The 1983 JOURNAL—a Continuing Perspective

After the fifty-first year of publication of the JOURNAL and on the eve of the XII Leprosy Congress in New Delhi, it again seems appropriate to review the progress that has been made in the last year in our understanding of leprosy. As reflected in these pages, 1983 was another year of steady progress marked by refinements in our knowledge over broad fronts. In the March issue the original article by Mukherjee, *et al.* (1–6)* pointed out that subcutaneous venous involvement (leprous phlebitis) occurs in a very high percentage of lepromatous patients and may be quite advanced in early lepromatous disease. Duncan, *et al.* (7–17) presented strong evidence for placental transmission of leprosy from active lepromatous mothers to their babies. Balybin and Nazarov (18–21) showed that basal levels of hydrocortisone are elevated in patients with lepromatous leprosy and that high proportions of active lepromatous patients, particularly relapsed cases, show exhausted reserve hydrocortisone-producing adrenal function as revealed under insulin load. Ahmed, *et al.* (22–28) found elevated total proteins and IgA concentrations in nasal washings, but not in the salivas, of borderline lepromatous (BL) and lepromatous leprosy (LL) patients. Holla, *et al.* (29–32) reported a series of 50 synovial biopsies from lepromatous leprosy patients with arthritis. In 36 cases, primary synovial involvement seemed to be responsible for the arthritis and in 14 patients the arthritis was associated with lepra reactions. Mshana, *et al.* (33–40) did not find significantly elevated antibody levels against bovine peripheral nerve myelin protein P_2 among leprosy patients. Saoji and Kelkar (41–44) studied 50 leprosy patients and found that none showed a deficiency of erythrocyte G-6-PD and that all showed the B+ variety of G-6-PD phenotype. Peters, *et al.* (45–53) found no mutagenic activity for clofazimine, ethionamide, prothionamide, rifampin, or dapsone, with or without metabolic activation in the Ames *Salmonella*/microsome assay system. Peters, *et al.* (54–63) studied the pharmacokinetics of prothionamide and prothionamide-S-oxide in rats and armadillos, showing that the two are metabolically interconvertible and that prothionamide does not induce its own metabolism. Ishaque (64–71) reported extensive studies of the respiratory activities of *Mycobacterium lepraemurium* using a variety of substrates. Matsuo (72–76) outlined an interesting technique using cycloheximide for the cultivation of *M. lepraemurium* in cell cultures. Kato (77–83) cultivated mycobacteria, tentatively designated "*Mycobacterium X*," from *M. leprae*-infected human and armadillo tissue in a liquid medium containing dimethylketone, dimethylsulfoxide, and tetradecane. Hirata (84–88) described the intracytoplasmic inclusions of *M. leprae* and *M. lepraemurium* in ultrathin serial sections of lepromata at the electron microscopic level.

In the Editorial section of the March issue, Hastings (89–104) reviewed the contents of the 1982 JOURNAL. The death of Howard Fieldsteel (105–106) was noted with sadness.

In the Current Literature section of the March issue Beeching and Ellis (129) pointed out the need for new, cheap antibacterial agents for leprosy. Li, *et al.* (130) found that R761 [3 (4-isobutyl-l piperazinyl) rifamycin SV] 150 mg daily was clinically active in 10 BL and LL patients. Andersen (130) described two cases of squamous cell carcinoma developing in long-established ulcers in leprosy patients. Duncan and Oakey (130–131) found that estrogen excretion was lower than normal in pregnant lepromatous leprosy patients, providing further evidence for diminished fetoplacental function in women with leprosy. Kundu, *et al.* (131) showed that corticosteroids were capable of rendering tuberculoid patients lepromin negative. Nigam, *et al.* (131) reported two cases of eosinophilia apparently due to rifampin. Sharma, *et al.* (132) pointed out the value of the solid, fragmented and granular (SFG) index in research and as a routine laboratory procedure. Shilo, *et al.* (132) found abnormalities in prolactin and thyrotropin secretion among lepromatous lep-

* Numbers in parentheses refer to page numbers in the INTERNATIONAL JOURNAL OF LEPROSY, Volume 51, 1983.

