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The 1988 JOURNAL—a Continuing Perspective

Our understanding of leprosy continued to grow in 1988. The XIII International Leprosy Congress at The Hague was a showcase of the wealth of new information available to us. In addition to the Congress Supplement, it again seems appropriate to review the progress in the field as reflected in the pages of the 1988 JOURNAL.

In the Original Articles of the March issue, Katoch, *et al.* (1–9)* presented evidence that pyrazinamide might have some effect against persisters in multibacillary leprosy. Pieters, *et al.* (10–20) presented results of field trials on subcutaneous depot injections of either dapsone or monoacetyldapsone at 4-week intervals. Excellent pharmacokinetics were obtained with both preparations, but the dapsone preparation was better tolerated. Marks and Grossetete (21–26) made the interesting observation that the rates of resorption of the anterior nasal spine and those of alveolar bone in the anterior maxilla were independent of each other in lepromatous leprosy. Chirmule, *et al.* (27–35) described the characteristics of a large subunit of ICRC bacilli which might be a candidate for an antileprosy vaccine. Gill, *et al.* (36–44) measured lepromin reactions in healthy, BCG-vaccinated volunteers who were given graded doses of heat-killed, armadillo-derived *Mycobacterium leprae* as a vaccine. There was a dose-response relationship between the vaccine dose and both the early and late lepromin reactions. Sengupta, *et al.* (45–49) coupled soluble *M. leprae* antigens to the surface of liposomes and used them as skin tests. The preparation elicited both early and late delayed-type hypersensitivity reactions similar to integral lepromin. Wu, *et al.* (50–55) measured anti-*M. leprae* antibodies by ELISA using phenolic glycolipid-I (PGL-I), whole *M. leprae,* and the natural disaccharide-octyl-bovine serum albumin (ND-O-BSA) as antigens. Practical problems were discussed in relation to the sensitivities and specificities of the assays. Jacob and Mathai (56–60) evaluated nerve biopsies in the diagnosis of primary neuritic leprosy. Nearly half of the patients had leprosy confirmed by biopsy of a representative cutaneous nerve. The entire spectrum of leprosy was seen in the biopsies. Gormus, *et al.* (61–65) reported a second sooty mangabey monkey with naturally acquired leprosy. The animal had been housed in direct contact with the first sooty mangabey diagnosed as having leprosy in 1979. The first signs of disease appeared in the second mangabey monkey in 1986, almost 7 years after the disease developed in the first animal.

In the Editorial section of the March JOURNAL, Foster, *et al.* (66–81) summarized a literature search relating diet to leprosy. Hastings (82–100) reviewed the 1987 JOURNAL.

In the Correspondence section of the March issue, Georgiev and McDougall (101–104) questioned current policies regarding slit-skin smear services in leprosy control programs in most parts of the world. The authors feel that the real value of slit-skin smears should be re-evaluated and that smears should be taken by highly trained, centralized and supervised personnel and not by unsupervised workers at small peripheral units. Jopling (104) commented on the results of lepromin testing in a study by Katoch, *et al.* Katoch (105–106) explained that Dharmendra lepromin was used instead of Mitsuda lepromin, and commented on the limited prognostic significance of lepromin positivity in paucibacillary patients on multidrug therapy (MDT) in their experience. Corcos (106–109) commented on a number of points made by Maier (IJL 55: 116–139, 1987). Srinivas (109–110) reported repigmentation of a tuberculoid lesion treated with topical 8-methoxypsoralen solution and exposure to sunlight. Singh, *et al.* (110–111) described a very interesting family in Libya in which eight members in three generations had histoid leprosy. Fujiwara (112–115) determined the D and L configuration of the sugar residues of the PGL of *M. leprae* and *M. bovis.* The absolute configurations of the three sugars of *M. leprae* were D for 3,6-di-*O*-methylglu-

* Numbers in parentheses refer to page numbers in the INTERNATIONAL JOURNAL OF LEPROSY, Volume 56, 1988.

cose and L for both the 2,3-di-*O*-methylrhamnose and 3-*O*-methylrhamnose. Baras and Levy (115–118) found no evidence that short-term storage of *M. leprae* in the cold affected viabilities as measured by mouse foot pad inoculations.

In the News and Notes department of the March issue, we were pleased to see the well-deserved 1987 Damien-Dutton Award being presented to Dr. W. Felton Ross (119–120). The deliberations of an informal meeting of eminent Indian leprologists was noted (120–121) in regard to the management of patients on MDT. The appointment of Dr. Hariharan Srinivasan as the new Director of the Central JALMA Institute for Leprosy in Agra, India, (121) as well as the appointment of Dr. Melville Christian as the new Director of Schieffelin Leprosy Research and Training Center, Karigiri, India (121–122) were noted. The appointment of Professor John Turk as the new Chairman of the Medical Advisory Board of LEPRA was noted (123). The well-deserved Prince of Asturias Prize for Science and Technical Research for 1987 was awarded to Dr. Jacinto Convit of Venezuela (124).

The Current Literature section of the March issue began with a report by Ali, *et al.* (131) of their experience with *Centilla asciatica* in the treatment of lepromatous leprosy. Gupta, *et al.* (131–132) found that the initial urinary desacetyl rifampin excretion in tuberculosis patients was significantly increased in those who developed hepatitis. Datz (134–135) reported that a leprosy patient with erythema nodosum leprosum (ENL) underwent a bone scan and there were bilaterally symmetrical double-stripe signs involving the distal tibias similar to those seen in hypertrophic osteoarthropathy. Fornage and Nerot (135) used ultrasound to diagnose an abscess of the common perineal nerve in a tuberculoid leprosy patient. Lamfers, *et al.* (136) reported a patient with both leprosy and AIDS. Mann, *et al.* (136) found that 11 out of 25 bacteriologically positive leprosy patients had measurable unilateral or bilateral perceptive deafness and suggested that leprosy seems to selectively involve the cochlea. Paksoy (136–137) summarized his experience with indeterminate leprosy.

Barros, *et al.* (138) studied 20 nerve biopsies of bacteriologically negative tuberculoid patients using a peroxidase-antiperoxidase method and anti-BCG antibodies. Antigen was found in all 20 of the nerve biopsies, mainly intracellularly, in the cytoplasm of epithelioid cells and, to a lesser degree, in Schwann, endothelial and plasma cells. Bharadwaj, *et al.* (138–139) found that anti-*M. leprae* antibodies as measured by the FLA-ABS test fell gradually in patients with inactive disease. A significant portion of multibacillary cases continued to show high antibody levels, implying the presence of continuous antigenic stimulus even after several years of clinically inactive disease. Britton (139) put forth the interesting hypothesis that exposure to ultraviolet (UV) light might favor the presentation of *M. leprae* antigens along a suppressive pathway in the skin. Britton, *et al.* (139–140) and de Wit, *et al.* (140) undertook sophisticated antigenic analysis of *M. leprae.* Gonzalez-Abreu and Gonzalez (140) found no evidence that a lepromin injection influenced an ELISA using the PGL-I of *M. leprae.* Mehta, *et al.* (140–141) observed that endothelial cells infected *in vitro* with live *M. leprae* released alkaline phosphatase but that no response was seen with heat-killed bacilli. Muthukkaruppan, *et al.* (141) found reduced CD2+ cells in the peripheral blood of bacteriologically positive lepromatous leprosy (LL) patients but normal levels of CD3+ cells. Peripheral blood mononuclear cells from healthy controls could be exposed to *M. leprae in vitro* and a decrease in CD2+ but not CD3+ cells could be seen. This phenomenon may be related to the nonspecific immunologic unresponsiveness seen in bacteriologically positive LL patients. Porichha and Bhatia (142) studied 36 histoid leprosy biopsies and found epithelioid cell foci in 5 and polygonal, foamy macrophages in 12 of the cases. Schmutzhard, *et al.* (142) measured urinary neopterin excretion as a correlate of cell-mediated immunity and found elevated neopterin excretion in 80% of leprosy patients but, surprisingly, no difference between tuberculoid and lepromatous patients. Sibley, *et al.* (143) found *in vitro* inhibition of phagosome-lysosome fusion in mouse macrophages containing freshly isolated live *M. leprae* but a majority of pha-

gosomes containing gamma-irradiated *M. leprae* underwent fusion with lysosomes. Verghese, *et al.* (144) presented evidence that the immunogenicity of *M. leprae* may be enhanced by conjugation with fluorescein isothiocyanate (FITC).

Bhagria and Mahadevan (144) described a modification of the fluorescein diacetate method of determining the viability of *M. leprae* by obtaining quantitative and nonsubjective measurements of fluorescence in a spectrofluorometer. Bharadwaj, *et al.* (144–145) found that *M. leprae* contained isocitrate lyase and malate synthase activities and concluded that *M. leprae* could metabolize via the glyoxylate bypass of the TCA cycle. Ibegbu, *et al.* (145) subjected cell sonicates of *M. leprae* to isoelectric focusing and chromatofocusing. The proteins of mycobacteria in general as well as *M. leprae* were acidic in nature and there were differences noted between untreated and autoclaved *M. leprae* preparations. Kato (145–146) described a multifactorial liquid medium used to grow acid-fast organisms from armadillo tissues containing *M. leprae.* Katoch, *et al.* (146) found that asparagine and glycerol favored the marginal increase and maintenance of ATP in *M. leprae* suspensions *in vitro.* Katoch, *et al.* (146) studied enzymatic activity in armadillo-derived *M. leprae* and concluded that the TCA cycle is operative.

Baskin, *et al.* (147) described three African green monkeys which were inoculated with *M. leprae.* One developed disseminated skin lesions, while the skin lesions in the other two eventually disappeared. At necropsy 5 years after inoculation, all three had active borderline-lepromatous disease in the peripheral nerves. Gelber (147) found minocycline to be active in *M. leprae*-infected mice. Job (147) reviewed the transmission of leprosy. Stallknecht, *et al.* (148) found that 7.5% (5/67) of wild armadillos in Pointe Coupee Parish, Louisiana, U.S.A., were serologically positive for antibodies against the PGL-I antigen of *M. leprae* by ELISA, and that 1.3% (1/74) were histopathologically positive as determined by the presence of acid-fast bacteria in nerves.

