CURRENT LITERATURE

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

General and Historical

Stanford, J. L., Torres, T. and Terencio de las Aguas, J. [Immunotherapy in lepromatous leprosy patients at Fontilles.] Fontilles **15** (1985) 309–312. (in Spanish)

After immunotherapy, there should be no severe reactions and the bacterial index should rapidly fall to zero. Biopsy should show resolution of histopathological changes and simple tests of immune function should show a return to normal. As far as possible there should be full neurological recovery. If all of this can be achieved, leprosy will be a different disease in the 21st century.—Authors' English Summary

Chemotherapy

Barss, P. Fatal dapsone agranulocytosis in a Melanesian. Lepr. Rev. **57** (1986) 63–66.

The death from agranulocytosis and septicemia of a young Melanesian male receiving unsupervised treatment with dapsone 100 mg daily for indeterminate leprosy is reported. The historical recognition and clinical management of agranulocytosis resulting from dapsone is discussed. Careful observation of leprosy patients for side effects during the initial weeks of treatment is recommended. This may include hospital admission and regular blood counts when possible.—Author's Summary

Chen, H.-S., Yeh, J.-C., Yang, C.-S., Lin, J.-F. and Lin, M.-L. [Acute interstitial nephritis associated with renal failure induced by rifampin—a case report.] J. Formosan Med. Assoc. **83** (1984) 1053–1057. (in Chinese)

Acute interstitial nephritis associated with renal failure caused by rifampin is a rare complication, which correlates with the methods of usage in the intermittent or interval regimens. No correlation was found between the severity of clinical manifestations and the total dose taken by the patients.

A 49-year-old woman first presented with uneven sizes of scalling, yellowish tuberculoid skin changes at the age of 27 years, and the pathologic diagnosis of lepromatous leprosy was made. She was treated with DDS 100 mg daily since then. Because of the persistent presence of leprosy bacteria in her skin lesions, she was treated by rifampin 600 mg monthly. But, unfortunately, she developed a high fever, nausea, vomiting, abdominal pain, and macular rashes a few hours after taking the second monthly 600 mg of rifampin, followed by oliguria, increased BUN, creatinine, GOT, GPT gradually. Plasma urea was up to 186 mg/dl, creatinine 17.4 mg/dl, GOT 35 u/ml, GPT 120 u/ml and urine revealed the presence of numerous RBCs and 3+ proteinuria. Kidney biopsy revealed acute interstitial nephritis and yellowish drug crystals were found in the lumens, sometime surrounded by the tubular epithelium. The diagnosis was sure by the clinical and pathological features. She was treated with prednisolone, supportive treatment and hemodialysis once. The renal and liver functions then returned completely to normal about 2 months later. This case and a review of the literature is discussed.—Authors' English Summary

Dos Santos Damasco, M. H., Talhari, S., Viana, S. M., Signorelli, M., Saad, M.

H. F. and Andrade, L. M. C. Secondary dapsone-resistant leprosy in Brazil: a preliminary report. Lepr. Rev. **57** (1986) 5–8.

In this first report of laboratory confirmation of the presence of dapsone-resistant *Mycobacterium leprae* in Brazil, the susceptibility to dapsone was studied in 12 patients clinically suspected of being resistant to dapsone.

The results showed that 8/12 strains were fully resistant to dapsone (66%), and 3/12 strains were partially resistant (25%). In 1/12 cases the organisms failed to grow in all groups of mice. Important indicators for dapsone resistance include irregular treatment, lepromas of the histoid variety, bacterioscopy with solid bacilli, and lack of response to dapsone therapy during 6 months.—Authors' Summary

Jamrozik, K. Dapsone syndrome occurring in two brothers. Lepr. Rev. **57** (1986) 57–62.

Two cases of dapsone syndrome occurring in brothers under treatment for multibacillary leprosy in Papua New Guinea are described. Both patients had rash, fever and jaundice, together with signs suggestive of chest infection. One patient died after developing a hemorrhagic diathesis, but the other improved rapidly after therapy with corticosteroids was commenced. Previous case reports of dapsone syndrome are reviewed.—Author's Summary

Johnson, D. A., Cattau, E. L., Jr., Kuritsky, J. N. and Zimmerman, H. J. Liver involvement in the sulfone syndrome. Arch. Intern. Med. **146** (1986) 875–877.

