CURRENT LITERATURE

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

General and Historical

Marcombe, D. and Manchester, K. The Melton Mowbray "leper head": an historical and medical investigation. Med. Hist. **34** (1990) 86–91.

For the last 40 years, the vestry of St. Mary's Church, Melton Mowbray (U.K.), has been home to a remarkable, yet little known, piece of medieval sculpture known locally as the "leper head" and linked by tradition to the nearby hospital foundation at Burton Lazars. Doubts have been cast on this over the years by both professional and amateur historians, who have alleged that the distinctive features of the head merely represent damage or are part of a broader and more commonplace medieval tradition of grotesques, good examples being on display in the south porch of Bakewell Church, Derbyshire. The purpose of the present paper is to examine the "leper head" in its historical and medical context in order to establish its likely provenance and identity.—(*From* the Article)

Richards, P. Leprosy: myth, melodrama and mediaevalism (The FitzPatrick Lecture 1989). J. R. Coll. Phys. Lond. **24** (1990) 55–62.

Leprosy, as an endemic disease, is dead in northern Europe. It gave its last gasp in the 1950s. It had a long run, probably about 2000 years. Around it has grown up over the centuries an extraordinarily complex and deep tradition of prejudice and fear, mirrored in behavior, language, and literature—a medieval tradition about to be taken over perhaps by a new disease, also not common but of high profile, AIDS.—Author's Conclusion

Chemotherapy

Biglino, A., Forno, B., Pollono, A. M., Busso, M., Arpinelli, F., Benedetti, M. and Pugliese, A. Effects of ofloxacin on cell-mediated immune response and lymphokine production. J. Antimicrob. Chemother. **25** (1990) 797–802.

The effects of orally administered ofloxacin on functional parameters of cell-mediated immunity were investigated in 15 patients with respiratory or urinary tract infections. Mononuclear leucocytes were obtained before administering the drug, 1 hr after the first dose, and days later. The cells were stimulated with lectins, tetanus toxoid, and Newcastle disease virus in order to assess mitogen- and antigen-induced lymphocyte proliferation and production of γ-interferon, interleukin-2 and α-interferon. An increase in proliferative response to pokeweed mitogen and a slight but significant decrease in α-interferon production were observed, while other parameters remained unaffected by treatment.—Authors' Abstract

Chopra, N. K., Agarawal, J. S. and Pandya, P. G. A study of relapse in paucibacillary leprosy in a multidrug therapy project, Baroda District, India. Lepr. Rev. **61** (1990) 157–162.

In order to judge the value of therapeutic regimens in paucibacillary leprosy, knowledge of incubation time of relapses is essential since this will define the length of time patients have to be followed up after treatment has been stopped. The prospec-

tive study of relapse includes paucibacillary cases of leprosy belonging to a nonlepromatous group consisting of tuberculoid, neuritic and indeterminate. Data are presented on the incubation time of 21 relapses after multidrug therapy in Baroda district; 76.19% of relapses occur during the first 2 years. This figure is most important in the analysis of results of drug trials in paucibacillary leprosy. This figure should also be relevant to regimens including drugs that are more bacteriocidal than dapsone, since the bacteriocidal activity has a bearing on the minimal necessary duration of treatment, but not on the incubation time of relapses. With the introduction of bacteriocidal drugs, e.g., rifampin, in multidrug therapy, the incidence of relapse is very low; hence, relapse rates fall to a very low level after multidrug therapy. Our study shows a mean relapse rate of 0.19% after multidrug therapy. Factors associated with the occurrence of relapse are discussed.—Authors' Summary

Coleman, M. D., Winn, M. J., Breckenridge, A. M. and Park, B. K. Inhibition of dapsone-induced methaemoglobinaemia in the rat. (Letter) Biochem. Pharmacol. **39** (1990) 802–805.

Pretreatment of male Wistar rats with cimetidine or piperonyl butoxide markedly reduced methemoglobin production by hydroxylated metabolites of dapsone. This was reflected by a significant increase in parent drug levels. Hence co-administration of a reversible metabolic inhibitor with compounds which undergo N-hydroxylation may result in fewer adverse reactions without change in pharmacodynamic activity.—*From* the Letter

Coleman, M. D., Winn, M. J., Breckenridge, A. M. and Park, B. K. Sex-dependent sensitivity to dapsone-induced methaemoglobinaemia in the rat. (Letter) Biochem. Pharmacol. **39** (1990) 805–809.

In summary, we have shown in the rat a marked sex difference, not only in the plasma disappearance of dapsone, but also in the tendency to develop dapsone mediated methemoglobinemia. Females may be protected from dapsone mediated oxidation of hemoglobin as a consequence of a lack of production of the toxic N-hydroxylated metabolites of the drug.—*From* the Letter

Dhople, A. M., Ortega, I., Seydel, J. K. and Gardner, G. D. Effect of brodimoprim on *Mycobacterium leprae in vitro* and in mouse foot-pads. Indian J. Lepr. **62** (1990) 76–86.

The new *in vitro* screening system reported earlier was adopted to determine anti-*Mycobacterium leprae* activity of a dihydrofolate reductase inhibitor, brodimoprim, and the results were compared with those obtained using the mouse foot-pad technique. Even though the MIC of brodimoprim against *M. leprae* was very high compared to other commonly used antileprosy drugs, in combination with dapsone it showed a remarkable synergistic activity in inhibiting the growth of *M. leprae* at concentrations much lower than the MICs of each of the drugs used singly. Similar effects were also demonstrated in mouse foot-pad experiments.—Authors' Abstract

Edstein, M. D., Veenendaal, J. R. and Rieckmann, K. H. Multiple-dose kinetics in healthy volunteers and in vitro antimalarial activity of proguanil plus dapsone. Chemotherapy **36** (1990) 169–176.

The multiple-dose kinetics of a daily dose of proguanil (200 mg) coadministered with dapsone (10 mg) was investigated in 6 healthy adult male volunteers. The kinetics of dapsone (DDS), monoacetyldapsone (MADDS), proguanil (PROG) and its active metabolite cycloguanil (CYCLO) were derived from plasma drug concentrations after the last maintenance dose. The following kinetic parameters (mean values) were estimated for DDS and PROG, respectively: maximum concentration (C_{max}) = 285 and 151 ng/ml, minimum concentration (C_{min} = 125 and 31 ng/ml, elimination half-life ($t_{½}$) = 23.3 and 18.3 hr, plasma clearance (Cl) = 0.032 and 1.27 l/hr/kg and apparent volume of distribution (V_{ss}) = 1.05 and 33.32 l/kg. The C_{max}, C_{min} and $t_{½}$ of CYCLO were 56 ng/ml, 17 ng/ml and 15.0 hr, respectively. The antimalarial activity of the proguanil/dapsone combination was assessed *in vitro* by measuring the inhibition of re-

invasion of two *Plasmodium falciparum* isolates grown in the presence of volunteers' sera. Both FC-27 [chloroquine (CQ)- and pyrimethamine (PYR)-sensitive] and Kl (CQ- and PYR-resistant) isolates were completely inhibited by the drug combination at steady-state concentrations. These findings suggest that the drug regimen may be effective against drug-resistant falciparum malaria.—Authors' Abstract

Eze, L. C., Okpogba, A. N. and Ogan, A. U. Acetylation polymorphism and leprosy. Biochem. Genet. **28** (1990) 1–7.

The sulfones are the drug of choice in the treatment of leprosy, with dapsone as the clear favorite. The major route for dapsone metabolism leading to its inactivation and excretion is via acetylation by hepatic N-acetyl transferase (NAT), as is the case with isoniazid (INH) and sulfamethazine (SMZ). The enzyme is known to exhibit genetic polymorphism. The object of the present study is mainly to determine the incidence of acetylator phenotype in a population of leprosy patients with a view to evaluating the degree of association, if any, between phenotype and the disease. Obviously, a knowledge of the incidence of the phenotypes may provide a valuable contribution to the institution of more rational and successful therapy. In the normal or control subjects, as well as in the leprosy patients, the frequency distribution histograms of the percentage acetylsulfamethazine in urine and serum samples are bimodal, and this indicates the existence of a genetic polymorphism. Based on the bimodality, individuals were classified as either "rapid" or "slow" acetylators, and the incidence of the slow acetylator phenotype of about 51% was observed in the leprosy population. This gives a relatively high incidence of the allele controlling the slow acetylator ($q = 0.73$). Although there is evidence that the mean percentage of SMZ acetylated in leprosy patients of the slow-acetylator phenotype is significantly higher than that observed for the same phenotype in the controls ($t = 4.86$, $p < 0.02$), statistical analyses show that there is no association between the slow-acetylator phenotype and the disease. Most of the individuals in the slow-acetylator phenotype tend to show some adverse reactions when a total weekly dose of 600 mg is given. Such adverse reactions include heightened lepra reactions, blurring of vision, and headache. These reactions, we think, are due to accumulation of the drug in the subjects. This therefore brings into sharp focus the desirability of knowing the acetylator phenotype of an individual before the initiation of dapsone therapy.—Authors' Abstract

Franzblau, S. G. Drug susceptibility testing of *Mycobacterium leprae* in the BACTEC 460 system. Antimicrob. Agents Chemother. **33** (1989) 2115–2117.

The susceptibility of *Mycobacterium leprae* to clinical and experimental antileprosy agents was assessed in the BACTEC 460 system. Nude-mouse-derived *M. leprae* (10^7 cells), incubated in BACTEC 12B medium at 33°C under reduced oxygen, maintained a fairly constant growth index ($^{14}CO_2$ evolution) for 2 to 3 weeks. At concentrations ranging from 0.031 to 2.0 μg/ml, dapsone, rifampin, clofazimine, ethionamide, ofloxacin, clarithromycin, and minocycline all effected reductions in the growth index within 1 to 2 weeks, the extent of inhibition increasing with the incubation time. An *in vivo* rifampin-resistant isolate displayed markedly reduced susceptibility to rifampin compared with an *in vivo*-susceptible strain. This system appears to be highly suitable for *in vitro* drug susceptibility testing of *M. leprae* [although it is more expensive and less sensitive than the Buddemeyer system].—AS/M. Hooper (Trop. Dis. Bull.)

Jansons, V. K. and Soggiu, A. Clofazimine and liposomes enhance the susceptibility of intracellular *M. avium* toward rifabutin. Curr. Microbiol. **20** (1990) 261–264.

The effects of rifabutin and clofazimine were studied on intracellularly growing *Mycobacterium avium.* Both drugs showed concentration-dependent inhibition of growth but no cidal effect at concentrations that can be reached in human serum. However, a combination of both drugs, even at lesser concentrations, exhibited cidal activity. Liposomes enhanced the susceptibility of the organism toward rifabutin but had no effect on the susceptibility toward clofazimine.—Authors' Abstract

Kakaiya, R. M., Dehertogh, D., Walker, F. J., Cummings, E. and Uzdejczyk, M. Rifampin-induced immune thrombocytopenia; a case report. Vox Sang. **57** (1989) 185–187.

In this report, a case of rifampin-induced immune thrombocytopenia with the following characteristics is described: a) thrombocytopenia follows intermittent drug administration; b) onset occurs within hours of drug ingestion; c) IgG antirifampin antibody binds *in vitro* to normal platelets only in the presence of rifampin; d) thrombocytopenia resolves quickly in the absence of rifampin; e) using immunofluorescence microscopy, IgG binding to normal platelets was seen with the patient's serum only in the presence of rifampin; and f) using fluorescence spectrofluorometry, an absence of rifampin binding to normal platelets was demonstrated. Although the serological studies are not definitive, the mechanism of thrombocytopenia in the patient can best be explained by the formation of immune complexes composed of rifampin-antirifampin antibody binding to platelets causing their rapid clearance from the circulation.—Authors' Abstract

Kar, P. K., Jha, P. K., Panaych, J. S. and Snehi, P. S. Clinico-histopathological study of multidrug therapy in indeterminate leprosy. Indian J. Lepr. **62** (1990) 98–103.

A study was undertaken in 42 patients with indeterminate leprosy to evaluate the efficacy of multidrug therapy (MDT) in indeterminate leprosy for 12 months. The main clinical finding was a single hypopigmented macule in 31 (73.8%) of the 42 cases. Histopathologically all cases showed lymphohistiocytic infiltration around skin appendages and dermal nerves. At the end of 6 months of MDT all the cases were evaluated clinically and 33 (85.5%) showed marked improvement or total inactivation, while the lesions were still active clinically in 21.4% cases. Histopathological examination of lesions in 30 patients showed complete histological resolution in 9 cases only. At the end of 1 year of treatment, it was found that 28 cases (66.3%) had become inactive and only 2 (4.7%) were found to be still active.—Authors' Abstract

Kaur, I., Ram, J., Kumar, B., Kaur, S. and Sharma, V. K. Effect of clofazimine on eye in multibacillary leprosy. Indian J. Lepr. **62** (1990) 87–90.

Seventy-six patients of multibacillary leprosy received clofazimine as part of multidrug therapy (MDT) for periods ranging between 6 and 24 months. Complete ocular examination including slit-lamp microscopy and examination of tears was carried out in all these patients. Reddish-brown conjunctival and corneal pigmentation was seen in 46% and 53% of the patients, respectively. Clofazimine crystals in tears were found in 32% of the patients. Apart from this, no other eye changes or symptoms attributable to clofazimine were observed.—Authors' Abstract

Munno, I., Arpinelli, F., Benedetti, M., Spoglianti, R. and Ferlini, A. The effect of ofloxacin on the immune system of elderly patients. J. Antimicrob. Chemother. **25** (1990) 455–458.

In 20 elderly patients with infectious diseases, some immune parameters were evaluated before and after treatment with ofloxacin. Results showed that the number of T cells, B cells, gamma-interferon plasma concentrations, and serum immunoglobulin levels were not affected following 10 days' treatment (600 mg per day). These data suggest that this antibiotic does not affect the immune parameters studied. However, inhibition of other immune functions cannot be excluded.—Authors' Abstract

Pattyn, S. R., Husser, J. A., Baquillon, G., Maiga, M. and Jamet, P. Evaluation of five treatment regimens, using either dapsone monotherapy or several doses of rifampicin in the treatment of paucibacillary leprosy. Lepr. Rev. **61** (1990) 151–156.

The objective of the present study was to define short-course treatment regimens for paucibacillary (PB) leprosy and to compare them with the "classical" dapsone treatment and the WHO-PB regimen. Five treatment regimens were studied and evaluated by the histologic evolution. The regimens were 1) dapsone 100 mg daily, nonsupervised for 3 years; 2) rifampin (RMP) 900

mg supervised, once weekly, 8 doses; 3) idem, 12 doses; 4) RMP 600 mg, once monthly, supervised, 6 doses and during this treatment dapsone 100 mg daily unsupervised; 5) RMP 600 mg together with dapsone 100 mg daily, supervised for 6 days. For each of these regimens there were between 114 and 195 person-years of follow-up. Results are comparable for the 5 treatment regimens, and reach 65–75% cure rates at 36 months and 80–90% at 48 months after the start of therapy. The relapse rate for all groups is about 0.5% per year. The difficulty for the diagnosis of relapse in PB leprosy is discussed. It is concluded that treatment of PB leprosy can be relatively simple but that a relatively long time is needed to evaluate its effect.—Authors' Summary

Proença, N. G. [Thalidomide: an eclectic medication in dermatology.] Rev. Paul. Med. **107** (1989) 41–46. (in Portuguese)

The authors review the indications for the use of thalidomide in dermatological conditions. They consider leprotic reaction, prurigo nodularis of Hyde, actinic prurigo, discoid lupus erythematosus, Weber-Christian panniculitis, recurrent mouth aphtosis, Behcet's syndrome, and pyoderma gangrenosum. The dramatic situation created by the use of thalidomide in the 1960s notwithstanding, interest in its use is warranted within certain limits due to its wide therapeutic action.—Authors' English Summary

Puavilai, S. and Timpatanapong, P. Short-course multi-drug therapy for leprosy patients. J. Med. Assn. Thailand **72** (1989) 33–36.

