CURRENT LITERATURE

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

General and Historical

Fleischer, A. B., Jr., Maxwell, B. A., Baird, D. B. and Woosley, J. T. Hansen's disease (leprosy): the North Carolina experience. Cutis **45** (1990) 427–434.

Hansen's disease presents a large public health problem throughout much of the world but it occurs infrequently in the United States. Only 8501 cases have been reported since 1921 and 81% of these have been from just six states. Typical of many states, North Carolina has had only 22 case reports over this 68-year period. We present two typical cases we have seen in the past year and briefly review some of the epidemiologic, clinical, and treatment aspects of the disease.—Authors' Abstract

Goodless, D. R. and Johnson, A. H. Hansen's disease update. J. Fla. Med. Assoc. 77 (1990) 520–525.

The incidence of Hansen's disease in the U.S. has increased, with most new cases appearing in California and Florida. The bulk of this increase can be attributed to the immigration of patients from countries where the disease is endemic. Because many immigrants from Caribbean basin countries settle in Florida, it is especially important for physicians here to be able to recognize this disease. An asymptomatic macule or patch may be the first recognizable feature. Alternatively, patients may present with an acute inflammatory episode known as a "reaction." Dapsone, rifampin, clofazimine, thalidomide, and prednisone are useful in treatment. With early recognition and treatment, potentially disabling neurological and ophthalmological sequelae can be avoided. Consultation with or referral to either the Miami Regional Hansen's Disease Center or the Gillis W. Long Hansen's Disease Center in Carville, Louisiana, may be helpful.—Authors' Abstract

Kato, L. The demystification of leprosy: a multifactorial problem. Acta Leprol. (Genève) 7 (1990) 199–204.

Abolishment of misbeliefs and misconceptions, unfounded fear and prejudice are factors as important in leprosy control as prevention, early detection and therapy. Concrete measures of demystification are proposed. Identify and divulge the absolute truth about leprosy. Calling leprosy "Hansen's disease" did not result in demystification. Patients know that the two terms are identical. Treating them as human beings attracts more patients to the healers that the Hansenologian ritual. Contrary to statements, no major advances are being made in the field of bacteriology, immunology, molecular biology, mode of transmission and epidemiology of leprosy. Not a single new drug has been discovered in 26 years. Vaccination is a dubious venture. The question arises as to whether the right priorities are promoted in leprosy research. Cultivation of the leprosy bacillus is the *sine qua non* of any further progress. This field of research is a lost and totally neglected priority. Consequently, we have no pharmacological model for badly needed ultrapotent antileprosy drugs. Syphilis is now cured with a single dose of penicillin. A drug as potent against leprosy should not be a mission impossible if an appropriate pharmacological model—the *in vitro* culture—is available. The multifactorial problem of demystification is a difficult but not an impossible task. Less sensationalism, more real progress in research, selecting the right priorities, achieving the "ultimate drug," shelter, food, shoes, soap and broom for every human on this planet constitute the road to demystification.—Author's Summary

Opromolla, D. V. A. [Teaching of hansenology in the universities.] Hansen. Int. **13** (1988) 27–33. (in Portuguese)

All postgraduate young doctors should be conscious of our major public health problems and should be able to diagnose and treat these endemic diseases. Hanseniasis is an infectious disease that has an especial affinity for peripheral nerves and by that a high potential to produce disability and deformity leading to stigma and social outcast. There are 5,546,000 known patients in the world and the WHO estimates that the real figure is around 12 million. In Brazil the registered number of patients is 259,000 but realistic estimations would increase it up to half a million. The disease spreads out all over Brazil but, in absolute figures the southeast region has the highest load. To cope with this problem one of the basic actions is training and teaching of hanseniasis in medical school is essential. As a systemic disease it should be present in all specialities involved leading to an increase of time devoted to the teaching of hanseniasis. This approach, which could be extended to other endemic diseases, will contribute to the eradication of many diseases that afflict our population. There is no reason for a public health budget if there are no trained personnel to use it.—Author's English Abstract

Stingl, P. [Leprosy; pathogenesis, classification, diagnosis, and treatment.] Hautarzt **41** (1990) 126–130. (in German)

Leprosy (hanseniasis) is caused by chronic infection with *Mycobacterium leprae*. The disease involves primarily the superficial peripheral nerves and the skin, but almost any organ can be affected. The clinical features vary and are determined by the host's immune response to the infection. A distinction is made between multibacillary and paucibacillary forms of leprosy. The multibacillary forms are lepromatous, borderline-lepromatous and borderline-borderline leprosy; the paucibacillary forms are tuberculoid and borderline-tuberculoid leprosy. The clinical features and the histological picture depend on the patient's immune response. Because effective chemotherapy has become available, leprosy can now be cured, and frightening disabilities are therefore preventable.—Author's English Summary

Chemotherapy

Cheng, J., *et al.* [Study on primary dapsone resistant leprosy.] Chin. J. Clin. Dermatol. **19** (1990) 176–178. (in Chinese)

Ninety-seven strains of *Mycobacterium leprae* recovered from patients with previously untreated multibacillary leprosy were tested for dapsone susceptibility. The specimens originated from Shanghai, Jiangsu Fujian and Anhui. Approximately 28% of the strains either did not infect the mice or the results of susceptibility were inconclusive due to the low proportion of viable organisms in the bacterial populations. Among the 70 strains in which dapsone susceptibility could be tested in mice, 31 (44.3%) strains were found to be primary dapsone resistant. Although the majority of the primary dapsone-resistant strains have been shown to be slightly or moderately resistant, one sixth of them were highly resistant.—Authors' English Abstract

Coleman, M. D., Hoaksey, P. E., Breckenridge, A. M. and Park, B. K. Inhibition of dapsone-induced methaemoglobinaemia in the rat isolated perfused liver. J. Pharm. Pharmaol. **42** (1990) 302–307.

We have investigated the disposition of dapsone (DDS, 1 mg) in the rat isolated perfused liver in the absence and the presence of cimetidine (3 mg). After the addition of DDS alone to the liver there was a monoexponential decline of parent drug concentrations and rapid formation of DDS-NOH (within 10 min) which coincided with methemoglobin formation (11.7 ± 3.0%, mean ± s.d.) which reached a maximum (22.6 ± 9.2%) at 1 hr. The appearance of monoac-

etyl DDS (MADDS) was not apparent until 30–45 min. Addition of cimetidine resulted in major changes in the pharmacokinetics of DDS and its metabolites. The AUC of DDS in the presence of cimetidine (1018.8 ± 267.8 μg min mL^{-1}) was almost threefold higher than control (345.0 ± 68.1 μg min mL^{-1}, $p < 0.01$). The half-life of DDS was also prolonged by cimetidine compared with control (117.0 ± 48.2 min vs 51.2 ± 22.9, $p < 0.05$). The clearance of DDS (3.0 ± 0.55 mL min^{-1}) was greatly reduced in the presence of cimetidine (1.03 ± 0.26 mL min^{-1} $p < 0.01$). The $AUC_{0\text{-}3\ h}$ for DDS-NOH (28.3 ± 21.2 μg min mL^{-1}) was significantly reduced by cimetidine (8.1 ± 3.40 μg min mL^{-1}, $p < 0.01$). In contrast, there was a marked increase in the $AUC_{0\text{-}3\ h}$ for MADDS (32.7 ± 25.8 μg min mL^{-1}) in the presence of cimetidine (166.0 ± 26.5 μg min mL^{-1} $p < 0.01$). The methemoglobinemia associated with DDS was reduced to below 5% by cimetidine. Hence, a shift in hepatic metabolism from bioactivation (*N*-hydroxylation) to detoxication (*N*-acetylation) caused by cimetidine, was associated with a fall in methemoglobinemia. These data suggest that the combination of DDS with a cytochrome P450 inhibitor might reduce the risk to benefit ratio of DDS.—Authors' Abstract

Das, R. K. and Roy, B. Evaluation of genotoxicity of clofazimine, an antileprosy drug, in mice in vivo. I. Chromosome analysis in bone marrow and spermatocytes. Mutat. Res. **241** (1990) 161–168.

Clofazimine, an antileprosy drug, was tested in mice for its cytogenetic effect in mouse bone marrow and testis. Bone marrow metaphase analysis in adult mice treated directly for different periods (1, 2 and 4 weeks, 40 mg/kg/day) and with different doses (4, 20 and 40 mg/kg/day for 7 days) as well as in young animals exposed through lactation for different periods (2, 3 and 4 weeks) revealed significant increases in chromosomol aberrations over the controls. Analysis of diakinesis-metaphase I stages also exhibited a significantly elevated incidence of chromosome aberrations over controls after treatment for different periods. On the basis of the present result, the drug may be considered a potential clastogen in mice.—Authors' Summary

Gelber, R. H. New developments in the antimicrobial treatment of leprosy. Antimicrob. Newslett. **6** (1989) 27–31.

There are a number of established agents available to treat leprosy. Unfortunately, resistance has been documented to each of them and each has serious drawbacks affecting its universal applicability. A number of promising newer agents are currently being evaluated. Authorities generally agree that combination chemotherapy is required, at least for lepromatous leprosy. The scientific basis for deciding on a specific regimen and the duration of therapy required remains slim.—Author's Conclusion

Jayalakshmi, P. and Ting, H. C. Dapsone-induced liver necrosis. Histopathology **17** (1990) 89–91.

A patient being treated with 100 mg dapsone and 200 mg chloroquine daily for 6 weeks for seborrhoeic dermatitis developed typical features of the "sulfone syndrome" and died due to massive liver necrosis.—Authors' Abstract

Job, C. K., Yoder, L., Jacobson, R. R. and Hastings, R. C. Skin pigmentation from clofazimine therapy in leprosy patients: a reappraisal. J. Am. Acad. Dermatol. **23** (1990) 236–241.

Skin biopsy specimens from two lepromatous leprosy patients with dark brown pigmentation who were receiving long-term clofazimine therapy were studied. Ceroid-lipofuscin pigment was demonstrated inside macrophages that contained numerous phagolysosomes. These contained lipids and clofazimine that appeared as electron-lucent vacuoles and a lipofuscin pigment that was electron dense, granular, and lamellated. Although the presence of the drug in tissues contributed to the skin pigmentation, the main cause was a drug-induced, reversible ceroid lipofuscinosis.—Authors' Abstract

Li, W., *et al.* [Observations on effect of MDT in multibacillary leprosy for five years.]

China Lepr. J. **6** (1990) 61–65. (in Chinese)

Six-hundred-forty-seven cases of active multibacillary leprosy were treated with rifampin, clofazimine and dapsone in 12 counties in Yangzhou District and Dongtai County during the period 1983 to 1988. The acceptance rate of MDT was 97%, and 347 cases have been observed for 5 years. The results showed that 80% of the patients whose BI was < 3 through 3 years of treatment and 90% of the patients whose BI was ≥ 3 through 5 years of treatment became skin-smear negative, respectively. However, in the patients with skin smears positive after 3 or 5 years' treatment, the BI was < 0.5 on the average. Up to now, 257 cases with negative skin smears have been followed up for 470 patient-years after cessation of MDT, and no relapse has been found.—Authors' English Abstract

Li, W.-H., Ye, G.-Y., Yang, Z.-M., Tao, M.-B., Luo, J., Wang, C.-J. and Ji, F. Effect of three-year multidrug therapy in multibacillary leprosy patients. Proc. CAMS PUMC **5** (1990) 37–40.

The feasibility and effects of a 3-year treatment using rifampin, clofazimine, and dapsone in multibacillary (MB) leprosy patients in Yangzhou Prefecture and Dongtai County (1983–1986) are reported. Among 591 active MB leprosy patients in the two areas, 569 (96.30%) were treated with this regimen. Of 303 cases available for analysis, 196 (64.7%) cases showed negative skin smears and clinical inactivity. The rest showed different degrees of improvement. The average reduction of the BI was 0.78. The intensity and frequency of ENL and neuritis decreased markedly with treatment. The main side effects were pigmentation and ichthyosiform changes of the skin, but these did not influence treatment.—Authors' Abstract

Ovcharova, G. D., Nacheva, R. N. and Dimitrova, D. B. [Potentiometric procedure for assay of rifampicin.] Antibiot. Khimioterap. **35** (1990) 8–10. (in Russian)

A potentiometric procedure for assay of rifampin was developed. The procedure implies titration of rifampin as a monofunctional acid by sodium hydroxide solution (0.1 mol/l) in 75% aqueous methanol. The constant ionic strength of the solution is provided by addition of KCl until its concentration is 0.1 mol/l, the titrant concentration being 10 times higher than the antibiotic concentration in the solution. This provides a precise determination of the concentration ionization constant of the antibiotic as a monofunctional acid (pKa 7.33 ± 0.01) and an insignificant dilution of the antibiotic solution during the titration promoting precise and reproducible results. The procedure error is 0.20%; the variation coefficient is 0.27%.—Authors' English Abstract

Recent trends in chemotherapy of paucibacillary leprosy. ICMR Bull. **20** (1990) 53–57.

In conclusion, the following points emerge, on analyzing the existing situation: a) The criteria used by WHO for selecting the paucibacillary patients are well conceived and even the 1982 criteria of classification evolved by WHO appear reasonable. b) MDT regimen recommended by WHO has helped in shortening the duration of treatment. However, treating these patients for just 6 months appears to be inadequate and there is a need of additional treatment with dapsone for 6 months. When reports of possible inadequacy of 6 months MDT started coming in, it was suggested that PB patients should be treated for 6 months or until inactivity was achieved. But subsequent experience has shown that late reactions and relapses are very high even in patients who had subsided by 6 months of treatment. It is therefore desirable that all PB patients be treated for 1 yr. It is expected that supplementing the WHO regimen with dapsone for 6 additional months will produce optimum therapeutic results and may also improve the acceptability of the program further. Many treating physicians find it hard to explain to their patients that persisting or worsening activity will subside, on its own, specially when they themselves are not convinced about it. c) The addition of initial 7 days of rifampin did not show any advantage in studies at the CJIL, Agra.

In recent years, newer drugs against leprosy have emerged and we can look forward

to newer regimens for treatment of different types of leprosy patients. Even with existing drugs, however, major advances have been made and with certain modifications in the existing regimens and a critical appraisal of emerging experience in the field, one can get optimal results.—From the Conclusions

Roy, B. and Das, R. K. Evaluation of genotoxicity of clofazimine, and antileprosy drug, in mice in vivo. II. Micronucleus test in bone marrow and hepatocytes. Mutat. Res. **241** (1990) 169–173.

The antileprosy drug, clofazimine, was tested for its possible genotoxicity using micronucleus (MN) tests in mice. A significantly higher incidence of MN in bone marrow erythrocytes, particularly in polychromatic erythrocytes, as well as in regenerated hepatocytes revealed a positive clastogenic effect of the drug. The drug also had a marked antimitotic effect as indicated by a negative correlation with the dose.—Authors' Summary

Yu, X., *et al.* [Three year follow-up after completing two year MDT for MB.] China Lepr. J. **6** (1990) 14–16. (in Chinese)

Thirty-one cases of active multibacillary leprosy were treated with rifampin, clofazimine, and dapsone for 2 years and then followed up after stopping the treatment. The patients showed marked improvement clinically during treatment. The bacterial index (BI) in the patients reduced by 0.8 each year during treatment. The clinical status and BI continue improving after stopping treatment. At the 36th month of follow up, the BI of 26 cases had become negative and histology showed marked improvement. The results indicated that multidrug therapy in the shorter course is effective for multibacillary leprosy patients. However, its long-term efficiency should be further observed.—Authors' English Abstract

Clinical Sciences

Chopra, N. K., Agrawal, J. S. and Pandya, P. G. Reactions in leprosy; a study of 250 patients in a multidrug therapy project, Baroda District, Gujarat, India. Int. J. Dermatol. **29** (1990) 490–493.

It was observed that all patients showing ENL were LL and those that showed reversal reaction were BB, BT and BL. In our series the incidence of the reactions among leprosy patients was 1.39% more in multibacillary (MB) cases (3.31%), as 235 of 7098 MB cases developed reactions. Our study shows that multidrug therapy lowers the incidence of reactional states in leprosy. Two-hundred-thirty-five MB cases developed ENL reactions between 6 months and 2 years of treatment and reversal reactions between 6 months and 1 year of treatment. The incidence of reactions was more common in the age group 21–40 years old (70.80%). In the observed series some precipitating factors such as intercurrent infection, routine and injudicious use of sulfones, rifampin, pregnancy, delivery and surgical intervention, and specific types of stress and strain were noted to have a definite relationship to the onset of reaction. Of 250 cases, 179 (71.6%) had an observed precipitating factor and 71 cases (28.4%) were of unknown etiology. Leprosy, because of its mutilating character and chronicity, has always been great challenge to physicians.—Authors' Conclusions

Courtright, P., Lee, H. S. and Lewallen, S. Training for primary eye care in leprosy. Bull. WHO **68** (1990) 347–351.

Reported are the results of a primary eye care training program for community-based leprosy control workers in the Republic of Korea. The 20-hour program emphasized the detection and management of lagophthalmos (and its complications) and chronic iridocyclitis. Leprosy patients in four resettlement villages were examined independently by the health workers and an ophthalmologist. Agreement between the health workers and the ophthalmologist was good

for the detection of most signs (lagophthalmos, acute iridocyclitis, and chronic iridocyclitis). Based on these preliminary results, it is recommended that primary eye care be included as a part of the training for leprosy paramedical workers.—Authors' Abstract

Dong, L., *et al.* [Surgical exploration of swollen peripheral nerves in 55 cases.] China Lepr. J. **6** (1990) 71–74. (in Chinese)

Fifty-five cases of swollen peripheral nerves whose diagnosis is very hard were surgically explored and histopathologically examined; 32 cases have been diagnosed as leprosy, being 58.2%, and the others as ulnar neuritis behind the elbow in 7 cases, common peroneal neurilemmocyst in 5, hypertrophic neuritis in 3, great auricular and superficial peroneal neuritis in 2 each, and mononeurofibroma, neuroamyloidosis, traumatic common peroneal neuritis and localized dermoneuritis in 1 each. In the past, swollen peripheral nerves with accompanying relevant dysfunctions were always regarded as a sign of the pure neuritic form of leprosy. On the basis of these results, the authors point out that it is really not so. The various causes of thickening of the peripheral nerves have been discussed. The authors believe that the surgical exploration of swollen peripheral nerves is not only harmless to the patients, but also helpful in diagnosis and decompression treatment, so long as the indications and explorative operation are right.—Authors' English Abstract

Flageul, B., Vignon-Pennamen, M. D., Wallach, D., Pennec, J. and Cottenot, F. [Late reversal reactions in leprosy.] Acta Leprol. (Genève) 7 (1990) 109–117. (in French).

Since the application of short duration multidrug therapy (MDT) in leprosy, it has been reported that reversal reactions (RR) may occur after withdrawal of treatment. Surprisingly, such "late reversal reactions" have never been described after monosulfonotherapy. Such RR, especially in endemic areas, may represent diagnostic and therapeutic difficult problems. We report 5 cases of late RR. In 4 cases (1 BT patient and 3 BL-LLs patients), the RR occurred 1½ months to 3 years after cessation of MDT. In the last case (form LLs), the RR happened 6 months after 14 years of monosulfonotherapy had been stopped. These observations strengthen the need of a complete clinical, bacteriological and immunological evaluation at the time of the diagnosis, more useful than a single bacteriological study, to differentiate late RR from relapses. Moreover, the last case confirms that late RR may occur after monosulfonotherapy.—Authors' English Summary

Fleming, A. F. Opportunistic infections in AIDS in developed and developing countries. Trans. R. Soc. Trop. Med. Hyg. **84** Suppl. 1 (1990) 1–6.