A patient being treated with dapsone developed a hypersensitivity reaction with typical features of the "sulfone syndrome," including fever, malaise, and hepatitis. All abnormalities rapidly reversed with discontinuance of the dapsone regimen and institution of prednisone therapy. Hepatic involvement may be a prominent feature of the sulfone syndrome and may be of the hepatocellular or cholestatic type. Based on our review of the [U.S.] Food and Drug Administration reports, this syndrome appears to be relatively uncommon, but physicians need to recognize that expression of this syndrome may be incomplete. More clinical data are necessary to better define the incidence and pathogenesis of sulfone-induced liver disease.—Authors' Abstract

Lakshmana Rao, S. S., Stanley, J. N. A., Kiran, K. U., Dharma Rao, T., Rao, P. R. and Pearson, J. M. H. The effect of dapsone in high and normal dosage on the clinical and cell-mediated immune status of patients with borderline (BT-BL) leprosy. Lepr. Rev. **57** (1986) 19–26.

Twenty-six patients with untreated borderline leprosy, 16 of whom (R group) had red raised lesions, indicating incipient reversal reaction, were allotted randomly to dapsone 1 mg or 4 mg/kg body weight/day for the initial 2 months of treatment. The R group patients on high dosage dapsone did not show significantly greater clinical improvement during the trial period. Before treatment, their immune response (leukocyte migration inhibition test) to sonicated (but not whole) *Mycobacterium leprae* was higher than that of the 10 patients with macular lesions (Q group). The response of Q group patients was unaffected by dapsone treatment, but in R group patients the response was reduced to Q group level after 1 month of dapsone treatment (both dosages). This suppression persisted for a week when dapsone was temporarily discontinued.—Authors' Summary

Levy, L. and Shepard, C. C. The number of *Mycobacterium leprae* in the pretreatment of biopsy-specimen does not determine the rate of response of patients with lepromatous leprosy to chemotherapy with acedapsone. Lepr. Rev. **57** (1986) 27–31.

In an attempt to explain wide patient-to-patient variation of the rate at which patients respond to chemotherapy with acedapsone, the relationship between the $\log_{10}$ of the number of *Mycobacterium leprae* in the patient's pretreatment skin-biopsy specimen, and the rapidity with which the organisms became noninfective for mice, was examined for a number of patients with previously untreated lepromatous leprosy, treated in the course of a clinical trial in Cebu, Philippines. Analysis

of the data failed to reveal such a relationship.—Authors' Summary

Mathur, A., Venkatesan, K., Girdhar, B. K., Bharadwaj, V. P., Girdhar, A. and Bagga, A. K. A study of drug interactions in leprosy—1. Effect of simultaneous administration of prothionamide on metabolic disposition of rifampicin and dapsone. Lepr. Rev. **57** (1986) 33–37.

A study has been undertaken to examine the potential effects of prothionamide (PTH) on the pharmacokinetics of rifampin (RMP), and dapsone (DDS) in 15 untreated leprosy patients. A daily administration of RMP and DDS for 7 continuous days followed by that of RMP, DDS, and PTH for 7 more days formed the drug schedule. RMP and DDS levels were estimated in timed blood samples collected on days 7 and 14. Twenty-four hour urinary excretions of the 2 drugs were also determined on days 7 and 14 of drug administration. The results showed a lack of any significant effect of PTH on pharmacokinetics of RMP and DDS.—Authors' Summary

Mehta, J., Gandhi, I. S., Sane, S. B. and Wamburkar, M. N. Effect of clofazimine and dapsone on rifampicin (Lositril) pharmacokinetics in multibacillary and paucibacillary leprosy cases. Indian J. Lepr. **57** (1985) 297–310.

A comparative pharmacokinetic study of Lositril (rifampin) was carried out in 6 multibacillary and 12 paucibacillary leprosy cases. The type of leprosy had no significant effect on rifampin pharmacokinetics. The effect of dapsone and clofazimine when given separately and in combination was studied on rifampin pharmacokinetics in each group of 6 patients. Within-group comparison revealed that clofazimine reduced rifampin absorption significantly ($p < 0.01$) and prolonged the time to reach the peak serum concentration ($p < 0.01$). Since MCR and Ke were also reduced significantly in the RC group, as compared with RDC group ($p < 0.02$ and $p < 0.05$, respectively), no significant alteration was seen in overall Auc and Cmax, although t0.5 was increased significantly ($p < 0.02$) in the RC group.

Dapsone alone did not produce any significant alteration in rifampin pharmacokinetic parameters, while dapsone with clofazimine reduced rifampin 1 hr serum levels ($p < 0.05$) and Auc ($p < 0.05$) significantly. Of the 3 groups, except the RC group, both RDC and RD groups were homogenous Ka, avd, Cmax, and Auc/t0.5 ratio of RC group were significantly different from those in the RD group, while KA and avd were significantly less ($p < 0.05$ and $p < 0.001$, respectively), and Cmax and Auc/t0.5 ratio were significantly more ($p < 0.01$) in the RC group. Since clofazimine reduced rifampin absorption, the difference in Ka and tp became more significant in the post-regimen phase ($p < 0.01$).—Authors' Abstract