Bian (148) described the decline in leprosy in Baoying County, Jiangsu Province, People's Republic of China. Gundersen (148–149) found leprosy to be prevalent in the lowlands and tuberculosis to be prevalent in the highlands in the Blue Nile Valley of western Ethiopia, and speculated on the possible reasons for this phenomenon. Lechat, *et al.* (149), using epidemiometric models, simulated the effect of MDT on the leprosy epidemic and found that it was quite considerable. Louis, *et al.* (149) described an epidemic of leprosy occurring in Rapa, a small island in French Polynesia, from 1922–1950. After peaks of 11/1000 in the incidence rate and 68/1000 in the prevalence rate, the outbreak decreased. Thomas, *et al.* (150) studied exposure to armadillos among Mexican-born lepromatous leprosy patients. A history of direct contact with armadillos was strongly associated with the disease. A measure of relative risk of leprosy was 2.7–3.5 for indirect exposure and 4.1–6.5 for direct exposure to armadillos in this population.

Boucher and Hirzel (151) followed a series of patients after surgical decompression of the posterial tibial nerve. Breger (151) compared results between Semmes-Weinstein monofilament sensory mappings and sensory nerve conduction tests. Fritschi (151) described five field tests for detecting early damage to peripheral mixed nerve trunks in leprosy. Jacobs, *et al.* (152) studied teased fiber preparations in nerve biopsies from leprosy patients and found that the most common abnormality was paranodal demyelination affecting successive internodes. Some fibers showed axonal atrophy, suggesting that the demyelination in some cases may be secondary to axonal changes. In other cases, there were focal areas of demyelination affecting whole internodes of many fibers at the same level across the nerve which suggested that these changes were caused by local factors.

Bahr, *et al.* (153) reported the extensive multiple skin test survey data on school children in Kuwait, and found that the mycobacterial species most commonly encountered was *M. leprae,* a remarkable finding in view of the very low prevalence of leprosy in that country. Britton, *et al.* (153) characterized a 70-kDa antigen of *M. bovis* which shares determinants with *M. tuberculosis* and *M. leprae.* Casal, *et al.* (154) reported *in vitro* susceptibility of *M. tuber-*

culosis to a new macrolide antibotic designated RU-28965. Crawford and Bates (154–155) examined 26 strains of *M. avium* complex isolated from patients with AIDS for plasmids. Plasmids were found in all of the strains, raising the possibility that they may play a role in virulence. Daffé, *et al.* (155) described a phenolic glycolipid (PGL) containing three sugars in *M. tuberculosis* (strain Canetti). These PGL compounds have now been described for *M. leprae, M. kansasii, M. bovis, M. marinum,* and now *M. tuberculosis.* Dickinson and Mitchison (155–156) compared the activities of rifampin and various newer rifamycins against *M. tuberculosis.* Ellis and Tayoub (156–157) found reduced plasma cortisol levels and reduced responses to ACTH in a substantial number of patients with acute pulmonary tuberculosis. Gilburd (157) measured IgG antibodies to PPD and a cytoplasmic antigen preparation from BCG in patients with active pulmonary tuberculosis and in healthy volunteers. Sensitivity and specificity of the ELISA with PPD amounted to 76.6% and 85%, respectively, while the respective figures using the BCG cytoplasmic antigen preparation were 90% and 95%. Lamb and Young (157) used T-cell cloning in conjunction with SDS-PAGE immunoblotting to determine the cellular immune response to *M. tuberculosis* and BCG. Onwubalili, *et al.* (158) found significant reductions in absolute numbers of total T cells, T4 cells, and B lymphocytes in the peripheral blood of active tuberculosis patients compared with normal controls. Shi, *et al.* (158–159) found thalidomide useful in the treatment of lupus erythematosus. Shoemaker, *et al.* (159) identified different strains of *M. tuberculosis* using restriction fragment analysis of chromosomal DNA. Stokes, *et al.* (160) showed that mice could be separated into naturally susceptible and naturally resistant strains based on the growth of *M. avium* 702 in the animals. Tsukamura, *et al.* (160–161) compared the *in vitro* antimycobacterial activities of ansamycin (rifabutin) and rifampin. In general, rifabutin was 2–4 times more potent than rifampin. Some rifampin-resistant *M. tuberculosis* strains were resistant also to rifabutin, others were sensitive. A similar pattern was seen with *M. avium* complex.

In the June Original Articles, Sirumban, *et al.* (223–227) found that untreated indeterminate and tuberculoid cases had an average healing time of approximately 2 years with a healing rate of 22.4% per year and a rate of downgrading of 0.57% per year. These careful observations re-emphasize the well-recognized phenomenon of self-healing or spontaneous regression in paucibacillary leprosy. Hodes and Teferedegne (228–230) reported five cases of tetanus in leprosy patients in Ethiopia. Neylan, *et al.* (231–237) explored illness beliefs in 61 leprosy patients in northern Thailand. Despite efforts at patient education, very few of these patients adopted the concept of bacterial infection to explain their illness. Leprosy was perceived as a series of acute disorders not necessarily related to one another. Suryawanshi and Richard (238–242) reviewed a large series of patients who had undergone cataract surgery in Karigiri, India. Patients with chronic insidious iridocyclitis tolerated the procedure satisfactorily as did patients with positive skin smears. Fine, *et al.* (243–254) analyzed over 6000 blood samples from total population surveys in northern Malawi for anti-*M. leprae* antibodies using an ELISA based on synthetic glycoconjugate antigen. The proportion of individuals classified as positive peaked at 20–30 years of age and then fell, and was consistently higher in females than in males. There was no evidence for higher seropositivity rates in household contacts of leprosy patients compared to noncontacts. These results provide little support for the potential value of ELISA tests based on the PGL-I antigen of *M. leprae* for field studies or the control of leprosy. Petchclai, *et al.* (255–258) developed a passive hemagglutination test for leprosy utilizing a synthetic disaccharide conjugated to bovine serum albumin and specific for the PGL-I antigen of *M. leprae.* Results using the test were similar to those using an ELISA for IgM antibodies to the same synthetic antigen. Grosset, *et al.* (259–264) demonstrated the bactericidal effects of 150 mg of ofloxacin per kg 5 days weekly for over 3 months in a kinetic experiment in mice infected with *M. leprae.* Mustafa (265–273) studied antigenic crossreactivity among *M. leprae,* BCG, and *M. w* using T-cell lines and clones

raised from BCG- and *M. leprae*-vaccinated subjects. The 65-kDa *M. leprae* and *M. tuberculosis* antigens were present in *M. leprae,* BCG, and *M. w. M. w* and *M. leprae* shared an 18-kDa antigen and an antigen designated 13B3 was shared by *M. leprae* and BCG. Vadiee, *et al.* (274–282) analyzed armadillo IgG and IgM antibody responses to *M. leprae.* Immunoblots developed for IgG antibodies to *M. leprae* showed multiple protein antigens while those developed for IgM antibodies showed predominantly reactions to carbohydrates. Cowley, *et al.* (282–290) presented the histologic and neurophysiologic characteristics of a guinea pig model of nerve damage in leprosy. The model involved intraneural injection of BCG to induce an epithelioid cell granuloma and the intraneural injection of cobalt-irradiated *M. leprae* to induce a macrophage granuloma. Job, *et al.* (291–295) reported intracellular *M. leprae* in neuronal cells and glial cells in the brains of nine-banded armadillos with lepromatous leprosy. Cree, *et al.* (296–301) measured the granuloma fraction, bacterial index, and histological classification in two biopsies from the same leprosy patient, either from opposing edges of the same lesion or from the edge of two separate lesions. There was little variation between biopsies from opposing edges of the same lesion, but there was considerable variation in the granuloma fraction between biopsies from the edge of different lesions in the same patient. There was a lesser degree of variation in the bacterial index between different lesions and there was little difference in histological classification. Meyers, *et al.* (302–309) presented the histopathological findings in skin biopsy specimens before and after immunotherapy of 60 LL or BL patients. The six histopathologists found changes in classification of reversal or upgrading toward the tuberculoid end of the leprosy spectrum in 90.5% of LL patients and in 83.3% of those initially classified as BL. The immunotherapy consisted of a mixture of autoclaved *M. leprae* and BCG.

In the Editorial section of the June issue, Antia and Birdi (310–313) point out the multitude of problems that are yet to be solved in developing an effective antileprosy vaccine and delivering it to a population susceptible to the disease. Mshana and Nilsen (314–322) critically reviewed the immunology of leprosy from a standpoint of clinical leprosy.

In the Obituary section of the June issue, we were saddened to note the passing of Professor Clovis Bopp (323), Professor Georg Klingmüller (324), and Mrs. Monina G. Madarang (325).

In the Correspondence section of the June issue, Ji, *et al.* (326–327) responded to a previous letter by Almeida which had questioned the conclusion that the susceptibility to dapsone of strains of *M. leprae* isolated from previously untreated patients has diminished since 1977. Devasundaram (328–329) described the construction of a simple portable device to remind patients with lagophthalmos to blink. Negesse (329–330) pointed out the discrepancy which frequently exists between the bacillary load found in the skin and the nerve in a leprosy patient, and raised questions regarding the classification, the immunology, and the appropriate treatment for patients in light of this finding.

In the News and Notes section of the June issue, the TALMILEP English Language Book List for 1988 was presented (331–335). Dr. R. Ganapati was elected President of the Indian Association of Leprologists (335, 338). Dr. Masahide Abe retired as Director of the National Institute for Leprosy Research in Tokyo after 32 years. The new Director is Dr. Tatsuo Mori, formerly Deputy Director of the National Leprosarium Tama Zensho-en (339). Dr. John R. Trautman retired as Director of the GWL Hansen's Disease Center at Carville, Louisiana, U.S.A. The new Director is Dr. John C. Duffy, Assistant Surgeon General, who was formerly Director of Medical Affairs on the staff of the U.S. Surgeon General and Chief Physician Officer of the U.S. Health Service (341).

In the Current Literature section of the June issue of the JOURNAL, Antia (342) points out the success in reducing leprosy in China using simple dapsone monotherapy and China's "barefoot doctor" approach. Char (342) provided a background for the founding of the Hansen's Disease

Association of Hawaii. Law (344) described the establishment of the Kalaupapa National Historical Park in Hawaii, U.S.A.