The acquired immune deficiency syndrome (AIDS) is fundamentally the same disease in all parts of the world, but the prevalence of microorganisms in an environment governs the patterns of disease arising from reactivated latent infections, invading pathogens and opportunistic infections. AIDS in Africa has certain characteristic presentations. Enteropathic AIDS is most common: *Cryptosporidium* and *Isospora belli* are identified in up to 60% of patients, but it is uncertain whether they are the causes of diarrhea. *Pneumocystis carinii* pneumonia is rare. Tuberculosis, both pulmonary and extrapulmonary, is the supreme complicating infection. Herpes zoster is frequently the first clinical presentation, and has a 95% positive predictive value for HIV positivity. Measles may be more frequent in infants born to HIV-infected mothers, and appears to be worse in HIV-infected children. There is accelerated progress of both diseases in patients infected by HIV and *Mycobacterium leprae.* Salmonellosis is frequent. There is no direct interaction between malaria and HIV but, by being a potent cause of anemia, malaria enhances transmission of HIV to children through blood transfusion. HIV-positive subjects are liable to new or reactivated visceral leishmaniasis with dissemination to unusual sites. Cerebral toxoplasmosis is common. There are no apparent interactions between HIV and helminths, although there is one report of hyperinfection with *Strongyloides stercoralis.* Cryptococcal

meningitis has high frequency. Infections with *Histoplasma encapsulatum* are common in tropical America, but there has been no increase of frequency of *H. duboisii* in Africa since the advent of AIDS.—Author's Abstract

Fleury, R. N. and Opromolla, D. V. A. [Virchowian hanseniasis, Lucio's phenomenon, cryptococcosis.] Hansen. Int. **13** (1988) 47–56. (in Portuguese)

A 75-year-old white male, for 3 years on treatment for virchowian hanseniasis, was admitted with active HD lesions, infiltration on the base of right lung, leg ulcer and malaise. After 2 days he developed purpura and hemorrhagic blisters in the limbs. The biopsy of these lesions revealed Lucio phenomenon. The patient worsened with mental confusion, psychomotor agitation and anisocoric pupils. On the 18th day of hospitalization, the patient died. Necropsy revealed virchowian infiltration, plenty of bacilli in the skin and viscera, as well as tuberculoid granuloma with acid-fast bacilli in the liver, spleen and bone marrow. These findings led us to review the patient's classification from virchowian to borderline. In the lungs, leptomeninges, renal papillae, prostate and thyroid, it was found loose tuberculoid granulomas with a great amount of fungi surrounded by a halo resembling *Cryptococcus neoformans.* These findings and the onset of Lucio phenomenon are discussed in a patient that had been treated for 3 years and still had several virchowian lesions and a great amount of acid-fast bacilli.—Authors' English Abstract

Garg, R., Agarwal, J. K., Singh, G. and Bajpai, H. S. Thyroid function in leprosy. Indian J. Lepr. **62** (1990) 215–218.

Thyroid function tests were carried out in 43 cases of leprosy. The study subjects included cases of tuberculoid, borderline and lepromatous leprosy and those with lepra reaction. The parameters studied included serum cholesterol, protein-bound iodine, serum T_3 and serum T_4 levels. The levels of serum cholesterol and protein-bound iodine were normal in all four groups of leprosy patients. However, the mean serum T_3 and T_4 were low in all four groups. The difference in the levels of serum T_3 was statistically significant only in the lepra reaction group. The levels of T_4 were statistically significantly decreased in borderline leprosy, lepromatous leprosy and in lepra reaction.—Authors' Abstract

Girdhar, A., Lavania, R. K., Malaviya, G. N. and Girdhar, B. K. Histoid lesion in nerve of a lepromatous patient. Lepr. Rev. **61** (1990) 237–241.

This report pertains to a patient who had untreated diffuse lepromatous disease of 8- to 10-years' duration. Two peripheral nerves were beaded, which on biopsy showed histoid features. Because of its rarity, the case is reported.—Authors' Summary

Guillet, G., Roudaut, M. M., Guillet, M., Hily, M., Bellein, M. and Constant-Desportes, M. Leucocytic alkaline phosphatase activity in leprosy: a possible guide in the follow up of leprosy. Acta Leprol. (Genève) **7** (1990) 163–168.

In order to investigate a possible involvement of phagocytic cells in the various types of leprosy, we undertook the study of enzymatic activities in circulating leukocytes. The activity of leukocytic alkaline phosphatase was studied by histochemical techniques on blood smears in 31 patients presenting with leprosy, aged between 4 and 73, and in 11 noninfected people. The 31 patients suffering from leprosy were distributed as: 14 lepromatous leprosy of which 6 had not yet been treated and 8 were under treatment; 9 cases of tuberculoid leprosy of which 7 had been treated and 2 had not yet; 3 cases of borderline leprosy which had all been treated; and 5 patients whose form of leprosy was indeterminate (before treatment). The distribution of the different values we obtained shows a very significant difference ($p < 0.001$) between patients with and without leprosy (respectively, 33.8 ± 7.3 and 109.8 ± 12.5). Moreover, the decrease of the alkaline phosphatase activity correlated with the severity of the disease (47.2 ± 11.4 in tuberculoid leprosy and 20.6 ± 9.3 in lepromatous leprosy), thus suggesting that the evaluation of leukocytic alkaline phosphatase activity should be advised as a possible prognosis guide in

indeterminate leprosy.—Authors' Summary

Hörnsten, P., Keisu, M. and Wiholm, B.-E. The incidence of agranulocytosis during treatment of dermatitis herpetiformis with dapsone as reported in Sweden, 1972 through 1988. Arch. Dermatol. **126** (1990) 919–922.

During the 17-year period 1972 through 1988, a total of 7 cases of agranulocytosis associated with the use of dapsone for the treatment of dermatitis herpetiformis were reported in Sweden. The median age of the patients involved was 61 years; three of them were male. The median duration of dapsone treatment was 7 weeks and the daily prescribed dose was 100 mg. Based on sales and prescription data, the crude relative risk of agranulocytosis during dapsone treatment of dermatitis herpetiformis was 50, and the total risk was 1 case per 3000 patient years of exposure to dapsone. In relation to the number of new cases of dermatitis herpetiformis, agranulocytosis was estimated to develop in 1 of 240 to 425 patients receiving dapsone therapy. Patients should be instructed to seek medical care immediately in case of fever.—Authors' Abstract

Hu, Y., *et al.* [Selenium contents in hair of normal persons and leprosy patients in Qin and Ba Mountain Regions of Shaanxi Province.] China Lepr. J. **6** (1990) 78–81. (in Chinese)

The Qin and Ba Mountain ranges are located in the southern part of Shaanxi Province. Although both regions are endemic for leprosy, there is a difference in the disease endemicity. Besides leprosy, the Ba Mountain region is also well known for its endemicity of Kaschin-Beck disease and a kind of degenerative arthritis is known to be associated with deficiency of selenium. Analysis of the selenium content in hair shows that there is a significant decrease gradually in the following order: L leprosy > T leprosy > healthy persons in Ba Mountain region > healthy persons in Qin Mountain region, but no significant difference between L patients living in Qin and Ba Mountain regions. The possible significance of these differences is discussed in the text.—Authors' English Abstract

Jadhav, V. H., Jadhav, M. V., Sapatnekar, S. M. and Joshi, P. B. Fibrinolytic phenomenon in leprosy. Indian J. Lepr. **62** (1990) 208–214.

Fibrinolytic activity in 81 patients with different types of leprosy and in 32 normal healthy controls was studied by the euglobulin lysis time method. Fibrinolytic activity was markedly decreased in patients with lepromatous leprosy and those with ENL reaction. Decline in fibrinolytic activity during ENL was independent of frequency of attacks. Fibrinolytic activity was partly restored after subsidence of ENL reaction, although it failed to attain normal levels. Cutaneous vasculitis seems to be most probable cause of fall in fibrinolytic activity in lepromatous leprosy and ENL reaction.—Authors' Abstract

Lamba, P. A. and Rohatgi, J. Leprotic keratopathy in India. Indian J. Lepr. **62** (1990) 186—192.

Corneal affections cause severe ocular morbidity in leprosy. Poor nutrition and low socioeconomic status make the eyes prone to repeated secondary infections which makes the pattern of corneal disease in this country different from that reported in Western literature. A study of 250 patients shows that leprotic keratopathy has four different patterns. Primary leprous keratitis was seen in 56.5% of cases, while secondary leprous keratitis (groups B, C and D) constituted 57.7%. In the later group, the ocular morbidity could be prevented by controlling infection and prevention of concomitant diseases. Cases of lepromatous leprosy showed a consistently higher incidence of different types of corneal involvement than tuberculoid cases.—Authors' Abstract

Lu, B., *et al.* [Survey of ocular diseases among 1692 cases of leprosy in Guangdong Province.] China Lepr. J. **6** (1990) 7–11. (in Chinese)

The examination of 75 ocular items in 1692 hospitalized leprosy patients, the majority of them had been cured, shows that the prevalence rate of ocular diseases is 90.9% without sexual difference and the blindness rate is 8.8%. The mean age of these patients is 53 years, and most of them are

affected with various disabilities. Blindness and reduced vision are more in women and in cured patients than in men and in active cases. It is obvious that the longer the duration of leprosy, the higher the incidence rates of leprous ocular diseases and blindness will be. Treatment as early as possible during lepra reaction and in the initial stages of ocular diseases will maintain normal vision, indicating that leprosy-caused blindness is preventable. Most of ocular diseases in leprosy are in the anterior section of the eye, and blindness and lower vision occur mostly in paucibacillary patients because they are apt to be affected with exposure ophthalmia and its sequelae. In multibacillary patients iridocyclitis is less seen, but cataract more. The authors regard ocular diseases and blindness in leprosy as so severe that it is necessary to train leprosy control workers and to mobilize ophthalmologists for activity controlling them in a planning way.—Authors' English Abstract

Nigam, P. K. and Singh, G. Mucosal and genital lesions in histoid leprosy. Int. J. Dermatol. **29** (1990) 207–208.

The histoid lesions in this patient were mainly confined over the face, buttocks, and extremities. Three to 50 lesions may be present in one patient; however, the presence of more than 200 lesions in this patient indicates a severe form of the disease. The eyebrows were not lost, although the lesions were present there (an observation similar to that of Price and Fitzherbert). Lesions present over the genitalia, including glans and scrotum, as seen in this case are rarely described. Presence of conductive deafness due to partial blockage of external auditory meatus by the nodules was an additional feature. Mucus membrane involvement in the form of lesions over the hard and soft palates and the mucosa around the lips is known to occur, although infrequently. The nasal mucosa, which is affected quite early in lepromatous leprosy and in advanced cases leads to destruction of nasal cartilage, was normal even after 6 years of uncontrolled disease, which shows that nasal mucosal involvement is relatively uncommon even in the severe forms of histoid leprosy.—Authors' Discussion

Nogueira, L. A. D. A case of isolated tuberculoid leprosy of brachial cutaneous nerve. Acta Leprol. (Genève) **7** (1990) 153–155.

The author relates a rare case of cutaneous-brachial nerve mononeuritis in a Hansen's disease patient, presenting a pure neural tuberculoid form, with spontaneous drainage of abscess.—Author's Summary

Patki, A. H. Multiple Beau's lines due to recurrent erythema nodosum leprosum. (Letter) Arch. Dermatol. **126** (1990) 1110–1111.

Beau's lines are transverse grooves on the nail plate that develop as a consequence of any acute illness or stressful condition. First described by Beau in 1846, they occur as a result of myocardial infarction, measles, mumps, pneumonia, or pulmonary embolism. A case is described where multiple Beau's lines were observed in a patient in whom the lines could be attributed to recurrent attacks of erythema nodosum leprosum, or a type 2 lepra reaction.—From the letter

Patki, A. H. Pterygium inversum unguis in a patient with leprosy. (Letter) Arch. Dermatol. **126** (1990) 1110.

Pterygium inversum unguis is a relatively recently described condition affecting the nails. It consists of a distal extension of the hyponychium with its fusion to the undersurface of the nail plate. The distal nail groove that separates the hyponychium from the nail plate becomes obliterated. The condition may be congenital, familial, or acquired. A patient with leprosy and pterygium inversum unguis is described.—From the letter

Pavithran, K. Non-pruritic eczemas as presenting manifestation of leprosy. Indian J. Lepr. **62** (1990) 202—207.

Three patients who presented with eczemas as manifestation of leprosy are described. One of them having lepromatous leprosy had extensive areas of acquired ichthyosis. He developed asteatotic eczema on the legs. The pathophysiologic mechanisms for the development of ichthyosis and as-

teatotic eczema in this patient are briefly discussed. The second patient, with tuberculoid leprosy, presented with allergic contact eczema due to neomycin which he had applied over the plaque for scaling and crusting. The third patient, also with tuberculoid leprosy, presented with features of nummular eczema. Dryness of the skin that resulted from leprosy had led to the development of nummular eczema in this case. One peculiarity noted in all these eczemas was that they were nonpruritic.—Author's Abstract

Ponnighaus, J. M., Fine, P. E. M., Gruer, P. J. K. and Maine, N. The anatomical distribution of single leprosy lesions in an African population, and it implications for the pathogenesis of leprosy. Lepr. Rev. **51** (1990) 242–250.

Data on the anatomical sites of single leprosy lesions found in 635 newly diagnosed and biopsy-confirmed leprosy patients are presented. These patients were found during total population surveys carried out by the Lepra Evaluation Project, a prospective longitudinal study of the epidemiology of leprosy in Karonga District, Northern Malâwi. There was a striking excess of single lesions on the face and the back of the arms, compared to the distribution of skin surface area, and a deficit on the legs, regardless of age. There is some evidence for a sex difference in lesion distribution among adults, with facial and arm lesions being relatively more common in females and back lesions being more common in males. The excess of lesions on the face compared to the lower limbs is similar to data from Uganda, but very unlike data from Burma and elsewhere in Asia. Overall, the distribution of lesions does not suggest a pattern reflecting entry of *Mycobacterium leprae,* nor does it suggest an association with anatomical distribution of the nervous or vascular system. It is argued that the distribution reflects the influence of some "local" environmental or behavioral factors.—Authors' Summary

Saxena, N., Sharma, R. P. and Singh, V. S. Serum iron and total iron binding capacity in leprosy patients. Indian J. Lepr. **62** (1990) 219–222.

Serum iron and total iron binding capacity was estimated by Ramsay's method in 40 leprosy patients having different types of leprosy and 20 normal subjects serving as controls. Significantly low serum iron and total iron binding capacity were observed in lepromatous leprosy patients.—Authors' Abstract

Saxena, U., Ramesh, V., Misra, R. S. and Mukherjee, A. Nodularity of nerves in treated leprosy. Int. J. Dermatol. **29** (1990) 497–499.

Ten patients with fully treated paucibacillary leprosy, mainly tuberculoid, had asymptomatic nodules present along the peripheral nerves that persisted even after the skin lesions had completely subsided and treatment was stopped. Histopathology of the nodules revealed no signs of activity of the disease. The evolution, follow-up care, and significance of these nodules are discussed.—Authors' Abstract

Sehgal, V. N. and Joginder. Slit-skin smear in leprosy. Int. J. Dermatol. **29** (1990) 9–16. (116 refs)

Slit-skin smear examinations should form an integral part of leprosy diagnosis, treatment, and prognosis. Laboratory services in most of the control units, however, are unsatisfactory. Classification of a MB case into PB is a serious repercussion of relying upon slit-skin smears for treatment. Not only may the treatment of such cases be inadequate, but it also may be a perpetuating factor for drug resistance. Therefore, arrangement should be made for regular training and supervision of laboratory workers and checking of their equipment. A system of quality control by random checking of smear results by establishing regional reference laboratories should be instituted.—From the article

Sehgal, V. N. and Lamba, P. A. Ocular changes in leprosy. Int. J. Dermatol. **29** (1990) 175–182.

It is now established that *Mycobacterium leprae* may affect the eye either indirectly (paucibacillary) or directly (multibacillary). The former is in consequence to the involvement of the 5th and 7th cranial nerves,

resulting in an insensitive cornea and infranuclear facial palsy. Thus, exposure keratitis and its sequelae and lagophthalmos are its common clinical presentations. The direct invasion by the organism may manifest in the form of supraciliary and ciliary madrosis, keratitis and its sequelae. In addition, the affliction of the uveal tract is of considerable clinical significance and may be recognized by a variety of unique clinical features, namely, iritis, iridocyclitis, iris pearls, iris holes, and atrophy. Pupillary involvement, denervation hypersensitivity, and formation of cataract are its other salient features.

The importance of these clinical features are discussed. Ocular involvement in leprosy is one of the major causes of blindness. Should the diagnosis be made early, these changes may be prevented by appropriate therapy. However, manifest clinical lesions should be managed by an expert ophthalmologist.—From the article

Shi, C., *et al.* [Contents of 10 kinds of elements in hair and serum of Tibetan leprosy patients in Gansu Province.] China Lepr. J. **6** (1990) 81–85. (in Chinese)

The levels of calcium, magnesium, copper, zinc, iron, chromium, nickel, strontium, manganese, and lead in the hair and blood of 50 cases of leprosy and 50 healthy controls have been determined with an atomic absorption photometer, and the results showed that the contents of calcium, copper, zinc, iron, and manganese in the hair of leprosy patients all are significantly lower than in controls ($p < 0.001$) and strontium level is higher ($p < 0.001$), but the levels of magnesium, chromium, nickel, and lead have no differences between them ($p > 0.05$). The levels of copper, zinc, iron, and manganese in blood of leprosy patients are significantly lower than in controls ($p < 0.001$) and chromium ($p < 0.05$), strontium and nickel ($p < 0.01$) are higher, but calcium, magnesium, and lead show no differences between the hair and the blood. The authors consider that further investigation is needed to determine whether the changes of the contents of these elements in the hair of leprosy patients are pathogenetic factors in leprosy or the results of the disease. They suggest giving Tibetan patients with leprosy some preparations of zinc, copper, iron, and manganese as complementary treatment on a trial basis.—Authors' English Abstract

Tu, Y., *et al.* [Oral and maxillofacial deformity in leprosy.] China Lepr. J. **6** (1990) 1–7. (in Chinese)

The purpose of this study was to investigate the oral and maxillofacial destruction caused directly or indirectly by leprosy and to formulate suggestions for dental-occlusal rehabilitation of the leprosy patients; 1155 cases were examined: multibacillary 842, paucibacillary 308 and 5 cases uncertain, with ages ranging from 15 to 90. The average age was 55.7; 994 cases (86.1%) were found with disfigured face and 483 cases (41.8%) suffered from sensory impairment of various-sized areas of the face. A μamp electric dental pulp test was carried out for 770 cases; 233 cases (30.2%) showed retarded pulp reaction, 291 (37.8%), no reaction. Multibacillary cases had a higher occurrence of retarded and no reaction than paucibacillary ($p < 0.01$). The diminishing pulp reaction to the electric pulp test in leprosy patients has not been previously reported. The gross destruction of oral tissues was predominantly on the palate and was always found along the midline. The statistical significance of the occurrence in the multibacillary vs paucibacillary patients was $p < 0.01$. Oral hygiene was generally poor; caries prevalence rate was 84.5% and the mean carious teeth per person was 5.23. Periodontal disease was found in 887 cases (76.8%). The tooth mortality score was 69.5% and the mean tooth loss per person was 7.7 teeth. According to the data gained from this pilot examination, 50% of patients need operative dental work, 72% need periodontal treatment and 67% need prosthodontic restoration. The authors suppose that the poor dental condition of leprosy patients is due to segregation and neglect by the dental profession.—Authors' English Abstract

Verdier, M., Denis, F., Sangare, A., Léonard, G., Sassou-Guesseau, E., Gave, A., Al-Qubati, Y., Rey, J. L., N'Gaporo, I., Doua, F. and Hugon, J. Antibodies to human T lymphotrophic virus type 1 in pa-

tients with leprosy in tropical areas. (Letter) J. Infect. Dis. **161** (1990) 1309–1310.

Human T lymphotropic virus type 1 (HTLV-1), the causative agent of adult T-cell leukemia (ATL) and non-Hodgkin's lymphoma, has been associated recently with chronic myelopathy. In 1969, cases of chronic spastic paraparesis were described in patients with leprosy in New Caledonia, a Pacific island near Australia. Considering that leprosy patients live in regions with high HTLV-1 prevalence, particularly sub-Saharan Africa, such neurologic symptoms among leprosy patients could be explained by HTLV-1 infection. A preliminary study reported high HTLV-1 antibody prevalence in a single group of leprous patients. Thus, we conducted a larger serologic survey in several tropical areas to evaluate the prevalence of HTLV-1 antibodies among leprous patients. Samples from leprosy patients (1493) and controls (1866) were collected from 1986 to 1988 in four tropical countries: the Ivory Coast, Congo, Senegal, and Yemen.

