cutaneous forms of the disease. High correlation was observed between gamma interferon production and lymphocyte proliferation assays in both diseases. Resistant forms of both diseases showed significant reactivity, while the severe progressive forms were characterized by insignificant responses in both assays. Localized cutaneous leishmaniasis is characterized by variability in gamma interferon production, which may be of prognostic value in longitudinal studies.—Authors' Abstract

Rojas-Espinosa, O. [Cellular anergy in lepromatous leprosy.] Dermatol. Rev. Mex. **30** (1986) 46–59. (in Spanish)

An attempt is made to integrate a model on the cell interactions that lead to the development of a cell-mediated immune response and those points where alterations (excess or deficiency) have been found in lepromatous leprosy are pin-pointed. Such alterations, individually or collectively, can explain the unresponsiveness of lepromatous patients to antigens from *Mycobacterium leprae*. Among the observed alterations we may count: the absence of *M. leprae*-reactive T lymphocytes, the absence of interleukin-2 producing T lymphocytes, the absence of T lymphocytes bearing the receptor for IL-2, the excess of suppressor T lymphocytes, the presence of suppressor macrophages, the suppressive activity exerted by *M. leprae* itself, etc. The possibility of suppression by anti-idiotypic factors and antibodies is also discussed, and a model is presented to explain the anergy to *M. leprae* while responsiveness toward other mycobacteria (BCG and *M. tuberculosis*) is preserved.—Author's English Summary

Samuel, N. M., Grange, J. M., Samuel, S., Lucas, S., Owilli, O. M., Adalla, S., Leigh, I. M. and Navarrette, C. A study of the effects of intradermal administration of recombinant gamma interferon in lepromatous leprosy patients. Lepr. Rev. **58** (1987) 389–400.

Twenty-six leprosy patients (23 lepromatous, 2 borderline tuberculoid and 1 with indeterminate disease) were treated with recombinant gamma interferon (rIFN-γ) intralesionally. Patients were divided into three groups: Group A received 10 μg dose of rIFN-γ for 3 consecutive days; Group B, 20 μg for 3 days and Group C, 20 μg for 5 days. Twenty-three pairs of skin biopsies and 25 pairs of radial cutaneous nerves were obtained prior to, and 2 days following, the last injections of rIFN-γ. Leprosin A skin tests were negative before and after rIFN-γ. Injections of rIFN-γ induced indurated swelling characteristic of delayed type hy-

persensitivity in all patients. Histologically, rIFN-γ caused localized edema, influx of mononuclear cells and eosinophils; epithelioid cell transformation and rapid reduction in the numbers of acid-fast bacilli in the majority of the patients. Immunocytochemical analysis revealed an increase in pan T cells, with equal numbers of T8 and T4 phenotypes, and increased expression of HLA-class II antigens of macrophages, epithelial cells and keratinocytes. These immunological changes indicate a shift in the immune spectrum of lepromatous leprosy. These results suggest that rIFN-γ may be used in lepromatous leprosy as an adjunct to chemotherapy.—Authors' Summary

Samuel, N. M., Jessen, K. R., Grange, J. M. and Mirsky, R. Gamma interferon, but not *Mycobacterium leprae,* induces major histocompatibility class II antigens on cultured rat Schwann cells. J. Neurocytol. **16** (1987) 281–287.

In order to investigate the possible role of Schwann cells in immune reactions, and in particular their involvement in the response to infection with *Mycobacterium leprae,* it was determined under what conditions Schwann cells express major histocompatibility complex class II (MHC class II) antigens, since these molecules are thought to have a key role in antigen presentation during cellular immune responses.

In situ and *in vitro* preparations from newborn and adult rat sciatic nerves were used as a model system to examine this question. Schwann cells in dissociated cell cultures did not express immunohistochemically detectable amounts of MHC class II antigens. Teased nerve preparations from the sciatic nerves of healthy adult rats showed no detectable immunolabeling of either myelin-forming or non-myelin-forming Schwann cells.

When dissociated Schwann cell cultures derived from the sciatic nerves of either neonatal or adult rats were treated with 10, 50 or 100 units of gamma interferon, MHC class II antigens were detectable on the surface of some Schwann cells 48 hr after addition of the interferon. By 72 hr, 32.29 ± 3.9% of Schwann cells in the cultures from neonatal rats and 53.32 ± 5.4% of Schwann cells in cultures from adult rats, identified by the presence of intracellular S-100, were clearly MHC class II-positive, especially at doses of 50 and 100 units per ml of gamma interferon. Some, but not all, of the fibroblastic cells were very weakly MHC class II-positive. Infection of the cultures with *M. leprae* did not induce MHC class II antigen expression in either Schwann cells or fibroblasts.

These results suggest that one of the functional roles of Schwann cells is the presentation of foreign antigens to T lymphocytes during nerve infection, leading to activation or augmentation of the cellular immune response. With respect to *M. leprae* in particular, it is therefore possible that infected Schwann cells might be capable of participating in the normal immune response to *M. leprae.*—Authors' Summary

Scollard, D. M. A review of immunopathologic studies of human leprosy lesions *in situ.* Hawaii Med. J. **47** (1988) 54–58.

The spectral concept of immune responses in leprosy was originally based primarily on clinical and histologic observations. Subsequent studies of immunologic function have primarily used peripheral blood lymphocytes *in vitro* to demonstrate and examine the specific unresponsiveness of lepromatous cells to *Mycobacterium leprae.*

The composition of cells in leprosy lesions, however, is very different from that in the peripheral blood, and detailed studies of human skin lesions *in situ* are now possible using immunohistochemical techniques, injecting lymphokines directly into the lesions, cloning cells from biopsies, and using suction-induced blisters to sample intralesional cells and tissue fluid.

Such studies have shown that T-helper cells outnumber T-suppressor cells in tuberculoid leprosy, and that this is reversed in lepromatous leprosy. Distinctive microanatomic distributions of some cell types have also been correlated with clinical immune status. Production of gamma-interferon (γINF) upon stimulation with *M. leprae* is reduced in lepromatous disease; the associated failure of macrophage activation can be reversed *in vivo* with recombinant γINF. Soluble IL-2R is present in compa-

rable quantities in all types of uncomplicated lesions, suggesting a state of immunologic equilibrium across the spectrum, but reversal reaction lesions contain higher levels of sIL-2R and greater numbers of activated cells.

Together, this array of new techniques for the study of the immunopathology of leprosy *in situ* are dramatically changing the pace and the direction of research in this disease.—Author's Summary

Shannon, E. J., Chehl, S., Job, C. K. and Hastings, R. C. Adoptively transferred reactivity to *M. leprae* in nude mice infected with *M. leprae.* Clin. Exp. Immunol. **70** (1987) 143–151.

Reversal reactions are manifestations of delayed hypersensitivity to *Mycobacterium leprae* and are thought to be usually accompanied by manifestations of effective cell-mediated immunity (CMI) as measured by bacterial clearing. These experiments were designed to study the induction of reversal reactions in *M. leprae*-infected, congenitally athymic nude mice using adoptive transfer of CMI. Splenic cell suspensions derived from unimmunized heterozygous nu/+ mice, and those vaccinated with heat-killed *M. leprae,* viable BCG and a mixture of the two antigens were diluted to contain 10^4, 10^5, 10^6, 10^7 lymphocytes/0.1 ml and infused intravenously into multibacillary nude mice. The production of reversal reactions in leprous nude mice in response to adoptively transferred CMI was studied in a quantitative fashion. Dose-responsive induction of reversal reactions, apparent by foot pad inflammation and swelling, decreased morphological indices (MI) of the bacteria and mononuclear cell infiltrations, histopathologically, were observed. For nude mice receiving cells primed with 3.9×10^5 living BCG alone, the effective dose 50% (ED_{50}) was 1.0×10^6 lymphocytes to induce reversal reactions. For those receiving cells primed with 10^7 *M. leprae,* the ED_{50} was 3.7×10^5 lymphocytes. For nude mice receiving cells primed with a mixture consisting of half the above dose of BCG plus half the above dose of *M. leprae,* the ED_{50} was 6.8×10^4 lymphocytes.—Authors' Summary

Urteaga-Ballon, O. [Phagocytic syndrome in lepromatous leprosy patients and in armadillos infected with Hansen's bacillus.] Dermatol. Rev. Mex. **30** (1986) 36–45. (in Spanish)

A specific histopathologic syndrome characterized by a proliferation of multinucleated giant cells phagocyting globi of *Mycobacterium leprae* in the spleen and lymph nodes of lepromatous patients and armadillos infected with *M. leprae* is herein reported. Simultaneously, another phenomenon of specific erythrophagocytosis was observed inside the sinusoids of liver and spleen of infected animals. A relationship between these findings and the immunopathologic changes in leprosy patients could explain the polymorphism of the disease.—Author's English Summary

Microbiology

Allen, B. W. Excretion of viable tubercle bacilli by *Blatta orientalis* (the oriental cockroach) following ingestion of heat-fixed sputum smears: a laboratory investigation. Trans. R. Soc. Trop. Med. Hyg. **81** (1987) 98–99.