Short-course multidrug therapy (MDT) for leprosy patients was evaluated in terms of effectiveness, recurrence rate, and side effects. Of the 108 patients studied, 48.1% defaulted. This MDT appeared to be quite effective in controlling leprosy. The medication could be stopped at 6 months in 83% of the paucibacillary patients. The medication was continued further in 17% of paucibacillary patients because of persistent skin lesions clinically and histopathologically. Recurrence occurred in 2.3% of the paucibacillary patients. The effect of this regimen for multibacillary patients is difficult to evaluate because of the small number of patients studied. Side effects of this regimen occurred in 5.4% of the patients. Leprosy reaction occurred in two patients with borderline lepromatous leprosy.—Authors' Summary

Quigley, J. M., Fahelelbom, K. M. S., Timoney, R. F. and Corrigan, O. I. Temperature dependence and thermodynamics of partitioning of clofazimine analogues in the *n*-octanol/water system. Int. J. Pharm. **58** (1990) 107–113.

The partition coefficient of eight N^2-substituted phenazines was measured at four temperatures (range 20–55°C) in the *n*-octanol/water system. The apparent modal partition coefficients, K_m', were calculated from the distribution results. Plots of log K_m vs. T^{-1} were linear and the thermodynamic parameters for the solute transfer were evaluated from the Van't Hoff isochore. A relationship between log K_m and log P was derived.—Author's Summary

Seydel, J. K., Wempe, E. G., Rosenfeld, M., Jagannathan, R., Mahadevan, P. R. and Dhople, A. M. *In vitro* and *in vivo* experiments with the new inhibitor of *Mycobacterium leprae* brodimoprim alone and in combination with dapsone. Arzneim. Forsch. **40** (1990) 69–75.

The antibacterial effect of brodimoprim alone and in combination with dapsone has been studied *in vitro* in cell-free systems and in whole mycobacterial cells as well as *in vivo* in mice and humans. The obtained inhibitory effects *in vitro* and *in vivo* against model mycobacterial strains and *Mycobacterium leprae,* the pharmacokinetic properties in humans and its synergistic effect with the most used drug in the chemotherapy of leprosy, dapsone, make brodimoprim a promising candidate in the therapy of leprosy.—Authors' Summary

Stone, O. J. Sulfapyride and sulfones decrease glycosaminoglycans viscosity in dermatitis herpetiformis, ulcerative colitis, and pyoderma gangrenosum. Med. Hypothes. **31** (1990) 99–103.

Shortly after the introduction of sulfa drugs, sulfapyridine was found to have unique therapeutic properties, unrelated to antibacterial activity. Later, sulfones were found to share the same properties. The disorders initially improved were dermatitis herpetiformis, pyoderma gangrenosum, subcorneal pustular dermatosis, acrodermatitis continua, impetigo herpetiformis and ulcerative colitis. They were also sometimes helpful in many other disorders. They are effective in select disorders characterized by edema followed by granulocytic inflammation or edema followed by vesicle or bullae formation. The sulfones work in low doses in leprosy and their mode of action is not fully understood. Several pieces of experimental information are available. It is proposed that these drugs are entering or influencing the protein moiety of glycosaminoglycans and decreasing tissue viscosity. This decreased tissue viscosity prevents edema and dilution of tissue fluid and decreases acute inflammation and vesicle and bullae formation.—Authors' Abstract

Clinical Sciences

Balkrishna and Bhatia, M. S. Dapsone induced psychosis. J. Indian Med. Assn. **87** (1989) 120–121.

Dapsone and the allied sulfones have been used extensively in a variety of diseases (mainly leprosy and dermatitis herpetiformis) on account of their efficacy and relatively less cost. The side effects of dapsone are rare and include hemolytic anemia, dermatitis and, least commonly, psychosis. Here, a case of dapsone-induced psychosis in a patient without family history of psychosis is being reported.—(*From* the Article)

Barbançon, O., Rath, S. and Al Quabati, Y. Hansen's disease: computed tomography findings in peripheral nerve lesions. Ann. Radiol. **32** (1989) 579–581.

Hansen's disease induces hypertrophic neuropathy. Computed tomography (CT) was performed on ulnar, median, peroneal and tibial posterior nerves where there is clinically presumed lesion. The CT findings (diameter and density) have correlated well with intra-operative findings. CT is a reliable method to study peripheral nerve lesions in Hansen's disease patients.—Authors' Summary

Bogaert, H., Saleta, B., Sanchez, E. and Garcia, B. Trophic leprosy ulcers: treatment with topical and systemic phenytoin. (Letter) Int. J. Dermatol. **29** (1990) 156–157.

Given the need for more effective treatment for these lesions, and because of the reports that phenytoin (PHT) promotes wound healing, we have treated a group of leprosy patients afflicted with trophic ulcers of the leg and plantar area during the past 18 months with topical and systemic PHT with good results. Our data indicate that phenytoin is a valuable agent in the treatment of trophic ulcers associated with leprosy. Its effectiveness is emphasized by the chronicity of the ulcers we treated and by the failure in all patients of the best treatments (including bed rest). In addition, 20 of the 27 patients were ambulatory, and so PHT was effective in the absence of bed rest. Further evaluation of phenytoin in trophic leprosy ulcers with formal randomized, controlled trials is indicated.—(*From* the Letter)

Brandt, F., Zhou, H. M., Shi, Z. R., Rai, N., Thuladar, L. and Pradhan, H. Histopathological findings in the iris of dapsone treated leprosy patients. Br. J. Ophthalmol. **74** (1990) 14–18.

From 43 Nepalese leprosy patients, skin-smear negative and treated with dapsone (diaminodiphenyl sulfone), and without any sign of active leprosy or iritis, specimens from iridectomy during cataract surgery

were studied histopathologically. Of 49 iris specimens only six (12%) were found to be without any histopathological change. Atrophy of the iris stroma was seen in 63% and neovascularization in 6% of all cases. In 16% in which the dilator muscle could be detected, it was atrophic, and in 11% the pigmented epithelium was thinned and atrophic. Cellular inflammatory infiltrations were seen in 88% of all specimens. They were mostly slight in eyes which before operation had been without posterior synechiae of the iris. In most of the eyes in which posterior synechiae had been present, moderate or heavy inflammatory cell infiltrates composed of lymphocytes and plasma cells, often associated with macrophages, neutrophils, or eosinophils, were found. In five iris specimens acid-fast bacilli were present. This raises the question whether these can survive systemically despite dapsone chemotherapy in the iris, thus leading to dapsone-resistant leprosy and to recurrent iritis.—Authors' Abstract

Brooks, B. J., Jr., Alvarez, S. and Yoder, L. Leukopenia secondary to *Mycobacterium leprae*. J. La. State Med. Soc. **142** (1990) 35–36.

Hansen's disease (HD) is one of the major infectious diseases in the world, with an estimated total of 12 million cases. Physicians in North America, however, rarely see HD or its manifestations. Hematological manifestations of HD have been reported but are not well appreciated. We report a patient with leukopenia while under treatment for active HD who demonstrated mycobacterial involvement of the bone marrow.—Authors' Abstract

de Rojas, V. and Lastra, R. A. [Contribution of the psychological characterization of leprosy patients.] Rev. Cub. Med. Trop. **39** (1987) 45–52. (in Spanish)

A total of 150 patients, selected at random, was studied. Psychologic variables studied in these patients were: intellectual efficiency, personality traits, and psychical stability. Such variables were analyzed in relation to sex, race, clinical forms, years of disease evolution, incapacities, and sexual dysfunction. Psychical stability shows a hypochondriac profile that, in some clinical forms, is associated with depressive states. Unsafety, apprehensiveness, cautiousness, sagacity, and timidity are characteristics of the personality traits of these patients. Presence of incapacities and alterations in sexual function increase psychical disorders. Implications of these facts are discussed.—Authors' English Summary

Dhawan, V., Vaishnavi, C., Nanda, A., Kumar, B., Kaur, S. and Ganguly, N. K. Prostaglandin $F_{2\alpha}$ in leprosy—a preliminary study. Indian J. Lepr. **62** (1990) 45–49.

Prostaglandin $F_{2\alpha}$ was estimated in the sera of 50 patients in the leprosy spectrum to find out the status of prostaglandins in response to *Mycobacterium leprae*. Contrary to expectation, $PGF_{2\alpha}$ could be detected in only 28% of leprosy patients.—Authors' Abstract

Dixit, V. B., Chaudhary, S. D., Jain, V. K. and Sen, R. Primary involvement of scrotum in tuberculoid leprosy; a case report. Indian J. Lepr. **62** (1990) 120–122.

To the best of our knowledge, primary involvement of the scrotum in tuberculoid leprosy, as in the present case, has not been reported in the literature, although primary involvement of the sole of the foot and the hairy scalp has been reported. Scrotal skin, being nearer to core body temperature, is relatively warmer and is also an infrequent site for injuries. This might be the reason for the rare occurrence of primary leprosy lesions on the scrotum. Involvement of the scrotum justifies earlier reports that no area is immune to development of leprosy lesions.—*From* the Article

D'Souza, D., Das, B. C. and Thomas, I. M. Differential sensitivity of peripheral blood lymphocytes of untreated leprosy patients to mitomycin C. Mutat. Res. **240** (1990) 101–107.

The effects of a bifunctional alkylating agent mitomycin C (MMC), an effective inducer of chromosome aberrations and sister-chromatid exchanges (SCEs), have been studied in untreated leprosy patients. This

was done to study the mutagen sensitivity of the leprosy patients. The frequency of chromosomal aberrations induced by MMC (conc. 0.01 μg/ml) was 2.5% in controls, 3.6% in paucibacillary (PB), and 6.8% in multibacillary (MB) patients. The difference in the frequency of MMC-induced chromosome aberrations between the three groups studied was highly significant ($p < 0.01$). Cultures grown with MMC showed the frequency of SCEs/cell to be 12.70 ± 1.19 in controls, 19.97 ± 3.51 in PB, and 29.66 ± 5.92 in MB patients. The differences in the frequency of MMC-induced SCEs between the three groups were found to be highly significant ($p < 0.01$). The enhanced frequencies of spontaneous and MMC-induced chromosome aberrations and SCEs observed in PB and MB patients indicate a clear differential mutagen sensitivity between PB and MB patients who are known to have different immunological status and thereby differ in the severity of the disease.—Authors' Summary

ffytche, T. Importance of early diagnosis in ocular leprosy. (Editorial) Br. J. Ophthalmol. **73** (1989) 939.

The revival of interest in ocular leprosy will prove timely, since the disease now ranks as one of the major contributors to world blindness. Leprosy patients, with their loss of mobility due to the crippling deformities of the disease, should qualify for special consideration in these statistics. Sadly, the numbers with severe visual impairment and blindness are unlikely to diminish in the short term despite the widespread introduction of multidrug therapy in the management of the disease.

A word of caution needs to be added at this stage. Evidence is accumulating that some eyes in lepromatous leprosy may harbor living organisms or antigen long after the skin is bacteriologically negative, and ocular disease may recur after patients are released from control. This implies that some form of ocular supervision may need to be continued indefinitely in multibacillary disease irrespective of current practice. The problem of early diagnosis and detection of ocular involvement therefore becomes more pertinent, and it is here that solid information is lacking at present.—*From* the Editorial

Garg, R., Agrawal, J. K., Bajpai, H. S., Singh, G. and Srivastava, P. K. Glucose tolerance test in leprosy. Indian J. Lepr. **62** (1990) 50–54.

A glucose tolerance test (GTT) was carried out in 43 cases of leprosy. They included cases of tuberculoid, borderline, and lepromatous leprosy and those with lepra reaction. It was observed that a normal curve was common in tuberculoid leprosy. A flat glucose tolerance curve was observed in borderline and lepromatous leprosy. However, the diabetic curve was common in lepra reaction. Fasting blood sugar was low in lepromatous leprosy, and it tended to be marginally high in lepra reaction. Normal GTT response was observed in those with duration of disease between 0–6 months, flat curves in those with duration of disease between 7–12 months, while a diabetic curve was more common in those with disease duration of more than 2 years.—Authors' Summary

Garg, S. P., Kalra, V. K., Verma, L. and Mahajan, V. M. Conjunctival microbial flora in leprosy. Indian J. Lepr. **62** (1990) 39–44.

The conjunctival sacs of 71 leprosy patients, paramedical and medical personnel working in a leprosy home were cultured. None of these eyes had any pathology of the outer eye. Surprisingly, 46.2% of the culturally positive eyes carried accepted pathogens, *Staphylococcus aureus* being the commonest. Determining the preoperative bacterial flora and their elimination before undertaking intraocular surgery is recommended.—Authors' Abstract

George, J., Rajendran, M. and Bhatia, V. N. Serum β-glucuronidase in subtypes of leprosy. Indian J. Med. Res. [A] **91** (1990) 106–110.

Serum β-glucuronidase activity was estimated using phenolphthalein mono-β-glucuronic acid as substrate in 176 individuals including 72 lepromatous leprosy patients, 24 patients of borderline leprosy,

42 of borderline tuberculoid, and 38 healthy controls. Of these, 35 patients (20 with lepromatous leprosy, 5 with borderline leprosy and 10 with borderline tuberculoid) were untreated. The enzyme levels were increased significantly in all types of leprosy, the highest levels being seen in treated lepromatous leprosy patients (105.0 SU). There was also a significant difference in the enzyme activity between untreated patients and those on combined dapsone and rifampin therapy, in all three types of leprosy. Among untreated patients, the maximum value observed in lepromatous leprosy was 93.4 SU. The lowest enzyme level in healthy control was 19.5 SU and the maximum was 54.0 SU. The results suggest that in leprosy patients, especially in those on daily multidrug regimens, there is an extensive damage of leukocytes and liver cells where the enzyme is largely present.—Authors' Abstract

Guo, Y.-P., He, Y., Wang, J.-M., *et al.* [Leprous peripheral neuropathy: clinical observation in 11 cases and ultrastructural study of nerve in 2 cases.] Chin. J. Intern. Med. **28** (1989) 545–547. (in Chinese, English abstract on page 573)

Two cases of the tuberculoid form of leprosy associated with peripheral neuropathy, having biopsy of sural nerve performed, were reported. Pathologically, there was diffuse and massive infiltration of lymphocytes in the endoneurium and perineurium. The pathogenic organisms were found in the Schwann cells and endoneurium. The clinical features of leprous neuropathy were studied in 11 cases, and the clinical diagnosis, pathological features, pathogenesis and treatment of this disease are discussed. —Authors' English Abstract

Jha "Amar," A. K. Psoralene in repigmentation of tuberculoid leprosy. Indian J. Dermatol. **34** (1989) 9–12.

Photoactivated psoralens were studied in 60 cases of tuberculoid leprosy for the repigmentation of hypopigmented macules. It was observed that in 42 (70%) cases there was significant repigmentation within 6 months of therapy; in 5 (8.33%) cases there was mild-to-moderate repigmentation, and in 13 (22.64%) cases, there was no change. No significant untoward effects of drug were encountered, except in four patients (6.66%) who developed marked erythema and eczematous reaction.—Authors' Abstract

Kennedy, C., Chin A Lien, R. A. M., Stolz, E., van Joost, T. and Naafs, B. Leprosy and human immunodeficiency virus infection; a closer look at the lesions. Int. J. Dermatol. **29** (1990) 139–140.

A 35-year-old woman visited our venereal disease outpatient clinic to be tested for HIV infection. She had been working as a prostitute on the South American mainland, the Caribbean, and in New York City. She had never used intravenous drugs. Her medical history revealed that she had a hepatitis-B infection in 1978 and primary syphilis in 1984, for which she had been treated. Besides general symptoms of weight loss and anorexia, she had recently developed an anesthetic skin lesion on her right upper arm.

Upon dermatologic examination, a hypopigmented macule of 6–7 cm in diameter with a minimal elevated slightly erythematous border was observed on her right upper arm. The sensitivity to light touch in the center of this lesion was clearly diminished as compared to that of the surrounding skin. A small hypopigmented macule with normal sensation was also seen on the abdomen. Peripheral nerves were not enlarged and there were no signs of peripheral neuropathy.