In Senegal and Yemen seroprevalence was very low in leprous patients and controls (not statistically significant). For leprous patients in the Congo and Ivory Coast, the age-adjusted mean prevalence with direct standardization was 5.6% and 5.7%, respectively, which is statistically different from respective control prevalences ($p = 0.001$). In 6 of 9 geographic zones within these countries, differences also were statistically significant ($p = 0.001$). Seroprevalences in the Congo ranged from 0.5% to 23.1% and in the Ivory Coast from 0.9% to 23.1%. The highest HTLV-1 prevalences were in leprous patients living in post-cure villages (16.4% and 23.1%); there was no apparent difference between hospitalized and ambulatory leprous patients in the Ivory Coast and Congo. Cumulative data from the Congo and Ivory Coast, countries with the highest HTLV-1 seroprevalences, showed no statistical differences between lepromatous, tuberculoid, or borderline forms, even when age-adjusted rates were considered and between lepromatous and borderline (12.9%) and borderline and tuberculoid forms (10.7%). Indeterminate and borderline forms have comparable seroprevalence rates (8.2%). Among leprous patients, men are less seropositive (not statistically significant) than women: men and women, respectively, 7.7% and 11.1% in the Congo and 9.1% and 11.0% in the Ivory Coast. HTLV-1 seroprevalence increased with age for leprous patients from 5.9% to 11.5% in the Congo and from 1.4% to 29.8% in the Ivory Coast. Similar results were observed in controls: 2.5%–9.0% and 2.1%–9.0%. Similar findings were recently described in West Equatorial Africa.

No clear explanation can be given for this higher prevalence. Iatrogenic origin could be proposed, but lepromatous and tuberculoid patients are similarly infected. Another possibility is based on the fact that virus transmission may be related to sexual activity among confined groups. The high seroprevalence, particularly in post-cure villages, supports this argument: The high endogamy rate occurring in such clustered communities could be evoked. Cohorts and family follow-ups are now underway to clarify this point.—From the letter

Zhou, S., *et al.* [Level of G6PD in the sera of 81 leprosy patients.] China Lepr. J. **6** (1990) 21–22. (in Chinese)

The examination of glucose-6-phosphate dehydrogenase (G6PD) in the sera of 81 patients with leprosy shows reduction of the enzyme only in 7 cases, being 8.64%, and normal values in all of the 37 healthy controls. The authors believe that leprosy has nothing to do with deficiency of G6PD.—Authors' English Abstract

Immuno-Pathology

Azulay, R. D. Determination of different populations of blood lymphocytes in Brazilian patients with hanseniasis. Int. J. Dermatol. **29** (1990) 35–36.

The number of B and T lymphocytes were determined in the blood of 35 Brazilian patients with leprosy: 19 lepromatous (L), 9 borderline (B), 4 tuberculoid (T), and 3 in-

determinate (I) and also in a control group of 30 normal individuals. The results, were as follows: B lymphocytes, no differences between the patients with hanseniasis and the control group; T lymphocytes, there was an evident depletion in the patients with L compared to the control group and patients with T; and the average of T lymphocytes in B and I was lower than that seen in the control group and in patients with T. Despite this alteration they approach to what is found in the patients with T and the control group.—Author's Abstract

Bloom, B. R. New strategies for leprosy and tuberculosis and for development of bacillus Calmette-Guérin into a multivaccine vehicle. Ann. N.Y. Acad. Sci. **569** (1989) 155–173.

Tuberculosis and leprosy are devastating diseases in which cell-mediated immunity is required for resistance. Each one now can be controlled by multidrug chemotherapy, although that is expensive and requires long periods of treatment for which compliance is a major problem. Through recombinant DNA technology and modern immunology, major antigens recognized by T cells are being identified that may be important for developing new diagnostic tests and candidate vaccines. Because BCG vaccine is currently the world's most widely used vaccine, and is one of the safest and least expensive and a uniquely effective adjuvant, efforts have been made to develop a genetic system in mycobacteria that permits the introduction and expression of foreign genes in BCG vaccine substrains. We have recently developed successful strategies for expressing foreign genes in BCG by integration of recombinant temperate mycobacteriophages (lysogeny) and by plasmid transformation. In the case of leprosy, since there is no animal reservoir known to be involved in transmission to man, as was the case with smallpox, the hope is to develop an effective vaccine that will eradicate the disease from the face of the earth. The possibility is being pursued that a more effective anti-tuberculosis vaccine than BCG itself can be constructed in a recombinant BCG by introduction of specific antigens of *Mycobacterium tuberculosis* recognized by appropriate T-cell populations. Finally, the use of recombinant BCG vaccines expressing protective antigens from many infectious agents for which cell-mediated immunity is required for resistance gives hope for a novel multivaccine vehicle capable of being given at birth and simultaneously immunizing against several infectious diseases.—Author's Conclusions

Bottasso, O. A., Morini, J. C., Ramos G. and Segal-Eiras, A. T lymphocyte subpopulations in leprosy patients and their relation with circulating immune complexes. Allergol. Immunopathol. **18** (1990) 91–94.

The possible relationship between circulating immune complexes (CIC) and peripheral T-lymphocyte populations was studied in 13 active multibacillary leprosy (10 lepromatous—LL—and 3 borderline lepromatous—BL) and 19 matched controls. Theophylline-resistant T cells (The-R, a lymphocyte subpopulation displaying helper activity on B cells) and total T cells were assessed by means of the E-rosette technique, with and without previous theophylline incubation, 1 hr 37°C, respectively. CIC were quantified by ^{125}I-C1q binding test.

Although leprosy patients showed a statistical nonsignificant light depression in total T cells, the remarkable variability in circulating levels of The-R T cells enabled us to separate them into two well-delineated groups (in relation to this variable $p < 0.001$) with no difference in age, sex and bacteriologic state: a) leprosy patients with The-R T cells proportionally conserved (6 LL and 2 BL); b) leprosy patients with The-R T cells proportionally depressed (4 LL and 1 BL). Patients belonging to the latter group showed the highest statistically significant levels of CIC.

Even though we do not discard an unknown factor being responsible for our findings, we believe that this inverse relationship between elevated CIC and depressed The-R circulating T cells might be representing a lower helper activity on antibody synthesis intending to reduce its excessive production.—Authors' Summary

Colston, M. J. Leprosy. In: *Vaccination Strategies of Tropical Diseases.* Liew, F.

Y., ed. Boca Raton, Florida: CRC Press, Inc., 1989, pp. 166–172.

Much progress has been made over the last few years toward understanding the basic immunological features of leprosy, toward better methods of studying the immunochemical structure of the causative organisms, and toward developing a vaccine. Trials of "first generation" vaccines are now in progress, although because of the slow way in which the disease develops it will take some years before the outcome of these trials will become known. Recent advances in the molecular biology of the organism and cellular immunology of the host have raised the possibility of developing molecularly defined "second generation" vaccines, in which the different compartments of the immune response are selectively activated. However, there is a great deal of work to be carried out to find out how this selective activation can be carried out and how such a vaccine might be most effectively delivered.—Author's Summary

Converse, P., Ottenhoff, T. H. M., Work Teklemariam, S., Hancock, G. E., Dietz, M., Becx-Bleumink, M., Wondimu, A., Kiessling, R., Cohn, Z. A. and Kaplan, G. Intradermal recombinant interleukin 2 enhances peripheral blood T-cell responses to mitogen and antigens in patients with lepromatous leprosy. Scand. J. Immunol. **32** (1990) 83–91.

Thirty-one patients with lepromatous leprosy received recombinant interleukin 2 (IL-2) intradermally in doses ranging from 10 to 30 μg. Before injection and at time intervals of 2–21 days thereafter, samples of peripheral blood mononuclear cells (PBMC) were obtained. Single or multiple injections (1–3) of IL-2 did not modify the total number of circulating lymphocytes or the number of T cells and the CD4/CD8 T-cell ratio. However, IL-2 had a pronounced influence on the [^{3}H]thymidine incorporation in response to various stimuli 4–8 days after intradermal IL-2. Stimulation indices of three- to sevenfold above pre-IL-2 levels were observed with the polyclonal activator phytohemagglutinin (PHA) and enhanced thymidine incorporation occurred in the presence of antigens to which the patients were already sensitized, such as purified protein derivative and BCG. IL-2 had no effect on the unresponsive state of lepromatous leprosy patient T cells to the antigens of *Mycobacterium leprae.*—Authors' Abstract

Cruaud, P., Potar, M. C., David, H. L., Papa, F., Torgal-Garcia, J., Maroja, F. and Orsi-Souza, A. T. IgG and IgM antibodies immunoreacting with a 2,3-diacyl trehalose-2′-sulphate in sera from leprosy patients. Zentralbl. Bakteriol. **273** (1990) 209–215.

The distribution of IgG and IgM antibodies immunoreacting with the sulfolipid I (SLI) and sulfolipid IV (SLIV) of *Mycobacterium tuberculosis* was examined in sera from leprosy patients. It was found that the immunological reactions correlated with the clinical spectrum of leprosy; and in multibacillary patients, antibody titers declined in response to successful treatment. The serological patterns were similar to the PGL-I patterns, however, the IgG responses toward the sulfolipids were predominant over the IgM responses in the case of the sulfolipid antigens.—Authors' Summary

Esquenazi, D. A., Sampaio, E. P., Moreira, A. L., Gallo, M. E. N., Almeida, S. M. R. and Sarno, E. N. Effect of treatment on immune responsiveness in lepromatous leprosy patients. Lepr. Rev. **61** (1990) 251–257.

This study was performed in order to analyze whether the immune unresponsiveness to *Mycobacterium leprae,* largely seen in lepromatous patients, persisted after discharge from treatment. Lymphoproliferation and skin tests were performed using two mycobacterial antigens (*M. leprae* and BCG) in three groups of lepromatous (BL and LL) patients grouped by treatment status. Forty-seven percent of the lepromatous patients tested acquired reactivity to *M. leprae* after long-term treatment.—Authors' Summary

Evans, D. J., Norton, P. and Ivanyi, J. Distribution in tissue sections of the human groEL stress-protein homologue. APMIS **98** (1990) 437–441.

A monoclonal antibody (ML30) raised against the 65-kDa heat-shock protein of mycobacteria showed widespread staining of sections from standard paraffin-embedded human tissues. The staining had a granular pattern and was particularly marked in cells with abundant mitochondria. Increased staining was observed in the synovial lining, histocytes, and in the endothelium of reactive and rheumatoid synovium; it was also increased in the reactive lung alveolar lining. It is suggested that the antibody identifies an epitope in mitochondria of a protein homologous with the groEL heat-shock protein of bacteria.—Authors' Abstract

Foss, N. T., Pagnano, P. M. G., Bechelli, L. M. and Simoes, A. L. Lymphocyte blastogenesis and lepromin reactivity in leprosy patients and their parents. Acta Leprol. (Genève) 7 (1990) 119–128.

To determine whether there is an inherited familial trait linked to the lymphocyte blastogenesis test (LTT), under stimulation with PHA, lepromin and *Mycobacterium leprae* in culture medium containing autologous plasma, this test was carried out in patients with the polar forms of leprosy and their parents. The lepromin reaction was also studied in the patients and their parents because, since the test is negative in lepromatous (L) patients and a greater proportion of negativity is detected among their relatives, it might be assumed that the lymphocytes of these individuals could have a lower tendency toward blastogenesis than lymphocytes of tuberculoid (T) patients and their relatives. Thirty individuals were studied, 10 of them being leprosy patients (4 L and 6 T) and the remaining their parents; 115 LTT, including control and stimulated cultures, were performed. In the limited number of patients and parents studied, the results showed that mothers of either L or T patients displayed a similarly low response to the stimulants *M. leprae* and lepromin. The lepromin reaction was negative in all L patients and positive in 3 out of 8 parents, as well as in all the T cases and their fathers. Fathers and their T descendants were lepromin positive, and there was a certain relationship between this reactivity and blastogenesis. This might suggest a possible inherited familial trait related to a relative degree of resistance. However, further evidence from studies with larger numbers of subjects are required to support this hypothesis.—Authors' Summary

Hartskeerl, R. A., van Rens, R. M., Stabel, L. F. E. M., de Wit, M. Y. L. and Klatser, P. R. Selection and characterization of recombinant clones that produce *Mycobacterium leprae* antigens recognized by antibodies in sera from household contacts of leprosy patients. Infect. Immun. **58** (1990) 2821–2827.

A *Mycobacterium leprae* expression library was constructed in the vectors EX1, pEX2, and pEX3 and screened with a pool of 19 well-absorbed sera from household contacts of leprosy patients. Twelve selected recombinants that were further characterized differed clearly from recombinants selected with murine monoclonal antibodies. Whereas the monoclonal antibodies recognized mainly six recombinant antigens, the human sera from contacts reacted with a range of different recombinant antigens. None of the contact recombinant antigens was identical or related to well-characterized antigens from *M. leprae* or other mycobacteria selected with monoclonal antibodies, including proteins of the heat-shock families. Two groups of recombinant antigens could be distinguished: one that was recognized by all sera used in the pool and one that was recognized by only a limited number of sera. These antigens, selected with sera from household contacts of previously untreated lepromatous leprosy patients, may be relevant to the immune responses during the early phase of infection with *M. leprae*.—Authors' Abstract

Hirata, T. Low-magnification electron micrography of leproma in human skin based on semithin and ultrathin sectioning. Lepr. Rev. **61** (1990) 227–236.

Low-magnification electron micrography of leprosy lesions is described. The various cell types in the lesions, the relationships to leprosy bacilli, and the distribution of bacilli in the lesions of lepromatous leprosy

are neatly demonstrated in the low-magnified pictures.—Author's Summary

Kumar, V., Narayanan, R. B., Girdhar, B. K. and Malaviya, G. N. Isolation and characterization of infiltrates in the nerves of patients with neuritic leprosy. Acta Leprol. (Genève) 7 (1990) 157–161.

A study was done on the characteristics of infiltrating cells in the nerves of 9 patients with pure neuritic leprosy by preparing a single cell suspension. The patients had no skin lesions. Histopathological examination revealed that 2 of the 9 nerves showed granulomas characteristic of tuberculoid leprosy, while the remaining 7 had features of lepromatous granulomas. In the nerves showing tuberculoid granulomas, a high proportion of lymphocytes were T cells as they formed rosettes with sheep erythrocytes and only a few percent were EAC rosette-forming cells. On the other hand, the nerves showing lepromatous granulomas contained only occasional lymphocytes which formed E and EAC rosettes. Macrophages from the granulomas of all the nerves were esterase positive, peroxidase negative, contained *M. leprae,* and did not exhibit C3 surface receptors.—Authors' Summary

Lamb, J. R., Bal, V., Rothbard, J. B., Mehlert, A., Mendez-Samperio, P. and Young, D. B. The mycobacterial GroEL stress protein: a common target of T-cell recognition in infection and autoimmunity. In: *T-Cell Activation in Health and Disease.* Feldmann, M., *et al.,* eds. London: Academic Press, 1989, pp. 93–100.

The 65-kDa protein of mycobacteria is an immunodominant antigen for both T and B lymphocytes. Sequence analysis has revealed that this protein belongs to the highly conserved family of stress proteins, related to the GroEL gene product of *E. coli,* that are present in all cells from bacteria to man. We demonstrate here that human T cells from healthy individuals and disease sites are able to recognize determinants within the 65-kDa protein that are either specific for *M. tuberculosis* or are conserved between GroEL of mycobacterial, *E. coli* or human origin. The induction of T cells that recognize with crossreactive sequences of GroEL may provide an explanation for the autoimmune phenomena often associated with infection by microbial pathogens. However, both the magnitude and the biological significance of this component of the T-cell repertoire reactive with self-stress proteins will be influenced by local environmental factors as well as the MHC haplotype of the individual.—Authors' Abstract

Lavania, R. K., Girdhar, A., Girdhar, B. K. and Desikan, K. V. Histological changes in tuberculoid leprosy after fixed duration multidrug therapy of six months. Acta Leprol. (Genève) 7 (1990) 169–174.

The length of treatment advocated for leprosy has been very long and arbitrary. During the past few years, attempts have been made to reduce the length of treatment required. World Health Organization (WHO) has recommended 6 months' therapy for paucibacillary leprosy. The present study was undertaken to see the extent of histological changes that occur with this therapy. Thirty-four untreated tuberculoid (TT/BT) leprosy patients were biopsied initially and after completion of a fixed course of this treatment. Clinically, 50% of the patients showed regression of disease activity at the end of 6 months. Morphology of the lesions was studied, in clinically active and inactive cases on completion of therapy. It was found that after 6 months' therapy, histology of the lesions was similar, whether the case was active or not. After the prescribed treatment, biopsy showed marked reduction in the extent of granuloma, along with significant increase in lymphocytes and an increase in epithelioid cells in these granulomas.—Authors' Summary

Li, H., *et al.* [The comparative study of gelatin particle agglutination test (GPAT) and PGL-ELISA.] China Lepr. J. **6** (1990) 74–78. (in Chinese)

A comparative study of GPAT and PGL-ELISA was made on 47 leprosy cases, 103 household contacts, 15 tuberculosis patients, and 100 normal persons. The results show that the positive rate for normal persons from nonendemic areas is 5%, tuber-

culosis patients is 6.7%, multibacillary and paucibacillary leprosy patients are 93.3% and 59.8%, respectively. There was a high degree of agreement in the two tests as to antibody level ($r = 0.80-0.83$, $p = 0.0005$). Although the specificity and sensitivity of GPAT is lower than PGL-ELISA, it is ample enough for field work. Therefore, it can be concluded that GPAT is of practical value for the detection of leprosy, but further studies to improve its sensitivity are required.—Authors' English Abstract

Liang, Z., *et al.* [Determination of Langerhans' cells in the skin lesions of leprosy cases with immunohistochemical technique using wheat-germ agglutinin.] China Lepr. J. **6** (1990) 16–18 (in Chinese)

The determination of Langerhans' cells in the skin lesions of 61 leprosy patients with wheat-germ agglutinin (WGA) indicates that there is no significant difference between the densities of Langerhans' cells and positivity rates of WGA in the two polar forms of leprosy, and the reaction to WGA of Langerhans' cells is specific to the active lesions of the skin in leprosy.—Authors' English Abstract

Narayanan, R. B., Girdhar, B. K., Malaviya, G. N. and Sengupta, U. In situ demonstration of *Mycobacterium leprae* in leprosy lesions using monoclonal antibodies. Immunol. Lett. **24** (1990) 179–184.

Cryostat sections of skin and nerve lesions of leprosy were stained with monoclonal antibodies recognizing *Mycobacterium leprae* antigens and indirect immunofluorescence. In both the tuberculoid and lepromatous lesions, PGL-I, 55–65-kDa, 17-kDa protein antigens and crossreactive nonprotein antigens were present; 65-kDa antigens were seen mainly in the skin lesions of lepromatous leprosy. The infiltrates in both the skin and nerve granulomas of tuberculoid and lepromatous leprosy showed membranous staining with monoclonal antibodies recognizing PGL-I and 55–65-kDa antigens. Bacilli in the lesions and the cells in the lymph node granulomas of patients with tuberculosis or the infiltrates in the lesions of tinea corporis or sections of normal skin did not show any staining with these monoclonal antibodies. These results confirm that *M. leprae* antigens are present and are expressed on the infiltrating cells of leprosy lesions.—Authors' Summary

Ottenhoff, T. H. M. and Mutis, T. Specific killing of cytotoxic T cells and antigen-presenting cells by CD4+ cytotoxic T cell clones; a novel potentially immunoregulatory T-T cell interaction in man. J. Exp. Med. **171** (1990) 2011–2024.