Sputum smears were prepared from untreated patients in Hong Kong with tuberculosis, and heat-fixed over a Bunsen-burner flame. Feces from adult *Blatta orientalis* that had been allowed to feed intermittently on these smears for 4 weeks yielded *Mycobacterium tuberculosis* on culture in suitable liquid or solid media, even after the feces had been stored at room temperature (in the U.K.) in the dark for 8 weeks. The author recommends that unstained smears of material that may contain *M. tuberculosis* (or *M. leprae*) should be stored in closed insect-proof containers, particularly in tropical regions where insect infestation may be high.—(C. A. Brown, Trop. Dis. Bull.)

Chakrabarty, A. N. and Dastidar, S. G. *In vitro* cultivation of an acid-fast nocardioform chemoautotroph from mouse footpad-passaged strain of leprosy bacillus. Indian J. Exp. Biol. **25** (1987) 302–304.

An acid-fast nocardioform bacterium from the mouse foot pad into which a human strain of leprosy bacillus was passaged could be cultivated to purity on inorganic minimal medium supplemented with simple C (e.g., liquid paraffin, tetradecane) and N (e.g., NH_4-salts, urea, asparagine, gelatin) sources. It failed to grow altogether on any complex organic substrates, e.g., casein, tyrosine, xanthine, hypoxanthine, glucose, glycerol, peptone(s), beef and yeast extracts, egg-proteins, serum, blood and medium 199. Paraffin-urea minimal, paraffin-gelatin minimal or gelatin-minimal liquid media selectively allowed luxuriant growth of this organism which could be continuously propagated in series in these, as well as on their agar slants.—Authors' Abstract

Cocito, C., Coene, M. and Delville, J. [Microbiology of leprosy.] Med./Sci. **3** (1987) 461–470. (in French)

This review focuses on three kinds of leprosy-associated microorganisms: *Mycobacterium leprae* or ML (an acid-fast bacterium not multiplying axenically), LDC or leprosy-derived corynebacteria isolated from patients' granulomas and blood, and ADM or armadillo-derived mycobacteria. *M. leprae* has a peptidoglycan with glycine in place of L-alanine, a DNA with 56% G + C and a peculiar mycolic acid pattern. LDC are true corynebacteria (presence of corynomycolic acids and 56% G + C in DNA) with a special DNA restriction pattern (fully A-methylated GATC sequences) and some unusual traits of the cell-wall components. Contrasting with the genetic homogeneity of ML and LDC is the genetic heterogeneity of ADM (62 to 68% G+C, the range of genus *Mycobacterium*): the five ADM subgroups behave as distinct mycobacterial species. Putative implication of LDC in leprosy is based on: a) the repeated isolation of these organisms from leprosy granulomas (but not from normal skin); b) the genetic homogeneity of the group; and c) the facilitation of *M. leprae* growth produced in experimental animals by LDC. An immunological kinship of ML and LDC (crossreactivity between ML antigen A7 and LDC antigen M_1, 2 members of the TMA antigen family) has been observed.—Authors' English Summary

Dastidar, S. G., Das, S. and Chakrabarty, A. N. *In vitro* cultivation of a chemoautotrophic nocardioform bacterium from armadillo tissue infected with leprosy bacillus. Indian J. Exper. Biol. **25** (1987) 427–428.

A nocardioform acid-fast bacillus from armadillo tissues infected with leprosy bacilli could be cultivated, isolated and propagated in pure culture in liquid media such as paraffin urea minimal (PUM), paraffin gelatin minimal (PGM), gelatin minimal (GM) media and GM agar slants, all containing only simple sources of C (e.g., liquid paraffin, tetradecane, etc.) and N (NH_4-salts, urea, asparagine, gelatin, etc.) just like the human and mouse foot pad isolates of this organism reported earlier. It resembled a chemoautotroph. Studies on isolated colonies revealed the presence of a single type of bacterium only.—Authors' Abstract

De Kesel, M., Coene, M., Portaels, F. and Cocito, C. Analysis of deoxyribonucleic acids from armadillo-derived mycobacteria. Int. J. Syst. Bacteriol. **37** (1987) 317–322.

Armadillos are used for propagation of *Mycobacterium leprae* and are hosts of mycobacteria of the armadillo-derived mycobacteria (ADM) group. The deoxyribonucleic acids (DNAs) of isolates of the five phenetic subgroups of the ADM were analyzed and compared with the genomes of related bacteria. The guanine-plus-cytosine (G + C) contents of the DNAs were 62.2 to 67.1 mol% for different ADM strains, 56 mol% for *M. leprae* and leprosy-derived corynebacteria (LDC), and 62 to 71 mol% for reference mycobacteria. Restriction analysis showed neither adenine methylation in the GATC site (a specific trait of LDC strains) nor cytosine methylation in the CCGG and GGCC sites. Hybridization higher than 80% was obtained with DNA from isolates within the same ADM subgroups; whereas 17% to 50% hybridizations were observed with organisms from different ADM subgroups. Genomes of

ADM strains and reference mycobacteria were 15% to 40% homologous, except for subgroups IV and V whose DNAs were 54% to 62% homologous with *M. lepraemurium* DNA. Little or no homology between *M. leprae* and ADM genomes was found. We concluded that single ADM subgroups can be considered as distinct species within the genus *Mycobacterium*; they are genetically unrelated to the other leprosy-associated bacteria.—Authors' Abstract

Franzblau, S. G. and Hastings, R. C. Rapid *in vitro* metabolic screen for antileprosy compounds. Antimicrob. Agents Chemother. **31** (1987) 780–783.

Measurement of intracellular ATP of *Mycobacterium leprae* after direct *in vitro* exposure to antimicrobial agents was evaluated as a rapid means of identifying potentially useful therapeutic agents. Nude mouse-derived *M. leprae* were incubated in an axenic-modified Dubos medium in the presence or absence of antimicrobial agents for up to 3 weeks. ATP was then assayed by using the firefly bioluminescence technique. Rifampin, clofazimine, and ethionamide each effected a significantly accelerated rate of ATP decay compared with controls. Dapsone appeared inactive, possibly reflecting a general insensitivity of this system to compounds acting at certain loci. The system appeared suitable for assessing comparative activity of new structural analogs of clofazimine. Other active compounds included erythromycin, minocycline, chloramphenicol, gramicidin, and, to a lesser extent, cycloserine, cephalothin, ciprofloxacin, tetracycline, and gramicidin S. The penicillins, bacitracin, isoniazid, nalidixic acid, trimethoprim, polymyxin B, and griseofulvin were all inactive. The system appears sensitive to agents with various modes of action and may prove useful as a primary screen for antileprosy drugs.—Authors' Abstract

Fujiwara, T. and Izumi, S. Synthesis of the neoglycoconjugates of phenolic glycolipid-related trisaccharides for the serodiagnosis of leprosy. Agric. Biol. Chem. **51** (1987) 2539–2547.