Clinically, the lesions were compatible with borderline tuberculoid-midborderline (BT/BB) leprosy. Histologic examination of the biopsy specimens taken from the lesion on the upper arm showed perivascular and perineural lymphohistiocytic infiltrations with a tendency to granuloma formation. In and around the granuloma a mild extracellular edema was seen. Some of the histiocytes had foamy cytoplasm and in a Wade-Fite-stained preparation contained solid-staining acid-fast bacteria. The same histologic features, but with markedly less lymphocytic infiltrate, were observed in the specimen from the lesion of the abdomen. The histopathology was that of a borderline lepromatous (BL) leprosy in reaction. Virologic studies showed the following: HIV

Elisa, positive; HIV western blot technique, positive.

The lesions subsided quickly under antileprosy therapy consisting of dapsone 100 mg once daily, clofazimine 100 mg every other day, and rifampin 600 mg once every month, leaving only an anesthetic area on the upper arm. The lesion on the abdomen disappeared without a trace. Her general condition, however, worsened and hospitalization became necessary for progressive malaise, fatigue, weight loss, headaches, and a hemiparalysis of the right side of her body. Neurologic examination did not show any relationship with her leprosy; a neuroluetic infection and a cerebral *Toxoplasma gondii* infection were also excluded. The neurologic symptoms were compatible with an HIV encephalopathy confirming the diagnosis AIDS. A further deterioration in her condition could not be stopped. The patient died 3 months after she was admitted to the hospital.

Concomitant leprosy and HIV infections will especially occur in countries where both infections are endemic. An increase in the ratio of lepromatous to tuberculoid leprosy and thus an increase in the bacterial pool may be significant in these countries, especially as many patients with both leprosy and HIV infections will show a decrease in their CMI and will eventually develop AIDS-related complex (ARC) or full blown AIDS. A collapse in the immune system as seen in AIDS will allow a progression toward the lepromatous side. This may not manifest clinically as is shown in the reported patient. Combining these observations, we recommend that a patient positive for an HIV infection with clinical paucibacillary leprosy be regarded as multibacillary and should be treated accordingly.—*From* the Article

Lu, B.-X., *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 whom have been cured, shows that the incidence 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 common 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 disease will maintain normal vision, indicating that leprosy-caused blindness is preventable. Most of the 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 to ophthalmia and its sequelae. In multibacillary patients, iridocyclitis is less seen, but cataracts 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 actively controlling them in a planned way.—Authors' English Abstract

Porro, A. M., Yamashita, J. T., de Almeida, F. A., Yamada, S. and Michalany, N. S. [Association of Virchowian hanseniasis dermatopoly.] Med. Cut. Ibero Lat. Am. **17** (1989) 179–181. (in Portuguese)

The authors report a case of lepromatous leprosy associated with dermatopolymyositis and gastric adenocarcinoma. The literature is reviewed, and the authors discuss this association.—Authors' English Summary

Rajan, M. A. Eye in multidrug therapy. Indian J. Lepr. **62** (1990) 33–38.

The eyes of 237 multibacillary leprosy patients on multidrug therapy were studied for a minimum period of 2 years and a maximum period of 4 years. Ocular status remained unaltered in 75%, improved in 16%, and there was worsening in 9% during the study period. The changes in those worsened were of microscopic nature and seen mostly among those with long duration of disease and among reactors.—Author's Abstract

Saxena, U., Ravi, S., Ramesh, V., Misra, R. S. and Mukherjee, A. Multiple cutaneous

nerve abscesses on a healed tuberculoid patch. Lepr. Rev. **61** (1990) 180–182.

A case of healed tuberculoid leprosy (TT) with multiple superficial nerve abscesses involving the whole cutaneous network on the patch is reported. To the best of our knowledge multiple cutaneous nerve abscesses involving the entire subcutaneous plexus on a TT patch is a very uncommon observation.—Authors' Summary

Shah, P. K. D., Malhotra, Y. K., Lakhotia, M., Kothari, A., Jain, S. K. and Mehta, S. Cardiovascular dysautonomia in patients with lepromatous leprosy. Indian J. Lepr. **62** (1990) 91–97.

Autonomic functions were studied by six standard tests in 65 patients with lepromatous leprosy and 25 healthy controls. Dysautonomia was observed in 22 patients, all having the disease for more than 5 years. Associated peripheral neuropathy, judged clinically, was present in all except one patient. Of the 22 dysautonomic patients, 9 each had mild or moderate dysautonomia and 4 had severe dysautonomia as per the scoring schedule devised by us. Syncope, gustatory sweating, and impotence were the symptoms suggestive of dysautonomia, but not all affected patients reported these symptoms. Involvement of the sympathetic system was more frequent than that of the parasympathetic system. Statistically significant abnormality was seen with atropine ratio, standing 30:15 beat ratio, postural hypotension, and sustained hand grip test. The sustained hand grip test was the one which consistently gave abnormal results in all the 22 dysautonomic patients.—Authors' Abstract

Shwe, T., Thaung, U., Toe, M., Mya, M. M. and Myint, T. The effect of tetanus toxoid in leprosy patients. Indian J. Lepr. **62** (1990) 104–108.

Since cases of lepra reaction following smallpox vaccination and BCG vaccination had been reported, the effect of tetanus immunization on leprosy patients (whether it may provoke a lepra reaction or not) was studied. Three doses of purified tetanus toxoid (one ml initially, one ml after 6 weeks and one ml after 6 months) were given to 357 leprosy patients, and 60 patients living in the same environment were followed as controls. The antibody response following immunization was followed in six lepromatous leprosy patients using the toxin antitoxin neutralization test at the Lf/1000 level in mice and in three of them the antibody titer of leprosy patients rose to a satisfactory level. The number of lepra reactions in these patients was monitored for 9 months (2 months before vaccination, during the 6-month period of vaccination and 1 month after the last dose of vaccine). There was no significant rise in the number of patients with reaction following the vaccination.—Authors' Abstract

Suárez Moreno, O., Valdés-Portela Rodríguez, A. and Aparicio Gómez, J. [Levels of circulating immune complexes in a patient with lepromatous leprosy during a type 2 reaction.] Rev. Leprol. Fontilles **17** (1990) 375–378. (in Spanish)

We report the correspondence found among signs, symptoms and circulating immune complex levels. Those values diminish as the patient's evolution improves. The results are discussed; we suggest that more research is needed in this field.—Authors' English Summary

Immuno-Pathology

Adams, E., Garsia, R. J., Hellqvist, L., Holt, P. and Basten, A. T cell reactivity to the purified mycobacterial antigens p65 and p70 in leprosy patients and their household contacts. Clin. Exp. Immunol. **80** (1990) 206–212.

T-cell reactivity to the 70 kDa and 65 kDa (p70 and p65) protein antigens derived from *Mycobacterium bovis* BCG strain was studied by measuring the proliferative responses of peripheral blood mononuclear cells from members of an isolated Aboriginal community resident in the Torres Straits islands. In the nine index leprosy cases, the pattern of responsiveness to the purified antigens paralleled that to whole sonicates from *M. leprae* and BCG. In the 40 contacts of the index cases, a high correlation was observed between the responses to p70 and p65 as well as to the crude sonicates. Significant T-cell responses to the purified antigens, as well as the crude sonicates, were obtained with cells from the majority of contacts. Limiting dilution analysis of precursor frequencies in the contacts confirmed the immunogenicity of the purified antigens and excluded both a mitogenic component and the presence of suppressor cells in those moderate or low responders whose blood contained sufficient precursors to be tested. p70 appeared to be more potent in stimulating a proliferative response than p65 at equivalent protein concentrations. No correlation between responder status to either antigen or disease type was detected in families. These findings provide confirmation of the importance of p70 and p65 as major T-cell immunogens in man, and indicate that they are both potential candidates for inclusion in a bivalent vaccine for leprosy and tuberculosis.—Authors' Summary

Bloom, B. R. and Jacobs, W. R., Jr. 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 the 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.—Authors' Conclusion

Cree, I. A., Coghill, G. and Beck, J. S. Mast cells in leprosy skin lesions. J. Clin. Pathol. **43** (1990) 196–200.

The variability of mast-cell density within and between leprosy skin lesions was examined as a basis for future studies, and whether the number of mast cells in the lesion was determined by local or systemic factors was evaluated. The mast-cell density in the granuloma, skin appendages, and in-

tervening dermis was assessed by counting mast cells in glycol methacylate sections stained with Giemsa stain, and relating these counts to area measurements obtained by planimetry. In biopsy specimens taken from the edge of established lesions, the density of mast cells within the granulomas was considerably higher than that in the intervening dermis and was comparable with that found in the appendages. No major differences in mast-cell density were found between unaffected skin and the center or edge of individual lesions. Mast-cell densities in biopsy specimens from the edge of different lesions on the same patient were also similar, suggesting that the mast-cell density within the granulomas is independent of the site of the lesion and is determined systemically.—Authors' Abstract

Gao, X.-L., *et al.* [The histopathological observation on erector pili muscle in skin lesions of leprosy; prevention and treatment for skin disease control, Nanjing.] Chin. J. Clin. Dermatol. **19** (1990) 15–18. (in Chinese)

The erector pili muscles in skin lesions of 100 leprosy patients (I = 6, TT = 7, BT = 40, BB = 5, BL = 29, LL = 13) were observed. The authors found that the histopathological changes of erector pili muscles also showed spectral immunological changes from TT to LL. The main infiltrates were epithelioid cells or macrophages, lymphocytes were quite few, and Langhans cells and foreign-body giant cells were absent. Bundles of muscle fibers became extensively swollen, separated, and even fragmented because of the inflammatory infiltration or the formation of granuloma. The tissue reaction of TT and BT was strong, while that of BL and LL was slight, with BB intermediate between these two types. The bacteriological index of *Mycobacterium leprae* increased with upgrading of the types of leprosy. The morphology of *M. leprae* was integrated, and small clumps of *M. leprae* could be seen between muscle fibers in some cases. There were few inflammatory infiltrates around the bacilli.—Authors' English Abstract

Gonzalez-Abreu, E., Mora, N., Perez, M., Pereira, M., Perez, J. and Gonzalez, A. B. Serodiagnosis of leprosy in patients' contacts by enzyme-linked immunosorbent assay. Lepr. Rev. **61** (1990) 145–150.

Serum samples from 3336 contacts of leprosy patients were tested for antiphenolic glycolipid-I antibodies by enzyme-linked immunosorbent assay with the albumin coupled synthetic disaccharide antigen. The overall positivity rate was 9.3%. No significant differences were seen between a group of household contacts of lepromatous patients and those of the other types of the disease. The proportion of ELISA positives was slightly higher in the relatives as compared to workplace contacts and neighbors but significantly different only between the two former ($p < 0.05$). Among those contacts with absorbance values higher than 0.100, 5 new leprosy patients were diagnosed, 2 of them with positive skin smears. A sixth contact was detected with a very high absorbance value in whom no single skin lesion was found but whose lepromin reaction was 0 mm and the skin smear showed a bacteriological index of 3+.—Authors' Summary

Job, C. K., McCormick, G. M., Moses, R. L. and Hastings, R. C. Phagocytosis of *M. leprae* by cardiac muscle cells—a preliminary report. Indian J. Lepr. **62** (1990) 55–59.

Fetal cardiac muscle cells were shown to ingest *Mycobacterium leprae* easily within 20 min of exposure *in vitro*. This phagocytosis is considered nonspecific and facilitated by the lipid coat of the mycobacteria. The presence of *M. leprae* free in the cytoplasm of the muscle cells did not seriously affect the morphology or rhythmic contractions of the cells. The significance of the presence of *M. leprae* in somatic cells needs further study.—Authors' Abstract

Li, S. G., Elfernik, D. G. and de Vries, R. R. P. Phenotypic and functional characterization of human suppressor T-cell clones: II. Activation by *Mycobacterium leprae* presented by HLA-DR molecules to $\alpha\beta$ T-cell receptors. Hum. Immunol. **28** (1990) 11–26.

We have been studying human T-cell clones that suppress antimycobacterial T-cell responses but not T-cell responses to an unrelated antigen or mitogen. In the present paper we report our studies on the activation requirements of these suppressor-T-cell clones. The suppressor-T-cell clones could proliferate and produce interferon-γ upon stimulation with *Mycobacterium leprae* and other mycobacteria but not with unrelated antigens or autologous T-cells. Both suppressor and nonsuppressor clones react to a 36-kDa antigen of *M. leprae*. Thus far, we have not been able to demonstrate whether they see the same or different epitopes. The antigen-driven proliferation of suppressor-T-cell clones was, however, significantly lower than that observed for T-cell clones that did not mediate suppression. The proliferation of suppressor-T-cell clones to *M. leprae* antigens could be blocked by monoclonal antibodies to HLA-DR, $\alpha\beta$ T-cell receptor, interleukin-2 receptor, and, in the case of CD4-positive suppressor-T-cell clones, anti-CD4 monoclonal antibodies. DR restriction of the antigen presentation to these suppressor-T-cell clones was shown in mixing experiments using antigen-presenting cells as mononuclear cells from family members and unrelated individuals. These experiments also indicated that apart from regular DR restriction a hitherto unknown factor may be required for presentation to or activation of suppressor-T-cell clones that are present in the family members and unrelated individuals with the same ethnic and geographic background but absent in DR/Dw-matched healthy Dutch individuals.—Authors' 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' cell is specific to the active lesions of the skin in leprosy.—Authors' English Abstract

Mehra, V. and Modlin, R. L. T-Lymphocytes in leprosy lesions. Curr. Topics Microbiol. Immunol. **155** (1990) 97–109.

The study of T-cell subsets and their function in leprosy lesions continues to offer new insights into regulation of cell-mediated immunity in man. In addition, such studies provide a unique insight into the dynamics of the disease, leprosy. As we continue to learn from lesions, so we will continue to learn about leprosy and the immune response to pathogens in man.—Authors' Conclusion

Moudgil, K. D., Mishra, R. and Talwar, G. P. Comparative evaluation of enzyme immunoassays based on synthetic glycoconjugates and phenolic glycolipid-I for immunodiagnosis of leprosy. Indian J. Lepr. **62** (1990) 60–65.

Enzyme immunoassays (EIAs) based on synthetic glycoconjugates containing the terminal monosaccharide (M-BGG) or disaccharide (ND-BSA) residue of the trisaccharide component of phenolic glycolipid-I (PGL-I) for immunodiagnosis of leprosy are described. The results of the assays were compared with that of the EIA using PGL-I. All three assays were highly specific for leprosy. The percent positivity of active lepromatous leprosy (LL) patients with M-BGG was 78.05 in comparison to 85.36 with ND-BSA and 82.11 with PGL-I. Similarly, the positivity of tuberculoid (TT) leprosy patients in M-BGG assay was lower than that in EIAs using ND-BSA or PGL-I. However, the difference in the positivity of individual category of leprosy patients in the three EIAs was not statistically significant. The correlation between absorbance values of leprosy sera EIAs based on M-BGG and PGL-I, as well as that in assays using ND-BSA and PGL-I, was statistically significant.—Authors' Abstract

Naafs, B., Kolk, A. H. J., Chin A Lien, R. A. M., Faber, W. R., Van Dijk, G., Kuijper, S., Stolz, E. and Van Joost, T. Anti-*Mycobacterium leprae* monoclonal antibodies cross-react with human skin: an

alternative explanation for the immune responses in leprosy. J. Invest. Dermatol. **94** (1990) 685–688.

A panel of 17 mouse monoclonal antibodies (MoAb) raised against *Mycobacterium leprae* antigens was used to detect antigenic determinants in normal human skin. An indirect immunoperoxidase technique was used. Eight of the MoAb detected epidermal antigens similar to patterns well known for human sera. Five of these MoAb detected determinants in the dermis, too. These observations may indicate a certain degree of similarity between the antigenic determinants occurring in *M. leprae* and in the human host. We propose that such a similarity on the one hand may facilitate the survival of *M. leprae* in the human host when the antigens are not recognized as "non-self," a situation which seems to occur in lepromatous leprosy, when the patients' tissues are loaded with bacteria virtually without any immune response. On the other hand, *M. leprae* antigens which mimic host antigens may induce an auto-immune reaction against the host's own antigens, which could explain the immune reaction in tuberculoid leprosy and during a "reversal reaction" when *M. leprae* is not observed in the host tissues, but extensive granuloma formation occurs.—Authors' Abstract

Oftung, F., Shinnick, T. M., Mustafa, A. S., Lundin, K. E. A., Godal, T. and Nerland, A. H. Heterogeneity among human T cell clones recognizing an HLA-DR4,Dw4-restricted epitope from the 18-kDa antigen of *Mycobacterium leprae* defined by synthetic peptides. J. Immunol. **144** (1990) 1478–1483.