Cartel, *et al.* (345) found a mean relapse rate of 1.2% per year among multibacillary leprosy patients receiving life-long treatment with dapsone for more than 5 years. In all cases of relapse for which a mouse foot pad inoculation was carried out, the bacilli were dapsone resistant. Prevention of relapses by intensive treatment of inactive multibacillary patients still under dapsone monotherapy appeared to be a high priority for the control of the disease in Guadaloupe. Joseph (346) reported a patient with leprosy who developed photodermatitis due to dapsone, confirmed by clinical trial. Mac-Moune Lai, *et al.* (346) reported a patient who developed extensive papillary necrosis associated with rifampin therapy for renal tuberculosis. Orege, *et al.* (346–347) and Pattyn, *et al.* (347) reported favorable results with short-course multidrug regimens for paucibacillary patients. Samuel, *et al.* (347) tested bacilli from nine Nepalese children with multibacillary leprosy, in all except one of whom the index case was a relapsed multibacillary patient, and found that 7 of the 9 had primary dapsone resistance. The Subcommittee on Clinical Trials of THELEP (347) reported persisting viable *M. leprae* in approximately 10% of skin biopsy specimens during treatment with a variety of combined drug regimens. The proportion of positive specimens did not seem to vary with either regimen or the duration of treatment. A single large initial dose of rifampin plus daily dapsone was equivalent to rifampin plus dapsone plus clofazimine administered daily. None of the regimens appeared to be effective in eliminating persisters if given for 24 months. Zeis and Anderson (348) studied the effects of clofazimine on human mononuclear leukocytes *in vitro*. Clofazimine decreased sulphydryl content, inhibited mitogen-induced transformation, increased spontaneous luminol-enhanced chemiluminescence, and activated the arachidonic acid cascade. The antiproliferative activity of clofazimine was found to be related to both the pro-oxidative and prostaglandin synthesis enhancing effects of the drug on mononuclear leukocytes.

Aurora and Mukhija (349) reported pure neural leprosy in a 3½ year old female. Atkin, *et al.* (349) found 31 of 55 leprosy patients in Papua New Guinea to have an inflammatory peripheral polyarthritis associated with raised α_2 macroglobulin levels and not associated with the characteristics of ENL reactions or Charcot's joints. Castells, *et al.* (349–350) used thymopentin to treat 8 patients with long-standing lepromatous leprosy. There was said to be a steady improvement of the bacteriological status of the nasal mucus. He, *et al.* (350–351) found that leprosy patients had significantly less secretory IgA in their tears compared to normal controls. Kumar, *et al.* (351) undertook a time-motion study in leprosy clinics and determined that more than 90% of the time spent in the clinic by patients was in waiting in lines for various clinic services. Lagueny, *et al.* (351–352) studied peripheral neuropathy developing in patients due to thalidomide and found that the data best revealing the neuropathy, even when clinical abnormalities were not present, were a reduction in the sensory nerve action potential amplitude on the sural nerve, increase of somatosensory evoked potential latency following sural nerve stimulation, and reduction of sensory action potential amplitude on stimulating the median nerve at the wrist. Nigam, *et al.* (352) reviewed gynecomastia and testicular and epididymal involvement in 60 male patients with leprosy. Olivier (352) reviewed the psychiatric care provided leprosy patients at Carville from 1923–1985. Rao, *et al.* (353) reported that lepromatous leprosy patients have significant decreases in serum levels of vitamins A and E, a remarkable reduction in serum zinc, but normal levels of serum iron. Despite normal levels of iron, transferrin and ferritin, the hemoglobulin levels were significantly reduced in the lepromatous patients.

Barros, *et al.* (354–355) detected substantial amounts of mycobacterial antigen in 16 lymph nodes from leprosy patients using anti-BCG by the peroxidase-antiperoxidase method. Antigen persisted in the lymph nodes despite prolonged chemotherapy and

was not confined to any particular anatomical compartment of the lymph node. Bonfa, *et al.* (353) compared autoantibodies in malaria, leprosy, and systemic lupus erythematosus. There were considerable differences in the capacity of infectious agents to induce autoantibodies. Campbell, *et al.* (355–356) found that plasma from 53 of 67 leprosy patients inhibited the locomotion of normal human monocytes. This activity resided principally in a non-immunoglobulin, cell-directed inhibitor of 230,000 daltons molecular weight. Cutaneous explants from these patients spontaneously produced this leukotactic inhibitor *in vitro*. Ehrenberg and Gebre (356–357) point out the potential usefulness of rabbit monospecific hyperimmune sera to select *M. leprae* fractions in immunodiagnosis, in immune regulation studies, or as a tool to screen for mycobacterial products in phage lysates of *Escherichia coli*. Fliess, *et al.* (357) found no effect of *M. leprae* on the *in vitro* ability of neutrophils to phagocytose and kill *Candida albicans* and *C. pseudotropicalis*. Gaylord and Brennan (357–358) reviewed the current concepts of the immunology of leprosy. Given the number of complex and lipophilic products in mycobacteria, some of which can intercalate into membrane bilayers, much of the *in vitro* immunologic disturbance reported in leprosy using crude preparations of *M. leprae* as antigen may be pharmacologic. Kaplan, *et al.* (358–359) injected recombinant human gamma-interferon into the skin of lepromatous leprosy patients and found many of the changes associated with DTH responses with the exception that no Langerhans' cells accumulated in the dermis in association with helper T cells. Kardjito, *et al.* (359) measured skin test responses to four new tuberculins in patients with pulmonary tuberculosis and healthy subjects, and found that the response of tuberculosis patients was much lower than the response of healthy subjects—a pattern or reactivity observed previously in leprosy. These findings suggest that patients with mycobacterial diseases fail to respond to the shared or common mycobacterial antigens. Lamb, *et al.* (359–360) used a combination of recombinant DNA technology and peptide chemistry to determine the epitope specificity of clonal and polyclonal human T lymphocytes reactive with the 65-kDa antigen of *M. leprae*. T-cell epitopes were found in four amino acid sequences of the 65-kDa protein. Launois, *et al.* (360) produced T-cell clones capable of mounting a proliferative response to *M. leprae* from the peripheral blood of 3 leprosy patients, 2 with polar lepromatous disease and 1 with polar tuberculoid disease. The clones were produced either from *M. leprae*-activated or from tuberculin-activated polyclonal T lymphoblasts. *M. leprae*-reactive clones from one lepromatous patient displayed strong antigen-specific cytotoxicity toward autologous antigen-coated target cells. Levis, *et al.* (360) measured antibodies to lipoarabinomannan (LAM) in leprosy patients. Both IgG and IgM antibodies to LAM were related to bacterial index, except in patients with ENL in whom there was no correlation. The authors suggest that LAM may have a role in the pathogenesis of ENL. Mandock, *et al.* (360) found two antigenic fractions of *M. leprae* which were heat-labile. The remaining fractions contained heat-stable antigens. Marolia and Mahadevan (360–361) reported that peripheral blood-derived macrophages from both cured and active lepromatous leprosy patients were unable to respond to live *M. leprae in vitro* to produce superoxide anions. Normal healthy individuals' macrophages were able to do so. Mukherjee and Meyers (361) found heavy bacillation of vascular endothelial cells in a biopsy specimen of skin from a lepromatous leprosy patient. Munno, *et al.* (361) found improvement in the immune status of 6 LL patients following the administration of a synthetic thymic extract (TP-5 or thymopentin). Munro, *et al.* (361) described differential binding of two new monoclonal antibodies to epithelioid and giant cells, on the one hand, and macrophages in the surrounding mantle and normal tissue, on the other hand, in epithelioid granulomas. Praputpittaya and Ivanyi (362–363) raised anti-idiotype rabbit antibodies against monoclonal antibodies binding with the 35-kDa protein and the 12-kDa protein antigens of *M. leprae*. Rada, *et al.* (363) found that gamma-interferon production was closely related to lymphocyte proliferation assays in *in vitro* mononuclear cell cultures from patients with var-

ious forms of leprosy and American cutaneous leishmaniasis. Samuel, *et al.* (363–364) treated 23 lepromatous, 2 borderline tuberculoid, and 1 indeterminate leprosy patients with recombinant gamma-interferon intralesionally. Leprosin A skin tests were negative before and after the injections. Locally the injections produced DTH-like reactions. Samuel, *et al.* (364) induced the expression of major histocompatibility complex (MHC) class II antigens on Schwann cells *in vitro* with gamma-interferon but not with *M. leprae.* One of the functional roles of Schwann cells may be to present foreign antigens to T lymphocytes during nerve infections. Shannon, *et al.* (365) presented evidence that a combination of live BCG and killed *M. leprae* was a better immunogen in mice than either alone. Effects were measured by the ability of spleen cells from immunized heterozygote mice to induce reversal reactions in homozygous nude mice infected with *M. leprae.*

Allen (365) demonstrated viable *M. tuberculosis* from the feces of cockroaches allowed to feed on sputum smears from untreated tuberculosis patients which had been heat-fixed over a Bunsen burner flame. Cocito, *et al.* (366) reviewed the three kinds of leprosy-associated microorganisms: *M. leprae,* leprosy-derived corynebacteria (LDC), and armadillo-derived mycobacteria. Dastidar, *et al.* (366) described a nocardioform acid-fast bacillus isolated from armadillo tissues infected with *M. leprae* which grew on media containing only simple sources of carbon and nitrogen. Similar organisms were isolated from human and mouse foot pad tissues infected with *M. leprae.* Franzblau and Hastings (366–367) measured intracellular ATP in *M. leprae* after direct *in vitro* exposure to antimicrobial agents as a means of identifying potentially useful drugs. Fujiwara and Izumi (367) synthesized neoglycoconjugates of the PGL-related trisaccharides of *M. leprae* for use in serology. Gaylord, *et al.* (367) reported that most *M. leprae* monoclonal antibodies directed against carbohydrates recognized lipoarabinomannan. McNeil, *et al.* (368) established that the arabinogalactans of *M. leprae* and *M. tuberculosis* contain arabinofuranosyl and galactofuranosyl residues exclusively. The galactofuranosyl residues are either 5-, 6-, or 5, 6-linked. The Subcommittee on Clinical Trials of THELEP (368) found that 37% of 131 lepromatous leprosy patients admitted into controlled clinical trials in Bamako and Chingleput had bacilli with low or intermediate levels of resistance to dapsone. No patient harbored *M. leprae* of a high degree of resistance. Wheeler (369) demonstrated that *M. leprae* do not synthesize purines but do scavange purines from their environment. Nucleotides were not taken up directly by *M. leprae* but could be hydrolyzed first to nucleosides and then taken up. Wheeler (369) detected only one of three enzymes involved in purine biosynthesis in *M. leprae.* Low levels of phosphoribosyltransferases and high adenosine kinase activities were found in *M. leprae.*

Gelber (370–371) found clofazimine and ethionamide to have bactericidal activity in *M. leprae*-infected mice. Wang (371) found that skin scrapings provided adequate numbers of *M. leprae* for mouse foot pad inoculations.