The trisaccharide segment of the phenolic glycolipid-I of *Mycobacterium leprae* was synthesized effectively in the form of *p*-(2-methoxycarbonylethyl)phenyl glycoside by the condensation of *p*-(2-methoxycarbonyl ethyl)phenyl 4-*O*-benzyl-3-*O*-methyl-α-L-rhamnopyranoside and 2,3-di-*O*-methyl-4-*O*-(2,4-di-*O*-acetyl-3,6-di-*O*-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranosyl chloride in the presence of silver triflate and 1,1,3,3-tetra-*N*-methylurea, and subsequent selective deprotection. This was then coupled to BSA by the acyl azide method, giving NT-P-BSA. The NT-P-BSA showed very high reactivity and specificity to leprosy sera. The trisaccharide-BSA conjugate with a β-linked rhamnosylrhamnose unit (βT-P-BSA) was also synthesized.—Authors' Abstract

Gaylord, H., Brennan, P. J., Young, D. B. and Buchanan, T. M. Most *Mycobacterium leprae* carbohydrate-reactive monoclonal antibodies are directed by lipoarabinomannan. Infect. Immun. **55** (1987) 2860–2863.

Each of more than 30 monoclonal antibodies that had been raised against *Mycobacterium leprae* and previously classified as reactive with carbohydrate was shown to be directed against lipoarabinomannan, a prominent, highly pervasive, *myo*-inositol-phosphate-containing, crossreactive antigen within the leprosy bacillus. Some of the antibodies preferentially bound to the lipopolysaccharide of *M. leprae* rather than to that of *M. tuberculosis*, suggesting the presence of distinguishing structural features. The presence of alkali-labile inositol 1-phosphate in the lipopolysaccharide from *M. tuberculosis* and its apparent absence from the *M. leprae* product may account for the difference.—Authors' Abstract

Hottat, F., Coene, M. and Cocito, C. DNA methylation in leprosy-associated bacteria: *Mycobacterium leprae* and *Corynebacterium tuberculostearicum*. Med. Microbiol. Immunol. **177** (1988) 33–45.

The DNAs of two kinds of microorganisms from human leprosy lesion, *Mycobacterium leprae* and *Corynebacterium tuberculostearicum* (also known as "leprosy-derived corynebacterium" or LDC), have been analyzed and compared with the genomes of reference bacteria of the CMN

group (genera *Corynebacterium, Mycobacterium* and *Nocardia*). The guanine-plus-cytosine content (% GC) of DNA was determined by a double-labeling procedure, which is unaffected by the presence of modified and unusual bases (that alter both buoyant density and mid-melting-point determinations). Accordingly, the DNAs of seven LDC strains had GC values of 54–56 mol%, and that of armadillo-grown *M. leprae* a value of 54.8 ± 0.9 mol%. Restriction patterns disclosed no methylated cytosine in the DNA sequences CCGG, GGCC, AGCT, and GATC of either LDC or *M. leprae* DNA. N^6-methyladenine was present in the sequence GATC of all LDC strains, but was missing from the genomes of all other CMN organisms analyzed, including *M. leprae.* By HPLC analysis of LDC-DNA hydrolysates, it was found that N^6-methyladenine amounted to 1.8% of total DNA adenine, and was present exclusively within GATC sequences, which appeared all to be methylated. It is concluded that LDC represent a group of corynebacteria endowed with high genetic homogeneity and a unique restriction pattern, whereby their genome is easily distinguished from that of *M. leprae,* which has a similar base composition.—Authors' Abstract

McNeil, M., Wallner, S. J., Hunter, S. W. and Brennan, P. J. Demonstration that the galactosyl and arabinosyl residues in the cell-wall arabinogalactan of *Mycobacterium leprae* and *Mycobacterium tuberculosis* are furanoid. Carbohydr. Res. **166** (1987) 299–308.

By a complex process involving methylation, partial hydrolysis with acid, reduction with sodium borodeuteride, ethylation, further hydrolysis and reduction, and subsequent capillary gas-liquid chromatography-mass spectrometry of the derived alditol acetates, it was established that the arabinogalactans of *Mycobacterium leprae* and *M. tuberculosis* contain arabinofuranosyl and galactofuranosyl residues exclusively. Thus, the covalently bound, highly immunogenic arabinogalactan of mycobacteria, and presumably of other actinomycetes, is highly unusual, in that all of the glycosyl residues are in the furanoid form. Furthermore, by establishing that the galactofuranosyl residues are either 5-, 6-, or 5,6-linked, their linkage pattern was established, and the literature is corrected on this point.—Authors' Abstract

Subcommittee on Clinical Trials of the Chemotherapy of Leprosy (THELEP) Scientific Working Group of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. Primary dapsone resistance in Bamako and Chingleput: final report; THELEP. Lepr. Rev. **58** (1987) 209–218.

Approximately 37% of the 131 patients with lepromatous leprosy admitted into the THELEP controlled clinical trials in Bamako and Chingleput, whose *Mycobacterium leprae* obtained from pretreatment biopsy specimens could be tested in mice, have been found to harbor dapsone-resistant organisms, and are thought to represent instances of primary resistance to dapsone. The majority of these patients harbored strains of a low degree of resistance, one-fifth of these patients harbored organisms of an intermediate resistance, and no patient was found to harbor *M. leprae* of a high degree of resistance. No relationships were discerned between patient age, number of *M. leprae,* or disease classification on one hand, and primary resistance to dapsone on the other.—Authors' Summary

Venkatesan, K., Minnikin, D. E., Singh, H., Ramu, G. and Bharadwaj, V. P. Detection of mycobacterial lipids in skin biopsies from leprosy patients. FEMS Microbiol. Lett. **44** (1987) 167–172.

Lipids were extracted from small skin biopsies obtained from five lepromatous leprosy patients by employing a procedure designed to produce separate nonpolar and polar fractions. The defatted tissue was subjected to alkaline hydrolysis and the total fatty acids in the hydrolysate were converted to methyl esters by a phase transfer reaction using iodomethane. The composition of free lipids and methyl esters of fatty acids was analyzed by special thin-layer chromatographic systems. The presence of dimycocerosates of phthiocerol A, phthiocerol B, and phthiodiolone A, phenolic glycolipid-I, two phosphatidyl inositol mannosides and 2 mycolates—alpha- and

keto-mycolate—was demonstrated using reference lipid samples.—Authors' Summary

Wheeler, P. R. Biosynthesis and scavenging of purines by pathogenic mycobacteria including *Mycobacterium leprae*. J. Gen. Microbiol. **133** (1987) 2999–3011.

Purine biosynthesis *de novo* could not be detected in suspensions of *Mycobacterium leprae* isolated from armadillo tissue. In contrast, non-growing suspensions of other pathogenic mycobacteria, also isolated from infected host tissue did synthesize purines. Rates of synthesis, judged by incorporation of [2-^{14}C]glycine or [3-^{14}C]serine into nucleic acid purines were 600 times higher in *M. microti* and 110 times higher in *M. avium*—both isolated from infected mouse tissue—than the lowest possible rate detectable and therefore the highest possible rate in *M. leprae*. The rate of purine synthesis relative to purine scavenging (judged by comparing incorporation of [3-^{14}C]serine and [8-^{14}C]hypoxanthine into nucleic acid purines in suspensions of mycobacteria) varied only slightly—4-fold in *M. microti* and 6-fold in *M. avium*—whether organisms were harvested from media with or without purines, from media with a low nitrogen content but containing a purine, from mice or even with starved organisms. Thus, the failure of *M. leprae* to synthesize purines could not be explained as either a result of using non-growing mycobacteria in the incubations with ^{14}C-labelled precursors or as repression or inhibition of synthesis *de novo*. It appears that *M. leprae* requires a supply of the purine ring from its environment. Nucleotides, which may be the major sources of the purine ring in the intracellular environment, were not taken up directly by *M. leprae* but could be hydrolyzed first to nucleosides and then taken up.—Author's Abstract

Wheeler, P. R. Enzymes for purine synthesis and scavenging in pathogenic mycobacteria and their distribution in *Mycobacterium leprae*. J. Gen. Microbiol. **133** (1987) 3013–3018.