Mycobacterial antigens not only stimulate helper T cells that produce macrophage-activating factors, but also CD4+ and CD8+ cytolytic T lymphocytes (CTL) that lyse human macrophages. The mycobacterial recombinant 65-kDa heat shock protein (hsp) was previously found to be an important target antigen for polyclonal CD4+ CTL. Because of the major role of 65-kDa hsp in the immune response to mycobacterial as well as autoantigens, we have studied CTL activity to this protein at the clonal level. HLA-DR or HLA-DQ restricted, CD4+CD8− T-cell clones that recognize different peptides of the *Mycobacterium leprae* 65-kDa hsp strongly lysed EBV-BLCL pulsed with specific but not irrelevant peptide. No bystander lysis of B cells, T cells, or tumor cells was seen. Target cell lysis could not be triggered by PMA + Ca^{2+} ionophore alone and depended on active metabolism. Interestingly, these CD4+ CTL also strongly lysed themselves and other HLA-Class II compatible CD4+ (TCR-α/β or γ/δ) or CD8+ CTL clones in the presence of peptide, suggesting that CTL are not actively protected from CTL-mediated lysis. Cold target competition experiments suggested that EBV-BLCL targets were more efficiently recognized than CD4+ CTL targets. These results demonstrate that hsp65 peptide-specific HLA class II-restricted CD4+ T-cell clones display strong peptide-dependent cytolytic activity toward both antigen-presenting cells and, unexpectedly, CD4+ and CD8+ CTL clones, including themselves. Since, in contrast to murine T cells human T cells express class II, CTL-mediated T-cell killing may represent a novel immunoregulatory pathway in man.—Authors' Summary

Path, S. Detection of antibodies to 35 kD determinant of *M. leprae* in urine and serum of leprosy patients. Acta Leprol. (Genève) 7 (1990) 139–143.

Urine and serum samples from 67 subjects comprising 55 active cases of different types of leprosy and 12 normal controls were subjected to a monoclonal antibody-based urine antibody competition test (UACT) and serum antibody competition test (SACT), respectively. It was possible to demonstrate *M. leprae*-specific antibodies in the urine of 50% of the seropositive subjects. Urine antibody positivity was observed to the extent of 52% in BL/LL subjects, 50% in BB, and 43% in TT/BT types of leprosy.—Author's Summary

Patil, S. A., Katoch, K., Singh, K. P., Ramu, G. and Sengupta, U. Antibodies to phenolic glycolipid-1 of *Mycobacterium leprae* in urine of leprosy patients. J. Infect. Dis. **162** (1990) 281–282.

The present study was undertaken to find out whether *Mycobacterium leprae*-specific phenolic glycolipid-I (PGL-I) antibodies are excreted in the urine of leprosy patients and whether excretion in urine is related to levels in serum.

Anti-PGL-I IgG and IgM antibodies were found in the serum of 3 (23%) and 4 (31%) of 13 patients with tuberculoid leprosy, respectively; 3 (25%) and 6 (50%) of 12 individuals with borderline leprosy were positive for IgG and IgM antibodies, respectively. In patients with lepromatous leprosy, 10 (33%) and 24 (80%) of 30 were positive for IgG and IgM antibodies, respectively. All controls were negative for anti-PGL-I antibodies. Anti-PGL-I IgG and IgM antibodies were found in the urine of 7 (54%) and 3 (23%) of 13 patients with tuberculoid leprosy; 8 (67%) and 3 (25%) of 12 patients with borderline leprosy were positive for IgG and IgM antibodies, respectively. In patients with lepromatous leprosy, 25 (85%) and 11 (37%) of 30 were positive for IgG and IgM antibodies, respectively. No control was positive for anti-PGL-I antibodies. In view of the higher positivity for IgG antibody against the immunodominant and species-specific lipid antigen, PGL-I, in urine than in serum of subjects with tuberculoid leprosy, the screening of antibodies against PGL-I may be useful for diagnosis of early leprosy.—From the letter

Rastogi, N. and Frehel, C. Evidence that coating of *Mycobacterium leprae* surface antigens reduces its ability to hinder host microbicidal functions. Zentralbl. Bakteriol. **272** (1990) 337–346.

Mycobacterium leprae extracted and purified from experimentally infected armadillo was coated with rabbit sera raised against the total antigens of the following species of mycobacteria: *M. leprae, M. avium, M. bovis* BCG, and *M. fallax*. In addition, the bacteria were also coated either with serum from a lepromatous (LL) or a tuberculoid (TT) leprosy patient. The effectiveness of surface coating was verified by electron microscopy, with the aid of gold immunolabelling. The coated bacilli were phagocytized by mice bone-marrow-derived macrophages, and the phagosome-lysosome fusions (PLF) were assessed during phagocytosis using acid-phosphatase (AcPase) cytochemistry. As compared to control preparations (like-wise treated with nonimmune serum), significant but partial reversion of PLF inhibition was observed in all cases except when bacteria had been incubated with *M. fallax* antiserum (rapidly growing, nonpathogenic species). The results obtained suggest that some of the antimycobacterial antibodies may offer partial protection to the host during early events of infection by reverting the usual pattern of inhibition of PLF in infected macrophages.—Authors' Abstract

Restrepo, L. M., Barrera, L. F. and Garcia, L. F. Natural killer cell activity in patients with pulmonary tuberculosis and in healthy controls. Tubercle **71** (1990) 95–102.

Natural killer (NK) cell activity of freshly isolated peripheral blood mononuclear cells (MNC) or cells stimulated for 72 hr with 10 μg/ml of a sonicate antigen of *Mycobacterium tuberculosis* H37Rv were studied in healthy responder and nonresponder controls, as detected by lymphocyte proliferation with specific antigen, and in patients

with pulmonary tuberculosis. K-652 cells were used as targets in a 4 hr ^{51}Cr release assay. MNC from patients exhibited a significant decrease in NK function as compared with responder controls ($p < 0.02$). NK activity in responder individuals was highest 72 hr after incubation with antigen. Nonstimulated cells were not cytotoxic. MNC from healthy responder and nonresponder subjects incubated for 72 hr with antigen yielded a significant increase in the percentage NK cytotoxicity at all effector/target ratios studied ($p < 0.01$) as well as in the number of lytic units per culture ($p < 0.004$). However this increase was higher in responder individuals as compared to nonresponder subjects ($p = 0.02$). The response to antigen was not significant in the group of patients although a net increase was also observed in the whole group. Only 4 of 9 patients exhibited significant increased responses after antigenic stimulation, 3 showed moderate responses, 1 did not respond, and in a further patient a decrease was observed. The decreased NK activity could be secondary to abnormalities in the production of lymphokines by tuberculous patients. Although the role of nonspecific cytotoxic cells in tuberculosis is unknown, their alterations could contribute to the pathogenesis of the disease.—Authors' Summary

Rook, G. A. W. Mycobacteria, cytokines and antiobiotics. Pathol. Biol. (Paris) **38** (1990) 276–280.

We still do not understand the mechanism of immunity to mycobacteria in man, and convincing reproducible kill of *M. tuberculosis* by human macrophages has not been achieved. The pathways so far elucidated, involving gamma interferon, $1,25(OH)_2$ vitamin D3, and TNF release seem more likely to lead to immunopathology than to protection. Meanwhile the major problem for the clinician is the existence of "persister" bacteria, which are not eliminated by the immune response, even when therapy has greatly reduced the bacterial load. It seems unlikely that it will be possible to design antibiotics which will rapidly kill dormant persister bacilli, so new strategies for therapy may need to concentrate on modulation of the host response. The objectives of such therapies would be: a) "Reawakening" of dormant persisters, b) rapid immune recognition of persisters, c) suppression of the tissue-damaging pathway, d) enhancement of the optimally protective mechanism, but this has not yet been defined.—Author's Summary

Stanford, J. L., Bahr, G. M., Rook, G. A. W., Shaaban, M. A., Chugh, T. D., Gabriel, M., Al-Shimali, B., Siddiqui, Z., Shahin, A. and Behbehani, K. Immunotherapy with *Mycobacterium vaccae* as an adjunct to chemotherapy in the treatment of pulmonary tuberculosis. Tubercle **71** (1990) 87–93.

Forty-seven patients with adult-type pulmonary tuberculosis attending the Chest Diseases Hospital in Kuwait were given a single injection of 10^9 irradiation-killed *Mycobacterium vaccae* after 1 month of a 9-month course of chemotherapy. The patients were followed-up for 3 more months in double-blind comparison with 65 patients given an injection of saline (placebo). The immunotherapeutic injection produced a small local lesion in 44/47 patients, 18 of which ulcerated and produced small scars. Immunotherapy made no measurable difference to the bacteriological, biochemical, hematological, or radiological parameters measured. However, it was associated with significantly improved weight gain, reduced size of skin test response to tuberculin, increased lymphocyte proliferation to common mycobacterial antigens, and increased antibody levels to mycobacterial antigens. These changes in skin test and LTT responses were related and occurred in 29% of patients whose recognition of common mycobacterial antigens returned to normal. The remaining patients did not differ in these respects from those receiving placebo. The proportion of patients whose responses were improved was very similar to that achieved using the same immunotherapeutic agent in a group of treated multibacillary leprosy patients.—Authors' Summary

Suri Babu, C. S. S., Kannan, K. B., Bharadwaj, V. P. and Katoch, V. M. Lymphocyte arginase activity in leprosy—a pre-

liminary report. Indian J. Med. Res. [A] **91** (1990) 193–196.

Arginase activity was estimated in serum and lymphocytes of 22 healthy controls and 50 untreated leprosy patients across the spectrum. The patients included 21 lepromatous/borderline lepromatous (LL/BL); 20 borderline borderline/borderline tuberculoid (BB/BT) and 9 tuberculoid (TT) cases. Mean serum arginase levels were 1.51 ± 0.43, 1.41 ± 0.43, 1.24 ± 0.43 and 1.10 ± 0.026 μmoles/min/ml in LL/BL, BB/BT and TT patients and healthy controls, respectively. The lymphocyte arginase activity showed a similar increasing trend from TT to LL/BL. The mean lymphocyte arginase levels were 0.87 ± 0.31 μmoles/min/10^6 cells in healthy controls and 1.81 ± 0.40, 2.54 ± 0.60 and 5.48 ± 0.56 μmoles/min/10^6 cells in TT, BB/BT and LL/BL patients, respectively. The increasing trend especially in lymphocyte arginase levels across the spectrum of leprosy correlated with the degree of impairment in the protective cell-mediated immune response and also the extent of disease. The role of these pathophysiological alterations in relation to defect in immune response calls for investigation.—Authors' Abstract

Tausk, F. and Gigli, I. The human C3b receptor: function and role in human diseases. J. Invest. Dermatol. **94** (1990) 141S–145S.

The human C3b receptor (CR1) is a polymorphic glycoprotein which functions regulating the complement system by inhibiting the activation of C3 and C5, through its effect on their convertases, and serving as cofactor for factor I in mediating the degradation of C3b to its inactive fragment C3bi and further to C3d-g. The latter are then ligands for their respective receptors on leukocytes, CR3 and CR2. Additionally, CR1 on erythrocytes endows these cells with the capacity to deliver immune complexes (IC) to the reticuloendothelial system, resulting in their clearance from the circulation. On phagocytes, this receptor participates in the process of endocytosis of foreign particles.

There is a wide inherited variation of CR1 expression on erythrocytes (CR1/E) of different individuals. Patients with diseases which feature elevated levels of IC, such as systemic lupus erythematosus, leprosy, and AIDS, have a marked decrease of CR1/E, which may result in an altered clearance. This reduction appears to be related to disease activity, and the most probable site for CR1/E loss is during the transfer of IC to macrophages. Healthy neutrophils increase tenfold their expression of CR1 in response to the effect of chemoattractant peptides. Neutrophils from patients with AIDS display an altered response to stimulation. This defect may be of relevance in the process of endocytosis.—Authors' Abstract

Vinnik, L. A., Gerovich, L. M. and Balybin, E. S. [Angiotensin-converting enzyme in serum of tuberculosis and leprosy patients.] Probl. Tuberk. **5** (1990) 54–56. (in Russian)

Angiotensin-converting enzyme (ACE) levels in the serum of 15 patients with pulmonary tuberculosis and 9 with leprosy were measured by means of a spectrophotometric method. The serum produced from 10 blood donors was used as a control. Leprosy is accompanied by a sharp drop of ACE levels, which is attributed by the authors to a cellular immunodeficiency. In case of tuberculosis, a higher ACE level in blood often follows fibrosis formed in the lung along with a tuberculin hyperergia. The opinion that the ACE level reflects the tuberculosis or leprosy activity as well as the granulomatous tissue extension in tuberculosis patients has not been confirmed.—Authors' English Abstract

Volc-Platzer, B., Kremsner, P., Stemberger, H. and Wiedermann, G. Restoration of defective cytokine activity within lepromatous leprosy lesions. Zentralbl. Bakteriol. **272** (1990) 458–466.

Immunohistological studies of tuberculoid leprosy lesions (TT lesions) showed a dense, well-organized granuloma consisting of a central area with epithelioid and giant cells containing interferon-gamma (IFN-γ) and CD3+, CD4+ T helper/inducer ($T_{h/i}$) cells, a considerable proportion of which expressed the interleukin-2-receptor (IL-2 R). This central area was surrounded by round cells which consisted mainly of CD3+/

CD8+ T cytotoxic/suppressor ($T_{c/s}$) lymphocytes. The overlying keratinocytes (KC) were strongly positive for HLA-DR antigens on the surface, indicating high intralesional IFN-γ activity. In contrast, lepromatous leprosy lesions (LL lesions) showed a disorganized infiltrate composed by foamy cells and round cells, the latter mainly expressing the CD3+/CD8+ phenotype. IFN-γ activity could not be detected within the lesions. The KC overlying the infiltrate were consistently negative for HLA/DR reactivity pointing to a defective intralesional IFN-γ production in LL patients. Two out of four patients with LL leprosy could be sensitized with dinitrochlorobenzene (DNCB). The eliciting of DNCB skin reactions within the LL lesion led to the recruitment of new infiltrating cells; the resulting infiltrate resembled a local reversal toward the tuberculoid pole of leprosy.—Authors' Summary

Wiker, H. G., Harboe, M., Nagai, S. and Bennedsen, J. Quantitative and qualitative studies on the major extracellular antigen of *Mycobacterium tuberculosis* H37Rv and *Mycobacterium bovis* BCG. Am. Rev. Respir. Dis. **141** (1990) 830–838.

The *Mycobacterium tuberculosis* antigen 85 is a biologically important antigen. Tuberculosis patients may have strong antibodies against it, and their peripheral blood mononuclear cells respond to it with γ-interferon production and lymphocyte proliferation. Antigen 85 is actively secreted into the culture medium during culture *in vitro* and is known to bind human fibronactin. A double-antibody enzyme-linked immunosorbent assay (ELISA) for quantification of antigen 85 is described. A mouse monoclonal antibody, HYT27, was used as capture antibody in the assay. HYT27 was characterized in crossed immunoelectrophoresis and found to bind all three components of the antigen 85 complex. By radioimmunoassay, HYT27 was found to bind equally well to antigens 85A and 85B. In the ELISA assay, a rabbit anti-antigen 85 antiserum was used in the second antibody layer. The specificity of the assay was tested using several different antigen preparations. The purified BCG 85A and 85B components were compared, and there was a 10 times lower sensitivity for antigen 85A due to weaker rabbit antibodies toward this component. The purified components MPT44 and MPT59 from *M. tuberculosis* H37Rv were compared with the components of BCG and found to correspond to BCG 85A and 85B, respectively. *M. kansasii* and *M. avium* both contained partially identical antigens. Small amounts of antigen 85 were detected in *M. leprae* sonicates. Detecting antigen 85 by sensitive methods may be of great value in the early diagnosis of mycobacterial disease.—Authors' Summary

Zeis, B. M., Savage, J., O'Sullivan, J. F. and Anderson, R. The influence of structural modifications of dihydrophenazines on arachidonic acid mobilization and superoxide generation by human neutrophils. Lepr. Rev. **61** (1990) 163–170.

In this study the effects of nine dihydrophenazine derivatives, relative to clofazimine (B663), on the N-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP) stimulated release of superoxide anion and on the spontaneous generation of arachidonic acid by human neutrophils were investigated. Previous findings that the pro-oxidative activity of the agents depended largely on the substitution in position 2 of the phenazine molecule and on chlorination in the para-position of the phenyl and anilino rings were confirmed. Only riminophenazines, but not aposafranone derivatives or the imidazophenazine B621, could enhance superoxide release from activated neutrophils. The lack of chlorination of the phenyl and anilino rings could be compensated for by chlorine substitution in position 7 of the phenazine core. The priming effect of the agents on FMLP stimulated superoxide generation was completely prevented by the phospholipase A_2 inhibitor 4-*p*-bromophenacyl bromide. Furthermore pro-oxidative activities correlated closely with a stimulatory effect of the agents on arachidonic acid release. It was therefore concluded that dihydrophenazine derivatives with pro-oxidative properties can prime neutrophils for FMLP-stimulated superoxide release by modula-

tion of phospholipase A_2 activity.—Authors' Summary

Zhang, X., *et al.* [Antibody against PG1 and immunocomplex in the sera of leprosy patients with ENL.] China Lepr. J. **6** (1990) 18–21. (in Chinese)

The examination of anti-PG1 antibody and immunocomplexes in the sera of 32 leprosy patients with ENL and of 56 cases without ENL showed a significant difference ($p < 0.05$), i.e., in the former the level of the antibody decreased and that of the immunocomplex increased. After cure of ENL, the levels were restored to those before ENL. The authors point out that the changes in the contents of antibody and immunocomplex in the sera of leprosy patients have some effect on the occurrence of ENL, but still cannot explain its pathogenesis.—Authors' English Abstract

Microbiology

Andrew, P. W. and Boulnois, G. J. Early days in the use of DNA probes for *Mycobacterium tuberculosis* and *Mycobacterium avium* complexes. In: *Gene Probes for Bacteria.* London: Academic Press, 1990, Chapter 7, pp. 179–203.

A variety of approaches have been adopted for the isolation of DNA probes for the detection and identification of mycobacterial species. These range from total mycobacterial genomic DNA, randomly cloned fragments of DNA, and specifically designed, synthetic oligonucleotides representative of species-specific segments of rRNA. These probes have been used in a variety of hybridization protocols and several ways adopted to detect and quantitate hybrids. On the basis of the available evidence, it is not possible to make a rational decision as to the optimal route to take in probe design and use. An open mind is crucial if the promise of automated, rapid, and sensitive detection and identification of mycobacteria using DNA probes is to be realized. Progress to date gives cause for guarded optimism.—Authors' Summary

Bock, K., Hvidt, T., Marino-Albernas, J. and Verez-Bencomo, V. An n.m.r. and conformational analysis of the terminal trisaccharide from the serologically active glycolipid of *Mycobacterium leprae* in different solvents. Carbohyd. Res. **200** (1990) 33–45.

The ^{1}H- and ^{14}C-n.m.r. spectra of allyl 2-*O*-[4-*O*-(3,6-di-*O*-methyl-β-D-lucopyranosyl)-2, 3-di-*O*-methyl-α-L-rhamnopyranosyl]-3-*O*-methyl-α-L-rhamnopyranoside, a glycoside of the terminal trisaccharide found in the phenolic glycolipid I from *Mycobacterium leprae,* and those of the two component disaccharides, allyl 4-*O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-2,3-di-*O*-methyl-α-L-rhamnopyranoside and allyl 2-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-3-*O*-methyl-α-L-rhamnopyranoside have been assigned completely by 1D and 2D techniques. The preferred conformations, determined by chemical shift and n.O.e. studies, were different in D_2O, CD_3OD, and $CDCl_3$. The preferred conformation of the trisaccharide accorded with the results of hard-sphere exo-anomeric (HSEA) calculations.—Authors' Abstract

Chakrabarty, A. N., Dastidar, S. G., Das, S. and Chandra, A. K. Cultivation in vitro of acid-fast nocardioform chemoautotrophic bacteria from mouse foot-pads infected with human strains of leprosy bacillus. Indian J. Lepr. **62** (1990) 169–179.

Four acid-fast nocardioform bacteria could be isolated and cultivated as pure cultures *in vitro* from mouse foot pads (MFP), which were infected with serially passaged strains of human leprosy bacillus; the liquid mineral medium, such as paraffin urea minimal (PUM), paraffin gelatin minimal (PGM), gelatin minimal (GM), and GM agar (GMA) slants containing only simple sources of C and N were used, just like the human and the armadillo isolates of these organisms reported earlier. Morphologically,

metabolically and enzymologically, these were closely related to the previous ones and were also chemoautotrophic in nature. Serologically there appears to be a heterogenicity in these isolates, i.e., some of them showing higher affinity to nocardio forms, others showing significant binding to several mycobacteria. Normal (uninfected) mouse foot pad harvests were not found to harbor such organisms.—Authors' Abstract

Costa, H. C., de Souza, L. C. D., Martini, J. P. D., Opromolla, D. V. A. and del Giudice, A. C. [A comparative study of the various staining methods for mycobacteria.] Hansen. Int. **13** (1988) 37–41. (in Portuguese)

The present paper intends to show what coloration method for mycobacteria is the better. Samples was assessed and processed by hot Ziehl-Neelsen, cold Ziehl-Neelsen, Ziehl Gabbet and Ziehl-Neelsen with alkaline methylene blue. After microscopy by five different persons the method selected was the cold Ziehl-Neelsen.—Authors' English Abstract

Hartskeerl, R. A., Stabel, L. F. E. M., Hermans, C. J., Klatser, P. R. and Thole, J. E. R. Nucleotide and deduced amino acid sequence of a *Mycobacterium leprae* 12K protein. Nucleic Acids Res. **18** (1990) 1294.