Clark, *et al.* (371–372) found no acid-fast bacilli (AFB) in tissue sections from 237 nine-banded armadillos from central Texas, U.S.A. Gorodezky, *et al.* (372) demonstrated a significant association between HLA-DR3 and tuberculoid leprosy in a Mexican population. Merlin, *et al.* (372) presented a simplified sample survey methodology to evaluate prevalence rates for leprosy. Mittal (372–373) outlined the National Leprosy Eradication Programme (NLEP) in India.

MacMoran and Brand (374) studied 367 leprosy patients with insensitive hands and found that nonspecific infection and trauma were the reasons for bone resorption in 98% of the cases. Bone resorption can be arrested at any stage of the disease by appropriate therapy of splinting and control of infection. Patil and Srinivasan (374) measured pressures on the plantar aspects of standing leprosy patients and found that scars resulting from healed ulcers are discrete sites of very high pressures. Scar regions combined with foot deformity caused even higher levels of pressure.

Lambert, *et al.* (378) and Lévy-Frébault, *et al.* (378) analyzed mycobacteria for their mycolic acids and found this approach useful in characterizing mycobacterial species. Litvinov, *et al.* (378) found HLA-DR2 to

be more common in patients with tuberculosis than in healthy persons in Russia, and furthermore found that tuberculosis patients who were HLA-DR2+ had higher levels of antituberculous antibodies than tuberculosis patients who did not carry this antigen. Ma, *et al.* (379) measured IgG antibody to *M. tuberculosis* antigen 5 by ELISA and found that the test was 89% sensitive and 94% to 100% specific. Rastogi, *et al.* (379–380) evaluated a series of drugs on mycobacteria multiplying extracellularly and intracellulary in the continuous murine macrophage cell line J-774.

In the Original Articles of the September issue, Rea (383–388) demonstrated a high prevalence of testicular involvement in LL patients as judged by elevated FHS and LH values and a high prevalence of decreased total or free serum testosterone levels. Androgen deficiency was present in 5% of BL and in 43% of LL subjects. Dhand, *et al.* (389–393) found prolonged phrenic nerve conduction time and/or reduced amplitude of diaphragm muscle action potentials in 9 of 22 BL–LL patients and 6 of 18 BT–TT leprosy patients. Diaphragm movements were normal in all patients on fluoroscopy. Agusni (394–400) measured the velocity of blood flow in cutaneous lesions of leprosy patients by a noninvasive laser-Doppler technique. The blood flow velocity reflected the granuloma fraction, was higher in stable BL/LL lesions, and was considerably increased in BT lesions in reversal reaction. Thangaraj, *et al.* (401–407) studied epidermal changes in lesions of leprosy patients undergoing type 1 and type 2 reactions. The changes in both types of reactions were remarkably similar and indicated that local T-cell activation leading to the production of terminal lymphokines such as gamma-interferon with subsequent induction of Ia on epidermal cells may be an important event in both types of reactional leprosy states. Boerrigter, *et al.* (408–417) presented results of 503 paucibacillary leprosy patients treated with the WHO-recommended multiple-drug regimen. Two of 480 patients relapsed during the first year after completion of treatment; 24 developed type 1 reactions in the first 12 months following the completion of therapy. Jesudasan, *et al.* (418–421) studied 517 household contacts of 113 cases of mouse foot pad confirmed, secondary dapsone resistance. The attack rates of leprosy were comparable to those among household contacts of lepromatous cases in general. Twenty-seven contacts developed multibacillary leprosy and two, possibly three, had detectable primary dapsone resistance. An additional 48 paucibacillary leprosy cases developed among these household contacts and none showed any evidence of dapsone resistance. Vadiee, *et al.* (422–427) showed an association between high levels for IgG antibodies against PGL-I in *M. leprae*-infected armadillos and a longer life span suggesting relative resistance to the infection. Rojas-Espinosa, *et al.* (428–436) presented evidence of an early macrophage activation in *M. lepraemurium*-infected mice which subsequently disappears allowing the mycobacteria to disseminate. Job, *et al.* (437–442) presented a patient with lepromatous leprosy and ENL who developed focal tuberculoid granulomas in the ENL lesions. Malaty, *et al.* (443–448) studied the eyes in *M. leprae*-infected sooty mangabey monkeys and found histopathological evidence of lepromatous leprosy. Bacilli were detected in the corneal stroma, blood vessel walls, and corneal nerves. Smida, *et al.* (449–454) compared long, reverse transcriptase generated stretches of the primary structure of the 16S ribosomal ribonucleic acid of *M. leprae* to a variety of mycobacterial species and related taxa. Homology values were calculated and evolutionary distances derived which allowed the construction of a phylogenetic tree. The authors conclude that *M. leprae* is a true member of the slow-growing pathogenic mycobacteria, branching off intermediate to the other members of this subgroup.

In the Editorial section of the September issue, Deo (455–463) compared the immunology of lepromatous leprosy, on the one hand, and *M. avium-intracellulare* in AIDS, on the other, and made a case for similar approaches for an antimycobacterial vaccine to prevent or ameliorate both conditions.

In the Correspondence section of the September issue, Siddalinga Swamy and Ratnakar (464–466) described increased pigmentation of the skin along venous channels

in approximately 5% of leprosy patients with chronic plantar ulceration. Biopsies showed tortuosity and decreased size of the lumen of the vein together with marked thickening of the intima and media. The epidermis showed increased melanin pigment in the basal-cell layer. Klenerman and Hammond (466–468) measured vibration sensation with a biothesiometer and found significantly increased thresholds in the skin of leprosy patches compared to those of adjacent normal skin. Portaels, *et al.* (468–471) cultivated mycobacteria from 26 of 50 stool specimens from normal individuals. Fourteen of the 26 strains were *M. simiae,* 5 *M. gordonae,* 5 MAI complex, and 2 *M. malmoense.* Srinivas, *et al.* (471–472) reported a tuberculoid patient with comedones in the lesion thought to be secondary to coconut oil massaged over the affected site because the skin was dry.

In the News and Notes section of the September JOURNAL, Cheriyan and Srinivasan were both recognized by the government of India (473). A report on the two-day National Seminar on Social Science Research on Leprosy organized at the Gandhi Memorial Leprosy Foundation in Wardha was noted (473–474). We were deeply saddened by the tragic death of Dr. Melville Christian, Director of the Schieffelin Leprosy Research and Training Center in Karigiri (475). The retirement of Dr. A. Colin McDougall as Editor of *Leprosy Review* was noted together with the appointment of Professor J. L. Turk as the new Editor (476–477). LEPRA's Director Francis Harris retired (477).

In the Current Literature section of the September issue, Antia, *et al.* (481) found deoxyfructoserotinin to be active in six active LL patients. George, *et al.* (482) found that dapsone plasma levels gradually fell during concomitant administration of rifampin. Grosset, *et al.* (482) studied dapsone sensitivity in 13 strains of *M. leprae* isolated from new lepromatous leprosy cases in Senegal and found that 10 were resistant to dapsone, 7 at low level, 1 at intermediate level, and 1 at high level. This was the usual pattern in previously untreated patients. With acquired resistance, 62 of 69 relapsing patients showed resistance to dapsone, 6 at a low level, 21 at an intermediate level and 35 at high level. O'Sullivan, *et al.* (482–483) presented structure-activity-relationships among clofazimine analogs active against a strain of *M. smegmatis* 607 made resistant to clofazimine. Pieters, *et al.* (483) found that rifampin reduces the elimination half-life and plasma concentration of concomitantly administered dapsone. Raghavia, *et al.* (483) studied the causes and associations with absenteeism among leprosy patients attending outpatient clinics. Attendance irregularity was associated with nonlepromatous leprosy, backward and scheduled castes, the initial phase of treatment, illiteracy, lack of knowledge about the disease, unsuitable clinic timing, intolerance to dapsone, and "work." Salafia and Kharkar (483) report three cases of temporary generalized lymphadenopathy related to clofazimine. Smith (484) discussed hypersensitivity reactions to dapsone which were common in the late 1940s and early 1950s, then virtually disappeared, and have now reappeared in the last 5–6 years. Sreevatsa, *et al.* (484) found that 6 of 40 lepromatous leprosy patients treated for 2 years with MDT harbored drug-sensitive persisters. Zeis, *et al.* (485) presented structure-activity-relationships among 10 clofazimine derivatives on the inhibition of PHA-stimulated mononuclear cell proliferation.

Aggarwal, *et al.* (485) reported a case of tuberculoid leprosy presenting with a primary annular lesion on the sole of the foot. Arora and Mukhija (485) reported a case of malignant melanoma developing over a trophic ulcer. Balachandran, *et al.* (485) reported a case of nodular histiocytic lymphoma with clinical features simulating lepromatous leprosy. D'Souza, *et al.* (485–486) demonstrated bronchial hyporeactivity in lepromatous leprosy patients, suggesting postganglionic vagal fiber involvement in the disease process. Fain, *et al.* (486) reported that plasma exchange was useful in ENL. Mishra, *et al.* (486–487) reported a patient with BT leprosy with involvement of the hard palate. Pavithran (487) reported a patient who presented with a generalized erythematous maculopapular rash following ampicillin therapy with complete sparing of the hypopigmented patch of tuberculoid leprosy on the patient's face. Rajan, *et al.* (487) reported three cases of severe renal toxicity due to rifampin. Ramachan-

dran and Neelan (487) undertook detailed studies of borderline lepromatous and lepromatous leprosy patients and found definite involvement of the cardiovascular and genital systems with regard to autonomic function tests. Involvement of the parasympathetic system (vagus nerve) occurred early and was more common than involvement of the sympathetic system. Sympathetic damage was always associated with parasympathetic damage. The severity of the autonomic neuropathy was related to the duration of the disease. Singh, *et al.* (488) found that pityriasis versicolor was found more commonly among leprosy patients than among the general population. Zhou, *et al.* (489) reported that the suicide rate among leprosy patients was over 100 times higher than that of the general population in Baoying County, Jiangsu Province, in the People's Republic of China. Social discrimination against leprosy patients played an important role as a cause of suicide.