Three enzymes catalyzing the synthesis of four intermediates (phosphoribosylglycinamide, phosphoribosylaminoimidazole-succinocarboxamide, phosphoribosylaminoimidazole-carboxamide and AMP) in the purine biosynthetic pathway were detected in extracts of *Mycobacterium microti* and *M. avium*, even when the organisms had been grown in mice. However only one of the three enzymes, adenylosuccinate AMP-lyase (catalyzing the synthesis of the last two of the four intermediates listed above) was detected in *M. leprae*. Phosphoribosyltransferases, which convert adenine, guanine and hypoxanthine to the corresponding nucleoside monophosphates, and adenosine kinase were the major enzymes for purine scavenging in all mycobacteria studied. In contrast to enzymes in the synthetic pathway, evidence for metabolic regulation of the purine-scavenging enzymes was obtained. In particular, 20 80-fold differences in the activities of guanine phosphoribosyltransferase and adenosine kinase were observed when *M. microti* was grown in media with or without purines, or in mice. In *M. leprae*, activities of all phosphoribosyltransferases were low in comparison with activities in *M. microti* and *M. avium* (specific activity <2% when comparisons were made between extracts of host-grown mycobacteria). However, activity of adenosine kinase was higher in host-grown *M. leprae* than in host-grown *M. microti* or *M. avium*.—Author's Abstract

Experimental Infections

Baskin, G. B., Gormus, B. J., Martin, L. N., Wolf, R. H., Blanchard, J. L., Malaty, R., Walsh, G. P., Meyers, W. M. and Binford, C. H. Experimental leprosy in African green monkeys (*Cercopithecus aethiops*): a model for polyneuritic leprosy. Am. J. Trop. Med. Hyg. **37** (1987) 385–391.

Three African green monkeys (*Cercopithecus aethiops*) were inoculated intravenously and intracutaneously with *Mycobac-*

terium leprae derived from a naturally infected mangabey monkey. All developed cutaneous lesions at inoculation sites. One developed disseminated cutaneous lesions, while the cutaneous lesions in the other two regressed and eventually disappeared. The animals were examined at necropsy 5 years after inoculation. All three had active leprosy infection in peripheral nerves with extensive inflammation and fibrosis. The disease histologically resembled borderline lepromatous leprosy. These findings add a new dimension to animal models of leprosy.—Authors' Abstract

Brett, S. J. Regulatory interactions between macrophages and *Mycobacterium lepraemurium*-specific T-cell activation. Cell. Immunol. **110** (1987) 379–390.

The antigen-specific proliferative response of draining lymph node cells was found to follow a similar pattern in both C57BL and BALB/c mice following subcutaneous infection with *Mycobacterium lepraemurium* (MLM), although the two strains differed in their ability to control bacterial growth at the site of infection. The proliferative response, which was maximal 1–2 weeks postinfection, was T-cell dependent as it was abrogated with anti-Thy 1.2 + C treatment. The response was also abrogated by pretreatment with anti-Lyt 1.2 + C and slightly reduced by treatment with anti-Lyt 2.2 + C. The decline in T-cell responsiveness, at least from 4 to 8 weeks postinfection, may have been associated with prostaglandin production by inflammatory macrophages since it was partially restored by the addition of indomethacin. Also highly purified T lymphocytes from lymph nodes taken 6–8 weeks postinfection gave a strong antigen-specific proliferative response when reconstituted with optimal numbers of syngeneic antigen-presenting cells from uninfected mice. Proliferation was inhibited by peritoneal macrophages from *Corynebacterium parvum*-pretreated mice and macrophages from C57BL but not BALB/c mice infected with *M. lepraemurium* which had been elicited with heat-killed (HK) MLM and thioglycollate. Resident peritoneal macrophages from both C57BL and BALB/c mice infected subcutaneously with *M. lepraemurium* were slightly more inhibitory than normal macrophages but not as inhibitory as macrophages from *C. parvum*-pretreated mice. Macrophage-dependent inhibition of T-cell proliferation was partially reversed by the addition of indomethacin, suggesting that these cells were not defective in processing and presentation of HK-MLM antigens, and that the inhibitory effects were associated with prostaglandin production. Resident peritoneal macrophages from both C57BL and BALB/c mice infected subcutaneously with *M. lepraemurium* produced comparable or slightly elevated levels of IL-1 on stimulation with LPS or HK-MLM.—Author's Abstract

Brown, I. N. and Glynn, A. A. The *Ity/Lsh/Bcg* gene significantly affects mouse resistance to *Mycobacterium lepraemurium*. Immunology **62** (1987) 587–591.

Mouse resistance to infection with *Mycobacterium lepraemurium* was measured by counting the total number of intact acid-fast bacilli in the spleen 8 weeks after i.v. injection of a standard inoculation. The effect of Ity^r on resistance to *M. lepraemurium* was confirmed and the results extended to two Ity^r strains of mice, A and C57L, not previously tested. Resistance to *M. lepraemurium* was also examined in the F_1, backcross and F_2 generations of BALB/c × CBA crosses, and in the congenic strain B10.LLsh^r that is Ity^r. In all experiments the results were consistent with the view that resistance to *M. lepraemurium* is significantly affected by a gene close to or identical to the *Ity/Lsh/Bcg* gene on mouse chromosome 1. Sex had a marked effect on resistance to *M. lepraemurium*, so that the males of some genetically resistant strains were almost as susceptible as some genetically susceptible females.—Authors' Summary

Gelber, R. H. The killing of *Mycobacterium leprae* in mice by various dietary concentrations of clofazimine and ethionamide. Lepr. Rev. **58** (1987) 407–411.

The bactericidal activity of *Mycobacterium leprae* in mice of a range of dietary concentrations of clofazimine and ethionamide was studied by the proportional bac-

tericidal technique. The two highest concentrations of clofazimine studied, 0.01% and 0.003% were respectively 99.6 ± 0.2% and 98 ± 1.0% bactericidal. Although less killing was afforded by 0.001% and 0.0001% clofazimine, even the latter concentration retained significant bactericidal activity (84 ± 10% bactericidal). The minimal bactericidal dietary concentration of ethionamide was found to be approximately 0.02% (68 ± 13% bactericidal). Higher concentrations of ethionamide, 0.05% and greater, were consistently more active, at least 95 ± 3% bactericidal. It is noteworthy in these studies that significant bactericidal activity of both clofazimine and ethionamide was retained at lower dietary concentrations than had been demonstrated previously.—Author's Summary

Suárez Moreno, O., Gonzáles Segredo, A. B. and Castells, E. G. [Assay of foot pad technique for the multiplication of *Mycobacterium leprae* in different mouse lines existing in Cuba.] Rev. Cubana Med. Trop. **38** (1986) 297–299. (in Spanish)

Four lines of isogenic mice (IOR, CBA/CA, C17 and Swiss) and one of non-isogenic albino-Swiss mice were studied in order to know if any of those lines was definitively superior than the other ones, with regard to the multiplication of *Mycobacterium leprae* in foot-pad tissues. From results observed, it is concluded that albino Swiss mouse line is found among those yielding higher harvests, therefore, this line is useful to be used in this technique.—Authors' English Summary

Wang, H. [A comparison of skin scraping and skin biopsy in mouse foot pad experiments with *Mycobacterium leprae*.] Chin. J. Clin. Dermatol. **16** (1987) 180–181. (in Chinese)

The skin scraping and skin biopsy were compared in mouse foot pad experiments with *Mycobacterium leprae*. In 91 multibacillary leprosy patients, the specimens were taken by skin scraping in 46 patients, and by skin biopsy in 45 patients. The results showed that the rates of growth of *M. leprae* on foot pad were 82.6% and 86.7%, respectively. The *M. leprae* from skin scrapings multiplied significantly in the mouse foot pad. We found that this technique is simpler than that of biopsy, and is particularly suited to field conditions. The author suggests skin scraping be used in mouse foot pad experiment.—Author's English Abstract

Epidemiology and Prevention

Ashmalla, L. Impact of leprosy on family and intimate relationships. Int. J. Dermatol. **26** (1987) 305–307.

Ninety-eight families with leprosy patients as members were examined. Of these, only two families were identified where both husband and wife had the disease. The father was the known patient in 46 cases and the mother in 12 families. There were seven cases where the father and one son had the disease, while in one case it was the mother and son; 25 families presented a son or daughter with the disease, while their parents were apparently healthy. Siblings and cousins with the disease of healthy parents were seen in five families.