Stanley, J. N. A., Pearson, J. M. H. and Ellard, G. A. Ethionamide, prothionamide and thiacetazone self-administration. Studies of patient compliance using isoniazid-marked formulations. Lepr. Rev. **57** (1986) 9–18

The acceptability of ethionamide, prothionamide, and thiacetazone as potential companion drugs for the treatment of lepromatous leprosy was assessed in 2 small-scale studies carried out among outpatients in Hyderabad. Specially formulated tablets or capsules containing 6 mg isoniazid as an innocuous marker were prescribed and their ingestion demonstrated by collecting urine samples at surprise home visits and testing for the presence of isoniazid metabolites by a simple colorimetric procedure. About three quarters of the prescribed thioamide doses were ingested and daily doses of 125 mg ethionamide, and 125 or 250 mg prothionamide were of similar acceptability to the patients. Furthermore, prothionamide and dapsone could be given together in a single daily capsule without compromising the dapsone compliance of the patients. However, more extensive studies of thioamide compliance are required before these drugs can be confidently recommended for the treatment of lepromatous patients unable to tolerate clofazimine. Thiacetazone compliance was poorer, supporting the conclusion that thiacetazone should not be recommended for the treatment of leprosy.—Authors' Summary

Clinical Sciences

Armstrong, R. B., Nichols, J. and Pachance, J. Punch biopsy wounds treated with Monsel's solution or a collagen matrix. Arch. Dermatol. **122** (1986) 546–549.

Adjacent punch biopsy wounds in 20 subjects were treated with a collagen matrix or Monsel's solution. Both techniques were easy to use and were hemostatically effective. The collagen matrix produced less inflammation, had a lower incidence of wound infection, was associated with a faster reepithelialization rate, and healed with a modestly better appearance at 4 weeks than did Monsel's solution.—Authors' Abstract

Chung, T. H., Lee, K. S. and Suh, S. B. [Determination of high-density lipoprotein cholesterol and individual cholesteryl esters in leprosy patients.] J. Korean Med. Assoc. **28** (1985) 163–169. (in Korean)

Hypocholesterolemia, especially low levels of high-density liproprotein cholesterol in the serum of leprosy patients, has been reported from this laboratory. This study was carried out to determine the levels of high-density lipoprotein cholesterol and individual cholesteryl esters in the serum of 22 cases of nonlepromatous and 24 cases of lepromatous patients.

A slight decrease in total serum cholesterol was observed in both types of leprosy patients. Significantly decreased values of high-density lipoprotein cholesterol were found in leprosy compared with healthy subjects.—(*From* Authors' English Abstract)

Dash, R. J., Sriprakash, M. L., Kumar, B., Singh, S., Sharma, B. R. and Kaur, S. Adrenal cortical reserve in leprosy. Indian J. Med. Res. **82** (1985) 388–392.

Basal levels of serum cortisol as well as levels in response to insulin hypoglycemia and depot ACTH were determined in 22 patients of lepromatous leprosy, 14 of borderline lepromatous leprosy, 8 of borderline tuberculoid leprosy, and 6 of tuberculoid leprosy with a mean duration of illness for 2 to 7 yr. Five of the male patients studied had evidence of acute lepra reaction. Ten age-matched healthy subjects were similarly studied and served as controls. Cortisol was estimated by radioimmunoassay using WHO matched reagents. None of the patients had clinical evidence of adrenal cortical insufficiency. No significant differences in the basal and stimulated cortisol response parameters including peak, $\triangle$ and area under the response curve, were noted between the various groups of patients and the healthy controls. Cortisol responses were also normal in patients with acute lepra reaction. The data thus revealed normal adrenal cortical function in leprosy.—Authors' Abstract

Kozminska-Kubarska, A., d'Oniene, Y. and Assan, M. [Difficulties in clinically diagnosing leprosy.] Pol. Tyg. Lek. **40** (1985) 661–669. (in Polish)

The problems of leprosy do not concern only the doctors working in the countries where leprosy is endemic (e.g., in Africa) but, more and more, all dermatologists. In Europe there are many immigrants from endemic countries as well as Europeans working in the terrains of endemy. The authors discuss the different clinical methods of diagnosing leprosy and emphasize the role of exact clinical examination. On the basis of observed patients the differential diagnosis with different manifestations, hipopigmented macular lesions, erythematous infiltrated plaques of variable size, the papules and nodules, and the neurological troubles is presented. The authors conclude that more attention should be paid in the manuals edited in Europe to leprosy in differential diagnosis, especially in dermatology and in neurology.—Authors' English Abstract

Kumar, A. and Lakshmanan, M. Adhesive zinc tape treatment of uncomplicated ulcers amongst leprosy outpatients. Lepr. Rev. **57** (1986) 45–51.