Synthetic peptides have been used to exactly define a T-cell epitope region from the immunogenic 18-kDa protein of *Mycobacterium leprae.* Four *M. leprae* reactive CD4+ T-cell clones, isolated from two healthy individuals vaccinated with killed *M. leprae,* recognized a determinant initially defined by the peptide (38–50). However, fine mapping of the minimal sequence required for T-cell recognition revealed heterogeneity among the T-cell clones with regard to the N- and carboxyl-terminal boundaries of the epitopes recognized. MHC restriction analysis showed that the immunogenic peptides were presented to the T cells in an HLA-DR4,Dw4-restricted manner in all cases. The results suggest that a polyclonal T-cell response representing different fine specificities is directed toward a possible immunodominant epitope from the *M. leprae* 18-kDa antigen in individuals carrying this MHC haplotype.—Authors' Abstract

Ottenhoff, T. H. M., Wondimu, A. and Reddy, N. N. B. A comparative study on the effects of rIL-4, rIL-2, rIFN-γ, and rTNF-α on specific T-cell non-responsiveness to mycobacterial antigens in lepromatous leprosy patients in vitro. Scand. J. Immunol. **31** (1990) 553–565.

We have studied lepromatous leprosy (LL) as a human model disease for T-cell nonresponsiveness to specific mycobacterial antigens and studied the effect of rIL-4, rIL-2, rIFN-γ and rTNF-α thereon. T-cell nonresponsiveness to *Mycobacterium bovis* bacillus Calmette-Guérin (BCG) or purified protein derivative of *M. tuberculosis* (PPD) antigens could be overcome in 5 out of 8 nonresponder patients by rIL-2 and in 2 out of 8 by rIL-4. The ability of rIL-4 to overcome BCG/PPD nonresponsiveness was strongly dose-dependent. When rIL-2 and rIL-4 were added simultaneously, they seemed to synergize in their effect. T-cell nonresponsiveness to *M. leprae* could be overcome only in 2 out of 18 nonresponders by rIL-2 but not by rIL-4 alone. The ability of rIL-2 to overcome T-cell nonresponsiveness to *M. leprae* antigens became particularly marked when the recombinant 65-kDa heat-shock antigen of *M. leprae* was used instead of whole bacilli. Exogenously added rIL-4, and to a lesser extent rIL-2, strongly enhanced existing T-cell responses to BCG or *M. leprae* in the majority (8 out of 11) of responders. These findings may have implications for the *in vivo* manipulation of the immune response by recombinant lymphokines and vaccines.—Authors' Abstract

Pisa, P., Gennene, M., Söder, O., Ottenhoff, T., Hansson, M. and Kiessling, R. Serum tumor necrosis factor levels and disease dissemination in leprosy and leishmaniasis. J. Infect. Dis. **161** (1990) 988–991.

It has been suggested that tumor necrosis factor alpha (TNFα) may serve as an important antigen-independent host defense mechanism against parasitic organisms. Sera from 66 patients with leishmaniasis and 68 patients with leprosy, all from Ethiopia, were tested for TNFα using an enzyme-linked immunoassay. Sera from patients with the multi-parasitic/bacillary type of disease (visceral or diffuse cutaneous leishmaniasis and lepromatous leprosy), known to be associated with absent or low specific T-cell response, contained significantly higher TNFα titers than those of patients with pauci-parasitic/bacillary disease (localized cutaneous leishmaniasis and nonlepromatous leprosy). High titers of TNFα in the absence of a functioning T-cell response do not appear to confer resistance against *Leishmania aethiopica* and *Mycobacterium leprae.*—Authors' Abstract

Rao, K. N., Saha, K., Bhatia, V. N. and Gadi, S. *Toxoplasma gondii* antibody in patients of lepromatous leprosy. Jpn. J. Med. Sci. Biol. **42** (1989) 163–168.

Sera from 140 lepromatous leprosy patients (test group) and 120 normal persons, who showed no clinical signs of acute or chronic toxoplasmosis (control group), were studied for the presence of *Toxoplasma gondii* antibody by indirect hemagglutination and indirect-immunofluorescent antibody tests. Both tests showed a high incidence of *Toxoplasma* antibody in the test group in comparison with the control group. IgM and IgG classes of antibody responses were observed in both the groups, which signified recent as well as past infections in them.—Authors' Summary

Sathish, M., Esser, R. E., Thole, J. E. R. and Clark-Curtiss, J. E. Identification and characterization of antigenic determinants of *Mycobacterium leprae* that react with antibodies in sera of leprosy patients. Infect. Immun. **58** (1990) 1327–1336.

Antigenic determinants of *Mycobacterium leprae* were identified by screening a λgt11::*M. leprae* genomic library with two separate pools of sera from leprosy patients. A total of 45 recombinant clones were detected with pooled sera from 21 lepromatous (LL) leprosy patients and 5 additional clones specified polypeptides that reacted with antibodies in pooled sera from 30 borderline tuberculoid or tuberculoid leprosy patients. The recombinant clones that specified antigenic determinants that reacted with sera from LL patients were condensed into eight groups on the basis of DNA hybridization experiments among the *M. leprae* DNA insert fragments. In addition, 11 of the 45 recombinant clones did not hybridize to members of the eight groups nor to one another; these represent unique recombinant clones. None of the recombinant clones identified by screening with sera from tuberculoid leprosy patients hybridized to each other or to any of the 45 LL recombinant clones. The polypeptides specified by the recombinant clones were usually fusion proteins with β-galactosidase, ranging in size from 117 to 175 kilodaltons (kDa). Members of hybridization group III specified nonfusion proteins of 45 kDa. Only members of hybridization group I reacted with any of 30 monoclonal antibodies prepared against *M. leprae* proteins; recombinant proteins from these clones reacted with a single monoclonal antibody directed against the *M. leprae* 65-kDa protein. Thus, at least 22 new antigenic determinants of *M. leprae* have been identified on the basis of their reactivity to antibodies in sera from LL patients or sera from tuberculoid leprosy patients or both.—Authors' Abstract

Schlesinger, L. S. and Horwitz, M. A. Phagocytosis of leprosy bacilli is mediated by complement receptors CR1 and CR3 on human monocytes and complement component C3 in serum. J. Clin. Invest. **85** (1990) 1304–1314.

Mycobacterium leprae, an obligate intracellular pathogen, invades and multiplies within host mononuclear phagocytes. To understand *M. leprae* invasion better, we have investigated the role of phagocyte receptors and bacterium-bound ligands in phagocytosis of *M. leprae* by human monocytes. Complement receptors CR1 and CR3 mediate adherence and phagocytosis of *M. leprae* in nonimmune serum. Two monoclonal antibodies (MAbs) used in combination against CR3 inhibit adherence by up

to 90 ± 3%. Two MAbs used in combination against CR1 and CR3 inhibit adherence by up to 70 ± 1%. Single MAbs against CR1 or CR3 consistently inhibit adherence by 38–55%. In contrast, MAbs against other monocyte surface molecules, alone or in combination, do not significantly influence adherence. As studied by electron microscopy, 100% of monocyte-associated *M. leprae* are ingested in the presence of nonimmune serum and MAbs against CR3 markedly inhibit ingestion. Complement receptors CR1 and CR3 also mediate the low level of adherence observed in the absence of serum. Serum complement component C3 serves as a ligand on the bacterial surface in monocyte phagocytosis of *M. leprae.* Adherence of *M. leprae* to monocytes is enhanced by preopsonization (3.1 ± 1.1-fold increase) and is markedly reduced in <0.5% fresh serum (66 ± 7% reduction) or heat-inactivated serum (68 ± 3% reduction). Adherence is also markedly reduced in C3- or factor B-depleted serum; repletion with purified C3 or factor B increases adherence 4.3 ± 0.8- and 2.6 ± 0.2-fold, respectively. C3 is fixed to *M. leprae* by the alternative pathway of complement activation, as determined by a whole bacterial cell ELISA. By electron microscopy, monocytes ingest *M. leprae* by conventional phagocytosis. This study demonstrates that a) human monocyte complement receptors CR1 and CR3 mediate phagocytosis of *M. leprae*; b) complement component C3 on the bacterial surface serves as a ligand for complement receptors; c) complement component C3 binds to *M. leprae* by the alternative pathway of complement activation; and d) monocytes phagocytize *M. leprae* by conventional phagocytosis.—Authors' Abstract

Smith, D. L., Bahna, S. L., Gillis, T. P. and Clements, B. H. Atopy and IgE in patients with leprosy. J. Allergy Clin. Immunol. **85** (1990) 795–800.

The atopic status of patients with leprosy was assessed by medical history, physical examination, serum total IgE, and specific IgE antibodies to common allergens (by skin testing and RAST). Tests for specific IgE antibody to *Mycobacterium leprae* were performed by RAST and immunoblotting technique. We studied 28 patients with leprosy and 49 control subjects. The two groups did not differ significantly in the prevalence of atopic disease. The IgE level was significantly higher in the patients, however, than in the control subjects, whether there was atopy (296.1 versus 96.3 IU/ml) or not atopy (72.9 versus 18.9 IU/ml). Neither RAST nor immunoblotting technique detected significant levels of IgE antibodies to *M. leprae.* Our data indicate that leprosy was associated with increased total IgE level, but clinical atopy in patients with leprosy was similar to that in control subjects. The observed IgE increase in patients with leprosy appears to be generally nonspecific.—Authors' Abstract

Talwar, G. P., Zaheer, S. A., Mukherjee, R., Walia, R., Misra, R. S., Sharma, A. K., Kar, H. K., Mukherjee, A., Parida, S. K., Suresh, N. R., Nair, S. K. and Pandey, R. M. Immunotherapeutic effects of a vaccine based on a saprophytic cultivable mycobacterium, *Mycobacterium w,* in multibacillary leprosy patients. Vaccine **8** (1990) 121–129.

Immunotherapy with a vaccine consisting of autoclaved *Mycobacterium w* was given in addition to chemotherapy in 54 multibacillary, lepromin-negative patients belonging to BB, BL and LL types of leprosy. Thirty-seven patients with similar types of diseases received chemotherapy and placebo injections. The "vaccine" was repeated every 3 months. Bacterial clearance was more rapid in the vaccinated patients. Two lepromatous leprosy patients with an initial bacterial index (BI) of 1.8 and 2.8 became bacteriologically negative in 1 year. One LL patient with a BI of 6.0 had the BI fall to 0.16 after four doses of the vaccine. None of the LL patients belonging to the placebo group during the same time period became bacteriologically negative. Rapid bacterial clearance was accompanied by distinct signs of clinical improvement. One-hundred percent of BB, 85.7% of BL patients, and 61.5% of LL patients converted to lepromin positivity after four doses of the vaccine. A significant number of vaccinated patients demonstrated an upgrading in skin lesions histopathologically.—Authors' Abstract

Thole, J. E. R., Stabel, L. F. E. M., Suykerbuyk, M. E. G., De Wit, M. Y. L., Klatser, P. R., Kolk, A. H. J. and Hartskeerl, R. A. A major immunogenic 36,000-molecular-weight antigen from *Mycobacterium leprae* contains an immunoreactive region of proline-rich repeats. Infect. Immun. **58** (1990) 80–87.

The 36,000-molecular-weight antigen (36 kDa antigen) of *Mycobacterium leprae* is a major immunogenic protein carrying common and specific antigenic determinants recognized by antibodies and T cells in leprosy patients. Recombinant DNA clones containing the complete gene coding for the 36 kDa antigen, designated in this paper as PRA, were isolated from both lambda gt11 and cosmid libraries of the *M. leprae* genome. The DNA sequence of the *pra* gene coded for a polypeptide of 249 amino acids with a predicted molecular mass of 26,299 daltons. The deduced amino acid sequence revealed a proline-rich (42%) amino-terminal region containing a number of repeated sequences similar or identical to the sequence PGGSYPPPPP. The reactivity of four monoclonal antibodies (F47-9, F67-1, F67-5, and F126-5) was directed to this proline-rich region of the PRA protein. DNA sequence and immunological data indicated that the lambda gt11 recombinant Y3180, which was previously isolated by using antibody F47-9, specifies a fusion protein unrelated to PRA but containing a similar epitope recognized by F47-9.—Authors' Abstract

Vadiee, A. R., Gillis, T. P. and Shannon, E. J. Confirmation of a false-positive result associated with a competition inhibition assay used for detecting antibodies to a protein epitope of *Mycobacterium leprae.* Clin. Exp. Immunol. **79** (1990) 397–402.

A competitive antibody-binding assay (CABA) was developed to detect antibodies in infected armadillos and leprosy patients which compete with a *Mycobacterium leprae*-specific ^{125}I monoclonal antibody IIIE9 for the species-specific *M. leprae*-IIIE9 epitope on the 65-kDa protein. The results suggest that armadillos and leprosy patients produce antibodies that inhibit the binding of ^{125}I–IIIE9 monoclonal antibody to the IIIE9 epitope on crude, native 65-kDa protein preparations. When purified, recombinant 65-kDa protein was substituted for crude antigen, there was no evidence in the CABA of antibody to the IIIE9 epitope. False-positive results, possibly induced by steric hindrance, are likely to be associated with CABA which incorporate crude cell-wall extracts as solid-phase antigen.—Authors' Summary

Wang, C.-R., Liu, M.-F., Chen, M.-Y., Lin, T.-P., Cheng, C.-S. and Chuang, C.-Y. Enzyme-linked immunosorbent assay with BCG sonicate antigen for diagnostic potential of mycobacterial infection in Taiwan. Chin. J. Microbiol. Immunol. **22** (1989) 97–104.

The diagnostic potential of an enzyme-linked immunosorbent assay (ELISA) with bacillus Calmette-Guérin (BCG) sonicate antigen for detection of mycobacterial infections, including pulmonary tuberculosis and leprosy, has been evaluated in the Taiwan area. One-hundred blood samples were collected from 74 active and 26 inactive pulmonary tuberculosis patients of the Taiwan Provincial Tuberculosis Control Bureau. Another 50 samples were collected from 24 lepromatous, 23 tuberculoid, and 3 borderline leprosy patients at the Taiwan Provincial Lo-Sheng Leprosarium. The IgG anti-BCG sonicate levels were compared among patients with tuberculosis, active or inactive, patients with leprosy, and healthy individuals. Patients with tuberculosis, both active and inactive, and those with leprosy had higher BCG sonicate antibody levels and frequencies above the cut-off value than healthy subjects (for BCG-sonicate antibody, $p < 0.05$ for inactive tuberculosis, $p < 0.0001$ for others; for frequency above cut-off, $p < 0.001$ for inactive tuberculosis, $p < 0.0001$ for others). Among the three groups of patients, significant differences were noted in anti-BCG sonicate antibody levels, and there was no difference of frequency above the cut-off value (i.e., inactive tuberculosis had a lower level than active tuberculosis and leprosy, $p < 0.005$). In conclusion, an ELISA with BCG sonicate antigen could serve as a diagnostic aid for mycobacterial infection in Taiwan. However, it was not possible to differentiate dis-

ease activity in tuberculosis or to discriminate infectious species of mycobacteria. Purified mycobacterial antigens should be tried in further research to improve the specificity and sensitivity in serodiagnosis with ELISA.—Authors' Abstract

Wu, Q.-X., *et al.* [Detection of specific circulating immune complexes in leprosy patients by mouse monoclonal antibody against phenolic glycolipid-I.] Chung Kuo I Hsueh Ko Hsueh Yuan Hsueh Pao **11** (1989) 293–297. (in Chinese)

In this article, we first report the development of a new test for detecting specific circulating immune complexes (SCIC) in the sera of leprosy patients. This test was named monoclonal antibody specific binding assay (McAb/SBA). We screened for SCIC (PGL-I–IgG, PGL-I–IgM) in 200 serum batches from 140 leprosy patients, 20 tuberculosis patients, and 40 normal controls, and compared the McAb/SBA with the PGL-I/ELISA. The results indicated that: a) McAb/SBA was highly sensitive (90%) and specific (95%). Its Youden's Index was 90. Except for its specificity of 95%, the sensitivity (85%) and Youden's Index (85) of the PGL-I/ELISA test were lower than those of McAB/SBA; b) The positive rate (34/40) in paucibacillary patients using McAb/SBA was higher than that (28/40) in PGL-I/ELISA; c) The increase and decline of MOD values in McAb/SBA were associated with BI. McAb/SBA is a new method for detecting SCIC (PGL-I–IgG, PGL-I–IgM) in the sera of leprosy patients, and it is more sensitive than PGL-I/ELISA.—Authors' English Abstract

Microbiology

Biswas, S. K. Cultivation of *Mycobacterium leprae* in artificial culture medium. Indian J. Med. Sci. **43** (1989) 5–10.