The duration of marriage and details of history were taken in each case. The relation between close contact and the development of leprosy is discussed.—Author's Abstract

Clark, K. A., Kim, S. H., Boening, L. F., Taylor, M. J., Betz, T. G. and McCasland, F. V. Leprosy in armadillos (*Dasypus novemcinctus*) from Texas. J. Wildlife Dis. **23** (1987) 220–224.

Tissue sections from 237 nine-banded armadillos (*Dasypus novemcinctus*) from 51 central Texas counties (U.S.A.) were examined microscopically for acid-fast bacilli and/or lesions of leprosy. Neither was found. A review of the literature relative to the incidence of leprosy from armadillos in Texas indicates that residents of counties along the Texas Gulf Coast may be at risk of contracting leprosy by handling infected

armadillos or their tissues.—Authors' Abstract

Gonçalves, A. [The epidemiology and control of leprosy in Brazil.] Bol. Of. Sanit. Panam. **102** (1987) 246–256. (in Spanish)

Leprosy, by virtue of its high rate of endemism in Brazil (with about four-fifths of all known cases in the South American continent), constitutes a public health problem in that country. This article analyzes the aspects of its behavior in accordance with current criteria of magnitude, importance, vulnerability, and institutional priority, taking into account the extent of the social damage that disabling lesions (depending on their location and spread) cause to those afflicted with them. The Ministry of Health supervises control efforts at the prescriptive and coordinating levels, while operations are the responsibility of the health secretariats. The paper considers the control operations carried out by six central-level areas of the program: institutional articulation, the promotion of science and technology, manpower training, formulation of technical standards, epidemiological monitoring of the endemic areas, and administrative monitoring of the programming and supply operations. The strategies adopted in each of those activities and the most representative results thereof are presented.—Author's English Summary

Gorodezky, C., Flores, J., Arevalo, N., Castro, L. E., Silva, A. and Rodriguez, O. Tuberculoid leprosy in Mexicans is associated with HLA-DR3. Lepr. Rev. **58** (1987) 401–406.

HLA-A, -B, -C, and -DR antigens were investigated in a total group of 76 leprosy patients, classified according to the system of Ridley and Jopling in 30 TT and 46 LL individuals. A group of 100 healthy subjects were included for comparison. Patients and controls were all Mexican Mestizos born in and inhabitants of Mexico. Typing of blood group systems was also performed. All TT patients showed a positive lepromin skin test, while all LL patients were negative to the specific antigen. The distribution of red-cell antigens was similar in both groups. The results of HLA typing demonstrated a significant association of DR3 with the tuberculoid type ($\chi^2 = 11.85$; $p = 0.0007$; $p_c = 0.04$). The RR value for DR3 carriers was 4.93 and the EF was 0.24. It is concluded that a class II-linked susceptibility gene plays an important role in the expression of tuberculoid leprosy. This gene is closely linked to DR3 in the Mexican population.—Authors' Summary

Li, Z. [Eight cases of leprosy in one family.] Chin. Lepr. J. **3** (1987) 86–87. (in Chinese)

The author reports that a mother with leprosy had eight children, of whom seven have suffered from leprosy with the exception of a daughter who married and it is unknown whether she has the disease or not. This suggests household aggregation of leprosy.—Author's English Abstract

Merlin, M., Drevet, D., Josse, R., Josseran, R. and Cottenot, F. [A sample survey: one objective method of evaluating leprosy prevalence in an endemic area.] Acta Leprol. (Genève) **5** (1987) 163–176. (in French)

The authors submit a simplified sample survey methodology designed to evaluate prevalence rates of leprosy. The system proposed uses a cluster sampling technique. A cluster is a randomly selected group of households. In each household visited by the epidemiological teams all the inhabitants of the target group are interviewed and examined.

Various sample sizes are used (from 6500 to 12,000 people) according to the expected prevalence rate of the studied area. All of the new cases detected through these surveys are reported to the national departments in charge of leprosy programs.

Two surveys are already finished (Equatorial Guinea, Cameroon); a third one is on the way.—Authors' English Summary

Mittal, B. N. Current status of National Leprosy Eradication Programme in India. J. Commun. Dis. **19** (1987) 37–41.

Leprosy still continues to be a major public health and social problem in India. The

disease is associated with high degree of social stigma, prejudice, and ignorance, leading to social ostracism in some communities.

Extension of case-detection procedures to newer areas, rapid increase in population, long course of disease, and application of newer techniques in the program strategies have all contributed to the increase of the estimated leprosy cases in India from 2.56 million in 1961 to 3.2 million in 1971 and 4.0 million in 1981. The disease exists in all the 31 States/UTs with variation in the prevalence rates and population at risk. Of the total population of 750 million, about 430 million are estimated to be at risk, living in the areas with a prevalence rate of 5 and more per thousand of population; 201 districts in the country have been identified to have a prevalence rate of 5 and more per thousand of population; 76 of these districts have a prevalence rate of 10 and more per thousand of population.

With the discovery of a number of highly effective drugs and regimens of treatment of cases, effective control of leprosy has become a reality. The control program in vogue since 1955 has been redesignated as National Leprosy Eradication Programme in 1983 with the goal of arrest of disease activity in all the known cases by the year 2000 A.D. This implies a break in the transmission besides the cure of all the known leprosy cases. The program has been included in the 20 Point Programme, 1986 and 100% central assistance is provided to all the 31 participating States/UTs. This paper presents the statistical information available regarding leprosy and strategies being conceived to eradicate this scourge.—Author's Abstract

Ponnighaus, J. M., Fine, P. E. M., Bliss, L., Sliney, I. J., Bradley, D. J. and Rees, R. J. W. The Lepra Evaluation Project (LEP) in Northern Malawi. I: Methods. Lepr. Rev. **58** (1987) 359–375.

The methodology employed in a total population survey carried out by the Lepra Evaluation Project (LEP) in Karonga District, Northern Malawi (Central Africa) is described in detail. After a pilot study in 1979, the survey started in March 1980 and was completed in August 1984. Four (later five) field teams visited households systematically across the district. Approximately 112,000 people were interviewed and examined. Preliminary analysis indicates that varied according to the sex of the paramedical examiners. The methods of collection 98% of individuals resident in the survey area who could and should have been examined for clinical leprosy were examined. Completeness of examination of women and processing of extensive data concerning a variety of possible risk factors for *Mycobacterium leprae* transmission and clinical disease are described. The paper serves as a background to a series of publications on various aspects of leprosy.—Authors' Summary

Talhari, S., Torrecila, M. A. A. and Talhari, A. C. A study of leprosy and other skin diseases in school children in the state of Amazonas, Brazil. Lepr. Rev. **58** (1987) 233–237.

During the period 1979–1982, 100,939 school children were examined for leprosy and other skin diseases. One hundred seven cases of leprosy were discovered: 16 with lepromatous type, 12 with indeterminate type, 11 with borderline, and 68 with tuberculoid type. The most frequent skin diseases found were dermatozoonosis, superficial mycosis, pyoderma, warts, pytiriasis alba and naevus.—Authors' Summary

Xiong, D., *et al.* [Epidemiological survey of leprosy in a Gangzi Autonomous County, Sichuan Province.] Chin. Lepr. J. **3** (1987) 75–76. (in Chinese)

In 1982 an epidemiological survey of leprosy in GanZi Prefecture, Sichuan Province, showed that the prevalence rate is 0.985%. It is estimated that there still are some patients in the early stage of the disease who have not been found and therefore this county is, in fact, still a highly endemic area. The higher prevalence in the county might be due to lower cultural and economical levels with poor health habits. The lower prevalence of leprosy in the local herdsmen might be due to protein being their staple food.—Authors' English Abstract

Rehabilitation

Chaise, F. and Boucher, P. [Long-term results of surgical decompression of the posterior tibial nerve in neuropathy of Hansen's disease.] J. Chir. (Paris) **124** (1987) 315–318. (in French)

Results are reported of surgery to the posterior tibial nerve affected by leprosy in 50 patients. A total of 90 neurolyses were performed using a similar technique. Study of the effect of surgery on the course of plantar sensitivity showed that three groups of nerves can be distinguished. Nerves in group 1 (21 totally paralyzed nerves) responded poorly to surgery (38% useful results) while on the contrary nerves in group 3 (non-paralyzed nerves) represented the ideal indication, surgery being truly prophylactic. In group 2 nerves a useful result was obtained in 82%. Indications for use of this surgical procedure are discussed, and more particularly the parameters affecting the quality of the results: severity of lesion and immunologic type of disease.—Authors' English Summary

MacMoran, J. W. and Brand, P. W. Bone loss in limbs with decreased or absent sensation: ten year follow-up of the hands in leprosy. Skeletal Radiol. **16** (1987) 452–459.