The operational feasibility of ordinary adhesive zinc tape treatment of ulcers under field conditions, was studied on 89 uncomplicated superficial ulcers among 50 leprosy

outpatients. Deep ulcers with or without sinus and purulent discharge were not considered fit for tape treatment. All the 13 hand ulcers and 62 (82%) of the 76 plantar ulcers healed in 3.8 ± 2.1 and 9.5 ± 7.6 weeks of tape treatment, while patients were ambulatory. The tape treatment was found to be effective, economical, acceptable, and convenient to patients, and operationally feasible. The available adhesive leucoblast may be used for ulcer treatment in field and hospital situations.—Authors' Summary

Missi, S. M., de Almeida Neto, E., Schaf, S., Gonçalves, C. R., Rodrigues, C. J. and Margarido, L. C. [Contribution to the study of specific arthritis in leprosy patients.] Rev. Hosp. Clin. Fac. Med. Sao Paulo **40** (1985) 22–26. (in Portuguese)

Five patients with leprosy and articular manifestations were studied. The histology of the synovial membrane was studied, as well as clinical and laboratorial investigations. The patients were classified as virchowian (3 cases), virchowian in reaction type erythema nodosum (1 case), and reactional tuberculoid (1 case). The biopsy showed acid-fast bacilli only in virchowian patients.

These findings are not explained by the physiopathologic models usually proposed. We suggest a possible direct involvement of *Mycobacterium leprae* in the pathogenesis of arthritis in leprosy.—Authors' English Summary

Obasi, O. E. This is not leprosy but porphyria cutanea tarda. Trop. Geogr. Med. **37** (1985) 352–355.

Three cases of porphyria cutanea tarda (PCT) misdiagnosed as leprosy were seen between 1978 and 1984 at Kaduna, Nigeria. All 3 patients had been heavy drinkers of a native alcoholic beverage, "burukutu," as well as beer for several years. Alcohol abstinence and oral chloroquine therapy produced satisfactory remission of the disease. This is believed to be the first report of cases of porphyria cutanea tarda from Nigeria.—Author's Abstract

Walton, R. T., Fritschi, E. P. and Umapathy, V. A. Treatment of plantar ulcers in leprosy patients in the community with adhesive zinc tape. Lepr. Rev. **57** (1986) 53–56.

The prevalence of plantar ulcers in 1483 leprosy patients attending village clinics in South India was 4.3%. Patients with "simple" ulcers, i.e., involving only skin and subcutaneous tissue containing no necrotic bone or fibrous tissue and not obviously infected, were randomly allocated to treatment with zinc oxide impregnated adhesive plaster (zinc tape) or conventional antiseptic-soaked gauze dressings. The 2 groups were comparable in age, sex, type of leprosy, the length of time the ulcer had been present, and the distance walked each day.

The area of the ulcer was estimated before treatment and after 1 month. Four ulcers treated with zinc tape healed completely compared with 2 in the control group and mean ulcer area fell from 91.9 ± 11.3 mm^2 (mean ± SEM) to 42.4 ± 15.5 mm^2 in the zinc tape group, and from 89.8 ± 13.9 mm^2 to 56.7 ± 17.4 mm^2 in the control group.

It is concluded that zinc tape is at least as effective as ordinary dressings in healing ulcers. It is more acceptable to patients than untidy, dirty bandages and so deserves more widespread use.—Authors' Summary

Immuno-Pathology

Alvarenga, F. de B., Nunes Sarno, E., Figueiredo, A. de A., Gattas, C. R., and Porto, J. A. [Distribution of Langerhans' cells in the epidermis of hanseniasis patients.] Med. Cut. Iber. Lat. Am. **13** (1985) 187–191. (in Portuguese)

Intra-epidermal OKT+ and OKIa+ cells were identified and counted in 25 cases of leprosy (7 lepromatous, 7 borderline, 8 tuberculoid and 3 indeterminate). No significant variations were found in the number of Langerhans' cells (OKT6+) in the clinical forms of the disease, nor marked variations determined in the relation of OKT6+/OKIa+ intra-epidermal cells. Nevertheless, significant variation in the number of Lan-

gerhans' cells were noted in several cases independent of the clinical form of the disease.—Authors' English Summary

Cho, S.-N., Hunter, S. W., Gelber, R. H., Rea, T. H. and Brennan, P. J. Quantitation of the phenolic glycolipid of *Mycobacterium leprae* and relevance to glycolipid antigenemia in leprosy. J. Infect. Dis. **153** (1986) 560–569.