Previously, Shinnick, *et al.* reported the sequence of a *M. tuberculosis* 12K protein which was about 43% homologous with the GroES protein of *Escherichia coli.* With two monoclonal antibodies, F116-13 and F116-14 directed to a 12K antigen from *M. leprae* (A. H. J. Kolk, manuscript in preparation), we selected a number of recombinant phages from the λgt11::*M. leprae* library. The selected recombinants appeared to encode two different 12K proteins as fusion products with β-galactosidase. The complete genes were obtained from a cosmid library of *M. leprae.* The sequence of one of them, here designed as *mla12A,* is presented.—From the article

Hunter, S. W., Rivoire, B., Mehra, V., Bloom, B. R. and Brennan, P. J. The major native proteins of the leprosy bacillus. J. Biol. Chem. **265** (1990) 14065–14068.

This study addresses a major obstacle to vaccine development for leprosy, the isolation and characterization of the native protein antigens of the leprosy bacillus. *Mycobacterium leprae* harvested from armadillos was subjected to a simple fractionation protocol to arrive at the three major subcellular fractions, cell walls, cytoplasmic membrane, and soluble cytoplasm. The application of extensive detergent phase separations to membrane fractions allowed removal of lipoarabinomannan and the mannosyl phosphatidylinositols, and the recognition and purification of two major membrane proteins (MMP) of molecular mass 35 kDa (MMP-I) and 22kDa (MMP-II); recovery of these proteins was about 0.5 mg each per g of *M. leprae.* MMP-I is *N*-blocked and is perhaps a lipoprotein. End group analysis on MMP-II indicates a new protein. Three major cytoplasmic proteins (MCP) of molecular mass 14 kDa (MCP-I), 17 kDa (MCP-II), and 28 kDa (MCP-III) were also recognized. MCP-I, the most abundant protein in *M. leprae,* represents 1% of the bacterial mass. End group analysis of the first 30 residues and immunoblotting studies demonstrate sizeable structural homology to a protein from *M. tuberculosis* but immunological distinctiveness. MCP-I, which also occurs in a highly immunogenic peptidoglycan-bound form, is a primary candidate for future vaccine development. The cell walls of *M. leprae* are also characterized by one major extractable protein, also of molecular mass 17 kDa. Thus, the major antigens of the leprosy bacillus, protein and carbohydrate alike, are now nearer to complete definition.—Authors' Abstract

Liesack, W., Pitulle, C. and Stackebrandt, E. Development of a highly specific diagnostic 23S rDNA oligonucleotide probe for *Mycobacterium leprae.* Lett. Appl. Microbiol. **11** (1990) 96–99.

A 21-mer DNA oligonucleotide probe targeting the 23S rRNA of *Mycobacterium leprae* was developed and its high specificity demonstrated by dot-blot hybridization. Even under relaxed hybridization and washing conditions (20°C below T_m) the

probe was highly selective in that positive signals were only detected with *M. leprae*, about half of the slow-growing and one of the fast-growing mycobacteria and *Gordona bronchialis*. At more stringent washing temperatures (16°C below T_m) only the rRNA of *M. leprae* was detectable.—Authors' Abstract

Plikaytis, B. B., Gelber, R. H. and Shinnick, T. M. Rapid and sensitive detection of *Mycobacterium leprae* using a nested-primer gene amplification assay. J. Clin. Microbiol. **28** (1990) 1913–1917.

By using a set of four nested oligonucleotide primers, a two-step polymerase chain reaction assay for the detection and identification of *Mycobacterium leprae* that does not require the use of radioactively labeled hybridization probes was developed. The nested-primer procedure amplified a 347-base-pair product from *M. leprae* genomic DNA. No amplification products were produced from DNAs of 19 other *Mycobacterium* species, 19 non-*Mycobacterium* species, mouse cells, or human cells. Minor amplification products were observed with three additional *Mycobacterium* species, i.e., "*M. lufu*," *M. simiae*, and *M. smegmatis*. These products were easily distinguished from the *M. leprae* product by size and restriction enzyme cleavage patterns. The assay could amplify the 347-base-pair product from samples containing as little as 3 fg of *M. leprae* genomic DNA—the amount of DNA in a single bacillus. The assay also amplified target sequences in crude lysates of *M. leprae* bacilli isolated from tissue biopsy specimens from infected animals and humans. The entire assay, from sample preparation to data analysis, can be completed in less than 8 hr.—Authors' Abstract

Thangaraj, H. S., Lamb, F. I., Davis, E. O., Jenner, P. J., Jeyakumar, L. H. and Colston, M. J. Identification, sequencing, and expression of *Mycobacterium leprae* superoxide dismutase, a major antigen. Infect. Immun. **58** (1990) 1937–1942.

The gene encoding a major 28-kilodalton antigen of *Mycobacterium leprae* has now been sequenced and identified as the enzyme superoxide dismutase (SOD) on the basis of the high degree of homology with known SOD sequences. The deduced amino acid sequence shows 67% homology with a human manganese-utilizing SOD and 55% homology with the *Escherichia coli* manganese-utilizing enzyme. The gene is not expressed from its own promoter in *E. coli* but is expressed from its own promoter in *M. smegmatis*. The amino acid sequences of epitopes recognized by monoclonal antibodies against the 28-kilodalton antigen have been determined.—Authors' Abstract

Williams, D. L., Gillis, T. P., Booth, R. J., Looker, D. and Watson, J. D. The use of a specific DNA probe and polymerase chain reaction for the detection of *Mycobacterium leprae*. J. Infect. Dis. **162** (1990) 193–200.

A DNA probe encoding ~80% of the 18-kDa protein gene of *Mycobacterium leprae* was isolated and tested for specificity by assessing hybridization of the probe to genomic DNA from taxonomically related and unrelated DNA samples. The 360-base-pair (bp) probe was specific for *M. leprae* DNA and did not hybridize with genomic DNA from 18 species of bacteria nor with DNA from human, murine, and armadillo sources. Oligonucleotide primer were synthesized corresponding to the 5′ and 3′ ends of the 360-bp fragment to yield a fragment of similar size on amplification of *M. leprae* DNA by the polymerase chain reaction (PCR). A simple procedure for DNA extraction from *M. leprae*-infected tissues was developed that provided suitable template DNA for amplification. The PCR test was specific for *M. leprae* DNA from human and murine sources and detected *M. leprae* DNA in biopsies from leprosy patients and from control and uninfected human skin biopsy preparations seeded with as few as 100 *M. leprae*.—Authors' Abstract

Experimental Infections

Coelmo, A. A. M., Gontijo Filho, P. P., Fonseca, L. deS., da Silva, M. G. and Costa, H. C. [Mycobacteria isolated from armadillos (*Dasypus novemcinctus*) inoculated with *Mycobacterium leprae.*] Hansen. Int. **13** (1988) 42–46. (in Portuguese)

The authors report the isolation of two mycobacteria from armadillo livers and spleens, inoculated with *Mycobacterium leprae* in the Kato medium. They discuss the results.—Authors' English Abstract

Job, C. K., Drain, V., Truman, R. W., Sanchez, R. M. and Hastings, R. C. Early infection with *M. leprae* and antibodies to phenolic glycolipid-I in the nine-banded armadillo. Indian J. Lepr. **62** (1990) 193–201.

Nine-banded armadillos were intravenously infected with 10^9 *Mycobacterium leprae.* IgM antibodies to PGL-I were evaluated three times during the 6 months before and every 2 months after the infection. A thorough autopsy examination was done on animals that died or were sacrificed at intervals of 3, 4, 6, 12, 15 and 18 months after the infection. Three animals which had acquired the infection in the wild, and one experimentally infected animal showed significant increases in antibody levels corresponding to their high bacterial load. In the other five experimentally infected animals, *M. leprae* infection was established in the cells of the reticuloendothelial system (RES) long before the IgM antibody levels to PGL-I became positive. It is possible that in human leprosy also *M. leprae* may enter and multiply in the RES initiating antibody production during the incubation period before clinical disease with neuritis becomes manifest.—Authors' Abstract

Karanth, S. S., Springall, D. R., Kar, S., Gibson, S. J., Royston, J. P., Banerjee, D. K. and Polak, J. M. Time-related decrease of substance P and CGRP in central and peripheral projections of sensory neurones in *Mycobacterium leprae* infected nude mice: a model for lepromatous leprosy in man. J. Pathol. **161** (1990) 335–345.

We have previously shown the depletion of cutaneous calcitonin gene-related peptide (CGRP)- and substance P-containing nerves in human leprosy. The aims of this study were to investigate the temporal effects of leprosy on nerves in skin and spinal cord. Tissues were taken from nude mice, 6 and 12 months after inoculation of *Mycobacterium leprae* into the hindfoot pads, and from ape-matched controls. Sections were immunostained with antisera to substance P or CGRP. After 6 months of infection, substance P- and CGRP-immunoreactive nerves were reduced in skin from all body area; by 12 months, the reduction was substantially greater. In the spinal cord, sensory fibers immunoreactive for substance P had decreased compared with controls at 6 and 12 months [by 60% (0.022 mm^2) and 80% (0.048 mm^2), respectively, $p < 0.001$], as with CGRP [30% (0.018 mm^2, $p < 0.02$) and 40% (0.028 mm^2, $p < 0.01$), respectively]. CGRP immunoreactivity was completely absent in motor neurones after 12 months of infection. Loss of CGRP- and substance P-immunoreactive fibers in skin and spinal cord, and CGRP in motor neurones, is in accord with impaired pain sensation and muscle weakness in leprosy.—Authors' Summary

Lemieux, S., Gosselin, D., Lusignan, Y. and Turcotte, R. Early accumulation of suppressor cell precursors in the spleen of *Mycobacterium lepraemurium*-infected mice and analysis of their *in vitro*-induced maturation. Clin. Exp. Immunol. **81** (1990) 116–122.

Spleen cells harvested from mice infected intraperitoneally with *Mycobacterium lepraemurium* 11–17 weeks prior to harvest acquired the capacity to inhibit concanavalin A (ConA) induced proliferation of normal spleen cells when precultured for up to 24 hr in mitogen-free medium. The *in vitro*-induced suppressor activity correlated with the length of the preculture period, the time postinfection and the infecting dose. These

findings were interpreted as an indication that suppressor-cell precursors accumulated in the spleen of infected mice during the early phase of the disease. The interaction of infection-dependent, adherent suppressor-cell precursors and infection-independent, nonadherent regulatory cells is necessary for the suppressor activity to develop. Both the cells which transmit the inductive signal and the precursor cells which mature into active suppressor cells are radiosensitive; whereas suppressor activity itself is a function of radioresistant adherent cells. Preculture of cells for a short period, before they were cocultured with ConA-stimulated normal spleen cells, allowed the detection of suppressor cells before they were deleterious to the infected host and also turned out to be a relevant *in vitro* model for characterization of suppressor cell development during *M. lepraemurium* infection.—Authors' Summary

McDermott-Lancaster, R. D. and McDougall, A. C. Mode of transmission of *M. leprae* infection in nude mice. Int. J. Exp. Pathol. **71** (1990) 689–700.

Athymic (nude) mice were experimentally infected with *Mycobacterium leprae* via the alimentary and respiratory tracts and through the skin. Animals were allowed to inhale aerosols of *M. leprae* or had bacilli instilled into the nostrils or directly into the lungs. Others were fed *M. leprae* by gastric tube or had bacilli placed on the tongue. Attempts were also made to transmit *M. leprae* from infected foot pads by *Aedes aegyptii* mosquitoes. The most successful infections resulted from nasal instillations and from bacilli inoculated onto the tongue surface: in these cases heavy systemic infections occurred. *M. leprae* was also shown to survive passage through the alimentary tract and bacilli recovered from the feces were capable of causing infection in recipient nude mice. The possible epidemiological significance of these findings for the transmission of leprosy in man is discussed.—Authors' Summary

Roch, F. and Bach, M.-A. Strain differences in mouse cellular responses to *Mycobacterium lepraemurium* and BCG subcutaneous infections. I. Analysis of cell surface phenotype in local granulomas. Clin. Exp. Immunol. **80** (1990) 332–338.

C57BL/6, BALB/c and CBA mice were subcutaneously infected with either *Mycobacterium lepraemurium* (MLM) or BCG, and studied for bacillary growth, granuloma size of infected foot pads and draining lymph nodes (DLN), and DLN cell surface phenotype. Whereas, BCG-infected mice controlled the infection and developed early and large granulomas, MLM-infected mice exhibited major strain variations in their resistance to the infection, as well as in the granuloma size and kinetics. C57BL/6 mice, highly resistant, displayed early and regressive granulomas; BALB/c mice showed lower resistance and early granulomas that grew continuously; CBA mice, highly susceptible, developed late, soft, phagocyte-rich granulomas. Important strain differences in lymph node lymphocyte subset distribution could be observed prior to any infection: C57BL/6 mice displayed higher B-cell percentages than both of the other strains and BALB/c mice showed the highest CD4/CD8 ratios, followed by CBA and C57BL/6 mice. BCG and MLM infections both induced similar changes of these parameters in all three strains: that is a decrease of the B-cell percentage and a decrease of the CD4/CD8 ratio, and the strain differences observed in uninfected mice persisted. On the other hand, DLN cells stimulated by the infecting bacillus and interleukin 2 also displayed an increase of the CD8 T-cell percentage as compared with normal lymph node cells, but this phenomenon was much less pronounced in BALB/c mice, whether infected by MLM or BCG, and in MLM-infected CBA mice, than in BCG- or MLM-infected C57BL/6 (B6) mice. Thus, the ability of C57BL/6 mice to generate an early and persistent CD8 T-cell response to mycobacteria may contribute to their resistance to MLM.—Authors' Summary

Shi, Z., *et al.* [Phacogenic endophthalmitis in an armadillo experimentally infected with *M. leprae.*] China Lepr. J. **6** (1990) 86–88. (in Chinese)

In 130 eyes of 68 armadillos infected with *Mycobacterium leprae,* in addition to the

lesions related to the leprosy infection, one eye with phacogenic endophthalmitis was found. In this eye, the lens capsule was ruptured and the lens matter was released outside the capsule. An allergic inflammatory reaction around the lens matter mixed with foreign body reaction and cholesterol crystal formation and cyclitis membrane formation were present. No distinct evidence of a previous trauma was seen, and so the cause of the rupture of the lens was not determined. In the other eye of the same animal, focal ball-like thickenings of the lens capsule and pavement of the endothelial cells on the anterior angle and the anterior surface of the peripheral ⅕ iris were seen. The focal lens capsule thickening had also been seen in other eyes in this series. These pathologic changes encountered by chance in so small a number of armadillo eyes were of interest. They seemed not related to the *M. leprae* infection. The pathology of these lesions was similar to that seen in human eyes.—Authors' English Abstract

Vadiee, A. R., Harris, E. and Shannon, E. J. The evolution of antibody response in armadillos inoculated with *Mycobacterium leprae.* Lepr. Rev. **61** (1990) 215–226.

Plasma from 30 armadillos (*Dasypus novemcinctus*) was collected prior to inoculation and at approximately 3-month intervals for a period of 1–3 years. These animals were inoculated intravenously with $6.1 \times 10^8 \pm 2 \times 10^8$ ($x \pm SD$) armadillo-derived *Mycobacterium leprae.* These samples were analyzed for antibodies of IgM and IgG class to phenolic glycolipid-I (PGL-I) and to sonicated *M. leprae* components using ELISA and immunoblotting techniques, respectively. We had previously observed among a group of 11 armadillos that some animals produced and maintained a high IgG antibody response to PGL-I. In this study, an animal's ability to produce and maintain an elevated IgG anti-PGL-I response was significantly correlated with its ability to delay dissemination of the infection and its ability to survive longer. When the animals were moribund, a significant decrease in the IgG anti-PGL-I absorbance value was observed. The detection of PGL-I in the plasma samples collected from moribund armadillos suggested that high concentrations of PGL-I in the plasma may have contributed to a drop in absorbance values by the formation of non-lattice-type immune complexes *in vivo.* As detected by immunoblotting, the IgM and IgG responses to antigens derived from sonically disrupted *M. leprae* were directed toward molecules with broad bands of immunoreactivity ranging from 21- to 45-kDa. There were no distinguishing features of these antibody responses among armadillos as was evident with the IgG anti-PGL-I responses.—Authors' Summary

Epidemiology and Prevention

Abel, L., Cua, V. V., Oberti, J., Lap, V. D., Due, L. K., Grosset, J. and Lagrange, P. H. Leprosy and BCG in southern Vietnam. (Letter) Lancet **1** (1990) 1536.

In Vietnam the prevalence of leprosy is about 1.5 per 1000, 30%–70% of cases (depending on the region) being lepromatous, the most infectious form. We have done a case-control study of the protective efficacy of BCG in southern Vietnam. BCG seems to be protective against nonlepromatous leprosy in southern Vietnam, as observed in other areas. The efficacy (80%) is close to that reported in the Uganda study; however, more patients are needed for a reliable estimate. BCG had no protective efficacy against lepromatous leprosy, which is consistent with the immunological status of the two subtypes of leprosy patients considered; BCG is not expected to be effective in lepromatous patients, who have defective antimycobacterial cellular immunity. These conclusions, have important implications for the control of leprosy in countries with a high proportion of lepromatous cases and indicate that the distinction between lepromatous and nonlepromatous is important in the evaluation of the protective role of BCG.—From the letter

Brightmer, M. I. New cases of leprosy in the Cross River Region, Nigeria. Lepr. Rev. **61** (1990) 273–281.

Rates of leprosy cases newly reporting during 1986 are examined for a region of southeastern Nigeria. Figures reveal that in part of the region which was designated in 1987 as a new state, half of the administrative units had new case reporting rates higher than in adjacent areas, while the other half had very few cases reporting in 1986. Possible explanations are offered and the implications of the pattern for leprosy control in the new state are examined.—Author's Summary

Cen, Y., *et al.* [Trial forecast of incidence with grey calculation in leprosy.] China Lepr. J. **6** (1990) 23–26. (in Chinese)

The incidence of leprosy each year in the period 1956 to 1981 in Zhanjiang City of Guangdong is forecast with the equation GM (1, 1) of grey calculation, and the result is compared with the results of dynamic number sequence fitting and exponential curve equation. The authors found that forecasted value according to the grey calculation has a better fit with actual value; its short-term forecasting effect is better and the long-term has a larger error, but the error is less than that of dynamic number sequence fitting and exponential curve equations.—Authors' English Abstract

Rao, P. S. and Sirumban, P. Screening of registered leprosy cases and its effects on prevalence rate. Indian J. Lepr. **62** (1990) 180–185.

Prevalence rates in 6 endemic districts in Andhra Pradesh, India, with a population of 168.71 lakhs (1981 census), were studied before and after screening of registered cases. The screening was carried out as part of multidrug treatment project implementation. After such screening, a sharp fall in the registered prevalence rate, by 26.2% on the average, was observed in all the districts. About 34.8% of the total cases were declared as released from control. The implication of these findings regarding registered cases fit for such release and the overall registered prevalence rates in the country must be kept in mind.—Authors' Abstract

Sekkat, A., Sedratti, O., Bellahmer, F., Zaoui, F., Fikri, M., Khaldi, M., Filali, B., Rollier, R., Alaoui, B., D'Khissy, L., Adnani, M. A. and Rollier, B. [Synthesis of seven years of systematic surveys on leprosy in Morocco.] Acta Leprol. (Genève) 7 (1990) 129–138. (in French)

Between 1980 and 1987, 12 systematic surveys were made on a population of 254,979 people, of whom 236,868 were actually examined (92.61%); 422 suspected cases were identified, i.e., a global detection rate of 1.66‰ of which only 241 reported to Aïn-Chock Hospital for further tests (55%). Out of these 241 suspected cases, 217 proved as having leprosy, i.e., a 90% correlation between the clinical suspicion and the biological identification. The 181 suspected cases who never reported to the hospital and the 16 leprosy patients whom we lost sight of constitute as a whole 46.68% of the suspected cases first identified. This shows an obvious lack of coordination between the local authority and the medical service. The 185 confirmed cases of leprosy are shown in the table below and compared with those of the Central Statistical Office.