Baumgart, *et al.* (490) found the IgM PGL-I ELISA to have limited value as a screening method for the detection of new cases in a high prevalence village in Papua New Guinea. Many normal persons, particularly children, had elevated IgM anti-PGL-I antibodies, presumably a consequence of early subclinical infection. Bhatia, *et al.* (490) demonstrated bacilli with auramine staining of histopathological sections from different types of treated leprosy cases which were negative by Fite-Faraco staining. Booth, *et al.* (490) sequenced the gene for the 18-kDa protein antigen of *M. leprae* and deduced its amino-acid sequence. A second open reading frame downstream from the 18-kDa coding sequence coded for a putative protein of 137 amino acids. Neither this nor the 18-kDa amino-acid sequence had significant homologies with any proteins in the established data bases. Britton, *et al.* (490–491) found the IgM anti-PGL-I response useful in signifying the presence of active leprosy, particularly in multibacillary cases, and found that it had the potential to monitor the response of leprosy patients to therapy and to detect subclinical leprosy in contacts. Britton, *et al.* (491) identified antigens of *M. leprae* by immunoprecipitation with sera from leprosy and tuberculosis patients. Douglas, *et al.* (491) found 10% skimmed milk or nonfat dry milk to be suitable as a blocking agent for ELISA in the detection of antibodies in leprosy. Gonzalez-Amaro, *et al.* (491–492) found immune contrasuppressor cell activity in the peripheral blood mononuclear cells of some lepromatous leprosy patients but not in cells from either tuberculoid patients or healthy contacts. Jeevan and Asherson (492) demonstrated a beneficial effect of recombinant interleukin-2 (IL-2) in BALB/c mice infected with *M. lepraemurium* or with *M. bovis* BCG. Kumar (492) showed the proliferation of mast cells and their degranulation in histoid skin nodules as compared to surrounding normal skin where the cells were mainly intact. Lamb, *et al.* (492) purified the recombinant 65-kDa antigen of *M. leprae* and showed that it stimulated both *in vitro* lymphoproliferative and *in vivo* DTH responses in mice immunized with killed *M. leprae*. Lyons, *et al.* (493) studied IgG and IgM antibodies to the PGL-I antigen of *M. leprae* by ELISA in 77 multibacillary leprosy patients and found no correlations to disease type, induration, bacillary load, reactional status, or concurrent secondary infection. Melancon-Kaplan, *et al.* (493) purified cell walls of *M. leprae* and showed them to be antigenic to T cells. Further purification to a large peptidoglycan-protein complex retained the immunological activity but proteolysis destroyed it. Mittal and Nath (493) demonstrated the efficacy of dendritic cells in presenting particulate mycobacterial antigens using an *in vitro* lympholiferative assay. Modlin, *et al.* (493–494) characterized the T-lymphocyte subsets and frequency of antigen-reactive T cells in leprosy lesions. Mshana, *et al.* (494) showed that *in vitro* infection of mouse peritoneal macrophages with live but not heat-killed *M. kansasii* significantly reduced the expression of Ia antigen following stimulation with lymphokines. Narayanan (494–495) reviewed the current status of the immunopathology of leprosy granulomas. Rawlinson, *et al.* (495–496) studied genetic susceptibility to infection with *M. leprae* in multiple-case families of Australian Aborigines. The model which best fits the data was for a gene on chromosome 6 in close linkage with the HLA haplotype, with two alleles, autosomal

recessive inheritance and penetrance of 90%. On this basis, lepromatous disease type, rather than disease susceptibility, may be controlled by genes linked to the MHC gene complex. Robinson and Mahadevan (496) reviewed the properties of the delipidified cell wall of *M. leprae* and proposed that it could be a potent immunomodulator for immune deficient cells of leprosy patients. Rook (496) reviewed the immunology of the mycobacterioses. Samuel, *et al.* (496) treated a group of BT leprosy patients with repeated injections of BCG plus killed *M. leprae* and showed that leprosin A conversion rates were significantly increased compared to BT patients not receiving the injections. Volc-Platzer, *et al.* (496–497) studied skin biopsies from 21 patients along the spectrum of leprosy and found in multibacillary forms of the disease that there was significant IL-1 expression, absent IL-2R-bearing cells, and absent HLA-DR reactivity of the overlying keratinocytes indicating an overall defective production of gamma-interferon in the lesion. Wilkinson, *et al.* (497) used DNA-mediated gene transfer to express HLA class II molecules in mouse L cells. Genes were transferred and expressed which encoded the DR2-β a and DR2-β b products of the DR2Dw2 haplotype of the DR2Dw2-restricted T-cell clones tested. All used the DR2-β a chain as their restriction element as measured by their response to the presentation of *M. leprae* antigen on these transfectants. Xu, *et al.* (498) injected PHA into the skin lesions of bacteriologically positive patients with excellent local effectiveness in clearing bacilli reported in 93.6% of the cases.

Chakrabarty, *et al.* (498) isolated nocardia-like organisms repeatedly from multibacillary leprosy patients. Franzblau (498–499) reported the ability of *M. leprae* to oxidize palmitic acid during incubation in an axenic medium. Franzblau, *et al.* (499) reported the incorporation of radiolabeled palmitic acid into the specific PGL-I antigen of *M. leprae* in an axenic medium. Wheeler (500) measured rates of incorporation of hypoxanthine in suspensions of *M. leprae* with and without added antileprosy agents. Fukunishi (501) described electron-microscopic findings in the peripheral nerve lesions of *M. leprae*-infected nude mice. Kazda, *et al.* (501) inoculated *M. leprae* and *M. intracellulare* simultaneously into nude mice and observed an acceleration of the infection compared to animals receiving *M. leprae* alone. Kohsaka, *et al.* (501–502) showed that the susceptibility of the beige mouse to infection with *M. leprae* was not more than that of normal mice. Malaty and Togni (502) studied the eyes of *M. leprae*-infected nine-banded armadillos and found AFB in all layers of the corneal stroma. The bacilli seem to reach the eye by the neural and/or vascular route. Samuel, *et al.* (502) infected human Schwann cells in tissue culture with *M. leprae.* Vaishnavi, *et al.* (503) found renal lesions, AFB, and immune complex deposits in the kidneys of *M. leprae*-infected Swiss albino mice. Vaishnavi, *et al.* (503) gave *M. leprae*-infected Swiss albino mice preformed immune complexes and found evidence that the immunosuppression caused by immune complexes was enhanced in the presence of *M. leprae* infection. Yogi and Nakamura (503–504) presented results of inoculations of *M. leprae* into the upper lip of nude mice. Yogi and Nakamura (504) inoculated *M. leprae* into congenitally asplenic mice and found no evidence of enhanced multiplication of the bacilli.

Chanteau, *et al.* (504) evaluated serology based on the PGL-I antigen of *M. leprae* in leprosy patients and their household contacts. The predictive value of a positive result of the test was very low ($< 2.4\%$) and the predictive value for a negative result was high ($> 99.9\%$) in this area of low prevalence for leprosy (1.78/1000). Gao (505) detected 131 new leprosy cases in a total of 2089 household contacts in 103 families with leprosy in Yiyuan County of Shandong Province (People's Republic of China). The prevalence rate of leprosy in the household contacts was 62.7/1000 compared to the rate in the local population of 1.1/1000. Contacts of multibacillary leprosy patients showed a prevalence of 109/1000 and the prevalence in contacts of paucibacillary cases was 14.6/1000. Kim (505–506) described the epidemiology trends of leprosy in Korea. The prevalence rate in 1965 was estimated to be 2.6/1000 and at present the prevalence rate is estimated to be about 0.8/1000 for a total of 32,000 cases. Ma (506–507) reviewed the epidemiology of leprosy

in the People's Republic of China. In 1949 there were estimated to be 500,000 patients and in 1984 this had fallen to 100,000 cases. Saikawa (508) provided chemoprophylaxis for leprosy household children in Okinawa, and noted a lower incidence among those treated than among those not treated. Shu, *et al.* (508) identified 150 household contacts of leprosy patients as being positive for antibodies to the PGL-I antigen of *M. leprae* by ELISA. Of these, 131 showed a positive Mitsuda skin test. Zhou, *et al.* (509) found that leprosy affects the life span only slightly, apart from its effect on the suicide rate, in Baoying County, Jiangsu Province, People's Republic of China.

Rao, *et al.* (510) surgically decompressed the posterior tibial neurovascular bundle in leprosy patients with anesthetic soles. There was an improvement in the sweat gland function on the soles of the feet of more than half of the patients studied. Zhang, *et al.* (510) modified Brand's extensor-to-flexor four-tailed graft operation and reported satisfactory results in three patients.

Aziz, *et al.* (510–511) compared two 3-drug regimens given for 6 months with a 3-drug regimen for 12 months in ambulatory tuberculosis patients. Default rates were 20%–27%, sputum conversions 56%–85%, and at the end of 2 years there was an overall failure rate of 30%–40%. Bhattacharya, *et al.* (511) hybridized dot blots containing DNA isolated from *M. tuberculosis* with ^{32}P-labeled total *M. tuberculosis* DNA under high stringency conditions. Under these conditions, it was possible to abolish hybridization with all mycobacteria tested except *M. bovis*. By using different probes, *M. tuberculosis* could be distinguished from *M. bovis*. Feureisl and Papezova (511–512) found no advantage of levamisole added to standard drugs in the treatment of new cases of pulmonary tuberculosis. Lazarova, *et al.* (512) pointed out the advantages of the fluorochromes auramine OO and rhodamine B in the detection of bacilli in skin biopsies from patients with cutaneous tuberculosis. Markov, *et al.* (512–513) found serologic tests for specific antibodies by solid-phase enzyme immunoassay to be useful in detecting reactivation and recurrence of disease in tuberculosis patients who have completed therapy. Pao, *et al.* (513) used *M. tuberculosis* DNA probes to detect *M. tuberculosis* in uncultured clinical specimens. The overall sensitivity and specificity of the DNA probes in detecting *M. tuberculosis* were 90.5% and 83.8%, respectively. Pospelov, *et al.* (513–514) presented evidence for the association between the development of tuberculosis in Russian populations and HLA-DR2. HLA-DR3 was less frequent in patients with tuberculosis than in the healthy controls. Sadoff, *et al.* (514) protected mice against sporozoite challenge by orally immunizing the animals with attenuated *Salmonella typhimurium* transformed with the *Plasmodium berghei* circumsporozoite protein gene. Storrs, *et al.* (515) reported instances of superdelayed parturition in armadillos in captivity.