Chemical and immunologic procedures have been developed for quantitation, in the body fluids of patients with leprosy, of phenolic glycolipid-I, the major specific antigen of the leprosy bacillus. Serum samples were extracted with $CHCl_3/CH_3OH$ and fractionated on columns of silicic acid. Thin-layer chromatography with a sensitivity of about 500 ng allowed detection of the glycolipid in untreated lepromatous and borderline patients, and high-pressure liquid chromatography gave a quantitation of 0.8–3.7 μg/ml of serum from 4 patients. An ELISA-inhibition assay with polyclonal antibodies to glycolipid corroborated these figures. Dot-ELISA on nitrocellulose with polyclonal and monoclonal IgG and antibodies allowed for much greater sensitivity (500 pg) and semiquantitative evaluation. Small quantities of glycolipid were present in the urine of patients with lepromatous leprosy. In sera obtained from patients undergoing chemotherapy, the amount of glycolipid declined sooner than did titer of antibody. This experimental approach is applicable to diagnosis of leprosy, bacillary quantification, and standardization of skin-test reagents and vaccines.—Authors' Abstract

Elferink, B. G., Ottenhoff, T. H. M. and de Vries, R. R. P. Epstein-Barr virus-transformed B cell lines present *M. leprae* antigens to T cells. Scand. J. Immunol. **22** (1985) 585–589.

We have investigated whether or not Epstein-Barr virus-transformed lymphoblastoid B cell lines (EBV-BLCL) are able to present *Mycobacterium leprae* to antigen-reactive T-cell lines and clones. Such EBV-BLCL would provide us with a homogeneous and unlimited source of antigen-presenting cells. Antigen-triggered proliferation of T cells has been studied with co-cultures either with autologous or allogeneic irradiated EBV-BLCL. Our results show that EBV-BLCL are able to present *M. leprae* as efficiently as peripheral blood mononuclear cells, and that they also function in an HLA-DR-restricted fashion. Apart from their possible *in vivo* relevance, these results have important practical implications, in particular for the generation and study of *M. leprae*-reactive T-cell clones.—Authors' Abstract

Haanen, J. B. A. G., Ottenhoff, T. H. M., Voordouw, A., Elferink, B. G., Klatser, P. R., Spits, H. and de Vries, R. R. P. HLA Class-II-restricted *Mycobacterium leprae*-reactive T-cell clones from leprosy patients established with a minimal requirement for autologous mononuclear cells. Scand. J. Immunol. **23** (1986) 101–108.

This report describes an effective method for the cloning of *Mycobacterium leprae*-reactive T lymphocytes with Epstein-Barr-virus transformed autologous B cells as antigen-presenting cells. The two advantages of this method are that it drastically reduces the number of autologous peripheral blood mononuclear cells ($<10^7$ cells) needed to obtain and propagate these T-cell clones (TLC), and that it enables us to expand individual TLC to large numbers of cells ($>10^8$). Thus, the major obstacles for the cloning of T lymphocytes—especially important with regard to patients—are bypassed. Thus far, TLC from 3 leprosy patients have been established. These TLC are HLA class-II-restricted in their *M. leprae*-directed response. A marked enhancement in antigen responsiveness was observed after further expansion of several TLC, some of which turned from nonresponder into responder TLC. Four tested TLC displayed strikingly different antigen recognition patterns when tested against a number of other mycobacterial antigens; one TLC so far recognizes only *M. leprae* antigens.—Authors' Abstract

Holzer, T. J., Nelson, K. E., Schauf, V., Crispen, R. G. and Andersen, B. R. *Mycobacterium leprae* fails to stimulate

phagocytic cell superoxide anion generation. Infect. Immun. **51** (1986) 514–520.

Mycobacterium leprae is an intracellular pathogen that is ingested by and proliferates within cells of the monocyte/macrophage series. Mechanisms by which intracellular pathogens resist destruction may involve failure to elicit a phagocyte "respiratory burst" or resistance to toxic oxygen derivatives and lysosomal enzymes. We have studied the ability of *M. leprae* and *M. bovis* BCG to stimulate the generation of superoxide anion (O_2^-) *in vitro* by human blood neutrophils and monocytes and murine peritoneal macrophages. *M. leprae* bacteria failed to stimulate significant O_2^- release except at high bacteria-to-cell ratios (>50:1) whether or not they were pretreated with normal serum or serum from patients with lepromatous leprosy. Either viable or irradiated BCG, on the other hand, stimulated the 3 cell types to release significant amounts of O_2^- when challenged with as few as 10 organisms per cell. Serum pretreatment enhanced the release of O_2^- by the 3 cell types. Preincubation for 18 hr with viable *M. leprae* did not inhibit the ability of monocytes to respond with an oxidative burst to phagocytic stimuli. The failure of *M. leprae* to stimulate phagocyte O_2^- generation may be an important factor in its pathogenicity.—Authors' Abstract

Jacobs, W. R., Docherty, M. A., Curtiss, R., III and Clark-Curtiss, J. E. Expression of *Mycobacterium leprae* genes from a *Streptococcus mutans* promoter in *Escherichia coli* K-12. Proc. Natl. Acad. Sci. U.S.A. **83** (1986) 1926–1930.