A novel procedure in the cultivation of *Mycobacterium leprae* in combined Dubos/Löwenstein-Jensen medium after addition of thyroxine sodium is reported. This has been found to be successful since the organisms, after multiplying vigorously in the thyroxine containing Dubos medium, have produced a visible colony on the surface of Löwenstein-Jensen medium during 8–16 wks of incubation at 37°C. The enhanced growth of this recalcitrant organism is due to the stimulating effect of thyroxine as well as a supply of ready-made basic nutrients in the synthetic Dubos medium. Intradermal inoculation of the bacterial suspension from the subculture into the foot pad of cortisone-treated mouse revealed an early appearance of specific histological lesion of leprosy with infiltration of nerve fibers by lepra cells. The methodology, described here for *in vitro* cultivation, may open up a new era in the preparation of purified vaccine, the study of *in vitro* drug sensitivity, and as such ensure rapid eradication of leprosy.—Authors' Summary

Dastidar, S. G. and Chakrabarty, A. N. Cultivation of a nocardioform acid-fast chemoautotrophic bacterium from armadillo tissues infected with *Mycobacterium leprae.* Indian J. Med. Res. [A] **91** (1990) 98–105.

A nocardioform bacterium was isolated from the spleen tissue of an armadillo infected with *Mycobacterium leprae* and easily propagated in pure culture in mineral salt medium supplemented with only simple C and N sources (e.g., liquid paraffin, tetradecane, ammonium salts, urea, asparagine, gelatin, xanthine, hypoxanthine, etc.). Complex organic substances, e.g., tyrosine, caseine, peptone, meat extract, egg proteins, serum, blood, yeast extract as well as medium 199, did not support the growth of this organism. Microscopically, the organism consisted of acid-fast, long, slender rods which originated from long, fragmented hyphae, or sporulating mycelial tufts; it was acid-fast (at $<4.0\%$ H_2SO_4) which was pyridine-susceptible. It produced DOPA-oxidase and catalase and was lysozyme resistant; this grew best under reduced O_2 tension, at pH 7.0 to 8.0 and 28°C. Serologically, it appeared to be only weakly related to the

prototype human multibacillary leprosy-derived (reference) nocardioform strain, *Nocardia brasiliensis* and *N. caviae,* but was variably related to several mycobacteria strains.—Authors' Abstract

Dhople, A. M. and Ortega, I. An *in vitro* culture method for screening new drugs against *Mycobacterium leprae.* Indian J. Lepr. **62** (1990) 66–75.

An *in vitro* culture system has been devised for the maintenance and growth of *Mycobacterium leprae* in a cell-free medium. Cells from 4-week-old cultures could be transferred to fresh medium, and normal growth was observed in subcultures. Using this system, the MICs of dapsone and rifampin were determined. Dapsone at 25 ng/ml and rifampin at 300 ng/ml completely inhibited the growth of host-grown as well as *in vitro*-adapted *M. leprae.* It was further shown that the effects of both the drugs were bactericidal; this observation was subsequently confirmed using the mouse foot-pad technique.—Authors' Abstract

Lamb, F. I., Singh, N. B. and Colston, M. J. The specific 18-kilodalton antigen of *Mycobacterium leprae* is present in *Mycobacterium habana* and functions as a heat-shock protein. J. Immunol. **144** (1990) 1922–1925.

A monoclonal antibody previously thought to be specific for *Mycobacterium leprae* has been found to crossreact with a cultivable mycobacterium, *M. habana* TMC5135. The epitope is present on a protein of identical molecular mass (18 kDa) in both species. When *M. habana* is subjected to heat shock, expression of the protein is significantly increased; whereas other forms of environmental stress do not increase its expression. Since immunization of mice with *M. habana* results in protection against infection with *M. leprae,* the possibility of using a molecular genetic approach to investigate the role of this protein in protective immunity is raised.—Authors' Abstract

Rook, G., Lydyard, P. and Stanford, J. Mycobacteria and rheumatoid arthritis. (Editorial) Arthritis Rheum. **33** (1990) 431–435.

Evidence for the involvement of a mycobacterial 65-kDa heat-shock protein (hsp65) (or of crossreactive autoantigens) in the etiology of rodent models of arthritis and of human rheumatoid arthritis (RA) has become more provocative following the recent discovery that a change in the glycosylation of IgG, originally described in RA, has also been observed in rodent models of arthritis and in human mycobacterioses. What is the relationship between these two sets of findings, and do they point to a mycobacterial etiology for RA? Experimental findings are analyzed and two hypotheses are discussed.

Neither the arthritis models in which hsp65 plays a role, nor the human or animal conditions in which G0 levels are elevated, have been shown to be exclusively mycobacterial in origin. It is conceivable that many hsp65-containing organisms are equally important. The antibody and skin-test studies with mycobacterial antigens in RA are suggestive, but do not yet provide genus-specific proof that mycobacteria play a role in RA. Nevertheless, it is possible to make a case for a special role for mycobacteria in RA in humans, and we propose two hypotheses.

First, mycobacteria possess relevant adjuvant properties and readily induce raised G0 levels, and some patients with classic mycobacterial infections develop inflammatory arthritides. Therefore, since there are mycobacterium-like organisms that are extraordinarily difficult to detect or grow in culture infection cannot, at present, be ruled out.

An alternative speculation, suggested by the role of the gut flora, is a changing degree of exposure to environmental mycobacteria. The mycobacteria are a largely saprophytic genus. They are so abundant in some environments that direct Ziehl-Neelsen staining of soil or water samples can reveal their presence. The immune response must have evolved in the presence of massive quantities of mycobacteria, which may be needed for the correct "setting" of the immunologic network or T-cell repertoire. However, as a result of changed lifestyles and modern water supplies, their presence in the human gut now varies considerably, being, for example, more common in Africa than in Europe, and it is not clear whether

these organisms are truly commensal. Thus, exposure to the mycobacterial heat-shock protein, unlike exposure to that of commensal genera, is a variable that depends on how and where one lives. Could this factor explain the changing incidence of RA?—*From* the Editorial

Experimental Infections

Brandt, F., Zhou, H. M., Shi, Z. R., Kazda, J., Dhople, A. M., Kolk, A. and Schmidt, D. S. The pathology of the eye in armadillos experimentally infected with *Mycobacterium leprae.* Lepr. Rev. **61** (1990) 112–131.

One-hundred-twenty-seven eyes from 66 *Mycobacterium leprae*-inoculated armadillos were studied histologically and some ultrastructurally. Inflammatory reactions were found in the following extraocular tissues: the eyelid, including the orbicularis muscle and the third eyelid, extraocular muscles, tear gland and Harder's gland. The early and slight changes of the intraocular tissues, small amounts of lymphocytes, plasma cells and macrophage infiltrations were confined to the area around the anterior angle specifically within the trabeculae and the adjacent ciliary body, the root of the iris and the limbus region of the cornea. But in the cases with severe lesions, the whole uvea was densely infiltrated with large, foamy macrophages intermingled with small amounts of lymphocytes, plasma cells and frequently, neutrophils. No specific necrosis of the granulomas was seen. No explanation for the neutrophil infiltrations was given. The lesions in the cornea were significantly less severe than those in the uvea. Retinal lesions comprised of macrophage infiltrations were all obvious extensions of the adjacent uvea lesions. Acid-fast bacilli (AFB) were found within all tissues. The infection of the intraocular tissues in the armadillo eyes seemed to be mainly, if not solely, hematogenous.—Authors' Summary

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 hind foot pads, and from age-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 areas; 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

Epidemiology and Prevention

Carrazana Hernández, G. B. and Ferrá Torres, T. M. [A study of the incidence of leprosy in the city of Camagüey, Cuba.] Rev. Leprol. Fontilles **17** (1990) 353–362. (in Spanish)

A study about the incidence of leprosy was carried out in Camagüey City, Cuba, during 1978–1988. The diagnosis was based on four main criteria: immunology (lepromin test), histopathology (skin biopsy), bacteriology (elbow and ear lymph bacilloscopy), and clinical examination (morphology of the skin lesions and sensibility physical tests) according to the classification of Madrid. The incidence was of 330 cases, which is quite the same as that of Cuba in just a year (between 300 and 350 cases). The incidence rates varied between 6.6 and 22.5 per 100,000 inhabitants and they were higher than the national ones. The average was about 30 new cases each year. The average of early clinical forms (LI + LT) (52.4%) was slightly higher than that of the late ones (LL + LD) (47.6%). In a decreasing order, the clinical forms percentage were the following ones: LL (27.9%), LI (27.0%), LT (25.4%) and LD (19.7%). A slight predominance of females (53.6%) over males (46.4%) was seen. Eight cases under 15 years old were reported (2.4%) and 322 (98.6%) of 15 years and older. In adults, the ages between 25 and 64 represented 69.4%.—Authors' English Summary

Carrazana Hernández, G. E. and Ferrá Torres, T. M. [Epidemiologic indicators of leprosy in the city of Camagüey, Cuba.] Rev. Leprol. Fontilles **17** (1990) 363–373. (in Spanish)

A study of the main epidemiologic indices of leprosy was carried out in Camagüey municipality, Cuba, during 1984–1988. The incidence and its rates per 100,000 inhabitants, clinical forms, bacilloscopy before diagnosis, age groups, and sex were analyzed, as well as the prevalence and its rates per 1000 inhabitants and the movement of patients. Examinated and sick intradomiciliary and extradomiciliary contacts were pointed out. The results of the study have demonstrated that the incidence rates varied between 6.6 and 11.5 per 100,000 inhabitants (24 new cases each year). The percentage of late clinical forms (LL + LD) (48.8%) was similar to the early ones (LL + LT) (51.2%). The cases under 15 years of age represented just 1.7%. A slight predominance of females (54.5%) was observed. The prevalence rate decreased from 1.6 to 1.3 per 1000 inhabitants at the end of the five year period. Few sick intradomiciliary contacts (0.5%–1.7%) and extradomiciliary contacts (0.9%–6.3%) were detected.—Authors' English Summary

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

The incidence of leprosy each year in the period of 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 the forecasted value according to the grey calculation has a better fit with the actual value; its short-term forecasting effect is better and the long-term has a larger error, but the error is less than those of dynamic number sequence fitting and exponential curve equations.—Authors' English Abstract

de Rojas, V. [Various social characteristics of leprosy patients in the city of Havana.] Rev. Cubana Med. Trop. **39** (1987) 55–60. (in Spanish)

A study on some social and economic aspects of leprosy was carried out in a sample of 150 patients in Havana City. Results obtained are compared with data from the Census of Population and Housing, 1981.—Author's English Summary

Fine, P. E. M. and Rodrigues, L. C. Modern vaccines; mycobacterial diseases. Lancet **1** (1990) 1016–1020.

The continued importance of mycobacterial disease in most countries argues for

the value of good prophylactic vaccines. The current BCG preparations, though cheap, stable, safe, and widely used, are less than ideal because of the unpredictable nature of their protective efficacy in different populations. This drawback is exacerbated by the lack of any immunological correlate of protective immunity, and by the difficulty of making epidemiological assessments of efficacy. Most countries of the world currently recommend BCG vaccines for tuberculosis control. The cost-effectiveness of these programs is difficult to assess—again because of the variability and unpredictability of protection imparted by the vaccines. Even in some countries in which BCG seems to have provided good protection against tuberculosis, a decline in the disease has led to reappraisal of the value of routine BCG vaccination. Thus Sweden has discontinued routine BCG vaccination, and in the U.K. there is a shift toward selective vaccination of high-risk groups. The arguments take a very different form in countries where tuberculosis continues to be a major hazard to public health. There is evidence that the vaccines provide reasonable levels of protection against childhood forms of the disease in most populations, though they may have little impact against tuberculosis in older individuals (and thus on transmission of infection). The fact that BCG provides protection against leprosy increases its value in those countries in which leprosy persists. Thus, despite our inability to predict its precise effect, BCG is still judged worthwhile in many countries. But it is important that such programs do not detract from continued emphasis upon case finding and treatment, which remain essential for effective community control of tuberculosis and leprosy.

The complexities surrounding BCG haunt research on new mycobacterial vaccines. The variability in BCG's efficacy between different populations implies the existence of determinants of protective immunity that are not yet understood, and means that multiple trials may be necessary to demonstrate the general utility of any new vaccine. But the popularity of BCG means that it is difficult to identify populations at risk of tuberculosis (or leprosy) which have not already been exposed to BCG. And widespread belief in the value of BCG may raise ethical questions about the inclusion of placebo control groups in trials. Indeed, it is the successes as well as the failures of BCG that will dominate mycobacterial vaccine research for years to come.—Authors' Conclusions

Gupte, M. D., Anantharaman, D. S., Nagaraju, B., Kannan, S. and Vallishayee, R. S. Experiences with *Mycobacterium leprae*-soluble antigens in a leprosy-endemic population. Lepr. Rev. **61** (1990) 132–144.

Rees and Convit antigens prepared from armadillo-derived *Mycobacterium leprae* were used for skin testing in two leprosy-endemic villages to understand their use in the epidemiology of leprosy. In all, 2602 individuals comprising 202 patients with leprosy detected in a prevalence survey, 476 household contacts and 1924 persons residing in non-case households were tested with two antigens. There was a strong and positive correlation ($r = 0.85$) between reactions to the Rees and Convit antigens. The distribution of reactions was bimodal and considering reactions of 12 mm or more as "positive," the positivity rate steeply increased with the increase in age. However, the distributions of reactions to these antigens in patients with leprosy, their household contacts and persons living in non-case households were very similar. These results indicate that Rees and Convit antigens are not useful in the identification of *M. leprae* infection or in the confirmation of leprosy diagnosis in a leprosy-endemic population with a high prevalence of nonspecific sensitivity.—Authors' Summary

Howerth, E. W., Stallknecht, D. E., Davidson, W. R. and Wentworth, E. J. Survey for leprosy in nine-banded armadillos (*Dasypus novemcinctus*) from the southeastern United States. J. Wildl. Dis. **26** (1990) 112–115.

Ears from 853 nine-banded armadillos (*Dasypus novemcinctus*) from Alabama, Arkansas, Florida, Georgia, and Mississippi (U.S.A) were examined microscopically for evidence of leprosy. All were negative for both acid-fast bacteria (*Mycobacterium lep-*

rae) and lesions compatible with leprosy.—Authors' Abstract

Naik, S. S., Acharekar, M. Y. and Godbole, P. M. Leprosy survey in night high schools in greater Bombay. Indian J. Lepr. **62** (1990) 116–119.

A survey of 6096 students attending night high schools in Bombay, India, gave the prevalence rate of leprosy of 9.3 per 1000 this group; 10.5% of the cases identified were having more serious forms of leprosy characterized by nerve involvement or skin-smear positivity. Night-school screening has limited value because it can only be conducted in big industrial cities, and such surveys cover only a very small proportion of the population. However, in view of the current tendency of population shift from rural to urban areas and since such surveys can identify a number of established cases, it can be included among the other routine leprosy case-detection activities in big cities, where night schools exist.—Authors' Abstract

Varughese, P. V., Carter, A. O. and Wittes, R. Leprosy in Canada to 1988. Can. Dis. Wkly. Rep. **15** (1989) 233–238.