Cases	Survey finding	CSO
65 lepromatous	36.15%	75.37%
88 tuberculoid	47.57%	30.33%
32 indeterminate	17.18%	8.99%

The active survey mainly reveals the tuberculoid type, which can develop unnoticed and which does not induce the patient to seek medical advice. The distribution by sex and age does not show a significant difference from that of the Central Statistical Office. The teams' operational efficiency, although satisfactory, could be improved by reducing the daily number of individuals examined.—Authors' English Summary

Tonglet, R., Eeckhout, E., Deverchin, J., Bola, N., Kivits, M. and Pattyn, S. [Evaluation of an antileprosy program in Ueles (1975–1989).] Acta Leprol. (Genève) 7 (1990) 145–152. (in French)

FOPERDA, who took over and continued the work initiated in 1924 by the Congo Red Cross, is responsible for the program of fight against leprosy in the Ueles region

(Zaire). Important results have been obtained since 1975 in the framework of a specialized medical service. These results are exposed and discussed here. The evolution of the endemic leprosy in the region under survey allows one to contemplate new trends for the pursuit of the program in the coming years (controlled integration within polyvalent health services).—Authors' English Summary

Warndorff, D. K. and Warndorff, J. A. Leprosy control in Zimbabwe: from a vertical to a horizontal programme. Lepr. Rev. **61** (1990) 183–187.

In Zimbabwe leprosy control services were re-established in 1983, following the war of independence. Its main objectives were the nation-wide implementation of multiple drug treatment (MDT) and the integration of leprosy control into the general health services. The MDT regimens have led to a rapid reduction of the prevalence of leprosy. At the beginning of 1989, 357 patients were on treatment and 1299 under follow-up. Six-hundred twenty-seven new cases have been detected since 1984, which represents an annual case detection rate of 1.6 per 100,000. This seems a fair reflection of the incidence rate, since the new cases are characterized by a minority of patients under the age of 15 (4%) and a lepromatous percentage of 50%. Since the budget of the program has remained unchanged, integration of leprosy control into the general health services has become imperative. However, this transition is now hindered by a number of obstacles that were not foreseen at the start of the program, because they are in measure corollaries of the successful implementation of MDT. Most of the problems that leprosy control is facing in Zimbabwe could have been avoided if instruction in leprosy had been introduced into the curricula of the (para) medical training schools 20 years ago.—Authors' Summary

Zhou, S., *et al.* [Analysis of endemicity of leprosy in Hubai Province.] China Lepr. J. **6** (1990) 11–14. (in Chinese)

In Hubai Province, 13,804 cases of leprosy have been accumulated since 1949, of which 9526 cases (74.1%) have been cured; there remained 1324 active patients by 1986. The prevalence decreased from 0.17/1000 in 1956, at the highest, to 0.03/1000 by 1986, and the incidence from 4.25/100,000 in 1949, at the highest, to 0.03/100,000 at the same time, thus reaching the goal of controlling leprosy worked out by the Ministry of Public Health with both measures continuing to decline. The main measures taken in leprosy control are the use of various surveys for detection of patients as early as possible and the treatment of all detected patients.—Authors' English Abstract

Rehabilitation

Berhe, D., Haimanot, R. T., Tedla, T. and Taddesse, T. Epidemiological pattern of leprosy in Ethiopia: a review of the control programmes. Lepr. Rev. **61** (1990) 258–266.

Leprosy control started in a limited area of Ethiopia in 1956. Extended coverage of the country was achieved in the early 1970s. Review of the data from the control projects since 1976 revealed that leprosy is a disease of the Ethiopian highlands where prevalence rates as high as 7 per thousand have been recorded in some provinces, while the cumulative national average for the last 13 years was 2.6 per thousand. The paucibacillary form was predominant. However, unlike other African countries, a relatively high proportion of multibacillary leprosy was found in Ethiopia. The male-to-female ratio was 2:1 with the highest prevalence in the 15–44 years age bracket. Detection rates for new cases have shown a gradual decline since 1982, a year before multiple drug therapy (MDT) was introduced into the country. For the last 5 years the number of new cases has stabilized at 4700/year. These trends probably reflect a general reduction in the prevalence of leprosy in the country, while the conspicuous decline in 1982 is

most likely related to discharge of cases during screening before MDT. The new villagization policy of Ethiopia, with its effective reorganization of the populations, is believed to make control programs and supervision of MDT easier and presumably more effective. Similarly, more reliable prevalence and incidence studies could be undertaken with success.—Authors' Summary

Bourrel, P. [Surgical treatment for neurotrophic lesions of leprosy: application to other types of neuropathy.] Acta Leprol. (Genève) **7** (1990) 175–191. (in French)

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

Duerksen, F. and Virmond, M. Carvable silicone rubber prosthetic implant for atrophy of the first web in the hand. Lepr. Rev. **61** (1990) 267–272.

Muscular atrophy of the first web space in the hand is a common finding following ulnar nerve palsy, and this deformity is very stigmatizing among leprosy patients in some countries and cultures. We present our experience with the carvable, soft-silicone rubber block implant to correct this deformity. We discuss the procedure, results and advantages over other techniques. Fifteen operations were performed at the Lauro de Souza Lima Research Institute, Bauru, Brazil, during a period of 6 years. One complication was encountered due to an implant that was too large. The results were considered good in 12 instances and fair in 3.—Authors' Summary

Lopez del Rincón, V., Garcia, S. and Diaz, J. M. [Some psychosocial and epidemiologic characteristics of the leprosy patient in Artemisa Municipality.] Rev. Cubana Med. Trop. **42** (1990) 53–68. (in Spanish)

Psychosocial and hygienico-epidemiologic characteristics of the prevalence of leprosy in Artemisa Municipality, Havana Province, Cuba, were studied and compared with a control group. In relation to psychological stability, they are normal individuals. The general personal profile shows a personality structure disposed to neuroticism. The hygienic conditions are good. The majority of patients do not feel outcast and they have been incorporated into social and labor life. There are no mutilating disabilities in these patients. All those who need rehabilitation have it. The patients in this municipality know the main aspects of the disease.—Authors' English Summary

Shibata, T., Tada, K. and Hashizume, C. The results of arthrodesis of the ankle for leprotic neuroarthropathy. J. Bone Joint Surg. **72A** (1990) 749–756.

Twenty-four patients who had arthrodesis of one or both ankles for leprotic neuroarthropathy were followed for an average of 9 years and 5 months. At operation, after the removal of cartilage, joint debris, and sclerotic bones, the ankle joint was transfixed with a Küntscher intramedullary nail, and staples or Kirschner wires were used to control rotation. Fusion of bone was obtained in 19 (73%) of the 26 ankles. Failure to obtain fusion was due to postoperative infection in 4 patients, deficiency of the site of arthrodesis in 1 patient, and refracture through the site of fusion in 2 patients. When arthrodesis was successful, additional neuroarthropathic destruction of the mid-tarsal joint was halted, and the preoperative clinical symptoms of dull pain, local warmth,

swelling, and instability were relieved.—Authors' Abstract

Virmond, M. and Duerksen, F. [The actual situation of surgery and the global treatment of hanseniasis.] Hansen. Int. **13** (1988) 34–36. (in Portuguese)

In the last decades the neural component of Hansen's disease has achieved its place of prime importance among other manifestations of the disease. Provided that there is a close relationship between neural involvement and deformities and that hitherto antileprosy drugs are able only to kill and prevent bacillary growth and not able to interrupt the immunological features of the disease, we can expect a significant load of patients with some degree of disability including those in regular treatment. Surgery plays an important role in control programs since it has not just the single aim to restore lost function but also to prevent further damage and to improve patient's self-confidence.—Authors' English Abstract

Watson, J. M. Disability control in a leprosy control programme. (Editorial) Lepr. Rev. **60** (1989) 169–177.

This editorial begins with a quotation from the *Sixth Report of the WHO Expert Committee on Leprosy* to the effect that "prevention and management of impairments and disabilities, which have long been recognized as essential components of leprosy control programmes, should be implemented effectively." It goes on to consider the 6 specific managerial steps recommended by this Committee for the practical implementation of disability prevention and management at peripheral level: 1) "the team leader, normally a physician, accepts responsibility for prevention of primary and secondary impairments and disability as part of his or her responsibility for patient care"; 2) "specific, limited, measurable objectives are set for preventing and limiting disability, and activity plans based on these objectives are formulated"; 3) "impairment and disability records are included in the clinical recording system"; 4) "arrangements are made for the provision of protective footwear and other aids"; 5) "patients are instructed in self-care and in behaviour designed to prevent further disability"; and 6) "staff are trained to implement the disability prevention programme, to teach patients self-care and to monitor and support the practice of self-care by patients." Three tables and figures in this publication deal with: 1) action objectives and evaluation measurement; 2) a "disability section of an individual patient record"; and 3) a "simple disability review"—which makes provision for recording changes in disability status since the previous year (an element that has not been fully recognized in previous systems).—From *Trop. Dis. Bull.*

Zhang, F., *et al.* [Survey of disability in leprosy.] China Lepr. J. **6** (1990) 68–71. (in Chinese)

Two-thousand-seventy cases of leprosy with 1754 cures have been examined for their disabilities. The disability rate is 75.1% in multibacillary and 60.6% in paucibacillary cases. The higher disability rates in the authors' opinion are due to the fact that prevention of disability and rehabilitation have not been taken seriously for a long time in the past as well as to some social factors. The authors think that rehabilitation for leprosy is a task of top priority in our country.—Authors' English Abstract

Other Mycobacterial Diseases and Related Entities

Al-Aska, A. K., Chagla, A. H., Wright, S. G., Al-Mofleh, I., Al-Tameem, M. and Al-Shareef, N. Paradoxical response during chemotherapy of tuberculous cervical lymphadenitis: a report of four cases. Saudi Med. J. **11** (1990) 111–112.

Of 64 cases of tuberculous cervical lymphadenitis treated in Riyadh with antituberculosis drugs, 4 showed enlargement of the affected cervical nodes during the first few weeks of treatment. The mechanisms involved are unclear but may include hypersensitivity to a heavy antigenic load. The nodes eventually regressed and there were no relapses.—C. A. Brown (*Trop. Dis. Bull.*)

Avinoach, I., Amital-Teplizki, H., Kuperman, O., Isenberg, D. A. And Shoenfeld, Y. Characteristics of antineuronal antibodies in systemic lupus erythematosus patients with and without central nervous system involvement: the role of mycobacterial cross-reacting antigens. Isr. J. Med. Sci. **26** (1990) 367–373.

Sera of 16 patients with systemic lupus erythematosus (SLE) and active involvement of the CNS were examined for the presence of antibodies to human brain neurons, using indirect immunofluorescence of human brain tissue sections. Thirteen of the 16 patients (81%) had high antineuronal titers, which declined during convalescence, compared with 18 of 105 (17%) SLE patients who had no CNS disease. Competition assays showed that the binding of the antineuronal antibodies was blocked by mycobacterial glycolipids and bovine brain extracts. This finding suggests an additional link between mycobacterial infection and SLE.—Authors' Abstract

Baelden, M.-C., Vanderelst, B., Dieng, M., Prignot, J. and Cocito, C. Serological analysis of human tuberculosis by an ELISA with mycobacterial antigen 60. Scand. J. Infect. Dis. **22** (1990) 63–73.

An ELISA method for detecting serum antibodies against A60, an antigen prepared from the cytoplasm of *Mycobacterium bovis* BCG, has been applied to 385 subjects, namely, 197 controls (neonates, healthy adults, and tuberculin negative, nontuberculous patients), and 188 subjects at various stages of tuberculous infection and disease. Most IgM determinations gave negative results. While the neonates and normal adults had titers of IgG anti-A60 antibodies below the cut-off value, wide variations in antibody titers were observed among the various types of subjects infected by *M. tuberculosis*. The results obtained with nontuberculous subjects were: 100% negative IgG in neonates and healthy adult individuals and 6.4% "false positive" cases among 124 non-tuberculous patients. The percentage of serologically positive cases of tuberculosis was: 5.9% in latent active primary forms, 42.8% in patent active primary forms, and 82.8% in active postprimary forms. Tuberculous infections had a positivity rate of 14.7%, while inactive postprimary tuberculosis had a positivity rate of 50%. The results obtained with A60 can favorably be compared with other serum ELISA tests for tuberculous antibodies against purified or semipurified mycobacterial antigens. Anti-A60 ELISA IgG antibody test can be used to monitor the kinetics of humoral immunological response during tuberculous infection, disease and chemotherapy. A positive IgG ELISA test may support the diagnosis of active tuberculous disease.—Authors' Abstract

Bermudez, L. E. M. and Young, L. S. Recombinant granulocyte-macrophage colony-stimulating factor activates human macrophages to inhibit growth or kill *Mycobacterium avium* complex. J. Leuk. Biol. **48** (1990) 67–73.

Organisms belonging to the *Mycobacterium avium* complex (MAC) are associated with life-threatening bacteremia in patients with the acquired immunodeficiency syndrome (AIDS). As these organisms survive within macrophages, we examined the ability of recombinant human granulocyte-monocyte colony-stimulating factor (GM-CSF) to activate human monocyte-derived macrophages to inhibit the intracellular growth or kill the most mouse-virulent MAC strain in our collection that belongs to serotype 1. While unstimulated cells did not inhibit intracellular growth of MAC, macrophages activated by GM-CSF ($10–10^4$ U/ml) inhibited or killed up to 58 ± 5% of the initial inoculum. This activation was dose-dependent, with maximal change occurring with a dose of 100 U/ml after 72 hr exposure. Inhibition or killing was demonstrated if GM-CSF was given both before or after establishment of infection. The

combination of GM-CSF (10^2 U/ml) plus TNF (10^2 U/ml) augmented macrophage killing (range 31 ± 4%) compared with GM-CSF (10^2 U/ml) alone, but the combination of recombinant human interferon-gamma (IFNγ) plus GM-CSF resulted in a significant decrease in intracellular inhibition of growth or killing (13.3 ± 2%) compared with 57.7 ± 5% obtained with GM-CSF alone. These results indicate that: 1) GM-CSF can activate macrophages to inhibit intracellular growth or kill MAC; 2) killing may be augmented by TNF; and 3) IFNγ may impair GM-CSF-dependent macrophage activation.—Authors' Abstract

Best, M., Sattar, S. A., Springthorpe, V. S. and Kennedy, M. E. Efficacies of selected disinfectants against *Mycobacterium tuberculosis.* J. Clin. Microbiol. **28** (1990) 2234–2239.

The activities of 10 formulations as mycobactericidal agents in *Mycobacterium tuberculosis*-contaminated suspensions (suspension test) and stainless steel surfaces (carrier test) were investigated with sputum as the organic load. The quaternary ammonium compound, chlorhexidine gluconate, and an iodophor were ineffective in all tests. Ethanol (70%) was effective against *M. tuberculosis* only in suspension in the absence of sputum. Povidone-iodine was not as efficacious when the test organism was dried on a surface as it was in suspension, and its activity was further reduced in the presence of sputum. Sodium hypochlorite required a higher concentration of available chlorine to achieve an effective level of disinfection than did sodium dichloroisocyanurate. Phenol (5%) was effective under all test conditions, producing at least a 4-$\log_{10}$ reduction in CFU. The undiluted glutaraldehyde-phenate solution was effective against *M. tuberculosis* and a second test organism, *M. smegmatis,* even in the presence of dried sputum, whereas the diluted solution (1:16) was only effective against *M. smegmatis* in the suspension test. A solution of 2% glutaraldehyde was effective against *M. tuberculosis.* This investigation presents tuberculocidal efficacy data generated by methods simulating actual practices of routine disinfection.—Authors' Abstract

Böddinghaus, B., Rogall, T., Flohr, T., Blöcker, H. and Böttger, E. C. Detection and identification of mycobacteria by amplification of rRNA. J. Clin. Microbiol. **28** (1990) 1751–1759.

Oligonucleotides specific at a genus, group, or species level were defined by a systematic comparison of small-subunit rRNA sequences from *Mycobacterium tuberculosis, M. bovis, M. africanum, M. bovis* BCG, *M. avium, M. kansasii, M. marinum, M. gastri, M. chelonae, M. smegmatis, M. terrae, M. nonchromogenicum, M. xenopi, M. malmoense, M. szulgai, M. scrofulaceum, M. fortuitum, M. gordonae, M. intracellulare, M. simiae, M. flavescens, M. paratuberculosis, M. sphagni, M. cookii, M. komossense, M. phlei,* and *M. farcinica.* On the basis of the defined oligonucleotides, the polymerase chain reaction (PCR) technique was explored to develop a sensitive taxon-specific detection system for mycobacteria. By using *M. tuberculosis* as a model system, fewer than 10 bacteria could be reliably detected by this kind of assay. These results suggest that amplification of rRNA sequences by PCR may provide a highly sensitive and specific tool for the direct detection of microorganisms without the need for prior cultivation.—Authors' Abstract

Butler, W. R. and Kilburn, J. O. High-performance liquid chromatography patterns of mycolic acids as criteria for identification of *Mycobacterium chelonae, Mycobacterium fortuitum,* and *Mycobacterium smegmatis.* J. Clin. Microbiol. **28** (1990) 2094–2098.

Rapidly growing mycobacteria of clinical significance were identified by mycolic acids detected with high-performance liquid chromatography. Mycolic acids from whole cells were extracted, derivatized, and detected by a modified high-performance liquid chromatography procedure in less than 3 hr. Use of an internal standard allowed differentiation of *Mycobacterium chelonae* and *M. fortuitum* by comparison of relative retention times. Peak height ratios were used for subidentification of *M. chelonae* strains; however, *M. fortuitum* and *M. smegmatis* could not be separated by this system.—Authors' Abstract

Collins, D. M., Gabric, D. M. and de Lisle, G. W. Identification of two groups of *Mycobacterium paratuberculosis* strains by restriction endonuclease analysis and DNA hybridization. J. Clin. Microbiol. **28** (1990) 1591–1596.

Genomic DNA was prepared from four reference strains of *Mycobacterium paratuberculosis* and 46 isolates of this organism from New Zealand, Australia, Canada, and Norway, and also from two mycobactin-dependent "wood pigeon" strains. The DNA was characterized by restriction endonuclease analysis, both with and without DNA hybridization, with a probe specific to a repetitive DNA sequence in *M. paratuberculosis.* Both techniques differentiated *M. paratuberculosis* strains into two groups, but DNA hybridization revealed more differences between strains within the larger group. All the strains from cattle and many strains from other animals belonged to this group. The second group of nine strains included the Faroe Islands strain, all New Zealand sheep strains, and one New Zealand goat strain. Primary isolation of strains belonging to this group was difficult to achieve. DNA from acid-fast organisms harvested directly from intestinal tissues of sheep with Johne's disease was shown to have restriction and hybridization patterns identical to those of DNA obtained from *M. paratuberculosis* isolates cultured from the same tissues. Two Norwegian goat strains and the wood pigeon strains did not hybridize to the *M. paratuberculosis* probe and had restriction patterns very different from those of other *M. paratuberculosis* strains. The wood pigeon strains had restriction patterns very similar to those of strains of *M. avium,* indicating that they should be classified as that species. The presence of two distinct groups of *M. paratuberculosis* strains and their predominant distribution in different host animals may be significant in management of mixed-animal farming operations.—Authors' Abstract

de Wit, L., de la Cuvellerie, A., Ooms, J. and Content, J. Nucleotide sequence of the 32 kDa-protein gene (antigen 85A) of *Mycobacterium bovis* BCG. Nucleic Acids Res. **18** (1990) 3995.