Three hundred sixty-seven patients with insensitive hands have been studied by correlating radiologic findings with occupational and medical history in order to better define causal factors in bone resorption. This study indicates that nonspecific infection and trauma are the reasons for bone resorption in 98% of cases. The role of intermittent pressure seems to be in soft tissue breakdown, which then allows bone to become infected. Bone resorption can be arrested at any stage of the disease by appropriate therapy of splinting and control of infection.—Authors' Abstract

Patil, K. M. and Srinivasan, H. Measurement of pressure under leprotic feet using a barograph. J. Rehabil. Res. Dev. **24** (1987) 9–12.

This paper describes the measurement of pressure distribution under normal and leprotic feet using a barograph. The barograph consists of a glass plate illuminated at its edges by fluorescent lights. The top surface of the glass plate is covered by a thin sheet of opaque white plastic upon which the subject stands. Greater pressure levels cause more intimate contact between the plastic and the glass, which results in the breakdown of total internal reflections within the glass. When viewed from a 45 degree inclined mirror placed below the glass plate, the areas of contact of the foot can be seen with light intensity related to the applied pressure. The resulting image recorded photographically is scanned for pressure intensity patterns using a microdensitometer. The pressure intensities are calibrated using known weights over specified areas. The method establishes characteristics of pressure distribution under normal feet. It confirms that scars resulting from healed ulcers in leprosy subjects are discrete sites of very high pressures in the range of 90 to 110 N/cm^2. This is two to three times the pressure levels under normal feet. Scar regions combined with deformity of the foot increase these pressures to still higher levels and possibly cause ulcers. The quantitative values of pressures determined in this study for leprosy subjects during standing are helpful in identifying problem areas on the soles of the feet.—Authors' Abstract

Yan, L. [Investigation of 225 leprosy patients with deformity and disability.] Chin. Lepr. J. **3** (1987) 91–93. (in Chinese)

Ninety-two cases among 225 cured and active leprosy patients in Jiangling County have deformities and disabilities, accounting for 36.07%. The longer the duration of the disease and the older the patient's age, the higher the rate of deformity and disability and the degree, especially of the hand. The cause, relation to the forms of leprosy, and location of deformity and disability are analyzed. The author makes suggestions for the prevention of deformities and disabilities.—Author's English Abstract

Other Mycobacterial Diseases and Related Entities

Brett, S. J. and Butler, R. Interactions of *Mycobacterium lepraemurium* with resident peritoneal macrophages; phagocytosis and stimulation of the oxidative burst. Clin. Exp. Immunol. **71** (1988) 32–38.

Live *Mycobacterium lepraemurium* or ^{60}Co-γ-irradiated organisms stimulated a very weak oxidative burst compared with similar numbers of heat-killed organisms or with live *M. microti.* This was found to reflect the poor uptake of the living organisms rather than an absolute failure to stimulate an oxidative burst. It is possible, however, that phagocytosis of fewer than 3–4 bacteria may not trigger the respiratory burst. Preincubating live *M. lepraemurium* with sera from infected mice, but not with fresh normal mouse sera, resulted in enhanced phagocytosis with a concomitant increase in the oxidative burst. The level of opsonic activity correlated with the *M. lepraemurium*-specific antibody titers. The opsonic activity appeared to be mediated by antigen–antibody activation of the classical complement pathway as heat inactivation destroyed the activity.—Authors' Summary

Cynamon, M. H., Palmer, G. S. and Sorg, T. B. Comparative *in vitro* activities of ampicillin, BMY 28142, and imipenem against *Mycobacterium avium* complex. Diagn. Microbiol. Infect. Dis. **6** (1987) 151–155.

The *in vitro* activity of ampicillin, BMY 28142, and imipenem was evaluated against 21 clinical isolates of *Mycobacterium avium* complex by both a broth and an agar dilution method. The MIC_{90} by broth dilution for ampicillin, BMY 28142, and imipenem was 16 μg/ml, 8 μg/ml, and greater than 32 μg/ml, respectively. The MIC_{90} by agar dilution for ampicillin and BMY 28142 was 16 μg/ml.—Authors' Abstract

D'Arcy Hart, P., Young, M. R., Gordon, A. H. and Sullivan, K. H. Inhibition of phagosome-lysosome fusion in macrophages by certain mycobacteria can be explained by inhibition of lysosomal movements observed after phagocytosis. J. Exp. Med. **166** (1987) 933–946.

We have investigated the mechanism of the inhibition of phagosome-lysosome (P-L) fusion in macrophages known to occur after infection by *Mycobacterium tuberculosis* and by the mouse pathogen *M. microti.* We have used an *M. microti* infection and have studied, first, the saltatory movements of periphagosomal secondary lysosomes by means of visual phase-contrast microscopy (a similar use of the method having been previously supported by computer analyses). The movements became slow or static after ingestion of live but not of heat-killed *M. microti.* They were unaffected by a fusiogenic mycobacterium *M. lepraemurium.*

Second, we studied the behavior of a normally fusiogenic unrelated organism, *Saccharomyces cerevisiae,* after its phagocytosis by cells already containing live *M. microti* ingested 18 hr previously. We observed, using a fluorescent assay of fusion, that many of these yeast phagosomes now also failed to fuse with the lysosomes; in contrast, when the host *M. microti* had been heat killed the yeast phagosomes fused normally. These observations were extended by ultrastructural quantitative analyses of P-L fusion, which confirmed the nonfusion of phagosomes of live *M. microti* and, more particularly, the change to nonfusion from the normal fusion behavior of the separate phagosomes of accompanying yeasts.

Third, we have assembled evidence against the likelihood that these *M. microti*-induced phenomena are nonspecific, i.e., secondary to a general depression of activity of heavily infected host cells. The evidence includes the feasibility of adjusting the degree of infection so as to facilitate visual assessment of organelle movements without the presence of detectable damage to the cells studied; the absence of lysosomal stasis after comparable infection with another mycobacterium of comparable virulence (*M. lepraemurium*); and the reversibility of the stasis. We conclude that inhibition of lysosome saltatory movements (and consequently its secondary effect on the associ-

ated yeasts) is a significant, specifically induced phenomenon.

From these observations and considerations, therefore, in conjunction with the analogous inhibition of lysosomal movements in normal macrophages by some chemical inhibitors of P-L fusion, and our suggestion that this association is causally related, we now suggest that *M. microti*-induced focal lysosomal stasis is also the main means by which the inhibition of P-L fusion is brought about by this organism. This concept is strengthened by the observations on *S. cerevisiae,* which provide strong evidence that stasis can cause suppression of fusion.—Authors' Summary

Gilpin, T. P. and Hammond, M. Active case-finding—for the whole community or for tuberculosis contacts only? S. Afr. Med. J. **72** (1987) 260–262.

The prevalence of tuberculosis in the household contacts of 67 smear-positive patients was compared with that in a "non-contact" population. The prevalence of smear-positive cases among adult contacts was 3.03% as opposed to 1.35% in non-contacts; 27.9% and 11.43% respectively of children in the two groups had positive tuberculin tests (Heaf grade III or IV). The differences in children are statistically significant and could be used to justify the contention that active case-finding in underdeveloped areas should be limited to intensive contact-tracing. It is argued, however, that this may be an inherently conservative response that will not meet the needs of tuberculosis control. A plea is therefore made for a redistribution of resources in order to meet these needs.—Authors' Summary

Hanson, P. J. V., Thomas, J. M. and Collins, J. V. *Mycobacterium chelonei* and abscess formation in soft tissues. Tubercle **68** (1987) 297–299.