Leprosy is a rare disease in Canada, with an average of only 26 newly reported cases (1 per million population) identified annually in recent years. Almost all cases involve foreign-born Canadian residents from leprosy-endemic areas. In recent years, no confirmed indigenous transmission of the disease has been reported, nor is likely to occur, due to rapid implementation of medical therapy following the diagnosis of a case. However, reports show that leprosy did occur indigenously among native-born Canadians in several foci across the country during the 19th and early part of this century. During the past two decades, the annual number of newly reported cases of leprosy has ranged from 6 to 39 (0.3 and 1.6 cases per million population). Compared to the 1970s, the overall annual incidence for the period 1980–1988 has been higher (25 cases compared to 12). A similar increase has also been observed in the United States as a result of an increasing immigrant population from endemic areas.—*From* the Article

Rehabilitation

Chaturvedi, R. M. and Kartikeyan, S. Employment status of leprosy patients with deformities in a suburban slum. Indian J. Med. **62** (1990) 109–112.

In a poor slum area in suburban Bombay, a study of 129 leprosy patients with deformities revealed that only 46% were employed before the appearance of deformities, and most of them had lost their jobs after deformities had appeared. Health education on care of anesthetic extremities did not have the desired impact on the patients; many of them had worsening of their deformities during the phase of their employment because they had to take up any kind of work in order to make a living. They were mostly poorly educated and lacked special skills. The only feasible alternative in this kind of situation appears to be a selective community-based rehabilitation of leprosy patients with deformities.—Authors' Abstract

Guinn, B. Hansen's disease in south Texas. Health Ed. **14** (1983) 46–47.

While Hansen's disease control and maintenance is accepted by public health agencies, too often it remains a disease apart in the total health care delivery system. Isolation of this disease from the mainstream of medical care (medical education, public education, research, rehabilitation, and health promotion) remains the final obstacle to complete management. Separate iso-

lated facilities and personnel are costly and in a broad sense offer less hope for a solution than integration into the health care delivery systems of every community. Fortunately, this situation is gradually changing. The modern Hansen's disease worker is taking the lead in the belief that the disease need no longer become a permanent catastrophe for the patient; that instead he or she can be rehabilitated successfully, take gainful employment, and maintain a normal life.—*From* the Article

Iyere, B. B. Leprosy deformities: experience in Molai Leprosy Hospital, Maiduguri, Nigeria. Lepr. Rev. **61** (1990) 171–179.

A total of 410 patients (288 males, 122 females) aged between 9 and 60 years with an average age of 32.5 years were assessed for deformities of the eyes, hands and feet. The objectives were to find out the number and types of leprosy deformities in the leprosy population of the hospital, the proportion of those deformed among them, and to establish the deformity baseline for the hospital. The study lasted 1 year; 38.78% (26.59% males, 12.20% females) of those investigated had one or more deformities. Apart from plantar and palmar insensitivity, which accounted for 17.91% and 17.24% of all deformities, the most frequent deformities were mobile claw hand 12.94%, plantar ulcers 10.78% and palmar ulcers 5.97%, respectively. With the exception of eye deformities, males accounted for a higher proportion of all deformities. Hand deformities were the most frequent of the three parts of the body studied. The patients' problems were highlighted and the need for adequate management and self-care were emphasized.—Author's Summary

Krishnamurthy, K. V. and Rao, S. P. A study of leprosy affected beggars in Aska (India). Indian J. Lepr. **62** (1990) 113–115.

A study conducted among beggars in and around Aska, Orissa, revealed 41 of them to be leprosy patients. Almost all had taken treatment and had been released from control. Only two of them were mildly positive in their skin smears for AFB. All of them had disabilities and deformities. It is evident that at least in this area beggar leprosy patients cannot be contributing to the transmission of the disease. Their treatment regularity record was also very good.—Authors' Abstract

Richard, B. M. Interosseous transfer of tibialis posterior for common peroneal nerve palsy. J. Bone Joint Surg. **71B** (1989) 834–837.

The interosseous route remains popular for tibialis posterior tendon transfer for drop-foot. It leaves a smaller range of movement than the circumtibial route, but lengthening the calcaneal tendon may improve this. The results of this present series indicate that, in order to predict a good functional result, the ankle must be held in at least 20° of dorsiflexion at the time of tendon transfer.—Author's Abstract

Other Mycobacterial Diseases and Related Entities

Anargyros, P., Astill, D. S. J. and Lim, I. S. L. Comparison of improved BACTEC and Lowenstein-Jensen media for culture of mycobacteria from clinical specimens. J. Clin. Microbiol. **28** (1990) 1288–1291.

A 4-month trial involving 2563 routine clinical specimens was conducted to compare the improved BACTEC TB system (12B medium) with the conventional Lowenstein-Jensen (LJ) media for the isolation, identification, and susceptibility testing of mycobacteria. One-hundred sixty-two mycobacterial isolates were recovered, 147 (91%) with BACTEC and 118 (73%) with LJ media. Of these, 62 were *Mycobacterium tuberculosis* complex strains, 59 (95%) of which were isolated with BACTEC and 54 (87%) of which were isolated with LJ media. Of the remaining 100 isolates, which were mycobacteria other than tuberculosis (MOTT), BACTEC and LJ media detected

88% and 64%, respectively. The contamination rate was significantly higher in BACTEC (5%) than in LJ media (3.3%). The mean isolation time for *M. tuberculosis* complex with BACTEC was 15.5 days, compared with 25.6 days with LJ. For MOTT, the mean isolation times were 5.8 and 21.4 days, respectively. Identification of 32 *M. tuberculosis* complex isolates and 38 isolates of MOTT by the BACTEC NAP (*p*-nitro-α-acetylamino-β-hydroxypropiophenone) inhibition test gave 100% agreement with conventional biochemical identifications. The results of susceptibility testing of 18 *M. tuberculosis* complex isolates with BACTEC agreed completely with those obtained by the resistance ratio method.—Authors' Abstract

Bermudez, L. E. M., Young, L. S. and Gupta, S. 1,25 Dihydroxyvitamin D_3-dependent inhibition of growth or killing of *Mycobacterium avium* complex in human macrophages is mediated by TNF and GM-CSF. Cell. Immunol. **127** (1990) 432–441.

Vitamin D_3 (D_3) has been shown to activate several macrophage functions. To determine whether D_3 could activate macrophages to kill or inhibit intracellular growth of *Mycobacterium avium* complex (MAC), human monocyte-derived macrophages were treated with D_3 (10^{-7}, 10^{-8}, and 10^{-9} M) 24 hr before or for 48 hr after MAC infection. All three concentrations were associated with inhibition of growth or killing of MAC in a dose-dependent fashion (28 ± 4% and 22 ± 3% of killing and inhibition of growth, respectively, at pharmacological concentrations) when added to the monolayer before injection or 60.4 ± 6%, 50.4 ± 3%, and 41.4 ± 6%, respectively, when added to the monolayers after infection. We found that D_3-treated macrophages produced increased concentrations of tumor necrosis factor (TNF) and granulocyte-monocyte colony stimulating factor (GM-CSF). Subsequently, macrophages were activated by D_3 in the presence of anti-TNF or anti-GM-CSF antibody: At 10^{-9} M of D_3 there was no inhibition of D_3-dependent macrophage activation by anti-TNF antibody, whereas anti-GM-CSF antibody was associated with 100% inhibition. At 10^{-8} M of D_3, anti-TNF antibody inhibited 35 ± 6% of killing, and anti-GM-CSF antibody was associated with 100% inhibition. At 10^{-7} M of D_3, anti-TNF antibody inhibited 58 ± 4% and anti-GM-CSF antibody 89 ± 3% of killing. D_3 treatment is associated with anti-MAC activity in human macrophages, and this activity appears to be mediated by both TNF and GM-CSF.—Authors' Abstract

Brandwein, M., Choi, H.-S. H., Strauchen, J., Stoler, M. and Jagidar, J. Spindle cell reaction to nontuberculous mycobacteriosis in AIDS mimicking a spindle cell neoplasm; evidence for dual histiocytic and fibroblast-like characteristics of spindle cells. Virchows Arch. [A] **416** (1990) 281–298.

We report five patients with AIDS who had an unusual spindle-cell proliferation in the lymph nodes and skin caused by nontuberculous mycobacteriosis. The spindle-cell proliferation in these tissues may mimic a spindle-cell neoplasm and pose a diagnostic problem if an infectious etiology is not suspected. The fibroblast-like spindle cells contained numerous acid-fast bacilli. They were strongly positive for antibody markers of monocyte/macrophage and leukocyte derivation: Leu M3, Mo-9, T-200, and HLA-DR, and variably positive for alpha-1 anti-chymotrypsin and lysozyme. Ultrastructurally, these spindle cells were predominantly fibroblast-like with poorly developed features of macrophages. These results reveal the dual macrophage and fibroblastic character of the spindle cells and probably imply a functional differentiation rather than a histogenetic one.—Authors' Summary

Brown, M. A., Farrell, C., Newton, P. and Child, R. P. Thalidomide, pregnancy and renal failure. Med. J. Aust. **152** (1990) 148–149.

A 26-year-old woman with upper limb phocomelia as a result of thalidomide embryopathy developed renal failure that required dialysis during pregnancy. The pregnancy was complicated by dialysis difficulties, uncontrollable hypertension, and deteriorating renal function resulting in fetal

loss at 26-weeks' gestation. The patient was left with end-stage renal failure and recently has undergone cadaveric renal transplantation. This case highlights the widespread effects, including urinary-tract abnormalities, that thalidomide may have and illustrates the peculiar difficulties in managing such a patient during and after pregnancy.—Authors' Abstract

Cambiaso, C. L., Van Vooren, J. P. and Farber, C. M. Immunological detection of mycobacterial antigens in infected fluids, cells and tissues by latex agglutination; animal model and clinical application. J. Immunol. Meth. **129** (1990) 9–14.

We devised an immunoassay for the detection of mycobacterial antigens in cell lysates and in tissue extracts which is based on the agglutination of latex particles coated with anti-*Mycobacterium bovis* $F(ab')_2$, followed by counting of non-agglutinated particles. *M. bovis* cell lysates were tested and a reference curve was established, having a lower limit of detection of 15–20 mycobacteria. We were able to detect mycobacterial antigens in cell lysates from bronchoalveolar washings and in spleen and liver lysates obtained from experimentally infected rabbits. Antigens were also detected in 10 out of 11 samples obtained from patients with proven tuberculous infection. These samples were readily distinguished from 32 negative control samples after pepsin treatment. In contrast, periodate treatment of samples to destroy carbohydrate abolished all reactivity. Following gel filtration chromatography, we identified three peaks with antigenic properties in samples of all types. The detection of mycobacterial carbohydrate antigens by latex agglutination and particle counting should be a useful adjunct in the diagnosis of tuberculosis.—Authors' Abstract

Clancy, L. J., Kelly, P., O'Reilly, L., Byrne, C. and Costello, E. The pathogenicity of *Mycobacterium tuberculosis* during chemotherapy. Eur. Respir. J. **3** (1990) 399–402.

We used the guinea pig as an experimental model to investigate the pathogenicity of *Mycobacterium tuberculosis*. Sputum samples were injected subcutaneously into guinea pigs and the animals were killed and an autopsy performed after 8 weeks. The likelihood of the sputum samples producing tuberculosis in the guinea pig was related to culture positivity rather than to duration of chemotherapy. This study does not support the belief that a change in pathogenicity occurs during treatment of pulmonary tuberculosis.—Authors' Abstract

Dobson, G., Minnikin, D. E., Besra, G. S., Mallet, A. I. and Magnusson, M. Characterization of phenolic glycolipids from *Mycobacterium marinum*. Biochim. Biophys. Acta **1042** (1990) 176–181.

The phenolic glycolipids from two strains of *Mycobacterium marinum* have been isolated and characterized. The glycolipids from *M. marinum* MNC 170 were principally glycosides of diacyl C_{37}, C_{39} and C_{41} phenolphthiocerols A, but in *M. marinum* MNC 842, these lipids were accompanied by glycosides of diacyl phenolphthiodiolones A and novel phthiotriols A with the same overall chain-lengths. The main acyl components of the phenolic glycolipids from *M. marinum* MNC 170 were C_{26} dimethyl and C_{27} and C_{29} trimethyl-branched fatty acids, but in the lipids of *M. marinum* MNC 842, the C_{27} trimethyl acid was the only principal component. The sugar composition of all these glycolipids had been previously shown to correspond to 3-*O*-methylrhamnose.—Authors' Abstract

Gabriel, S. E., Conn, D. L. and Luthra, H. Rifampin therapy in rheumatoid arthritis. J. Rheumatol. **17** (1990) 163–166.

Several second-line antirheumatic agents possess both immunosuppressive and antimicrobial properties. Rifampin is an antimicrobial agent recently found to exhibit immunosuppressive activity in both animal and human studies. Intraarticular rifamycin SV, a rifampin derivative, has been reported to cause dramatic improvement in gonarthritis in 15 patients with rheumatoid arthritis (RA). These reports, along with the personal observation of spontaneous improvement of arthritic symptoms in 2 patients with RA treated with rifampin at our institution, prompted us to conduct a pilot

study using oral rifampin at 600–1200 mg daily in 8 patients with active, adult onset, seropositive RA. Although no clinically important or statistically significant improvement occurred in any of the outcome variables measured ($p > 0.12$), the power of this study to detect such differences was limited. Alkaline phosphatase increased modestly in 7 patients. One patient developed an acute, drug-induced, flu-like syndrome with marked elevation of liver enzymes which resolved promptly with drug withdrawal. We conclude that the potential effectiveness of oral rifampin therapy in RA is doubtful.—Authors' Abstract

Gilleron, M., Venisse, A., Fournie, J.-J., Riviere, M., Dupont, M.-A., Gas, N. and Puzo, G. Structural and immunological properties of the phenolic glycolipids from *Mycobacterium gastri* and *Mycobacterium kansasii*. Eur. J. Biochem. **189** (1990) 167–173.

Mycobacterial species-specific antigens belong to the three following classes: phenolic glycolipids (Phe Gl), acyltrehalose-containing lipooligosaccharides and polar glycopeptidolipids. These antigens have been chemically defined and alkali-labile epitopes were found to characterize the lipooligosaccharide antigen type. In the present study the major *Mycobacterium kansasii* phenolic glycolipid epitope, namely Phe Gl K-I, was delineated as the distal monoacetylated disaccharidic residue: 2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl-(1→3)-2-*O*-methyl-4-*O*-acetyl-α-L-fucopyranose. This acetoxy group is required for K-I epitope recognition demonstrating that alkali-labile epitopes also occur in the phenolic glycolipid antigen class. Using immunoelectron microscopy, the Phe Gl K-I epitope was localized around the electron-transparent layer on the *M. kansasii* cell-wall surface. Furthermore, two new phenolic glycolipids, namely Phe Gl K-III and Phe Gl K-IV, were discovered in minute amounts. They were purified and characterized by their retention time in direct-phase column HPLC. These molecules are also *M. kansasii* antigens, whose epitopes differ from that of Phe Gl K-I. The complete family of phenolic glycolipids Phe Gl K-I, K-II, K-III and K-IV was found in both rough and smooth variants of both *M. kansasii* and *M. gastri* species.—Authors' Abstract

Hasløv, K., Andersen, A. B., Ljungqvist, L. and Weis Bentzon, M. Comparison of the immunological activity of five defined antigens from *Mycobacterium tuberculosis* in seven inbred guinea pig strains. The 38-kDa antigen is immunodominant. Scand. J. Immunol. **31** (1990) 503–514.