Proteins of the antigen 85 complex are abundantly secreted into the culture supernatant of a variety of mycobacteria. These proteins are known to be responsible for the high affinity of mycobacteria to fibronectin. The 32-kDa protein (antigen 85A) appears to be a major stimulant of cellular and humoral immunity toward mycobacteria both in mice and man. The gene encoding the 32-kDa protein of *Mycobacterium tuberculosis* has recently been identified by us.—From the article

Dorozhkova, I. R., Karachunsky, M. A. and Kochetkova, E. Y. [Features of qualitative changes in mycobacterial population in new elderly and senile cases of pulmonary tuberculosis during their treatment.] Probl. Tuberk. **4** (1990) 7–10. (in Russian)

Clinicobacteriological investigations were applied to 142 new cases of pulmonary tuberculosis at the age of 60 to 89 years. The control group consisted of 132 patients of young and middle ages (from 17 to 40 years). The form of the process, its extent and the character of the destructions in them were the same as those in the elderly and senile patients. It was shown that the pathogen bacterial forms in the elderly and senile patients were much more frequent than L-forms of *M. tuberculosis* (67.6% and 42.9%, respectively). The tubercle bacilli were mainly isolated from pure cultures (45.8%). L-transformants of *M. tuberculosis* in the elderly and senile patients were markedly less frequent than in the patients of the control group (69.7%) with analogous forms of tuberculosis. The frequency of L-form and their rapid reversion into the initial bacterial form of *M. tuberculosis* (28.0%) and the same period of isolating both the bacterial and L-forms were the distinctive features of the L-forms isolated from the elderly and senile patients. It was suggested that L-forms of *M. tuberculosis* played an important role in reactivation of the specific process.—Authors' English Abstract

Drabick, J. J., Duffy, P. E., Samlaska, C. P. and Scherbenske, J. M. Disseminated *Mycobacterium chelonae* subspecies *chelonae* infection with cutaneous and os-

seous manifestations. Arch. Dermatol. **126** (1990) 1064–1067.

A 75-year-old man who had been receiving corticosteroids for treatment of chronic obstructive pulmonary disease presented with nodulopustular skin lesions, bone pain, and constitutional symptoms. Evaluation revealed a disseminated infection with *Mycobacterium chelonae* subspecies *chelonae*, with cutaneous and osseous involvement documented by histopathologic studies and cultures. The bone involvement is a novel observation for this subspecies. The patient was successfully treated with a three-drug regimen of tobramycin sulfate, erythromycin stearate, and ciprofloxacin hydrochloride. We present a discussion of the case in the context of the literature.—Authors' Abstract

Dutt, A. K., Moers, D. and Stead, W. W. Smear-negative, culture-positive pulmonary tuberculosis; six-month chemotherapy with isoniazid and rifampin. Am. Rev. Respir. Dis. **141** (1990) 1232–1235.

We have shown in Arkansas that 9 months of therapy with isoniazid (INH) and rifampin (RIF) can achieve lasting success in 95% of cases with sputum-smear-positive pulmonary tuberculosis. It seemed likely that when the tubercle bacilli were less numerous, i.e., could not be seen on microscopy, less therapy would suffice. Thus, in January 1980, we began giving only 6 months of treatment to patients in whom at least one sputum culture showed *Mycobacterium tuberculosis* but at least three sputum smears showed no organisms. The regimen for adults is INH 300 mg and RIF 600 mg daily for 1 month followed by INH 900 mg and RIF 600 mg twice weekly for another 5 months. To date, 286 patients with an average age of 68.2 yr have been treated in this manner. Associated medical conditions were present as "risk factors" in 23.7%. The full course of therapy could not be completed in 75 patients (26.2%), largely because of side effects of the drugs and nontuberculosis deaths in this group of elderly patients. Side effects of the drugs requiring change of drug(s) occurred in 33 patients (11.5%), but major side effects occurred in only 8 (2.8%), 4 (1.4%) with toxic hepatitis and 4 with hematologic toxicity. The side effects in 25 patients (8.7%) were not life-threatening and were due to drug intolerance. Treatment failed during therapy in only one patient. The full 6-month course of therapy was completed by 211 patients. During follow-up from 3 to 107 months (median, 45 months), 5 of 211 patients (2.4%) relapsed, all with drug-susceptible organisms. Life table analysis did not show significant difference in survival between patients treated for 6 months (three negative smears) and those treated for 9 months (smear-positive). An overall success of 97% was achieved, which is comparable to the success of 9 months in smear-positive cases. Thus, shortening of therapy for less serious cases can be achieved without loss of effectiveness.—Authors' Summary

Friedland, I. R. The booster effect with repeat tuberculin testing in children and its relationship to BCG vaccination. S. Afr. Med. J. **77** (1990) 387–389.

One-hundred-twenty-seven children, aged 6 months–14 years, attending a day-care center in Pretoria, had two Mantoux tuberculin tests performed 8 weeks apart. On initial testing 19.7% of the children had reactions $\geq$ 10 mm and positive tests were commoner in the older children—who had received BCG vaccination twice. On repeat testing a significant increase in the mean tuberculin reaction size was noted and 13% of the children converted to tuberculin positivity. Since an extensive search revealed no evidence of active tuberculosis in either children or adults at the day-care center, it was concluded that the observed enhancement of the tuberculin reactions was due to the booster effect. This phenomenon was most marked in preschoolers with a BCG scar. It is important to recognize that boosting can occur in children and may be confused with true conversion to tuberculin positivity caused by infection with *Mycobacterium tuberculosis*.—Authors' Summary

Fries, J. W. U., Patel, R. J., Piessens, W. F. and Wirth, D. F. Genus- and species-specific DNA probes to identify mycobacteria using the polymerase chain re-

action. Mol. Cell. Probes **4** (1990) 87–105.

Differential diagnosis of *Mycobacterium tuberculosis, M. avium,* and other mycobacteria remains a lengthy process. Recently, the use of DNA probes has been proposed as a new approach for a more specific and rapid diagnosis. Here, we report the cloning and sequencing of a genus-specific probe for *Mycobacterium* and a species-specific *M. avium* probe. The genus-specific probe hybridizes with DNA from nine ATCC type strains and 13 isolates of mycobacteria but not to nonmycobacterial DNA. In addition, the cloned fragment could also be amplified by polymerase chain reaction (PCR) in DNA of ten different mycobacterial type strains. The *M. avium*-specific probe hybridizes strongly to sequences amplified in *M. avium* but not other mycobacterial or nonmycobacterial DNA. Amplification of the target sequence by PCR allowed the detection of 1 fg of all mycobacterial DNA tested for the genus-specific probe and 1 fg of *M. avium* DNA for the species-specific probe.—Authors' Abstract

Gorin, I., Vilette, B., Gehanno, P. and Escande, J. P. Thalidomide in hyperalgic pharyngeal ulceration of AIDS. (Letter) Lancet **2** (1990) 1343.

Some patients with AIDS have pharyngeal ulcerations which are always hyperalgic, interfere considerably with nutrition, and contribute to general deterioration. With the exception of cytomegalovirus infection, which produces ulcerations of the lower digestive tract, the cause of these manifestations is unknown. We are not aware of any effective treatment, and patients so affected may need high doses of morphine which produce incomplete relief. We have recently treated with thalidomide three AIDS patients with pharyngeal ulcerations: in all three the lesions disappeared completely, leading to a rapid cure.—From the letter

Grange, J. M., Yates, M. D. and Boughton, E. The avian tubercle bacillus and its relatives. J. Appl. Bacteriol. **68** (1990) 411–431.

The avian tubercle bacillus and its relatives are clearly an extremely important group of environmental saprophytes and pathogens of birds and mammals, including man. There is very strong evidence that the taxa known as *Mycobacterium avium, M. intracellulare, M. lepraemurium,* and *M. paratuberculosis* are really variants of a single species. For practical reasons these specific names will probably be retained although, unless distinguished by agglutination serology, the first two taxa will usually be grouped together as *M. avium-intracellulare* (MAI). Human disease ranges from self-limiting lymphadenitis through localized pulmonary and nonpulmonary lesions to disseminated disease, the latter being a common complication of AIDS. There is some evidence that a particular genetic variant of MAI is associated with AIDS, and it has been postulated that this may contribute to the weakening of the host defenses. Infection of animals is widespread, involving many species, and MAI are frequently isolated from healthy animals. Disease is a particular problem in zoo mammals, possibly associated with the stressful conditions under which they live. Johne's disease, caused by *M. paratuberculosis,* is a serious and economically important affliction of cattle and other farm animals, and *M. lepraemurium* affects cats as well as rats. After the tubercle and leprosy bacilli, the avian tubercle bacillus and its relatives are the most important and prevalent mycobacterial pathogens affecting man and animals, and there are compelling reasons to believe that they will continue or even increase as such in the years to come.—Authors' Conclusions

Henry, D., Bailey, C. C. and Lewis, I. J. Thalidomide in the treatment of graft-*versus*-host disease. Biomed. Pharmacother. **44** (1990) 199–204.

The success of allogeneic bone marrow transplantation has been restricted by the occurrence of graft-versus-host disease (GVHD). Attempts at prevention and treatment of GVHD have resulted in only a limited improvement, and the morbidity and mortality rate remains high. Thalidomide has been known to have immunosuppressive properties for over 20 years, but it has only recently been used in GVHD. Evidence is now accumulating as to its value both in animal models, and in humans where most

benefit has been seen in chronic GVHD. We report our experience using thalidomide in GVHD following allogeneic bone marrow transplantation and review the literature.—Authors' Summary

Hermans, P. W. M., van Soolingen, D., Dale, J. W., Schuitema, A. R. J., McAdam, R. A., Catty, D. and van Embden, J. D. A. Insertion element IS*986* from *Mycobacterium tuberculosis*: a useful tool for diagnosis and epidemiology of tuberculosis. J. Clin. Microbiol. **28** (1990) 2051–2058.

IS*986* of *Mycobacterium tuberculosis* belongs to the IS*3*-like family of insertion sequences, and it has previously been shown to be present in multiple copies in the chromosome of *M. tuberculosis*. In this study we investigated the value of a IS*986*-based DNA probe in the diagnosis and epidemiology of tuberculosis. IS*986* was found only in species belonging to the *M. tuberculosis* complex. Independent isolates of *M. tuberculosis* complex strains showed a very high degree of polymorphism of restriction fragments which contained IS*986* DNA. In contrast, *M. bovis* BCG vaccine strains as well as clinical isolates of *M. bovis* BCG contained one copy of IS*986*, which was present at the same location in the chromosome. Different *M. tuberculosis* isolates from a recent *M. tuberculosis* outbreak showed an identical banding pattern. We concluded that IS*986* is an extremely suitable tool for the diagnosis and epidemiology of tuberculosis.—Authors' Abstract

Hoffner, S. E., Olsson-Liljequist, B., Rydgård, K. J., Svenson, S. B. and Källenius, G. Susceptibility of mycobacteria to fusidic acid. Eur. J. Clin. Microbiol. Infect. Dis. **9** (1990) 294–297.

Fusidic acid was shown to be effective *in vitro* against 30 clinical isolates of *Mycobacterium tuberculosis* at concentrations of 32–64 mg/l, concentrations which are readily achieved in serum. All but one of 17 *M. avium* complex strains were resistant to fusidic acid at concentrations up to 64 mg/l. However, synergistic effects were shown for 11 of the 17 strains when fusidic acid was combined with ethambutol. Five of the strains were fully susceptible to the combination of fusidic acid (64 mg/l) and ethambutol (4 mg/l). It is suggested that fusidic acid should be evaluated clinically as a potential supplementary drug for treatment of mycobacterial infections.—Authors' Abstract

Hörhold, C. and Böhme, K.-H. Formation of progesterone and 1-dehydroprogesterone from cholesterol in fermentation cultures of *Mycobacterium aurum*. J. Steroid Biochem. **36** (1990) 181–183.

The formation of progesterone and 1-dehydroprogesterone from cholesterol in fermentation cultures of *Mycobacterium aurum* ATCC 25790 was studied with the aim of clarifying the microbial pathway. The C_{22}-intermediate (20S)-20-carboxy-1,4-pregnadien-3-one was microbiologically converted via the undetectable corresponding aldehyde into the C_{22}-alcohol. However in the fermentation broth without microorganisms, but containing 2,2′-bipyridyl and copper ions, synthetically prepared C_{22}-aldehyde was oxidized to the corresponding C_{21}-compound 1-dehydroprogesterone, suggesting that the enzymatically originated C_{22}-aldehydes may be immediately chemically oxidized to the corresponding C_{21}-ketones.—Authors' Summary

Jittinandana, A. Problems of tuberculosis treatment in Thailand. J. Med. Assoc. Thai. **72** (1989) 601–605.

Problems of tuberculosis treatment in Thailand are an obstacle in the national tuberculosis control program. Reasons concerning the problems on the health provider side being the most important are the budget and the health personnel attitude and behavior, convenience of service, distance of service, health provider-consumer social relation, social support and health service quality. On the health consumer side are patient attitude and behavior and patient economy. The most important understanding to the problems is the socioeconomic status of the nation and health providers are responsible for the problems.—Authors' Summary

Joesoef, M. R., Remington, P. L. and Tjipthoherijanto, P. Epidemiological model

and cost-effectiveness analysis of tuberculosis treatment programmes in Indonesia. Int. J. Epidemiol. **18** (1989) 174–179.

An epidemiological model of tuberculosis, based on the natural history of tuberculosis and the control programs in Indonesia, was constructed. This model was used for estimating future tuberculosis-prevented cases and costs for three treatment strategies—the 100% standard course, the 100% short course, and the existing strategy (a combination of 65% standard course and 35% short course)—in accordance with the master plan of the Indonesian Government's tuberculosis control program. A cost-effectiveness analysis of the three strategies confirmed that the short-course strategy was the most cost-effective. Sensitivity analysis, which applied a broad range of parameters, continued to confirm the short-course strategy as the most cost-effective. If the short-course strategy had been applied in 1980 instead of the existing strategy (using the most likely parameters), the short-course strategy would prevent 1.8 million sputum-positive cases and would save 61.0 million dollars by the year 2000.—AS (*Trop. Dis. Bull.*)

Kazda, J., Stackebrandt, E., Smida, J., Minnikin, D. E., Daffe, M., Parlett, J. H. and Pitulle, C. *Mycobacterium cookii* sp. nov. Int. J. System. Bacteriol. **40** (1990) 217–223.

Strains of a new type of slowly growing scotochromogenic mycobacterium were isolated repeatedly from sphagnum vegetation and surface water of moors in New Zealand. These strains grew at 31°C and 22°C but not at 37°C and possessed catalase, acid phosphatase, and arylsulfatase activities. They did not split amides, and most of them were susceptible to antituberculotic drugs. Furthermore, they did not tolerate 0.1% $NaOH_2$ and 0.2% picric acid and did not grow on compounds used as single carbon sources and single nitrogen and carbon sources. The internal similarity of the strains as determined by numerical taxonomy methods was 96.6% ± 3.09%. The whole-mycolate pattern is unique in that it has not been found previously in 23 species of slowly growing mycobacteria. Evaluation of long-reverse-transcriptase-generated stretches of the primary structure of the 16S rRNA confirmed that these organisms belong to the genus *Mycobacterium*. The phylogenetic position of these bacteria is unique; they are situated between slowly growing pathogenic and rapidly growing saprophytic species. The strains are not pathogenic for mice, guinea pigs, and rabbits, they provoke a nonspecific hypersensitivity reaction to bovine tuberculin. Hence, they are considered members of a new species of nonpathogenic, slowly growing mycobacteria, for which the name *Mycobacterium cookii* is proposed. Strain NZ2 is the type strain: a culture of this strain has been deposited in the American Type Culture Collection as strain ATCC 49103.—Authors' Abstract

Khomenko, A. G., Golyshevskaya, V. I., Maslova, L. I., Kalmykova, G. N. and Uvarova, O. A. [Chemotherapeutic efficacy of flurenizid, a new antituberculous pharmaceutical, in an experiment.] Probl. Tuberk. **6** (1990) 3–7. (in Russian)

The efficacy of a chemotherapeutic effect of flurenizid, a new antituberculous drug, was experimentally demonstrated. Flurenizid is an aromatic heterocyclic derivative. As estimated on the models of hematogenic disseminated and destructive pulmonary tuberculosis, a chemotherapeutic dose of the drug was 20 and 50 mg per kg body weight of an animal. Phagocytotic stimulation and fibrillogenetic intensification represent one of the mechanisms of its action. The most pronounced efficacy of flurenizid was noted when it was combined with isoniazid.—Authors' English Abstract

Khomenko, A. G., Litvinov, V. I., Chukanova, V. P. and Pospelov, L. E. Tuberculosis in patients with various HLA phenotypes. Tubercle **71** (1990) 187–192.

Tuberculosis patients and healthy subjects from six ethnic groups of the Soviet Union were HLA-A, -B, -C, and DR typed. The frequencies of the HLA-A, -B and -C antigens differed among the ethnic groups. With all groups, however, patients with tuberculosis showed a significantly increased frequency of HLA-DR2 and a reduced frequency of HLA-DR3 type. Unfavorable dymanics of tuberculosis was significantly associated with an increased incidence of B15 and DR2 and a reduced incidence of B27

and DR3. Family studies revealed that the inheritance of susceptibility to tuberculosis (from parent to offspring) is associated with the inheritance of certain HLA haplotypes. Tuberculosis patients bearing the DR2 antigen had increased levels of IgG antibodies to PPD and the frequency of B7 and, more particularly, DR2 was higher in anergic patients.—Authors' Summary

Kossiy, N. M., Gergert, V. Y. and Abramova, Z. P. [Impact of acute respiratory viral infection on the immunity parameters of pulmonary tuberculosis patients.] Probl. Tuberk. 7 (1990) 33–36. (in Russian)

To study the impact of acute respiratory viral infection (ARVI) on the course of pulmonary tuberculosis, 150 cases with this condition were under observation. These patients were divided into two groups: 88 subjects who had ARVI and 62 persons who did not have it, being in hospital. In both groups those suffering from infiltrative and focal pulmonary tuberculosis were predominant. ARVI is conducive to the aggravation of a specific process in the lungs, which was registered in 27.3% of the cases who had had ARVI, and impedes the reactions of cellular immunity to restore, which can be observed during chemotherapy. Among those who had ARVI, 68.4% of the patients demonstrated a decrease in T cells and blast transformation with PHA. A significant drop in the number of T lymphocytes and their functional activity, as a consequence of ARVI, promotes the deterioration of the above specific process. ARVI affects the efficacy of the inpatient treatment and decreases the proportion of patients with cavity closure.—Authors' English Abstract

Kumar, S., Ojha, V., Ganguly, N. K. and Kohli, K. K. Presence of gamma glutamyl transferase in *Mycobacterium smegmatis*. Biochem. Int. **20** (1990) 539–548.

The presence of gamma glutamyl transferase (GGT) has been established in *Mycobacterium smegmatis*. The 10,000 × *g* supernatant demonstrated only hydrolase activity and did not exhibit any transpeptidase activity. Most of the transferase activity was recovered in 100,000 × *g* supernatant, demonstrating that GGT is a cytosolic enzyme. Maximum activity of GGT was observed at 2 days of growth, and the activity decreased significantly until the seventh day of growth when the mycobacteria were grown as a stationary culture. The km for gamma glutamyl-p-nitroanilide was found to be 0.074 mM and Vmax for the reaction approached 11.9 nmol per min per mg protein. L-serine + borate was found to be a competitive inhibitor (Ki 12.05 mM) for GGT activity. The pH optimum for GGT activity was observed between 7.5 to 8.5, and temperature above 35°C rapidly inactivated the enzyme activity. To the best of our knowledge, this is the first report which unequivocally establishes the presence of GGT activity in 10,000 × *g* supernatant of *M. smegmatis*.—Authors' Summary

Lacave, C., Quémard, A. and Lanéelle, G. Cell-free synthesis of mycolic acids in *Mycobacterium aurum*: radioactivity distribution in newly synthesized acids and presence of cell wall in the system. Biochim. Biophys. Acta **1045** (1990) 58–68.