Genomic libraries of *Mycobacterium leprae* DNA partially digested with *Pst* I were constructed in the expression vector pYA626, which contains the promoter region from the *Streptococcus mutans* gene encoding aspartate β-semialdehyde dehydrogenase, which is very efficiently expressed in *Escherichia coli*. We have detected several clones that complement a mutation in the citrate synthase gene of *E. coli*. Southern blot analysis demonstrated that the complementing DNA was *M. leprae* DNA. Sodium dodecyl sulfate/polyacrylamide gel analysis of polypeptides produced by minicells containing the citrate synthase-complementing recombinant molecules demonstrated the production of a 46-kD polypeptide. When the citrate synthase-complementing fragment was cloned in pYA626 in the reverse orientation, the recombinant molecule was no longer able to complement the mutation in the citrate synthase gene and no longer produced the 46-kD polypeptide. When the DNA fragment was cloned in the *Pst* I site of pHC79, so as to allow expression from the β-lactamase promoter, the resulting recombinant failed to complement the mutation in the *E. coli* citrate synthase gene yet still produced the 46-kD polypeptide, but in one fourth the amounts than when expressed from the *S. mutans asd* promoter. This demonstrates that *M. leprae* translational sequences can be recognized by *E. coli* translational machinery. Promoter expression vectors can be used to obtain expression of protein antigens to be used for early diagnosis of leprosy or components of a vaccine and proteins that are targets of potential antileprosy drugs.—Authors' Abstract

Koster, F. T., Teuscher, C., Matzner, P., Umland, E., Yanagihara, D., Brennan, P. J. and Tung, K. S. K. Strain variations in the murine cellular immune response to the phenolic glycolipid I antigen of *Mycobacterium leprae*. Infect. Immun. **51** (1986) 495–500.

The cellular immune response to the *Mycobacterium leprae*-specific phenolic glycolipid I was examined in inbred mice immunized with *M. leprae* by *in vivo* delayed cutaneous hypersensitivity and *in vitro* lymphocyte proliferation. Whereas all mouse strains responded to *M. leprae*-induced delayed-type hypersensitivity and lymphocyte proliferation, only BALB.K was responsive in both assays to the glycolipid. Responsiveness was determined in part by non-*H-2* genes, while the influence of *H-2* genes was not apparent. Among congenic BALB/c mice differing only at *Igh-C* allotype loci, variations in responsiveness were found in both delayed-type hypersensitivity and lymphocytes proliferation assays, indicating a possible role for *Igh-C* loci-linked

genes. Unresponsiveness in the lymphocyte proliferation assay to the glycolipid was inherited as a dominant trait in one set of responder × nonresponder F_1 progeny. We conclude that after immunization with *M. leprae* organisms, the cell-mediated responses to the glycolipid, endowed with a single carbohydrate epitope, are under polygenic control, predominantly non-*H-2*-linked genes.—Authors' Abstract

Modlin, R. L., Mehra, V., Jordan, R., Bloom, B. R. and Rea, T. H. *In situ* and *in vitro* characterization of the cellular immune response in erythema nodosum leprosum. J. Immunol. **136** (1986) 883–886.

We sought to evaluate cell-mediated immune responses in erythema nodosum leprosum (ENL), a reactional state occurring in lepromatous leprosy. Skin biopsies from patients with leprosy were studied with monoclonal antibodies against T lymphocyte antigenic determinants, interleukin 2 (IL-2), and IL-2 receptors (Tac) by using immunoperoxidase staining of frozen sections. Peripheral blood lymphocytes from 18 ENL patients were tested *in vitro* for lepromin-induced suppression of ConA stimulation. Serial studies of 7 lepromatous patients who developed ENL during the course of the study showed increases in both the Leu-3a : Leu-2a ratio and the number of IL-2+ cells. IL-2+ cells comprised 0.3% of the cells in all of the ENL lesions studied as compared with the 0.03% found in nonreactional lepromatous lesions ($p < 0.001$). Lepromin-induced suppression of the ConA response, present in nonreactional lepromatous patients, significantly decreased in patients developing the ENL reaction, but returned after recovery from ENL. These changes in tissues and peripheral blood suggest that the pathogenesis of ENL is related to cell-mediated immune processes. Despite these immunologic changes, however, ENL patients do not recover antigen-specific skin tests or eliminate *Mycobacterium leprae*.—Authors' Abstract

Panteleev, O. A. and Vaneeva, L. I. [Indirect enzyme-linked immunosorbent assay, its accuracy and sources of errors.] Zh. Mikrobiol. Epidemiol. Immunobiol. **3** (1986) 95–99. (in Russian)

The study of the accuracy of the enzyme-linked immunosorbent assay has revealed that the accuracy of this assay is low. The influence of instruments (dispensers, photometers, plates) on the accuracy of the assay has been studied. As shown in this study, the main sources of error are titration procedures and differences in the adsorption and optical properties of available plates.—Authors' English Abstract

Experimental Infections

Dhople, A. M., Johnson, K. J., Williams, S. L., Zeigler, J. A., Cook, C. A. and Storrs, E. E. Nicotinamide adenine dinucleotide glycohydrolase in normal and leprous armadillos. Microbios **28** (1985) 17–20.