We have examined the immunological activity of five affinity-purified protein antigens from *Mycobacterium tuberculosis* in seven inbred and one outbred guinea pig strains. The test systems were measurements of delayed-type hypersensitivity (DTH) responses, lymphocyte stimulation assays (LS), and antibody response measurements. The results showed significant differences in the immunogenicity of the single-protein antigens and, when the antigens were considered separately, highly significant guinea pig strain differences. The outbred guinea pig strain behaved as a DTH high responder to all antigens studied. The order of magnitude of the DTH responses was not usually correlated with that of the corresponding antibody responses for the individual guinea pig strain-antigen combinations. In particular, when compared with the other strains, strain 2 guinea pigs generally gave the lowest DTH, but the highest antibody responses. A 38,000 molecular weight protein, possessing *M. tuberculosis* complex-specific B-cell determinants, appeared immunodominant in 5 out of 7 strains. Our DTH data in the inbred strains further suggest the presence of an *M. tuberculosis*-specific T-cell epitope. A T-cell line, 11D9, derived from the high-responder guinea pig strain 13 reactive to this protein, was shown to be able to confer a tuberculin-like skin reaction *in vivo*. LS assays with recombinant 38-kDa protein and truncated versions of the protein mapped the 11D9-defined T-cell epitope to the middle part of the molecule.—Authors' Abstract

Harboe, M., Wiker, H. G., Duncan, J. R., Garcia, M. M., Dukes, T. W., Brooks, B. W., Turcotte, C. and Nagai, S. Protein

G-based enzyme-linked immunosorbent assay for anti-MPB70 antibodies in bovine tuberculosis. J. Clin. Microbiol. **28** (1990) 913–921.

MPB70 is a highly species-specific protein which is secreted from *Mycobacterium bovis* during culture. To investigate whether antibodies against MPB70 can be used as an indicator of infection with *M. bovis,* an enzyme-linked immunosorbent assay was developed, based on the use of biotinylated protein G, to provide a common indicator for antibody formation in different species. During experimental infection with *M. bovis* in cattle, a characteristic pattern of anti-MPB70 antibody production was observed with an initial flat plateau followed by a marked rise 18 to 20 weeks after infection. Skin testing with bovine tuberculin purified protein derivative (PPD), which was shown to contain antibody-reactive MPB70, was a potent stimulator of antibody production in infected animals. In experimentally infected cattle, we observed an inverse relationship between antibody activity and delayed-type hypersensitivity skin-test reactions. In natural *M. bovis* infections, skin testing with PPD was also a potent stimulator of anti-MPB70 formation. Comparison between the enzyme-linked immunosorbent assay for antibodies to MPB70 and that for antibodies to the widely crossreacting *M. bovis* BCG antigen 85B in animals with *M. bovis, M. avium, M. paratuberculosis,* and *Corynebacterium pseudotuberculosis* infections showed that formation of antibody to MPB70 was highly specific for infection with *M. bovis.* The use of an MPB70-containing PPD preparation for skin testing followed by this anti-MPB70 assay is a highly specific indicator of *M. bovis* infection. Adjustment of the test conditions is expected to provide an increased sensitivity of the procedure for the diagnosis of natural *M. bovis* infections.—Authors' Abstract

Heifets, L. B. and Lindholm-Levy, P. J. MICs and MBCs of Win 57273 against *M. avium* and *M. tuberculosis.* Antimicrob. Agents Chemother. **34** (1990) 770–774.

A new quinolone, Win 57273 [1-cyclopropyl-7-(2, 6-dimethyl-4-pyridinyl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolonecarboxylic acid], synthesized by Sterling Research Group, was tested *in vitro* against *Mycobacterium tuberculosis* and *M. avium* strains. The broth-determined MICs of this agent ranged from 1.0 to 4.0 μg/ml for *M. tuberculosis* strains and from 0.25 to 8.0 μg/ml for *M. avium* strains. A distinctive feature of this agent, in comparison with ofloxacin and ciprofloxacin, is its substantially greater activity at the low pHs. For *M. avium* strains, the MICs of Win 57273 were 2.0 μg/ml or less for 54.5% of strains at pH 6.8 and 85.5% of strains at pH 5.0. Win 57273 was more active than ciprofloxacin against *M. avium* strains, and this difference was very substantial for all *M. avium* strains at pH 5.0. Taking into account that the predominant locations of these organisms *in vivo* are within the phagosomes and phagolysosomes of macrophages, i.e., in acidic environments at pH 5.0 or lower, the greater activity of Win 57273 at low pH makes this quinolone especially promising for *M. avium* infection. The bactericidal activity of Win 57273 for *M. avium* strains was the same as that of ciprofloxacin, with MBCs from 4.0 to 16.0 μg/ml.—Authors' Abstract

Heifets, L. B., Lindholm-Levy, P. J. and Flory, M. A. Bactericidal activity *in vitro* of various rifamycins against *M. avium* and *M. tuberculosis.* Am. Rev. Respir. Dis. **141** (1990) 626–630.

Minimal inhibitory and bactericidal concentrations (MICs and MBCs) of rifampin (RMP), rifabutin (RBT), rifapentine (RPT), CGP-7040, and P-DEA were determined for 50 *Mycobacterium avium* strains in 7H12 liquid medium radiometrically under various pH conditions. Half were isolated from patients with AIDS and the other half from patients without AIDS but with pulmonary disease. The MICs and MBCs were also determined in 7H12 broth for *M. tuberculosis* strains. The MIC results obtained with *M. tuberculosis* strains, and the serum peak levels in humans, were used as standards for interpretation of the MICs and MBCs of the rifamycins for *M. avium.* The bactericidal activity of all rifamycins for *M. avium* was substantially lower than for *M. tuberculosis.*

The majority of *M. avium* strains was within the "susceptible" category, e.g., comparable to susceptible *M. tuberculosis* strains, when tested with CGP-7040 and RPT, and all of them were "moderately susceptible" when tested with P-DEA. On the basis of *in vitro* bacteriostatic and bactericidal activity, it seems that three agents, RPT, P-DEA, and CGP-7040, have more potential than do RMP and RBT against *M. avium* disease.—Authors' Summary

Helbert, M., Robinson, D., Buchanan, D., Hellyer, T., McCarthy, M., Brown, I., Pinching, A. J. and Mitchell, D. M. Mycobacterial infection in patients infected with the human immunodeficiency virus. Thorax **45** (1990) 45–48.

Of 207 homosexual or bisexual patients with the acquired immune deficiency syndrome (AIDS), 24 with the AIDS-related complex, and 39 with asymptomatic HIV infection, 32 patients were found to have mycobacterial infection. *Mycobacterium tuberculosis* was found in 13 patients with AIDS and in two with the AIDS-related complex. *M. avium-intracellulare* was found in 15 patients with AIDS and was disseminated in 12. One patient was infected with *M. kansasii* and one with *M. ulcerans.* Invasive procedures were frequently required to obtain positive bacteriological results. Subclinical carriage of *M. avium-intracellulare* and other mycobacteria thought to be nonpathogenic was common in patients seronegative for the human immunodeficiency virus and at all stages of human immunodeficiency virus infection. All but one isolate of *M. tuberculosis* were fully sensitive to standard antimycobacterial antibiotics. Response to treatment was usually rapid. *M. avium-intracellulare* isolates were all resistant to first line agents *in vitro,* and antibiotics such as ansamycin and amikacin were required to obtain a clinical response.—Authors' Abstract

Hermans, P. W. M., Schuitema, A. R. J., Van Soolingen, D., Verstynen, C. P. H. J., Bik, E. M., Thole, J. E. R., Kolk, A. H. J. and van Embden, J. D. A. Specific detection of *Mycobacterium tuberculosis* complex strains by polymerase chain reaction. J. Clin. Microbiol. **28** (1990) 1204–1213.

During the screening of a *Mycobacterium tuberculosis* lambda gt-11 gene library with monoclonal antibodies, we detected a recombinant clone, lambda PH7311, which contained a mycobacterial DNA insert that hybridized specifically with DNA of *M. tuberculosis* complex strains. Part of this insert was sequenced and used for the development of an *M. tuberculosis* complex-specific polymerase chain reaction (PCR). Only strains belonging to species of the *M. tuberculosis* complex group contained an amplifiable fragment of 158 base pairs (bp). This fragment was absent in all strains tested belonging to 15 other mycobacterial species. After amplification by PCR and dot-blot hybridization with a digoxigenin-labeled oligonucleotide, the limit of detection of purified genomic *M. tuberculosis* DNA amounted to a quantity corresponding to 20 bacterial cells. By this technique about 10^3 *M. tuberculosis* bacteria were detectable in sputum. Using PCR, we were also able to detect *M. tuberculosis* cells in clinical material such as pleural fluid, bronchial washings, and biopsies, and these results were comparable with those obtained by classical bacterial culture. Of 34 *M. tuberculosis* strains, 5 did not carry the amplifiable 158-bp fragment, which occurs usually as a single copy in the chromosome. Evidence is presented that the 158-bp fragment is located near a repeated sequence in the chromosome. We presume that strains which do not carry the 158-bp fragment have lost a chromosomal segment by a genetic rearrangement induced by the repetitive DNA element.—Authors' Abstract

Hiu, I.-J. Extraction and localization by electron microscopy of an immunosuppressor fraction from *Mycobacterium bovis* bacillus Calmette-Guérin (BCG). APMIS **98** (1990) 244–248.

BCG has been used all over the world to immunize against tuberculosis. Nevertheless, in certain areas (South India) BCG vaccines failed to show any protective efficacy. Furthermore, immunosuppressive cell populations have been reported in experimental mycobacterial infection in mice. The pres-

ent work reports the localization and isolation of an immunosuppressor fraction from BCG. This lipid fraction called WDB inhibited the skin reactivity of delayed-type hypersensitivity (DTH) to the test antigen CEWA (crystalline egg white albumin) in guinea pigs and depressed the production of immune antibody to SRBC (sheep red blood cells) in mice. WDB is a glycolipid with an approximate mol.wt. of 62,000. By electron microscopy, WDB was located among the BCG extracellular metabolic products (ECMP) surrounding the BCG cell wall.—Author's Abstract

Hoffner, S. E., Källenius, G., Petrini, B., Brennan, P. J. and Tsang, A. Y. Serovars of *Mycobacterium avium* complex isolated from patients in Sweden. J. Clin. Microbiol. **28** (1990) 1105–1107.

The serovars of clinical isolates of *Mycobacterium avium* complex from 24 acquired immunodeficiency syndrome (AIDS) and 140 non-AIDS patients in Sweden were studied by using type-specific antisera. A wide distribution of serovars was seen. Serovar 6 was predominant in both groups of patients, isolated from 33% and 16% of the AIDS and non-AIDS patients, respectively. The results indicate geographical as well as disease-related differences in the distribution of *M. avium* complex serovars of clinical importance.—Authors' Abstract

Katz, P., Yeager, H., Jr., Whalen, G., Evans, M., Swartz, R. P. and Roecklein, J. Natural killer cell-mediated lysis of *Mycobacterium-avium* complex-infected monocytes. J. Clin. Immunol. **10** (1990) 71–77.

Since the precise mechanism of host responses to infection with *Mycobacterium-avium* complex (MAC) is unclear and since cytotoxic lymphocytes may be involved in the destruction of cells infected with intracellular pathogens, we investigated the ability of normal peripheral blood lymphocytes to kill MAC-infected monocytes in a short-term isotope release assay. Nylon wool-passed lymphocytes lysed MAC-infected but not uninfected monocytes during a 4-hr assay. Infected monocytes were less sensitive to cell-mediated killing than the standard natural killer (NK) cell-sensitive cell line K562, although the kinetics of lysis were similar. The release of lymphocyte-derived mediators such as tumor necrosis factor, interleukin-2 (IL-2), and interferon-alpha and -gamma could not be implicated as a cause of monocyte death. Through the use of cell-specific monoclonal antibodies plus complement, the phenotype of the effector cell was that of an NK cell (CD3 negative, partially CD8 negative, and CD16 positive). The use of highly purified, negatively selected NK cells confirmed these results. NK cell-mediated lysis of infected monocytes decreased MAC viability, indicating that this cytotoxic activity would not favor dissemination of the organism. The killing of MAC-infected monocytes was reduced by K562 cells, suggesting that these targets shared common recognition/binding structures. These results suggest that NK-cell function may be important in the prevention of or response to MAC infection and may help explain the predilection of AIDS patients to develop widespread disease.—Authors' Abstract

Khomenko, I. S., Chukanov, V. I., Gergert, V. Y. and Utkin, V. V. [Tuberculous chemotherapy in combination with corticosteroids and immunomodulators.] Probl. Tuberk. **1** (1990) 24–28. (in Russian)

One-hundred-forty-eight patients with common forms of pulmonary tuberculosis in an outbreak phase and the presence of secondary immunodeficiency were observed. Caverns were found in 80.4% and bacterial excretion in 87.16% of the cases. Group 1 (71 persons) received chemotherapeutic drugs only; group 2 (21 persons), chemotherapeutic drugs and T-activin; group 3 (33 persons), chemotherapeutic drugs and corticosteroids; and group 4 (23 persons), chemotherapeutic drugs, corticosteroids and T-activin. The bacterial excretion in all the groups was found to be the same. The regression of infiltrative changes in the lungs by the sixth month of treatment was more significantly registered in the groups of patients on a regimen containing chemotherapeutic drugs, corticosteroids and T-activin. Cavern closure rate appeared to

be the lowest in subjects receiving chemotherapeutic drugs and corticosteroids; the addition of T-activin increases the cavern closure index. The combination of chemotherapeutic drugs, corticosteroids and T-activin promotes the normalization of the cellular immunity, and increases the efficacy of pulmonary tuberculosis treatment.—Authors' English Abstract

Kuo, C.-C. and Grayston, J. T. Amino acid requirements for growth of *Chlamydia pneumoniae* in cell cultures: growth enhancement by lysine or methionine depletion. J. Clin. Microbiol. **28** (1990) 1098–1100.

Amino acid requirements for the growth of two isolates of *Chlamydia pneumoniae* were studied and compared with those of one strain of *Chlamydia trachomatis* in a HeLa 229 cell culture. It was shown that among 13 amino acids in Eagle minimum essential medium, *C. pneumoniae* required all amino acids except lysine. A true requirement for arginine, isoleucine, leucine, threonine, and valine could not be determined because depletion of 100% of these amino acids caused cell detachment. Consequently, a requirement for these amino acids was based on 90% depletion. *C. trachomatis* biovar *trachoma* required all amino acids except threonine, which was indeterminable. Depletion of 100% and 90% of the lysine and 90% to 70% of the methionine was shown to enhance the growth of *C. pneumoniae*. This phenomenon was shown to be a property of *C. pneumoniae* because the effect of lysine and methionine reduction was also demonstrated in another human line, HL cells, and a mouse line, McCoy cells.—Authors' Abstract

Kurmanbayev, K. K., Agzamova, R. A., Balguzhinov, D. B. and Tieubergenov, E. T. [Epidemiologic risk of tuberculosis-affected cattle for people living in the northern regions of Kazakh, SSR.] Probl. Tuberk. **2** (1990) 13–15. (in Russian)

One of the main reasons of low decrease in the epidemiologic data on tuberculosis in the Republic is represented by an additional huge reservoir of tuberculous infection transmitted by the tuberculosis-infected cattle of which 90% reside in the areas of the northern Kazakhstan. As a consequence, a high tuberculosis morbidity of the rural population of the region, and its cattle breeders in particular, having threefold morbidity rates compared to other occupational groups, is recorded. The emphasis is made on the importance of the joint and concordant efforts of medical and veterinary workers to identify tuberculosis-infected population and animals, and to organize antituberculous activities in the identified foci to bring down an epidemiological risk of the tuberculosis-infected cattle.—Authors' English Abstract

Lacave, C., Lanéelle, M.-A. and Lanéelle, G. Mycolic acid synthesis by *M. aurum* cell-free extracts. Biochim. Biophys. Acta **1042** (1990) 315–323.

The first cell-free system capable of synthesizing whole mycolic acids: ($R_1CH\cdot(OH)CH(R_2)COOH$, with 60 to 90 carbon atoms) from [1-^{14}C]acetate is described, and preliminary investigations into some of its requirements and properties are reported. Biosynthetic activity for mycolic acids occurred in an insoluble fraction (40,000 × *g* pellet) from disrupted cells of *Mycobacterium aurum* (ATCC 23366-type strain); it produced mycolic acids, but a very small amount of non-hydroxylated fatty acids. The predominant product was unsaturated mycolic acid (type I), while oxo- (type IV) and dicarboxy- (type VI) mycolic acids were synthesized to a lesser extent. When [1-^{14}C]palmitic acid was used as a marker, no labelled mycolic acid was detected. The reaction required a divalent cation (Mg^{2+} or Mn^{2+}), $KHCO_3$ and O_2. Neither CoA, NADH, NADPH nor ATP was necessary, but CoA rather increased the synthesis of non-hydroxylated fatty acids. Glucose or trehalose were not required. Avidin inhibited the biosynthesis of the three types of mycolic acid, indicating the presence of a biotin-requiring enzyme in the reaction sequence and therefore a carboxylation step, but citrate had no allosteric effect. Iodoacetamide inhibited the system. These first data are in favor of a complex multienzyme system.—Authors' Abstract

McLean, L., Winrow, V. and Blake, D. Current status review: role of immunity to mycobacterial stress proteins in rheumatoid arthritis. J. Exp. Pathol. **71** (1990) 295–303.