Distribution of radiolabeling in different parts of the newly synthesized mycolic acids, by a cell-free system from *Mycobacterium aurum* previously described, is examined, [1-^{14}C] acetate being the precursor. By oxidation cleavage of mycolic acids and examination of the fragments, it was shown that acetate was not uniformly incorporated into the molecule: the methyl terminal part was not labeled, while the central fragments—between unsaturations or between oxygenated functions (oxo or ester) and unsaturations—presented the major part of radioactivity, suggesting the elongation of a preformed compound that the cell-free extract was unable to synthesize. Moreover, the side-chain R2-CH_2-COOH was only weakly labeled compared to the central fragments. Since non-hydroxylated fatty acids were not synthesized by the system, it is suggested that *de novo* C_{18} fatty acids may be elongated with C_2 units by the cell-free extract into C_{22} fatty derivative, only a low level of labeling being recorded (two C_2 units for all the molecule). A scheme is proposed to summarize the main results. Identification of *meso*-DAP which is a characteristic amino-acid of the peptidoglycan and *Actinomycetes* and analysis of the profiles of

total fatty esters, demonstrated that the cell-free extract is partly constituted by fragments of the cell wall as has already been noticed by examination of micrographs of the extract.—Authors' Abstract

Meindl, W., Friese-Kimmel, A., Lachenmayr, F., Buschauer, A. and Schunack, W. [The influence of agonists and antagonists of the histamine H_1- and H_2-receptor on the growth of *Mycobacterium tuberculosis* H37Ra. Arch. Pharm (Weinheim) **323** (1990) 267–272. (in German)

The influence of histamine H_1- and H_2-agonists and -antagonists on the growth of mycobacteria is described. While compounds which are strongly related to histamine improve the growth, predominantly H_1-antagonists inhibit bacterial growth.—Authors' English Abstract

Nikonenko, B. V., Mezhlumova, M. B., Apt, S. D. and Moroz, A. M. Local adoptive transfer of delayed-type hypersensitivity to tuberculin from *M. bovis* (BCG) infected mice. Folia Biol. (Praha) **35** (1989) 255–259.

Immunological properties of the cells mediating delayed-type hypersensitivity to tuberculin and genetic requirements of this reaction have been studied by the method of local adoptive transfer. Peritoneal cells from BCG-immunized mice transferred the reaction into unprimed recipients without any genetic restriction. In contrast, nonadherent peritoneal cells transferred the reaction only in H-2-compatible donor-recipient strain combinations. The use of H-2 recombinant strains has shown that delayed-type hypersensitivity to tuberculin in mice is restricted by the I-A locus. Monoclonal antibody against I-$A^k\beta$ abrogated (without complement) the transfer of the reaction to CBA recipients. The phenotype of nonadherent cells transferring the reaction has been shown to be Thy-1^+, Lyt-1^+, 2^-, L3T4^+.—Authors' Abstract

Obregón Fuentes, A. M., Valdivia Alvarez, J. A. and Ferrá Zalazar, C. [Serotyping of strains of non-tuberculous mycobacteria.] Rev. Cubana Med. Trop. **42** (1990) 148–155. (in Spanish)

Forty strains of mycobacteria, belonging to the *Mycobacterium avium-intracellulare-scrofulaceum* complex, isolated from symptomatic respiratory patients, were studied. For such study, the agglutination-adsorption technique was applied, using specific antisera elaborated at the Pedro Kouri Institute of Tropical Medicine, National Research Institute, with titers ranging close to 1:320. The results obtained demonstrated that the prevailing types were those of the species *M. intracellulare* (31 strains), prevailing serotypes 9 (Darden), 8 (Davis), 12 (Haweel) and serotype 26 followed by the species *M. avium* (3 strains) and *M. scrofulaceum* (2 strains).—Authors' English Summary

Olsen, W. P., Groves, M. J. and Klegerman, M. E. Cell mass of *Mycobacterium bovis* BCG estimated by gas chromatography. Biologicals **18** (1990) 83–88.

The presence of additives and large cellular aggregates in freeze-dried BCG vaccines precludes accurate measurement of total cell content by traditional methods. The possibility that extraction and quantitation of a cell membrane fatty acid may provide a suitable means of cell mass determination was tested. The palmitic acid methyl ester peak area determined by gas chromatography was directly proportional to the wet weight of freshly grown Tice-, Pasteur-, and Glaxo-substrain BCG, as well as the dry weight of the ampoule contents after removal of soluble material. Extraction of palmitic acid from Tice BCG vaccine was not appreciably affected by lyophilization and the calculated dry cell mass values of freeze-dried vaccine samples correlated well with particle number. This method, therefore, may be useful in measuring BCG cell mass during all stages of vaccine manufacture and storage.—Authors' Abstract

Pao, C. C., Yen, T. S. B., You, J.-B., Maa, J.-S., Fiss, E. H. and Chang, C.-H. Detection and identification of *Mycobacterium tuberculosis* by DNA amplification. J. Clin. Microbiol. **28** (1990) 1877–1880.

The polymerase chain reaction (PCR) was used to identify mycobacterial DNA sequences in uncultured clinical specimens. Two oligonucleotide primers derived from the sequence of a gene that codes for the 65-kilodalton antigen of *Mycobacterium tuberculosis* amplified DNA from all 11 species

of mycobacteria tested. Amplified DNAs of nontuberculosis mycobacteria were found to be approximately 20 to 40 bases shorter than those from *M. tuberculosis* and *M. bovis* BCG. DNA equivalent to that present in as few as 40 *M. tuberculosis* cells either alone or in the presence of DNA equivalent to that in 10^6 human cells could be detected. Results from analysis of cultured bacteria and clinical specimens showed PCR was sensitive and specific both in detecting mycobacteria and in differentiating *M. tuberculosis* and BCG from other species of mycobacteria. The PCR method with the primers reported here may become a useful tool in the early and rapid detection of mycobacterial infections in uncultured clinical specimens.—Authors' Abstract

Revuz, J., Guillaume, J.-C, Janier, M., Hans, P., Marchand, C., Soutevrand, P., Bonnetblanc, J.-M., Claudy, A., Dallac, S., Klene, C., Crickx, B., Sancho-Garnier, H. and Chaumeil, J. C. Crossover study of thalidomide vs placebo in severe recurrent aphthous stomatitis. Arch. Dermatol. **126** (1990) 923–927.

A multicentric crossover randomized trial of 100 mg of thalidomide vs placebo each for 2 months was conducted in patients with severe aphthous stomatitis of more than 6 months' duration. Seventy-three patients were included. Complete remission was obtained in 32 patients who received thalidomide and in 6 patients who received placebo. The confidence interval of the difference between the two treatments ranged from 25% to 53%. Most of the patients who did not achieve a complete remission had a dramatic improvement with regard to the number of aphthae when they were receiving thalidomide. Thirteen of 17 patients who had a complete remission while they were receiving thalidomide had a recurrence with placebo, 19 ± 9 (mean ± SD) days after stopping this drug. Side effects were significantly more frequent with thalidomide, especially drowsiness and constipation. We concluded that thalidomide in a dosage of 100 mg/d is an effective treatment of severe aphthous stomatitis but is not without some risk.—Authors' Abstract

Rosen, E. U. The diagnostic value of an enzyme-linked immune sorbent assay using adsorbed mycobacterial sonicates in children. Tubercle **71** (1990) 127–130.

We have evaluated the serodiagnosis of tuberculosis in children using mycobacterial sonicates in an enzyme-linked immunosorbent assay (TB ELISA), a method reported to have been used with success in adults. Attempts were also made to ascertain if prior BCG immunization would influence the outcome of the test. Using clinically diagnosed and notified cases of tuberculosis as well as subjects in whom the condition had been excluded as controls, it was found that the TB ELISA showed very low degrees of specificity and sensitivity, and consequently was not suitable as a diagnostic tool in identifying children aged 5 years or less with tuberculosis. In groups of older children, the TB ELISA appeared to be much more promising and gave results more in keeping with those found in adults. In very young infants who were free from tuberculosis we showed that there was a crossreactivity with BCG. Thus, it appears that, at present, serodiagnosis of tuberculosis in children is not practical.—Author's Summary

Sai Baba, K. S. S., Moudgil, K. D., Jain, R. C. and Srivastava, L. M. Complement activation in pulmonary tuberculosis. Tubercle **71** (1990) 103–107.

The alterations in serum/plasma levels of total hemolytic complement activity (CH50), complement components C3 and C3d, and circulating immune complexes (CICs) in patients with pulmonary tuberculosis were analyzed in relation to the severity of disease and treatment status. The mean levels of CH50, C3, C3d and CICs were significantly higher in untreated than treated patients and in normal controls. In the untreated group, the level of each of these four parameters except C3d was significantly higher in patients with far advanced disease than in those with moderately advanced disease; whereas the difference between treated patients and normal controls was not statistically significant for any of the four parameters tested. There were statistically significant correlations between levels of CICs and both C3 and C3d in the untreated tuberculosis patients. However, the correlations for the same parameters were not significant when treated patients

were considered. The CH50 levels in tuberculosis patients suggest a functional classical complement pathway, which is essential for immune complex solubilization. High C3d level in untreated patients is indicative of increased complement activation, which in turn shows significant correlation with levels of CICs. It appears that the intact and elevated complement proteins and their proper activation by CICs prevent tuberculosis from becoming a typical immune complex disease.—Authors' Summary

Sareen, M. and Khuller, G. K. Cell wall composition of ethambutol susceptible and resistant strains of *Mycobacterium smegmatis* ATCC 607. Lett. Appl. Microbiol. **11** (1990) 7–10.

Changes in the cell wall that accompany acquisition of ethambutol (EMB) resistance in a single-step mutant of *Mycobacterium smegmatis* ATCC 607 were analyzed. Quantitative changes were seen in the chemical constituents of the cell wall of resistant cultures in comparison with EMB-susceptible *M. smegmatis.* Alterations in the binding of 1-anilinonaphthalene-8-sulfonate (ANS) were suggestive of structural changes in the cell surface.—Authors' Abstract

Seldenrijk, C. A., Drexhage, H. A., Meuwissen, S. G. M. and Meijer, C. J. L. M. T-cellular immune reactions (in macrophage inhibition factor assay) against *Mycobacterium paratuberculosis, Mycobacterium kansasii, Mycobacterium tuberculosis, Mycobacterium avium* in patients with chronic inflammatory bowel disease. Gut **31** (1990) 529–535.

A mycobacterial etiology has been suggested for Crohn's disease. A slow-growing mycobacterium, biochemically and genetically identical to *Mycobacterium paratuberculosis,* the causative agent of enteritis in ruminants (Johne's disease), has been isolated from gut specimens of patients affected by Crohn's disease. If *M. paratuberculosis* or other mycobacteria play a role in the pathogenesis of Crohn's disease, then patients may have been sensitized to these mycobacteria or show an anergy immune reaction. We therefore investigated the T-cell-mediated immune response to sonicates of *M. paratuberculosis, M. kansasii, M. avium,* and *M. tuberculosis* in 35 patients with Crohn's disease, 28 with ulcerative colitis, and 25 controls using a macrophage inhibition factor assay on peripheral blood lymphocytes. Two types of reaction patterns were identified—that is, "responders" (subjects with a macrophage inhibition factor assay in which a dose-response relation was present and a percentage of inhibition exceeding 20%), and "nonresponders." There was no significant difference in the prevalence of responders (59%–80%) and nonresponders (20%–41%) to these mycobacteria between the group of Crohn's disease, ulcerative colitis, and control group. We found also that a large proportion of controls showed T-cell immunization to the mycobacteria which supports the contention that the antigens are practically commensal. Our results do not support the proposed involvement of mycobacteria in the pathogenesis of Crohn's disease.—Authors' Abstract

Sjöbring, U., Mecklenburg, M., Andersen, A. B. and Miörner, H. Polymerase chain reaction for detection of *Mycobacterium tuberculosis.* J. Clin. Microbiol. **28** (1990) 2200–2204.

A polymerase chain reaction for the specific detection of mycobacteria belonging to the *Mycobacterium tuberculosis* complex was developed. Using a single primer pair derived from the nucleotide sequence of protein antigen b of *M. tuberculosis,* we achieved specific amplification of a 419-base-pair DNA fragment in *M. tuberculosis* and *M. bovis.* After DNA was extracted from mycobacteria by using a simple, safe lysis procedure, we detected the 419-base-pair sequence in samples containing few mycobacteria. Preliminary data suggested that this technique could be applied to clinical specimens for early and specific diagnosis of tuberculosis.—Authors' Abstract

Tomioka, H., Saito, H., Sato, K. and Dawson, D. J. Arylsulfatase activity for differentiating *Mycobacterium avium* and *Mycobacterium intracellulare.* J. Clin. Microbiol. **28** (1990) 2104–2106.

Arylsulfatase activities (96-hr reaction) of various strains of *Mycobacterium avium* and *M. intracellulare,* as identified by a DNA probe test, were measured. The enzyme activities of *M. avium* strains were signifi-

cantly higher than those of *M. intracellulare* strains ($p < 0.005$ to $p < 0.025$). The enzyme activities did not vary with serovar; that is, the activities of serovars 1, 2, 8, and 9 (belonging to *M. avium*) were similar to each other, as were the activities of serovars 7, 12, 13, 14, and 16 (belonging to *M. intracellulare*). The results indicate the usefulness of the arylsulfatase test in distinguishing *M. avium* from *M. intracellulare* in an accurate manner.—Authors' Abstract

Veerman, G. M., Kelman, R., Colley, J. and Pike, J. G. Rapid confirmatory identification of *Mycobacterium bovis* using a dot blotting immunodetection technique. Vet. Microbiol. **22** (1990) 335–340.

A safe, cost-effective and accurate immunodetection technique for the rapid identification of *Mycobacterium bovis* colonies is described. One-hundred-thirteen *M. bovis* isolates were differentiated from other species of mycobacteria using a *M. bovis*-specific monoclonal antibody, with nitrocellulose membrane as the solid support. The technique confirms *M. bovis* identification in only 4 hr compared to 3 weeks for conventional antibiotic sensitivity tests.—Authors' Abstract

Vorobyev, A. A., Badukshanova, N. M., Dorozhkova, I. R., Sukhova, T. G., Khodorkovskaya, V. A., Kassirskaya, N. G. and Rybakova, A. M. [Identification of mycobacteria by gas-liquid chromatography.] Probl. Tuberk. **7** (1990) 46–50. (in Russian)

Gas-liquid chromatography was used to study the composition of fatty acids and hydrocarbons of different types of mycobacteria, including *Mycobacterium tuberculosis,* opportunistic mycobacteria and acid-fast saprophytes. In terms of composition of fatty acids and hydrocarbons, clinical and laboratory strains of *M. tuberculosis* are very similar. The cellular higher fatty acids of *M. tuberculosis* differ much from those of opportunistic mycobacteria and acid-fast saprophytes. The findings can be used for the identification and differentiation of different types of mycobacteria.—Authors' English Abstract

Wilbrink, B., Bijlsma, J. W. J., Huber-Bruning, O., Van Roy, J. L. A. M., Den Otter, W. and Van Eden, W. Mycobacterial antigens stimulate rheumatoid mononuclear cells to cartilage proteoglycan depletion. J. Rheumatol. **17** (1990) 532–537.

In a coculture with porcine articular cartilage explants unstimulated blood mononuclear cells (BMC) from patients with rheumatoid arthritis (RA), but not from healthy controls, induced proteoglycan depletion of dead cartilage. Specific stimulation of the RA BMC with *Mycobacterium tuberculosis* (MT), in comparison with concanavalin A, strongly enhanced the proteoglycan depletion of living cartilage; this was not found with the BMC of healthy controls. However, the MT-induced proliferative responses of the same BMC were similar in healthy controls and patients with RA. Neither the proliferative response nor the proteoglycan depletion was influenced by the presence of HLA-DR4 in the donor, whether patient with RA or healthy control. The proliferative responses of the RA BMC seemed to correlate inversely with the proteoglycan depletion. We conclude that stimulation of RA BMC with mycobacterial antigens may elicit effector pathways that induce proteoglycan depletion, independent of T-cell proliferation.—Authors' Abstract

Wood, P. M. D. and Proctor, S. J. The potential use of thalidomide in the therapy of graft-versus-host disease—a review of clinical and laboratory information. Leuk. Res. **14** (1990) 395–399.

This article reviews the historical development of thalidomide as an immunosuppressive agent and the current state of knowledge of thalidomide as an anti-graft-versus-host disease (GVHD) agent. The evidence suggests that metabolites of thalidomide act at an early stage in the antigen recognition-activation pathway of graft T lymphocytes and down-regulate normal lymphocyte responses. This effect seems to have beneficial effects in both acute and chronic GVHD, but the optimal mode of use in the clinical setting remains to be determined.—Authors' Abstract

Wu, C. H., Fann, M. C. and Lau, Y. J. Detection of mycobacterial antigens in cerebrospinal fluid by enzyme-linked immunosorbent assay. Tubercle **70** (1989) 37–43.

By use of commonly available antibodies against *Mycobacterium bovis* BCG, *M. tuberculosis* antigens can be detected by a rapid and sensitive double-antibody sandwich enzyme-linked immunosorbent assay (ELISA). The ELISA was dose-dependent and capable of detecting as little as 4 ng of antigens. Absorbance for 5 patients with confirmed tuberculous meningitis ranged from 0.150 to 0.600 with a mean value of 0.271 ± 0.190. For 134 non-meningitis control patients and 6 treated tuberculous meningitis patients, optical densities were 0.032 ± 0.009 and 0.029 ± 0.010, respectively. Specificity was demonstrated by the negative results (0.028 ± 0.006) with bacterial and cryptococcal antigens. Maximum crossreactivity with non-tuberculous mycobacterial antigens was less than 7%.—From *Trop. Dis. Bull.*

Yew, W. W., Kwan, S. Y.-L., Ma, W. K., Khin, M. A. and Chau, P. Y. In-vitro activity of ofloxacin against *Mycobacterium tuberculosis* and its clinical efficacy in multiple resistant pulmonary tuberculosis. J. Antimicrob. Chemother. **26** (1990) 227–236.

The *in-vitro* susceptibilities to ofloxacin of 159 clinical sputum isolates of *Mycobacterium tuberculosis,* comprising 95 isolates sensitive to all drugs, 31 isolates resistant to streptomycin or isoniazid or both, 27 isolates resistant to streptomycin, isoniazid and rifampin, and 6 isolates resistant to rifampin (and in 3 cases to other drugs) were determined. Favorable MICs of ofloxacin (0.63–1.25 mg/l) were demonstrated for 147 isolates (92%). Twenty-two patients with resistant strains (including one patient with rifampin intolerance) were studied: 10 were given 300 mg ofloxacin and 10 were given 800 mg ofloxacin, once daily in both cases, together with second-line accompanying drugs, for 9 months to 1 year. Two received 800 mg of ofloxacin once daily alone for similar periods. In the 300 mg-ofloxacin group and the 800 mg-ofloxacin group, 5 and 8 patients, respectively, achieved culture conversion; the rest failed. In the former group, the peak serum ofloxacin concentrations were 3.71–8.08 mg/l and the mean sputum/serum ratio was 0.85. In the latter group, the corresponding values were 10–18.7 mg/l, and 0.76, respectively. All patients tolerated the drugs well. Analyzing only patients with accompanying drugs, those on ofloxacin 800 mg once daily had more rapid sputum culture conversion than those on ofloxacin 300 mg once daily (Mann-Whitney Wilcoxon rank sum test: $p < 0.05$), indicating more rapid bacteriolysis and implying the definite efficacy of ofloxacin when used together with second-line accompanying drugs in the management of resistant tuberculosis.—Authors' Abstract

Yew, W. W., Kwan, S. Y. L., Wong, P. C. and Lee, J. Ofloxacin and imipenem in the treatment of *Mycobacterium fortuitum* and *Mycobacterium chelonae* lung infections. Tubercle **71** (1990) 131–133.

Two patients with *Mycobacterium fortuitum* and one patient with *M. chelonae* lung infections were treated with ofloxacin and imipenem, respectively. Of the former two, one had underlying inactive pulmonary tuberculosis and bronchiectasis and the other had silicosis. The latter had severe underlying bronchiectasis also. The treatments were well tolerated and the patients responded well.—Authors' Summary

Youle, M., Hawkins, D. and Gazzard, B. Thalidomide in hyperalgic pharyngeal ulceration of AIDS. (Letter) Lancet **2** (1990) 1591.

The suggestion that thalidomide is the only curative therapy available for intractable painful aphthous ulceration in AIDS is no longer true. Several workers have shown short courses of oral steroids to be effective in such hyperalgic ulceration of uncertain etiology. This has been our experience, and we have also had success with intralesional injection of steroids. In view of the possibility of peripheral neuropathy and the difficulty of obtaining thalidomide, we suggest that steroids may be a first-line treatment and that thalidomide should be reserved for the patients who do not respond.—From the letter