The levels of nicotinamide adenine dinucleotide glycohydrolase in the serum samples of healthy and leprous armadillos were measured. The levels were significantly elevated in leprous armadillos. When the particulate and soluble fractions of livers and spleens of these armadillos were examined, it was observed that the increase of the enzyme levels in serum were accompanied by an increase in these two components of the infected organs. The possibility of using this assay in monitoring leprosy infection in armadillos is discussed.—Authors' Abstract

Resnick, M., Bercouvier, H., Mor, N. and Levy, L. Unforeseen death of *Mycobacterium lepraemurium* in infected susceptible mice. J. Infect. Dis. **153** (1986) 368–369.

Systemic infection of susceptible inbred (including CBA) mice with *Mycobacterium lepraemurium* results in progressive disease that terminates in death of the mice. In its later stages, the disease is characterized by profound immunosuppression, and at the time of death the mice harbor enormous populations of bacteria, the number of or-

ganisms in the spleen and liver reaching 10^{10}–10^{11}/organ. In the course of harvesting large numbers of *M. lepraemurium* from moribund CBA mice, we discovered that the great majority of the harvested bacteria were dead.—(*From* the Report)

Epidemiology and Prevention

de Melo Caeiro, F., Carmona Teixeira, M. J. E. and Costa Pereira, M. F. [Hansen's disease in continental Portugal in 1984.] Fontilles **15** (1985) 283–307. (in Spanish)

A total of 2234 leprosy patients were living in continental Portugal in 1984, with a preponderance of males (55.6%) over females (44.4%). In both sexes there is a predominance of the lepromatous form. The average age of the patients is 58.9 years; the age at onset was 31.8 years. Most of the patients are unskilled workers. Of the 2234 patients, only 4% were born outside of Portugal. The prevalence rate of leprosy in Portugal is 24/100,000 inhabitants, with a distribution of focus throughout the country. The yearly incidence during 1975–1983 was between 0.57 and 0.31/100,000 inhabitants, with an average of 38 new patients yearly. Of the 344 patients diagnosed from 1975 to 1983, 16.6% were born outside of Portugal; the average age at onset was 48.4 years, and 50% had the lepromatous and 23.8% had borderline forms of the disease. The leprosy endemic in Portugal is now in a regressive phase.–(*Adapted from* Authors' English Summary)

Gonzalez de Canales, F. and Pinedo y C. Mendez, J. M. [Changes in the prevalence and in the annual rates of detection of new cases in an antileprosy campaign.] Fontilles **15** (1985) 269–273. (in Spanish)

An analysis was made of changes in annual detection rates of new leprosy cases and changes in overall prevalence of the disease in the province of Huelva over a 55-year period from 1930–1985. The annual detection rates are better than prevalence rates in signifying the beginning of the regression of the leprosy endemic.—(*Adapted from* Authors' English Summary)

Rehabilitation

Kumar, R. P. and Brandsma, J. W. A method to determine pressure distribution of the hand. Lepr. Rev. **57** (1986) 39–43.

A simple method to determine pressure distribution and to identify areas of localized high pressure of the deformed and often insensitive hand is presented. The method will also be useful to evaluate tool adaptations and the effect of surgery on the contact-bearing area of the hand.—Authors' Summary

Other Mycobacterial Diseases and Related Entities

Baig, M. M. E., Pettengell, K. E., Simjee, A. E., Sathar, M. A. and Vorster, B. J. Diagnosis of tuberculosis by detection of mycobacterial antigen in pleural effusions and ascites. S. Afr. Med. J. **69** (1986) 101–102.

We describe a method for the diagnosis of pleural and peritoneal tuberculosis by the detection of tuberculous antigens using an enzyme-linked immunosorbent assay. Eleven tuberculous pleural fluid and 10 tuberculous ascitic fluid samples were studied by this technique, using 10 nontuberculous pleural fluid and 14 nontuberculous ascitic fluid samples as controls. An absorbance value of 0.3 was found to separate the tuberculous groups from their controls to a statistically significant extent (ascitic fluid $p < 0.05$; pleural fluid $p < 0.01$).—Authors' Summary

Donta, S. T., Smith, P. W., Levitz, R. E. and Quintiliani, R. Therapy of *Mycobacterium marinum* infections; use of tetra-

cyclines vs rifampin. Arch. Intern. Med. **146** (1986) 902–904.