In December's Original Articles, Job and Chacko (523–526) took nasal biopsies from the anterior ends of both interior turbinates from 14 patients with ENL and six with reversal reactions. In 10 of the ENL patients there was histologic evidence of ENL in the nasal mucosa. In 2 of the 6 reversal reaction patients, both with lesions on the skin of the nose, there were edema and epithelioid cells in the nasal mucosa. Agis, *et al.* (527–536) measured anti-PGL-I antibody levels in untreated patients and their household contacts in Guadeloupe, and found statistically significantly higher seropositivity rates among contacts of multibacillary patients when compared to contacts of paucibacillary cases. One fourth of indeterminate patients were seropositive and had a negative Mitsuda lepromin, an immunological pattern seen in LL patients, and yet fulfilling criteria of paucibacillary disease for the purposes of WHO MDT. Gormus, *et al.* (537–545) followed mangabey monkeys inoculated with *M. leprae* and found that high IgG and low IgM antibodies to the PGL-I antigen were associated with less severe disease than monkeys showing high IgM, especially high IgM associated with low IgG antibodies. ShivRaj, *et al.* (546–551) tested sera from leprosy patients for IgG antibodies to HIV-1 by ELISA and Western blot. No sera were positive by ELISA but 33 of 43 patients were positive to one or more bands of HIV-1 proteins by Western blot; 14 positive only to the p55 band but another 14 of the 43 were also positive to the HIV-

1-specific antigen, p24. Lai A Fat, *et al.* (552–558) measured antibody production in biopsies of the nasal mucosa, lymph nodes, bone marrow, and skin lesions of untreated leprosy patients. Different antibody specificities were found at different sites in the same patient. Chakrabarty, *et al.* (559–565) studied sera from patients before and after reactions for their ability to solubilize preformed immune complexes *in vitro.* Lepromatous patients with or without ENL, as well as type 1 reactional patients, showed reduced capacity to solubilize immune complexes. Courtright (566–573) reviewed all 40 ocular surveys of leprosy patients which had been published and pointed out their methodological shortcomings. Roy and Das (574–579) evaluated the potential genotoxicity of dapsone in mice by following *in vivo* cytogenetic assays. Dapsone treatment of the mice was associated with increased incidences of clastogenicity. It seems clear that dapsone can induce chromosome damage. Portaels, *et al.* (580–587) studied the viability of *M. leprae* in armadillo tissues after freezing and thawing. When frozen tissues were subjected to a second freezing-thawing cycle, 65%–97% loss of viability was observed. A third freezing-thawing cycle was lethal for most of the *M. leprae.* Harris, *et al.* (588–591) measured the effects of antimicrobial agents on the incorporation of radiolabeled palmitic acid into the PGL-I antigen of *M. leprae,* and suggested that this system may prove useful in the screening of antileprosy agents. Reddi, *et al.* (592–598) carried out restriction fragment length analysis of mycobacterial species within the tuberculosis complex. *Alu* I-digested DNA of *M. tuberculosis* showed a specific pattern with bands of 5.6 kb and 4.8 kb which appeared to be species specific. Al-Mohaya, *et al.* (599–602) described an interesting patient with BL leprosy and ENL who developed a nephritic range proteinuria. Renal biopsy showed mesangial proliferative glomerulonephritis and epithelioid granulomas in the interstitium.

In the Editorial section of the December issue, Georgiev and McDougall (603–610) pointed out the advantages of blister calendar packs for the delivery of MDT under field conditions. Lennon (611–618) reviewed the role of health education in leprosy control.

In the Correspondence section of the December issue, Shetty and Antia (619–621) discussed the pathogenesis of nerve damage in leprosy. Schwann cells are preferentially parasitized by *M. leprae.* The question is raised as to whether or not the treatment of patients with antileprosy drugs is only helping in the formation of scar tissue as far as nerve damage is concerned. Levy (621–622) criticized Katoch, *et al.* (IJL 56: 1–9, 1988) in using pyrazinamide and isoniazid in patients when these drugs have not been shown to be active against *M. leprae* in the mouse foot pad. Katoch (622–624) responded that all results in mice cannot be extrapolated to humans and expanded on the rationale for the use of pyrazinamide against *M. leprae* persisters. Salafia and Kharkar (625) presented a patient who developed exfoliative dermatitis after thalidomide. Mohamed (625–627) presented a patient with BT leprosy consisting of a single patch occupying 27% of the patient's body surface area including an upper limb. Salafia and Kharkar (627–628) reported a massive reaction to lepromin A in a polar tuberculoid patient who was given the injection with a Dermo-O-Jet standardized to inject 0.1 ml with every shot. Ulceration developed over an original facial lesion and ulceration developed in a doughnut pattern around the site of the lepromin injection. Agarwal and Porichha (628–630) commented on skin smears following the Letter to the Editor by Georgiev and McDougall (IJL 56: 101–104, 1988). Smears are frequently inadequate because the matter is not moved from the level of theoretical discussion to actual practice. Most types of leprosy can be diagnosed and classified by the clinical features alone. Job, *et al.* (630–631) had earlier found that 2.02% of 494 wild armadillos had leprosy histopathologically in Louisiana, U.S.A. A similar study showed no evidence of *M. leprae* infection in 311 opossums, 17 raccoons, 56 nutria, and 51 rabbits from the same area. Kato (631–632) reported higher yields and more rapid growth of AFB from *M. leprae*-infected tissues if media previously used were modified. Antia, *et al.* (632–635) described the culture conditions found to be optimal for obtaining the growth of AFB

from *M. leprae*-infected armadillo tissues in dissociated Schwann cells *in vitro.*

In the News and Notes section of the December issue, the recipient of the 1988 Damien-Dutton Award was Mr. Hermann Kober of the Federal Republic of Germany, one of the co-founders of the German Leprosy Relief Association (GLRA) and current President of the International Federation of Anti-Leprosy Associations (ILEP) (636–637). The TDR components on the chemotherapy and immunology of leprosy were noted to have established a new joint subcommittee on field research in leprosy (640). The TDR steering committees on the chemotherapy and immunology of leprosy have singled out leprosy reactions and nerve damage as being of particular interest (641–642).

Book Reviews in December included the book by the International Cooperative Team for Evaluating Serological Tests in Leprosy entitled *A Trial to Compare Serodiagnostic Tests for Leprosy* (644), Sehgal's *Clinical Leprosy (Illustrated Second Edition)* (644–645), and *Studies on Leprosy by Bombay Leprosy Project 1976–1986* (645–646).

In the Current Literature section of the December issue, Aschhoff, *et al.* (647) estimated the overall minimum prevalence of secondary dapsone resistance to be 5.6% and the overall minimum prevalence of primary dapsone resistance to be 21% in their control area in south India. Deenabandhu and Kothandapani (648) presented a case of primary dapsone-resistant paucibacillary leprosy. Douglas, *et al.* (648) noted the decline of anti-*M. leprae* antibody levels in lepromatous leprosy patients under chemotherapy. Ellard, *et al.* (648–649) studied compliance in patients receiving prothionamide as part of a multiple-drug regimen. As measured by urine-test methods, approximately one half of the prescribed doses were ingested. Patki, *et al.* (650) reported two cases of "flu" syndrome in patients receiving rifampin once monthly. Pattyn, *et al.* (650–651) analyzed relapses occurring in leprosy patients treated with various rifampin-containing regimens. Two groups of relapses were observed: early relapses occurring <3.5 years after stopping treatment and late relapses occurring after that time.

Chattopadhyay and Gupta (651) reported two tuberculoid leprosy patients with primary hyperpigmented anesthetic lesions. Chaudhary, *et al.* (651) found elevated adenosine deaminase activity in leprosy patients compared to controls. D'Souza and Thomas (652) found various chromosome aberrations to be significantly higher in both lepromatous and tuberculoid leprosy patients' blood lymphocyte cultures than in those of controls. Koranne and Srivastava (653) described a patient with primary neuritic leprosy treated with dapsone and rifampin, who did not show any improvement. Nigam, *et al.* (653–654) studied 60 male leprosy patients for gonadal involvement. Lepromatous and borderline leprosy patients developed testicular pain and/or swelling. Altered sexual function was observed in 34 (57%) of the patients and 11 had altered sexual hair patterns. Nine patients had gynecomastia and 19 (35%) azoospermia, and 16 (27%) oligospermia. Ramu and Desikan (645) noted that patients with BT leprosy treated with sulfone monotherapy had a poor prognosis if they had more than 15 lesions or lesions covering three or more of the seven sectors of the body. Rao and Saha (654) found significant reductions in mean serum levels of vitamins A and E in leprosy patients compared to normal controls. Sane and Mehta (654) reported 12 cases of carcinoma arising from trophic ulcers of leprosy patients. Singh, *et al.* (654–655) found lowered serum testosterone levels in male leprosy patients. Serum FSH and LH levels were elevated in LL and BL patients and oligospermia was found in these same groups.

Alvarez-Mendoza, *et al.* (655) described a technique to demonstrate AFB in skin biopsies from indeterminate leprosy patients by mincing and grinding the tissue in phosphate-buffered saline and then treating it with NaOH and digesting with trypsin. Anderson, *et al.* (656) have used synthetic peptides in inhibition ELISA experiments and have located 10 of 14 known epitopes defined by different monoclonal antibodies to the *M. leprae* 65-kDa protein. Converse, *et al.* (656) separated the antigens of *M. leprae* by SDS-PAGE, electroblotted onto nitrocellulose paper, cut the blots into squares