rosy patients which were similar to those described in patients with primary testicular failure. Shulman, *et al.* (132–133) reported a dramatic downgrading reaction in a patient associated with griseofulvin therapy. Terencio de las Aguas (133) suggested that there is an increased frequency of diabetes among leprosy patients. Zhang, *et al.* (133) reported 20 cases of histoid leproma, 12 with subpolar LL, 4 with polar LL and 4 with borderline lepromatous leprosy. Bahr, *et al.* (133) delayed the addition of *M. leprae* antigens to cultures of peripheral blood mononuclear cells in an effort to allow suppressor cells to lose their activity during the preculture period. Most normal donors or tuberculoid leprosy patients showed enhanced responses but the effect was less common with lepromatous leprosy patients, suggesting that this type of suppressor reflects a normal mechanism which is diminished rather than increased in lepromatous patients. Chakrabarty, *et al.* (134) undertook sophisticated antigenic analysis of *M. leprae* and detected two glycoprotein antigens of 12,000 and 33,000 daltons which seemed to have *M. leprae*-specific determinants on crossreacting components. Humphres, *et al.* (134–135) found markedly depressed natural killer (NK) cell activities in patients with ENL and evidence that the patients' monocytes were responsible for the depression of NK activity. Kurup and Mahadevan (135) studied the effects of phagocytosis of live *M. leprae* on macrophages. Cholesterol esters accumulated, apparently due to reduced levels of esterase enzyme that could hydrolyze cholesterol esters, and this was associated with reduced protein synthesis by the macrophage. Mehra, *et al.* (136) reported that OKT8 (suppressor T cell)-depleted peripheral blood mononuclear cells from 6 of 21 borderline lepromatous-lepromatous patients responded *in vitro* to *M. leprae* and that lepromatous patients had elevated numbers of Ia+, TH_2^+/OKT8+, Fc receptor + (activated suppressor T cells) compared to normal controls. Melsom, *et al.* (136–137) studied cord sera from babies born to lepromatous mothers and found that 30% contained IgA class anti-*M. leprae* antibodies and 50% contained IgM class anti-*M. leprae* antibodies. None of the cord sera from babies of tuberculoid mothers or non-leprosy control mothers had detectable IgA or IgM anti-*M. leprae* antibodies. Prasad, *et al.* (1937) demonstrated that antigen-stimulated lymphokine preparations from cells of tuberculoid, but not lepromatous, patients inhibited the uptake of ^{3}H-thymidine by live *M. leprae* in macrophage cultures. Ramos-Zepeda, *et al.* (137) found that 40% of nodular lepromatous leprosy patients had a serum factor which could depress lymphocyte blast transformation in response to PHA. Ridley and Ridley (137) demonstrated HLA-DR (Ia-like) antigen in the skin lesions of 11 out of 11 polar tuberculoid (TT) patients, and 3 of 6 near tuberculoid cases in reaction, and in 0 of 38 other cases covering the spectrum from BT to LL. Rook (137–138) pointed out that the demonstration of suppressor cells in lepromatous leprosy does not prove that they are important in its pathogenesis. Saha, *et al.* (138) showed marked increases in C3d during ENL. Elevated C3d levels persisted after clinical remission of the ENL under treatment with prednisolone or chloroquine but C3d levels fell markedly in those ENL patients treated with clofazimine. Shepard, *et al.* (138–139) produced tolerance to intradermal challenge with *M. leprae* by administering 10^7 heat-killed *M. leprae* i.v. Intradermal immunization of tolerant mice partially sensitized the animals to *M. leprae*; mixtures of BCG and heat-killed *M. leprae* were no more effective than BCG alone.

Abou-Zeid, *et al.* (139), Cocito (140), and Delville (140) reported studies on leprosy-derived corynebacteria (LDC). Arabinogalactomannan may occur in the wall polysaccharide fraction of these organisms and contribute to the biochemical uniqueness of this group of bacteria. The immunological relatedness of LDC and mycobacteria has been demonstrated including the correspondence between the M component of LDC and antigen 7 of *M. leprae*. Small numbers of viable LDC facilitate the multiplication of *M. leprae* in the foot pads of mice. There are good correlations between LDC antigens and lepromin in skin tests both in patients and controls. Dhople (140–141) reported that *M. leprae* in infected tissues which had been stored at −76°C retained metabolic activity and infectiousness. Portaels, *et al.* (141–142) cultivated

"difficult to grow mycobacteria" from two of four armadillo livers infected with human-derived *M. leprae*. Their *in vitro* multiplication was only successful if the inocula contained more than 10^5 organisms, suspensions were pretreated with NaOH or HCl, and the media were adjusted to a pH of 5.4–5.7 and contained autoclaved mycobacterial suspensions. Rotberg (142) proposed that the term *Mycobacterium hansenii* be substituted for the term *M. leprae*. Sathish, *et al.* (142–143) found no correlation between the percent of solid or beaded bacilli in the inoculum and the ability of *M. leprae* to incorporate ^{3}H-thymidine in macrophage cultures. Brown, *et al.* (143) suggested that mouse resistance to *M. lepraemurium* is, at least in part, controlled by a gene with the same distribution as genes for resistance to other intracellular infections on chromosome 1. Galletti, *et al.* (143–144) reported that subcutaneous injections of 10^6 human *M. leprae* into hibernating ground squirrels resulted in generalized infection of the animals and spontaneous death. The number of mycobacteria was high in the skin during winter and decreased during summer. Kawaguchi, *et al.* (144) found that resistance and susceptibility of mice to *M. avium* seemed to be under genetic control. Martinez, *et al.* (144–145) reported the second case of a nine-banded armadillo in Argentina with a naturally acquired disseminated mycobacterial infection similar to that seen in armadillos experimentally infected with *M. leprae*. Fine (147–149) authoritatively reviewed the epidemiology of leprosy in light of newer knowledge. van Eden, *et al.* (150) found that the frequency of the HLA-DR3 phenotype was increased among TT patients and decreased among lepromatous (BL+LL) patients in Suriname. Cook (152) emphasized the importance of stressing the treatability of leprosy in combating the stigma of the disease. Soderberg, *et al.* (153) reported good results in treating plantar ulcers with adhesive zinc tape. Srinivasan, *et al.* (153–154) found that six months of steroid therapy reversed the motor paralysis in 75% of leprosy patients with "quiet nerve paralysis." Nash and Steingrube (155–156) evaluated mixtures of antituberculosis drugs for their *in vitro* effects on *M. tuberculosis* and *M. avium-intracellulare*, and found that the responses of individual isolates to representative drug combinations was not always predictable from the results of single-drug sensitivity assays. Nouri-Arai, *et al.* (156) found evidence that low-dose prednisolone improves defective suppressor cell activity in "autoimmune" chronic active hepatitis, a possibility which could explain the extraordinary sensitivity of ENL to steroids. Sanders, *et al.* (156–157) found that amikacin has potent activity against mycobacteria and merits further study as a therapeutic agent.