Mycobacterium chelonei was isolated from a breast abscess in a healthy 46-year-old non-lactating Caucasian woman. *In vitro* testing showed the organism to be resistant to conventional anti-tuberculosis agents but sensitive to tetracycline and erythromycin. Treatment with isoniazid, pyrazinamide and rifampin initially produced a good response but the subsequent development of multiple abscesses required the addition of tetracycline and finally a change to erythromycin and trimethoprim, on which recovery was complete.—Authors' Summary

Heifets, L. B. and Lindholm-Levy, P. J. Bacteriostatic and bactericidal activity of ciprofloxacin and ofloxacin against *Mycobacterium tuberculosis* and *Mycobacterium avium* complex. Tubercle **68** (1987) 267–276.

Minimum inhibitory concentrations (MICs) of ciprofloxacin were lower than MICs of ofloxacin for both *Mycobacterium tuberculosis* and *M. avium* complex strains. The MICs of both drugs for 41 *M. tuberculosis* strains were in a narrow range, and significantly lower than the achievable serum concentrations. The MICs of ciprofloxacin for 46 *M. avium* strains were in a wide range, and in only 28% were the broth-determined MICs of ciprofloxacin within the same range as for *M. tuberculosis* and lower than the achievable serum level. When compared with the concentrations achievable in macrophages, the broth-determined MICs of ciprofloxacin were lower than this level for 61% of *M. avium* strains. Both drugs were bactericidal against *M. tuberculosis* and *M. avium,* with a low MIC/MBC ratio.—Authors' Summary

Humphrey, D. M. and Weiner, M. H. Mycobacterial antigen detection by immunohistochemistry in pulmonary tuberculosis. Hum. Pathol. **18** (1987) 701–708.

A preliminary diagnosis of tuberculosis can be established by the detection of acid-fast bacilli (AFB) and confirmed by culture of the microorganism. To evaluate an alternative method of diagnosis, the distribution of mycobacterial antigens in lung tissue specimens was characterized by an indirect peroxidase-antiperoxidase method and was compared to the detection of AFB by Ziehl-Neelsen stain. Histologic specimens were obtained from 59 hospital patients. Of nine patients with mycobacterial disease, seven had antigen detected in tissue. In two patients with tuberculous pneumonia, the distribution of mycobacterial

antigens was approximately the same as that of AFB. In contrast, in four patients with caseating pulmonary granulomas, clumps of mycobacterial antigens were demonstrated in necrotic areas of the granulomas where there are few or no AFB. In one patient with *Mycobacterium intracellulare* infection, crossreactive antigens stained weakly. Antigen was not found in tissue from two patients; one had miliary lung granulomas, and the second had mediastinal lymph node granulomas. Mycobacterial antigens were not detected in specimens from 50 control patients with nonmycobacterial diseases. On the basis of this study of 59 cases, immunohistochemical detection of microbial antigens appears to be useful for establishing the mycobacterial etiology of caseating pulmonary granulomas.—Authors' Abstract

Jiménez Misas, C. A., Valdivia Alvarez, J. A. and Mazón Zamora, D. [Classification of *Mycobacterium tuberculosis* by phage-type markers in Havana City Province.] Rev. Cubana Med. Trop. **38** (1986) 141–145. (in Spanish)

Fifty strains of *Mycobacterium tuberculosis* isolated from patients living in Havana City Province, Cuba, by means of phage-typing techniques and using a set of 11 phages specific for *M. tuberculosis* were studied. Of total number of strains studied, 50% correspond to type A_0, 44% to type A_1, 2% to type A_2 and 4% to type A_3. Neither the rest of type A, nor types B and C are reported.—(AS, Trop. Dis. Bull.)

Khomenko, A. G. The variability of *Mycobacterium tuberculosis* in patients with cavitary pulmonary tuberculosis in the course of chemotherapy. Tubercle **68** (1987) 243–253.

Inoculation of guinea pigs with membrane-filtered homogenates prepared from the walls of open cavities in the lungs of experimental animals allowed us to detect invisible (ultra-fine) forms of the tuberculosis agent. The ultra-fine forms of *Mycobacterium tuberculosis* were detected directly by electron microscopy, and indirectly by culture on liquid semi-synthetic media and subsequent microscopy, and by injection of the pathological material into the experimental animals. Similar results were obtained in patients who, after 3 and 6 months of treatment with the triple drug chemotherapy, still had open cavities in the lungs although smear and culture examinations were negative. The proportion of detected ultra-fine forms increased during chemotherapy: by the third month of treatment they were detected in 82% of the patients with open cavities.

The invisible forms of *M. tuberculosis* are able to revert to the typical bacterial forms. The initial stage of this process is accompanied by the formation of coccoid forms of mycobacteria that can be detected when the material is inoculated onto semi-synthetic medium with 10% plasma and by microscopy of the sediment.

Inoculation of experimental animals with the filtrate of sputum or other pathological material containing these ultra-fine forms of mycobacteria is accompanied by development of a peculiar granulomatous inflammation characterized by macrophages, mononuclear cells and solitary epithelioid and giant cells.—Author's Summary

Khomenko, A. G., Dorozhkova, I. R., Makarevich, N. M., Dubina, I. and Shlosarek, M. [Joint experience with phage typing and identification of tubercle bacilli isolated in the USSR and CSSR.] Probl. Tuberk. **11** (1987) 51–56. (in Russian)

Under the program of cooperation between the Central Research Institute of Tuberculosis of the USSR Ministry of Public Health and the Institute of Hygiene and Epidemiology in Prague, 111 fresh strains of tubercle bacilli isolated from patients with pulmonary tuberculosis in various geographical areas of the USSR and CSSR were in parallel identified and phage typed with the International Standard Set of Mycobacteriophages. All the studied strains were identified as *Mycobacterium tuberculosis* v. *humanus*. Three phage types, i.e., 1, 2 and 7, clearly predominated among the mycobacterial isolates. The quantitative proportions of separate phage types of the cultures isolated in the USSR and CSSR markedly differed ($p < 0.01$): the frequency of all the three phage types among the Soviet strains was almost the same (35.3%, 31.37% and

29.41% respectively), while among the Czech strains phage types 1 (53.33%) and 2 (36.66%) markedly predominated and the number of phage type 7 amounted only to 10%.—Authors' English Abstract

Lambert, M. A., Moss, C. W., Silcox, V. A. and Good, R. C. Analysis of mycolic acid cleavage products and cellular fatty acids of *Mycobacterium* species by capillary gas chromatography. J. Clin. Microbiol. **23** (1986) 731–736.

After growth and experimental conditions were established, the mycolic acid cleavage products, constituent fatty acids, and alcohols of representative strains of *Mycobacterium tuberculosis, M. smegmatis, M. fortuitum* complex, *M. kansasii, M. gordonae,* and *M. avium* complex were determined by capillary gas chromatography. Reproducible cleavage of mycolic acid methyl esters to tetracosanoic (24:0) or hexacosanoic (26:0) acid methyl esters was achieved by heating the sample in a high-temperature muffle furnace. The major constituent fatty acids in all species were hexadecanoic (16:0) and octadecenoic (18:1 ω9-c, oleic) acids. With the exception of *M. gordonae,* 10-methyloctadecanoic acid was found in all species; moreover, *M. gordonae* was the only species tested which contained 2-methyltetradecanoic acid. *M. kansasii* was characterized by the presence of 2,4-dimethyltetradecanoic acid, *M. avium* complex by 2-eicosanol, and *M. tuberculosis* by 26:0 mycolic acid cleavage product. The mycolic acid cleavage product in the other five species tested was 24:0. Although a limited number of strains and species were tested, preliminary results indicate that this gas chromatographic method can be used to characterize mycobacterial cultures by their mycolic acid cleavage products and consitituent fatty acid and alcohol content.—Authors' Abstract

Lévy-Frébault, V., Goh, K.-S. and David, H. L. Mycolic acid analysis for clinical identification of *Mycobacterium avium* and related mycobacteria. J. Clin. Microbiol. **24** (1986) 835–839.