and tested the antigens directly on a T-cell proliferation assay. Peripheral blood T cells of healthy leprosy patient contacts responded preferentially to the lower molecular weight (< 70,000) antigens of *M. leprae*. The most prominent lymphoproliferative responses were in the regions of 11–16 kDa and 22–26 kDa. Gross, *et al.* (657) analyzed the leukocyte subsets in the granulomatous responses produced in lepromatous leprosy patients after inoculation with a mixture of *M. leprae* and BCG. The granuloma produced after *M. leprae*-BCG inoculation showed a pattern similar to tuberculoid granulomas. Harris, *et al.* (657–658) measured T-cell proliferative responses to *M. leprae* after immunization of mice and identified low-responder mice and high-responder mice. F_1 (high × low) hybrid mice were found to be low responders. The cellular basis of the low responsiveness did not result from a defect in antigen-presenting cells (APC) or the activation of suppressor T cells by *M. leprae*. When high-responder bone marrow was used to reconstitute irradiated F_1 mice, the chimeric mice which resulted were low responders. This suggested that the donor, high-responder lymphocytes became tolerant to antigenic determinants of *M. leprae* as they developed in the irradiated F_1 mice. The authors suggest that low responsiveness to *M. leprae* in low-responder and F_1 hybrid mice may result from tolerance to H-2 encoded antigens that crossreact with antigens of *M. leprae*. Holzer, *et al.* (658) presented evidence that BCG are easily recognized and slowly ingested by normal phagocytic cells, the majority of which respond with a strong oxidative burst. *M. leprae* appeared to only weakly stimulate phagocyte oxidative responses and were also slowly phagocytized *in vitro*. Kaplan, *et al.* (658–659) found that there was a reduction in the number of *M. leprae* in positive skin test sites to tuberculin 21 days after the skin test injections in bacteriologically positive lepromatous leprosy patients. Locniskar, *et al.* (659) produced human monoclonal antibodies which bound to *M. leprae*, PGL-I, and single-stranded DNA (ssDNA). The monoclonal antibodies bound to several autoantigens such as ssDNA, double-stranded DNA, and poly(ADP-ribose) but not RNA. The monoclonal antibodies were used to prepare a rabbit anti-idiotype antisera. Both PGL-I and ssDNA inhibited binding of idiotype to its anti-idiotype. Roberts, *et al.* (660) isolated cutaneous lymphocytes from the Mitsuda lepromin reaction of a tuberculin-positive individual not previously exposed to *M. leprae* and cloned them with Dharmendra lepromin and analyzed for antigen specificity. Lepromin-responsive cell lines and clones were derived and all lepromin-responsive clones proliferated in response to tuberculin as well as Dharmendra lepromin. Sibley and Krahenbuhl (661) presented evidence that infection of mouse macrophages with *M. leprae* impairs the ability of these macrophages to become activated by gamma-interferon by means, at least in part, of inducing the production of inhibitory levels of prostaglandin E_2. Young, *et al.* (662) determined that five immunodominant protein antigens studied in tuberculosis and leprosy bacilli were homologs of stress proteins. Infectious agents may respond to the host environment by producing these stress proteins and the host response to these stress proteins may provide a response to a broad spectrum of human pathogens containing or producing these abundant and highly conserved stress proteins.

Bhatia, *et al.* (663) found that auramine staining was more sensitive than Ziehl-Neelsen staining in detecting *M. leprae* on skin smears. de Wit and Klatser (663) characterized the 36-kDa antigen of *M. leprae*. Dhople, *et al.* (663) obtained evidence of bacterial growth in two media inoculated with *M. leprae* from armadillo tissues. The harvested bacilli after 16 weeks of incubation had a few of the important properties of *M. leprae* including growth in mouse foot pads. Subcultures were unsuccessful. Franzblau and Harris (663–664) presented evidence that the optimum temperature for maintenance of intracellular ATP and palmitic acid incorporation into PGL-I of *M. leprae* was 33°C. The pH optimum appeared to be 5.2–5.6 and the optimum gaseous environment appeared to be 2.5%–10% oxygen. Katoch, *et al.* (664) purified *M. leprae* from 23 leprosy patients and measured ATP content, morphological index (MI), and

FDA-EB staining of the bacilli. The ATP content per solidly staining bacillus was fairly constant. The ATP content per green-staining bacillus as measured by FDA-EB varied up to ninefold. Wheeler and Ratledge (664–665) reported that citrate, glucose, and pyruvate were taken up by *M. leprae in vitro* and that carbon from glycerol and palmitate was taken up and incorporated into lipids. *M. leprae* may be incapable of making acetyl-CoA from acetate. Young (665) discussed the possibility that intracellular infection with mycobacteria may induce the synthesis of stress proteins and that the highly conserved nature of these stress proteins may suggest that they may play a role in the possible induction of tolerance or of autoimmune pathology in these diseases.

Abel and Demenais (666) performed complex segregation analysis on 27 multigenerational pedigrees from Desirade, a Caribbean island where leprosy is highly prevalent. The authors suggest that the gene for susceptibility to leprosy per se and that for the susceptibility to nonlepromatous leprosy might be different, acting at successive stages of the immune response following infection with *M. leprae.* Pearson (666) pointed out that distance from established treatment centers does not always act as a deterrent for leprosy patients seeking treatment. Distance may be desirable so that the leprosy patients can maintain anonymity, and thus disguise diagnosis and avoid social ostracism in their home locality. Ponnighaus, *et al.* (666–667) presented the epidemiology of leprosy in northern Malawi.

Fortier, *et al.* (668–669) examined the protective effect of BCG on *Leishmania major* infections in mice. Viable BCG, but not heat-killed BCG or tuberculin, inoculated with *L. major* amastigotes into the foot pad of naive mice protected these animals from infection. BCG given intraperitoneally 10 days before infection of the foot pads with *Leishmania* also offered protection. Mor, *et al.* (669–670) studied the responses of mice macrophages to *M. lepraemurium* and found that there was a low release of superoxide anion. The authors suggest that *M. lepraemurium* may be taken into macrophages by a mechanism that bypasses the Fc receptor and other receptors that are capable of triggering the production of superoxide anion by macrophages. Mowszowicz, *et al.* (670) reported a patient who developed a cutaneous granuloma due to *M. vaccae* on the knee some 5 months after local trauma. The patient's lesions regressed following thermal therapy. Pabst, *et al.* (670–671) showed that sulfatide from the outer surface of *M. tuberculosis* blocked the priming of human monocytes cultured *in vitro. In vivo, M. tuberculosis* may use sulfatide to block macrophage activation and thereby resist being killed by macrophages. Zarco Olivo, *et al.* (671–672) described a patient with a sporotricoid presentation of an infection due to *M. chelonei* which responded to oral erythromycin.

The December issue contained the abstracts from the Twenty-Third Joint Leprosy Conference of the U.S.–Japan Cooperative Medical Science Program held at Nara University in Nara, Japan, 27–29 July 1988. Tsutsumi and Gidoh (676–677) reported the effects of potential antileprosy drugs on the growth of *M. leprae* in nude mice. Intraperitoneal injections of muramyl dipeptide plus dapsone resulted in lower counts of *M. leprae* than those found in mice receiving dapsone alone. Franzblau, *et al.* (677–678) reported the *in vitro* activity of a number of potential antileprosy drugs against *M. leprae* by following the oxidation of palmitic acid to radiolabeled CO_2 by the bacilli. Osawa and Akiyama (678) found that liposomes containing protamine or rifampin inhibited the intracellular multiplication of *M. leprae* in murine and human macrophages. Kohsaka and Ito (678) found that ofloxacin and minocycline were active in suppressing the growth of *M. leprae* in nude mice. Jacobs, *et al.* (678–679) reported the development, using a molecular genetic approach, of both the vectors and methodology for efficient gene transfer in mycobacteria. A novel mycobacteriophage vector was developed, a shuttle phasmid, which replicates in *E. coli* as a plasmid and in mycobacteria as a phage. By introducing and expressing foreign antigens in BCG, it should be possible to develop novel, recombinant multivaccine vehicles for a variety of infectious diseases. Clark-Curtiss (679) described a DNA probe which appears to be specific for *M. leprae* and which can detect approximately 4000 *M. leprae* cells. Mohagheghpour, *et al.* (679–681) found that the pellet fraction of sonicated *M. leprae* is

a T-cell immunogen. T-cell responsiveness to this preparation paralleled responsiveness to intact *M. leprae*. The 35-kDa protein of *M. leprae* seemed to be the major T-cell immunogen in the preparation. Hirata and Chyugun (681) suggested that *M. leprae* in human skin lepromas showed slightly different features compared to bacilli in nasal mucosal biopsies. Matsuo, *et al.* (681–682) showed that beta-glucuronidase binds to the mycobacterium HI-75, and that the binding site is trypsin sensitive. Quismorio and Rea (682) found that approximately 50% of LL patients had high-level IgM anticardiolipin antibodies and approximately 25% had high-level IgG antibodies. Absorption of leprosy as well as systemic lupus erythematosus sera with whole *M. leprae* did not remove the anticardiolipin antibodies, indicating the antibody response was not to an antigen expressed on the leprosy bacillus. Izumi, *et al.* (682) described the application of the *M. leprae*-specific gelatin particle agglutination test for leprosy serology. Mehra, *et al.* (682–683) purified *M. leprae* cell walls and showed that T-cell responses to this preparation mimicked those to intact *M. leprae*. The immunologic reactivity was destroyed by proteolysis but not by removal of mycolates and arabinogalactan. Several T-cell clones responding to these cell-wall preparations did not respond to soluble or recombinant *M. leprae* antigens but did respond to antigens of 16 kDa and 7 kDa contained on nitrocellulose transfers of *M. leprae* cell extract. Hunter, *et al.* (683) described the preparation of a protein complex from a cell wall of *M. leprae*. Monoclonal antibodies to this cell wall protein also react with the soluble 65-kDa protein of *M. leprae*. The cell wall protein can be prepared from the cell walls of *M. leprae* in such a fashion that it is virtually devoid of 65-kDa protein but still retains its immunoreactivity. T-cell lines established to cell walls, when tested for reactivity against sonicated *M. leprae* proteins separated by SDS-PAGE, react to proteins of molecular weight 7 kDa, 16 kDa, and 28 kDa. Krahenbuhl, *et al.* (683–684) showed that mycobacterial lipoarabinomannan treatment of murine or human macrophages rendered the macrophages unresponsive to gamma-interferon. The lipoarabinomannan-treated macrophages did not produce elevated amounts of prostaglandin E_2. Fukutomi, *et al.* (684–685) showed that macrophages are able to activate and to secrete IL-1 following phagocytosis of *M. avium* and *M. lepraemurium*. Kaplan and Cohn (685–686) described intact immune responses in tuberculin skin test sites in lepromatous leprosy patients. In 80% of the tuberculin-responsive lepromatous patients there was a 5000–10,000-fold reduction described in the numbers of AFB locally. Local responses to gamma-interferon and IL-2 resembled the local responses to tuberculin. Nakamura and Yogi (686–687) compared the susceptibility of nude mice from various genetic backgrounds to *M. leprae*. Young (687) reviewed the contributions of recombinant DNA expressing technology to leprosy and tuberculosis. Nomaguchi, *et al.* (687–688) described the recloning of the gene for the 65-kDa protein of *M. leprae* from the λgt11 to the pUC8 system and the subsequent purification of the 65-kDa protein. Barnes, *et al.* (688–689) presented evidence that CD4+CDw29+ cells are selectively concentrated at the site of disease in tuberculous pleuritis and that they are likely to play an important role in the local cell-mediated immune response to *M. tuberculosis*. By analogy, CD4+CDw29+ cells may play a similar role in leprosy. Izaki, *et al.* (689–690) expanded on their previous study which demonstrated that proteolytic activities such as plasminogen activator and elastase are induced in the tissue extract of experimental granulomatous inflammation, and presented evidence that an antiproteolytic reaction takes place simultaneously in these granulomas.