The mycobacterial 65-kDa stress proteins play a key role in certain animal models of inflammatory arthritis. However, the impression emerging is that the mechanism probably involves more than a simple cross-reaction between mycobacterial SP65 and either the host SP65 or a cartilage antigen, and that evidence for a primary role in human rheumatoid arthritis is lacking. A realistic role for immune responses against stress proteins might be the amplification or perpetuation of inflammation. If so, this is unlikely to be limited to arthritis.—*From* Authors' Summary

Merali, S., Zhang, Y., Sloan, D. and Meshnick, S. Inhibition of *Pneumocystis carinii* dihydropteroate synthetase by sulfa drugs. Antimicrob. Agents Chemother. **34** (1990) 1075–1078.

A new reversed-phase high-pressure liquid chromatography assay procedure for dihydropteroate synthetase (DHPS) that involves the elution of the enzyme incubation solution with a series of three solvents of decreasing polarity (ammonium phosphate buffer, 10% methanol, and 50% methanol) was designed. By this procedure DHPS was detected in *Escherichia coli* and *Pneumocystis carinii* with specific activities of 450 and 14 U/mg, respectively. A comparison of the effects of five sulfa drugs on *P. carinii* DHPS activity revealed that dapsone is the most potent of these drugs.—Authors' Abstract

Minnikin, D. E., Ridell, M., Bolton, R. C. and Magnusson, M. Recognition of novel glycolipid antigens from smooth variants of *Mycobacterium tuberculosis.* FEMS Microbiol. Lett. **67** (1990) 55–58.

A major polar and three minor slightly less-polar glycolipids were identified in extracts of two smooth (Canetti) strains of *Mycobacterium tuberculosis.* Immunostaining on thin-layer chromatograms and enzyme-linked immunosorbent assay (ELISA) of purified lipids demonstrated that the major and the two most polar of the minor glycolipids are potent antigens, reacting with homologous antisera and also with that raised against the type strain (H37Rv).—Authors' Summary

Munk, M. E., Shinnick, T. M. and Kaufmann, S. H. E. Epitopes of the mycobacterial heat shock protein 65 for human T cells comprise different structures. Immunobiology **180** (1990) 272–277.

T-cell recognition of foreign antigens is a result of a ternary complex between T-cell receptor, nominal peptide and major histocompatibility complex molecule. It has been proposed that the nominal peptide, which is presented by accessory cells to T cells, has a characteristic structure which can be predicted on the basis of physicochemical criteria. To further study this aspect, we stimulated T cells from normal human blood donors with synthetic peptides (each of approximately 15 amino acids in length) from the heat-shock protein 65 of *Mycobacterium tuberculosis-M. bovis.* We found that while the characterization of certain epitopes follows commonly used predictions, other epitopes cannot be predicted by known methods.—Authors' Abstract

O'Brien, R. J., Geiter, L. J. and Lyle, M. A. Rifabutin (ansamycin LM427) for the treatment of pulmonary *Mycobacterium avium* complex. Am. Rev. Respir. Dis. **141** (1990) 821–826.

During the period October 1983 through January 1988, the Centers for Disease Control (CDC) provided the experimental drug rifabutin (ansamycin LM427) to 406 patients with severe, progressive *Mycobacterium avium* complex pulmonary disease who had been unresponsive to standard therapy. Selected patients were randomly assigned to doses of 150, 300, or 450 mg rifabutin. Choice of companion drugs was left to the treating physicians. In the analysis of data from this program, we examined the relationship between response to treatment, as measured by bacteriologic sputum conversion, survival, weight gain, improvement in respiratory symptoms, and subjective assessment of clinical improvement, and a variety of patient and treatment variables. Al-

though in some of the analyses a higher rifabutin dose appeared to be associated with sputum conversion, survival, and clinical improvement, the drug did not have a marked effect on outcome. The role of rifabutin in the treatment of this disease will best be assessed in a controlled clinical trial.—Authors' Summary

Oren, B., Raz, R. and Hass, H. Urinary *Mycobacterium fortuitum* infection. Infection **18** (1990) 105–106.

Mycobacterium fortuitum, a common saprophyte usually found in water and soil, can also be isolated from sputum and gastric secretions of healthy carriers. Under certain conditions, significant clinical infections due to *M. fortuitum* do occur. Urinary tract infections are rarely caused by atypical mycobacteria. This report describes a urinary tract infection caused by *M. fortuitum* in a 73-year-old patient treated with corticosteroids for bronchial asthma, who was successfully treated with ofloxacin.—Authors' Summary

Ovdiyenko, N. P., Kosenko, V. I., Naimanov, A. K., Kadochkin, A. M., Antonov, B. I. and Gertman, M. I. [Specific category of mycobacteria isolated from cattle and environmental objects.] Probl. Tuberk. **2** (1990) 46–48. (in Russian)

The results of testing the slaughtered cattle material and environment objects for the presence of mycobacteria are presented. During 1984–1988 with a stable excretion of pathogenic *Mycobacterium,* the quantity of the isolated atypical mycobacteria tended to increase. In 1984 the atypical mycobacteria made up 24.1% of the cultures isolated from cattle (pathogenic ones being 75.9%); in 1985, 29.0%; in 1986, 31.4%; in 1987, 46.0% and in 1988, 55.8%. For the above period *M. bovis* amounted to an average of 98.8% with annual fluctuations between 96.65% and 99.1%. During the last 5 years *M. tuberculosis* cultures ranged from 0.9% to 3.3% (1.92% on the average). *M. avium* was isolated from cattle in 22 cases out of 212 samples of the examined material (10.3%). As a result of testing of 2397 samples of the environment objects taken from 34 farms, 391 (16.3%) atypical mycobacteria were isolated. It is necessary to continue, with regard to environmental conditions, the study of animal responses and atypical *Mycobacterium* carriage in different areas of the country.—Authors' English Abstract

Pinchuk, L. M., Lazovskaya, A. L. and Rachkova, O. F. [Identification of mycobacterium species by gas-liquid chromatography.] Probl. Tuberk. **3** (1990) 36–41. (in Russian)

Principles and characteristic features of gas chromatographic identification of mycobacterium from the fatty acid composition were considered. The results of their differentiation by gas chromatography agree with mycobacterium identification according to the complex of morphological, cultural and biochemical, and other characteristics. Copyrolysis has a number of advantages compared to the routine identification techniques, i.e., it reduces the time needed for the analysis down to 2–3 hours; allows one to use small portions of microbial mass; and provides for a complete automation of the procedure. The advisability of putting the gas chromatographic identification of mycobacterium species into practice of the antituberculosis medical and veterinary institutions is pointed out.—Authors' English Abstract

Rastogi, N., Goh, K. S. and David, H. L. Enhancement of drug susceptibility of *Mycobacterium avium* by inhibitors of cell envelope synthesis. Antimicrob. Agents Chemother. **34** (1990) 759–764.

Treatment of infections caused by *Mycobacterium avium* complex bacteria still remains a challenge since these organisms are resistant to a majority of antituberculous drugs. *M. avium* is very often linked with acquired immune deficiency syndrome-associated opportunistic infections. We earlier suggested that one of the strategies for circumventing multiple-drug resistance might be the enhancement of *M. avium* during susceptibility by inhibiting the synthesis of the outermost layer of its envelope, which appears to act as an exclusionary barrier for drugs. In this investigation, we have examined this strategy by

simultaneously using drugs and the following inhibitors of the *M. avium* cell envelope: *m*-fluoro-phenylalanine (an inhibitor of mycoside-C biosynthesis), DL-norleucine (an inhibitor of transmethylation reactions), ethambutol (an inhibitor of arabinogalactan synthesis), EDTA (a divalent-ion chelator), and colistin (an inducer of membrane flux of divalent cations). All the drugs were used in concentrations which were low enough for a possible medical application to be foreseen. This approach, tested on seven strains of the *M. avium* complex, showed that both *m*-fluoro-phenylalanine and ethambutol were interesting candidates because they caused significant enhancement of *M. avium* drug susceptibility.—Authors' Abstract

Roger, H., Thevenet, J. P., Souteyrand, P. and Sauvezie, B. Subcorneal pustular dermatosis associated with rheumatoid arthritis and raised IgA: simultaneous remission of skin and joint involvements with dapsone treatment. Ann. Rheum. Dis. **49** (1990) 190–191.

A 44-year-old white woman with rheumatoid arthritis for 19 years developed subcorneal pustular dermatosis. She had increased polyclonal IgA and IgA rheumatoid factor. After 4 months' treatment with dapsone 100 mg daily, the patient had neither skin lesions nor active joint disease.—Authors' Abstract

Römmele, G., Wirz, G., Solf, R., Vosbeck, K., Gruner, J. and Wehrli, W. Resistance of *Escherichia coli* to rifampicin and sorangicin A—a comparison. J. Antibiot. **43** (1990) 88–91.

Sorangicin A, a macrolide polyether antibiotic, and the ansamycin antibiotic rifampin inhibit DNA-dependent RNA polymerase to a similar extent. Resistance to sorangicin A is due to a mutation in the RNA polymerase which renders the enzyme less sensitive. Parallel investigations with rifampin revealed partial crossresistance, which was more marked in sorangicin A-resistant mutants than in rifampin-resistant mutants.—Authors' Abstract

Shankar, P., Manjunath, N., Lakshmi, R., Aditi, B., Seth, P. and Shriniwas. Identification of *Mycobacterium tuberculosis* by polymerase chain reaction. (Letter) Lancet **335** (1990) 423.

The correspondents briefly describe their use of a gene sequence coding for the MPB 64 protein and amplification of a 240 base-pair region. In tests on 23 clinical samples of 10 PCR-positive specimens 8 were also positive by smear and culture (the other 2 were negative). In 2 urine specimens positive by smear and culture but PCR-negative, a nontuberculosis mycobacterium was identified.—D. W. FitzSimons (Trop. Dis. Bull.)

Xu, S., *et al.* [A follow-up of 23 patients with SCLE.] Chin. J. Clin. Dermatol. **19** (1990) 6–9. (in Chinese)

This article reports the follow-up result of 23 patients with SCLE. The interval of follow-up ranged from 3 to 5.3 years. The morphology of recurring eruptions in 44.8% of the cases was similar to the original eruptions. The skin lesions of 17.4% of the cases cleared; 24.3% of the cases were accompanied with erythema multiformis lesions, and 12.2% of the cases developed erythema multiformis lesions after the disappearance of the original erythema annularis eruptions. Three cases are compatible with the diagnosis of SLE according to the diagnostic criteria of SLE of ARA (1982). The visceral involvement of all the cases studied was rare and mild; only one proceeded to SLE. Thalidomide was helpful. The eruptions began to subside in 12 days and cleared in 38 days, yet they often relapsed after the discontinuation of the drug.—Authors' English Abstract

Yagupsky, P. V., Kaminski, D. A., Palmer, K. M. and Nolte, F. S. Cord formation in BACTEC 7H12 medium for rapid, presumptive identification of *Mycobacterium tuberculosis* complex. J. Clin. Microbiol. **28** (1990) 1451–1453.

We evaluated cord formation in BACTEC 7H12 medium as a criterion for rapid identification of *Mycobacterium tuberculosis* complex. Kinyoun-stained smears, prepared from 270 radiometrically positive BACTEC 7H12 bottles, were examined independently by three observers. Smears

from 93.2%, 88.6%, and 83.0% of the *M. tuberculosis* complex cultures were read as cord positive, and smears from 97.3%, 97.8%, and 99.5% of the mycobacteria other than *M. tuberculosis* cultures were read as cord negative by the three observers, respectively. There was 93.3% agreement between the observers. The presence of cords in BACTEC 7H12 medium can be a reliable criterion for rapid, presumptive identification of *M. tuberculosis* complex.—Authors' Abstract

Yakrus, M. A. and Good, R. C. Geographic distribution, frequency, and specimen source of *Mycobacterium avium* complex serotypes isolated from patients with acquired immunodeficiency syndrome. J. Clin. Microbiol. **28** (1990) 926–929.

Isolates of *Mycobacterium avium* complex from 727 patients with acquired immunodeficiency syndrome (AIDS) were submitted by medical centers across the United States to the Centers for Disease Control for serotyping. We were able to type 630 (87%) of these isolates by our seroagglutination procedure. Almost all typeable isolates were *M. avium* (serotypes 1 to 6 and 8 to 11). Blood was the major specimen source for both *M. avium* and the nontypeable isolates. *M. intracellulare* serotypes made up only 3% of all isolates from AIDS patients, with sputum being the major specimen source. More than 50% of the isolates originated from either New York or California, with serotype 4 being isolated most frequently in New York and serotype 8 appearing most frequently in California. AIDS patients in Los Angeles had a significantly higher isolation frequency for serotype 8 and a significantly lower one for serotype 4 in comparison with patients in either San Francisco or New York City.—Authors' Abstract

Yang, X.-D., Gasser, J., Riniker, B. and Feige, U. Treatment of adjuvant arthritis in rats: vaccination potential of a synthetic nonapeptide from the 65 kDa heat shock protein of mycobacteria. J. Autoimmun. **3** (1990) 11–23.

Adjuvant arthritis induced by mycobacteria in rats is a widely used model of chronic arthritis. A previously described nonapeptide (Thr-Phe-Gly-Leu-Gln-Leu-Glu-Leu-Thr, amino acid sequence 180–188) from the recombinant 65-kDa heat-shock protein of *Mycobacterium bovis* BCG, which was found to contain a T-cell epitope recognized by both arthritogenic and protective T-cell clones *in vitro,* has been investigated for its vaccination and therapeutic potential in adjuvant arthritis in rats. The nonapeptide was found not to be arthritogenic, although the T cells from nonapeptide-immunized rats crossreact *in vitro* with mycobacterial antigens. Intraperitoneal administration of 0.1 mg nonapeptide in oil at day −20, or days −2, −1 and 0, resulted in a marked reduction of incidence and severity of adjuvant arthritis. The disease process and severity were also influenced by therapeutic treatment with 0.1 mg nonapeptide injected intraperitoneally at days 7 to 10. Interestingly, subplantar or intravenous application of the nonapeptide had no influence on the disease process. Deletion of the *N*-terminal threonine led to complete loss of *in vivo* activity of the nonapeptide.—Authors' Abstract

Zhan, T., *et al.* [Clinical observation on the treatment of cutaneous vasculitis with clofazimine.] Chin. J. Clin. Dermatol. **19** (1990) 12–14. (in Chinese)

Sixty-six patients with miscellaneous cutaneous vasculitis were treated with clofazimine in a dose of 150–200 mg/day. The average duration of treatment was 29.3 days; most of them needed 3–7 weeks. Satisfactory results were obtained: cured = 47 (71.2%), marked improvement = 10 (15.2%), improvement = 8 (12.1%); the overall effective rate was 98.5%. The results were more effective in the patients less than 50 years old with a duration of illness less than 6 months. All three groups of vasculitis showed satisfactory effects. The most commonly observed side effect was reversible pink to brownish-black pigmentation of the skin (27.3%). We believe that clofazimine is a facile, efficient, and safe component for the treatment of cutaneous vasculitis.—Authors' English Abstract

Zumla, A. and James, G. D. Sarcoidosis and leprosy—an epidemiological, clinical,

pathological and immunological comparison. Sarcoidosis **6** (1990) 88–96.

While the close relationship between sarcoidosis and tuberculosis has long been recognized, the similarity of sarcoidosis to leprosy has remained in the background. In most of the developing world, sarcoidosis has been apparently eclipsed by the high prevalence of these two common mycobacterial diseases. The relevant epidemiological, clinical, immunological, and pathological features of leprosy and sarcoidosis are compared and contrasted.—Authors' Abstract