We examined the mycolic acid composition of 133 strains belonging to MAIS complex (*Mycobacterium avium–M. intracellulare–M. scrofulaceum*) and MAIS intermediate strains and the related species *M. asiaticum, M. malmoense, M. shimoidei,* and *M. simiae.* The analysis revealed that about 10% of the strains identified as *M. avium–M. intracellulare* complex by conventional cultural and biochemical tests were in fact *M. simiae* strains according to their mycolate composition. Of 25 strains previously studied by the International Working Group on Mycobacterial Taxonomy, 2 (MAIS intermediate and *M. asiaticum*) presented patterns incompatible with the clusters to which they had been assigned. *M. malmoense* and both *M. simiae* serovars shared the same pattern with α-, α′-, and ketomycolates. We describe here the method used to identify the mycolic acid profiles in detail. We found it to be highly reproducible and convenient for use in mycobacterial reference laboratories.—Authors' Abstract

Litvinov, V. I., Pospelov, L. E., Gilburd, B. S. and Chernousova, L. N. [Dependence of levels of antituberculous antibodies on HLA-DR genotype of patients suffering from tuberculosis.] Probl. Tuberk. **7** (1987) 47–49. (in Russian)

Eighty-three patients with infiltrative and fibrocavernous tuberculosis of the lungs and 155 healthy volunteers were examined. Their HLA-DR genotypes and the levels of antituberculous IgG antibodies to PPD were determined. The findings indicated that in patients with tuberculosis and especially with its chronic fibrocavernous pattern the detection of antigen HLA-DR2 was more frequent than that in healthy persons. The level of antituberculous antibodies in the patients was also higher than that in the healthy volunteers. Moreover, in the tuberculous patients carrying HLA-DR2 antigen the level of antituberculous antibodies was significantly higher as compared to that in the tuberculous patients not carrying the antigen.—Authors' English Summary

Love, G. L. Nontuberculous mycobacterial skin infection resembling lepromatous leprosy. So. Med. J. **80** (1987) 1060–1061.

A leg ulcer in a 52-year-old renal transplant patient yielded foamy histiocytes con-

taining acid-fast bacilli subsequently identified as a Runyon group III *Mycobacterium*. Skin infection with these organisms is unusual, and the histologic appearance in this case suggested lepromatous leprosy.—Author's Summary

Ma, Y., Wang, Y. M. and Daniel, T. M. Enzyme-linked immunosorbent assay using *Mycobacterium tuberculosis* antigen 5 for the diagnosis of pulmonary tuberculosis in China. Am. Rev. Respir. Dis. **134** (1986) 1273–1275.

Measurement of serum IgG antibody to *Mycobacterium tuberculosis* antigen 5 by enzyme-linked immunosorbent assay was evaluated as a serodiagnostic test for pulmonary tuberculosis in China. The test was 89% sensitive and 94% to 100% specific with high accuracies of prediction. Among 82 tuberculous patients [with bacteriologically positive sputum smears or cultures], antibody titer was related to the extent of pulmonary disease. Among control subjects, false-positive tests were encountered among 5 of 52 persons with other pulmonary disease and not among 30 healthy subjects.—(AS/D. J. Girling, Trop. Dis. Bull.)

McIntyre, G., Belsey, E. and Stanford, J. L. Taxonomic differences between *Mycobacterium avium* and *Mycobacterium intracellulare* elucidated in man by skin tests with three new tuberculins. Eur. J. Respir. Dis. **69** (1986) 146–152.

New tuberculins called Aviumins A, B and C prepared from *Mycobacterium avium*, its proposed subspecies *M. avium brunense* and *M. intracellulare*, respectively, have been skin tested on school children in six countries as a part of larger studies. The results show that the reagents are recognized separately in most cases by the human immune system. Although there is some significant interdependence in sensitization to these reagents, the frequency of meeting the organisms must be very high since 33% of children with a mean age of 8 years produced positive responses to Aviumin A and 40% of them produced positive responses to Aviumin C. Besides age, other factors influencing responsiveness were BCG and sex. Both Aviumin A and B sensitization were significantly increased in the presence of a BCG scar; whereas Aviumin C tended to show the reverse trend. Sex had little effect on responses to Aviumins A and B but had an unexpected significant effect on Aviumin C, with more boys than girls producing positive reactions to it.—(AS, Trop. Dis. Bull.)

Orme, I. M. The dynamics of infection following BCG and *Mycobacterium tuberculosis* challenge in T-cell-deficient mice. Tubercle **68** (1987) 277–283.

The purpose of these experiments was to re-evaluate the usefulness of the thymectomized, irradiated, bone-marrow-reconstituted mouse (TXB mouse) as a model of the effect of immunodeficiency on resistance to mycobacterial infection. It was found that, although TXB mice had no resistance to intravenous infection with *Mycobacterium tuberculosis*, such mice were able to express moderate resistance to infection with the BCG vaccine, even when given in high doses. It is concluded, therefore, that rather than representing an animal devoid of immunological reactivity, the TXB mouse retains a residual capacity, albeit minimal, to express acquired immunity.—Author's Summary

Rastogi, N., Potar, M.-C. and David, H. L. Intracellular growth of pathogenic mycobacteria in the continuous murine macrophage cell line J-774: ultrastructure and drug-susceptibility studies. Curr. Microbiol. **16** (1987) 79–92.

The comparative action of seven drugs, namely, rifampin (RIF), ansamycin-LM 427 (ANS), streptomycin (SM), isoniazid (INH), pyrizinamide (PZA), clofazimine (CLF), and pristinamycin (PST), was studied both on extracellularly and intracellularly growing mycobacterial species *Mycobacterium bovis*, *M. tuberculosis*, and *M. avium*. All the drugs were used at their minimal inhibitory concentrations (MICs) and their obtainable serum levels in man; 10 × MICs, when less than the obtainable serum levels, were also tested. The action of drugs on extracellularly growing bacilli was tested with the Middlebrook 7H9-Tween medium; whereas for intracellular growth, an experimental model

using a continuous murine macrophage cell line J-774 was developed, and macrophage-mycobacteria interactions by use of cytochemistry, scanning and transmission electron microscopy were investigated. Extracellularly growing *M. avium* was resistant to all the drugs tested; however, when tested on intracellularly growing bacilli, both RIF and CLF were found to be bactericidal; whereas other drugs only delayed the bacterial growth. In the case of extracellularly growing *M. bovis* and *M. tuberculosis,* INH, RIF, and SM were active; whereas PZA was active only on *M. tuberculosis.* However, on intracellularly growing bacilli, only INH and RIF were found to be bactericidal for both species, CLF to a lesser extent in the case of *M. tuberculosis*; ANS and SM were bacteriostatic; whereas both PZA and PST were without any antibacterial effect. This investigation underlined the discrepancies concerning the action of drugs on extra- and intracellularly multiplying mycobacteria and the advantage of using a continuous cell line model while studying drug susceptibility of mycobacteria in relation to their intracellular growth.—Authors' Abstract

Suzuki, Y., Mori, T., Miyata, Y. and Yamada, T. The number of ribosomal RNA genes in *Mycobacterium lepraemurium.* FEMS Microbiol. Lett. **44** (1987) 73–76.

Southern hybridization of *Mycobacterium lepraemurium* DNA with 16S, 23S, 5S rRNA from *M. bovis* BCG was carried out. It was concluded that *M. lepraemurium* may possess a minimum set of rRNA genes and tRNA genes were linked to genes for 5S and 23S rRNA genes.—Authors' Summary

Tsukamura, M. Two groups of *Mycobacterium avium* complex strains determined according to the susceptibility to rifampicin and ansamycin. Microbiol. Immunol. **31** (1987) 615–623.

Mycobacterium avium-complex strains previously not exposed to any antituberculosis agents could be divided into two groups according to their susceptibility to rifampin and ansamycin, one group susceptible to 80 μg/ml rifampin and to 1.25 μg/ml ansamycin, and another resistant to these concentrations. In each group, the ratio of the minimal inhibitory concentration of ansamycin against that of rifampin was greatly different depending on the strain. This naturally occurring resistance to rifampin and ansamycin was frequently correlated to naturally occurring resistance to ethambutol, kanamycin, enviomycin, kitasamycin, and minocycline, but not correlated to that to isoniazid and sulfadimethoxine. Ansamycin was more active than rifampin against *M. bovis, M. kansasii, M. marinum, M. xenopi,* and *M. haemophilum.*—Author's Abstract