Of interest, in the closing remarks of the U.S. Leprosy Panel Chairman (690–691), Brennan notes that the reviewers of the U.S.–Japan Cooperative Leprosy Program have provided the guidelines that molecular biology, immunology, and vaccine development should be emphasized in the future.

From a personal perspective, a number of trends seem to be developing. In the field of chemotherapy there is evidence that pyrazinamide may have some effect against persisting viable *M. leprae*. Ofloxacin has been shown to be bactericidal in mice. Deoxyfructoserotonin has been reported to be active clinically. New side effects and drug interactions have been reported. Dapsone

has been associated with photodermatitis and can apparently induce chromosomal damage. Temporary generalized lymphadenopathy has been associated with clofazimine and renal toxicity, including extensive papillary necrosis, in a patient with renal tuberculosis with rifampin. Rifampin has been shown to shorten the half-life and increase the rates of excretion of dapsone. Thalidomide has been associated with exfoliative dermatitis. There has been some interest in structure activity relationships of clofazimine analogs. The transmission of dapsone-resistant *M. leprae* from documented secondary dapsone-resistant cases to household contacts is not clear cut. Only approximately 10% (or less) of the new cases in the household show primary dapsone resistance. Additionally, primary sulfone resistance is preponderantly low level, while secondary dapsone resistance is preponderantly high level. It was estimated that the relapse rates for multibacillary leprosy patients on life-long dapsone monotherapy for more than 5 years is 1.2% per year. It was brought out that one fourth of indeterminate patients are seropositive but have negative Mitsuda lepromin. This is the immunologic pattern of lepromatous patients and yet these individuals with indeterminate leprosy would fulfill the criteria of paucibacillary leprosy for the purposes of WHO-MDT. In a large study, persisting viable *M. leprae* were found in 10% of patients treated for 2 years with a variety of drug combinations. The type of regimen or the duration of treatment did not seem to affect the proportion of the patients with persisting viable organisms. It would thus seem that none of the present drugs nor combinations of drugs eliminate persisters. Many experienced leprologists would continue to offer chemotherapy to lepromatous patients harboring viable bacilli.

Much new information came to light in the field of clinical sciences. The regrettably high suicide rates among leprosy patients in some societies were noted. It was interesting that the rates of resorption of the anterior nasal spine and alveolar bone in the anterior maxilla are independent in lepromatous leprosy patients. A family was described in whom eight members in three generations had histoid leprosy. A patient was reported with both leprosy and AIDS. Evidence was presented for leprosy involving the cochlea. Untreated indeterminate and tuberculoid cases were shown to self-heal in an average of 2 years, an observation of no small importance in evaluating chemotherapy. It was interesting that leprosy is often perceived by the patient as being a series of acute disorders not necessarily related to one another. Over 90% of the time spent in the clinic by leprosy patients is spent waiting in line for various services in one system. Leprosy patients have decreased secretory IgA in their tears which may have a bearing on their susceptibility to conjunctival infections. Lepromatous leprosy patients have been shown to have decreased serum levels of vitamin A, vitamin E, and serum zinc. Several groups have emphasized the testicular involvement in borderline lepromatous and lepromatous leprosy with hypogonadism, decreased serum total or free testosterone, increased FSH and LH. There was an interesting case report of a generalized drug rash which spared a tuberculoid patch. An interesting report of pigmentation over leg veins in patients with plantar ulcers was made. Phrenic nerve involvement was noted in a substantial portion of patients as well as decreased bronchial reactivity in lepromatous leprosy patients, suggesting postganglionic vagal fiber involvement. In another series, autonomic dysfunction of the cardiovascular and genital systems was shown with parasympathetic involvement being more pronounced and earlier than sympathetic involvement.

In immuno-pathology, much new information is available. There is new emphasis by the U.S.–Japan Cooperative Leprosy Program on leprosy immunology. The interesting hypothesis was put forth that UV light exposure might favor presentation of *M. leprae* antigens along a suppressive pathway in the skin. Lepromatous leprosy patients and patients with type 1 reactions were shown to have a decreased capacity to solubilize preformed immune complexes. Both type 1 and ENL changes have been documented in the nasal mucosa of patients with these reactions. Changes in the epidermis of both type 1 and ENL reactive lesions both suggest T-cell activation with ultimate gamma-interferon production. A case was pre-

sented with focal tuberculoid granulomas in an ENL skin lesion. The pathogenesis of ENL is not clear. *In vitro* live *M. leprae* inhibit phagosome-lysosome fusion in macrophages and decrease the ability of gamma-interferon to activate the macrophage. This is associated with synthesis of prostaglandin E_2. The surface sulfatide of *M. tuberculosis* interferes with the activation of the host macrophage. Lipoarabinomannan also decreases the activation of macrophages by gamma-interferon but in this instance is not associated with an increased synthesis of prostaglandin E_2. It now seems clear that large numbers of live *M. leprae* can down-regulate macrophage function. There was a report of a large molecular weight, cell-directed, inhibitor of monocyte chemotaxis produced in the skin of leprosy patients. Systemic immunotherapy of borderline lepromatous and lepromatous patients with viable BCG plus killed *M. leprae* led to long-term upgrading in the disease classification histopathologically in skin biopsies. In mice, viable BCG plus killed *M. leprae* were better immunogens than either alone. A variety of local injections into the skin of lepromatous leprosy patients induced changes of delayed-type hypersensitivity, e.g., tuberculin in tuberculin-positive individuals, recombinant IL-2, and recombinant gamma-interferon. Local reductions in bacterial numbers occurred at the sites. Quite a number of groups are now interested in *M. leprae* cell walls as sources of *M. leprae* antigens recognized by T cells. T-cell epitopes have been identified on a variety of *M. leprae* proteins, e.g., the 65-kDa, 11–16-kDa, 22–26-kDa, 28–kDa, 16-kDa, and 7-kDa areas of either soluble proteins or preparations from cell walls of *M. leprae.* The 18-kDa peptide gene has now been sequenced. Two observations, one in armadillos and the other in monkeys, suggest that increased levels of IgG and decreased levels of IgM antibodies to PGL-I are associated with less severe disease in the *M. leprae*-inoculated animals. The suggestion has been made that lipoarabinomannan may play a role in ENL. *M. leprae* has been demonstrated inside neuronal cells and glial cells of the brains of armadillos with leprosy. Two antigen fractions of *M. leprae* have been described which are heat-labile. Immune contrasuppressor cells have been reported in lepromatous leprosy but not tuberculoid disease. More studies have suggested that there is a genetic susceptibility to leprosy per se and another gene for susceptibility to nonlepromatous leprosy. An interesting study suggested that H-2 encoded antigens in mice may crossreact with antigens of *M. leprae.* Much has been written regarding the immunodominant stress proteins in *M. leprae* which may be involved in crossed immunity, tolerance, autoimmune pathology, etc.

The pace of work has increased in the field of microbiology. *M. leprae* can use the glyoxalate bypass of the TCA cycle. Asparagine and glycerol favor maintenance of ATP in *M. leprae in vitro.* A number of systems have been described which can be used for *in vitro* drug susceptibility. One report indicates optimum *in vitro* conditions to be 33°C, pH 5.2–5.6, and 2.5%–10% O_2. A report indicated that the amount of ATP per solid *M. leprae* was relatively constant but that the amount of ATP per green-staining *M. leprae* by FDA-EB was quite variable. It was shown that *M. leprae* cannot synthesize purines but can scavenge purines efficiently. Nucleotides cannot be taken up but nucleosides are. The primary structure of the 16S ribosomal RNA places *M. leprae* with slow-growing pathogenic mycobacteria evolutionarily. Careful work has shown substantial losses of viability of *M. leprae* in tissues with freezing and thawing. Limited growth of AFB from *M. leprae*-containing tissues has been reported in dissociated Schwann cell cultures and in several artificial media. DNA probes have been constructed for *M. leprae* with high sensitivity in detection of the organism. A shuttle plasmid vector has been created which now sets the stage for BCG to be used as a recombinant multi-vaccine vehicle.

In the field of epidemiology, 7.5% of wild armadillos in Louisiana are positive for antibodies to PGL-I; 1.3% are positive histopathologically for leprosy. In another area, approximately 2% of wild armadillos were positive for leprosy histopathologically but none of 435 from four other wild animal species in the same locale had leprosy histopathologically. A study showed a strong association between a history of direct armadillo contact and leprosy among U.S. pa-

tients from Mexico. In epidemiometric models, MDT shows a substantial impact on the leprosy epidemic. An *M. leprae*-specific gelatin particle agglutination test for leprosy serology has been developed. In general, serologic tests for antibodies to PGL-I have shown limited usefulness under field conditions. As with earlier studies with the FLA-ABS test, it appears that infection with *M. leprae* is very common in endemic areas compared to the relatively few who actually develop overt disease which would benefit from treatment.

In the field of rehabilitation, there was a clear demonstration that nonspecific infection and trauma account for virtually all bone resorption in leprosy patients with insensitive hands.

In the field of other mycobacterial diseases, a great deal of work is under way. Different strains of *M. tuberculosis* can be identified using restriction fragment analysis of chromosomal DNA. Results of such studies in leprosy should be forthcoming.

From the perspective of the 1988 JOURNAL, there continues to be a steady stream of new information. At no time has there ever been more brain power, more enthusiasm, and more resources applied to the unsolved problems of the leprosy sufferer. No doubt as laboratory-based leprosy research becomes more and more sophisticated, it appears to be further and further removed from the frequently humble surroundings of the leprosy patient. From the perspective of the JOURNAL, it appears that we are in an era in which, in order to advance our knowledge of leprosy, it is sometimes necessary to advance our knowledge of basic science itself. Innovative applied research in leprosy, in many instances, will be the product of innovative basic leprosy research. There is a chain from the basic scientist's laboratory bench to the bedside of the most remote leprosy patient in an endemic area. We all have an obligation to keep that chain unbroken. The basic information continues to be amassed. Hopefully, more practical applications of this knowledge will be forthcoming. I look forward with impatient optimism to 1989.—RCH