We describe 4 patients with *Mycobacterium marinum* infections who did not respond to 2- to 6-week courses of therapy with tetracycline, minocycline, and doxycycline. All 4 patients had prompt responses to therapy with either rifampin alone (2 patients) or rifampin in combination with ethambutol. Results of antimicrobial sensitivity tests may be helpful in guiding therapy. Rifampin may be the drug of choice for treatment of these infections.—Authors' Abstract

Emori, K., Nagao, S., Shigematsu, N., Kotani, S., Tsujimoto, M., Shiba, T., Kusumoto, S. and Tanaka, A. Granuloma formation by muramyl dipeptide associated with branched fatty acids, a structure probably essential for tubercle formation by *Mycobacterium tuberculosis.* Infect. Immun. **49** (1985) 244–249.

Muramyl dipeptide, which does not induce epithelioid granuloma when injected alone dissolved in phosphate-buffered saline, could induce extensive granulomas in guinea pigs when chemically conjugated with branched, but not linear, fatty acids. Peptidoglycan fragments of *Staphylococcus epidermidis* could evoke epithelioid granulomas when incorporated in a water-in-oil emulsion. These findings suggest the importance of a lipid bound to muramyl dipeptide for granuloma formation. In view of the fact that mycobacteria uniquely contain large amounts of branched fatty acids, it was proposed that the complex of muramyl dipeptide and branched fatty acids, mostly mycolic acids, is a structure in tubercle bacilli responsible for tubercle formation.—Authors' Abstract

Hunter, J. M. and Arbona, S. Field testing along a disease gradient: some geographical dimensions of tuberculosis in Puerto Rico. Soc. Sci. Med. **21** (1985) 1023–1042.

The spatial pattern of reported tuberculosis incidence in Puerto Rico is characterized by numerous high–low gradients among contiguous municipios. Tuberculin testing of some 1500 subjects along one such gradient reveals that there is no difference in sensitivity and suggests that the gradients are artifacts of reporting. Correlative associations with tuberculin conversion were generally weak, except for age-dependency. Collected personal histories demonstrated that the web of familial and intergenerational relationships is a major force in perpetuating the disease. Concealment of infection, denial and poor compliance in chemotherapy regimens compound the difficulties of case discovery and case control. Interviews in a sample of 12 health centers confirmed that, without the presence of trained and assigned tuberculosis nurses, the health care providers' "index of suspicion" for tuberculosis is generally low. Absence of a tuberculosis clinic virtually dictates serious under-reporting of incidence in that municipio. Despite the success of Puerto Rico's control program over past decades, a reservoir of tuberculosis persists. The level of endemicity is relatively low but unsatisfactory in the context of public health aspirations.—(A.S. *From* Trop. Dis. Bull.)

Marchal, G., Milon, G. and Augier, J. Apparent increased sensitivity of mice to tuberculin by adding a non-specific inflammatory agent to the antigen. Tubercle **67** (1986) 61–67.

The delayed-type hypersensitivity (DTH) reaction at the site of tuberculin injection in immunized animals depends on the presence of sensitized T lymphocytes which interact with the antigen and recruit nonspecific phagocytic cells. The intensity of DTH reaction was found to be related to the nonspecific inflammatory stimulus created by antigen injection. The early plasma protein extravasation which occurred 0.5 hr after antigen injection was correlated with the intensity of DTH reaction measured 18 hr later. The addition to tuberculin of a nonspecific inflammatory agent (concanavalin A or sheep red blood cells) in a dose range without clinical inflammatory effect increased the apparent potency of tuberculin by a factor of 1000.—Authors' Summary

McMurray, D. N., Mintzer, C. L., Tetzlaff, C. L. and Carlomagno, M. A. The influence of dietary protein on the protective effect of BCG in guinea pigs. Tubercle **67** (1986) 31–39.

Specific pathogen-free, Hartley guinea pigs were vaccinated with viable bacille Calmette-Guérin (BCG) and given isocaloric diets identical in every nutrient except protein (control = 30%; low protein = 10%). A nonvaccinated group was maintained on the control diet. Five weeks later, all animals were infected with an aerosol-containing virulent, *Mycobacterium tuberculosis* H37Rv. On the same day, half of the protein-deficient guinea pigs were transferred to the control diet, while the remainder were maintained on the low protein (10%) diet. Animals from each diet treatment were tuberculin tested and sacrificed 1, 2, 3 and 4 weeks post-challenge. Protein-deficient guinea pigs exhibited diminished tuberculin reactions and loss of BCG-induced protection against virulent challenge as measured by the number of viable *M. tuberculosis* recovered from the lung and spleen. Renourished animals expressed normal levels of delayed hypersensitivity within 1 week of initiating the normal diet and were protected as well as vaccinated control guinea pigs against virulent respiratory challenge.—Authors' Summary