The June original articles began with a clear demonstration by Chaudhuri, *et al.* (159–168) of the ability of a single immunization with "*Mycobacterium w*" to convert about 60% of lepromin-negative, inactive BL/LL leprosy patients to lepromin positivity. Lynch, *et al.* (169–173) did not find significant elevations of serum IgE levels in active lepromatous leprosy patients compared to appropriate controls. Trach, *et al.* (174–178) showed that active lepromatous leprosy patients had significant reductions in circulating T cells as measured by standard, "active" or "high affinity" rosette-forming cells with sheep erythrocytes. Compared with normal controls, both lepromatous and borderline leprosy patients had increased percentages of cells forming rosettes with sheep erythrocytes coated with antibody and complement. Ridell (179–184) analyzed serological relationships among eight diphtheroid organisms isolated from leprosy patients and 25 strains representing *Corynebacterium, Mycobacterium, Nocardia, Rhodococcus,* and related taxa. The largest number of shared precipitinogens with six of the eight diphtheroid strains was with corynebacteria. Ridell (185–190) found that *M. leprae* share antigens with various species of mycobacteria and also with other species of related genera. *M. leprae* share more antigens with mycobacteria than with the other genera tested. Modderman, *et al.* (191–196) measured serum levels of dapsone (DDS) and monoacetyl DDS (MADDS) in 20 leprosy patients receiving weekly injections of 375 mg DDS in an oily vehicle and found that DDS levels of approximately 1 μg/ml were maintained. Sundararaj, *et al.* (197–202) compared the results of two surgical procedures for the correction of claw hand deformities in leprosy patients. Both operative procedures produced 95% satisfactory results. Andersen and Warndorff (203–204) reported a very

unusual case of a hyperactive leproma simulating an osteoclastoma in the distal metaphysis of the ulna. Gummer, *et al.* (205–210) studied the distribution of *M. leprae* in the hair follicle of the eyebrow in active lepromatous leprosy patients. Bacilli were found in the dermal papilla and outer root sheath of both anagen and telogen hair follicles but were rarely found in those cell lines continuous with the environment. Ridley (211–218) reported an elegant study in which tissue bacterial enumerations were undertaken across the leprosy spectrum using acid-fast staining, methenamine silver to demonstrate cell walls, and an immunoperoxidase technique to demonstrate nonparticulate mycobacterial antigenic material. In BT, BB, and BL, the degradation of cell walls, loss of acid fastness, and total elimination of bacilli are almost simultaneous. In LL the breakdown of cell walls is slow but mycobacterial antigenic material as detected by an anti-BCG serum is cleared as fast as it leaks out. Silva and Macedo (219–224) studied *M. leprae* in tissues of experimentally infected armadillos by transmission electron microscopy and demonstrated an apparently unique, symmetric membrane profile. Silva and Macedo (225–234) pointed out several aspects of the ultrastructure of mycobacterial cells relating to whether the cells are normal or altered, emphasizing the importance of fixation conditions.

We were fortunate to have a masterful review of the serology of leprosy by Melsom as a Guest Editorial in the June issue (235–252). The death of Sister Hilary Ross was noted with a deep feeling of loss (253).

In the Current Literature section of the June issue, Ramanathan and Ramu (271) studied the attitudes of 35 physicians working in leprosy and found that at least some revealed fears of being socially stigmatized and facing poor job prospects while working in this field. Baquillon, *et al.* (273) reported 2.3%–4.1% average yearly incidences of dapsone resistance among patients at risk in Bamako, Mali. Kulkarni and Seydel (274) isolated cell-free folate-synthesizing extracts from *E. coli*, "*M. lufu*," *M. smegmatis*, and *M. leprae* and showed that the high sensitivity of "*M. lufu*" and *M. leprae* to dapsone, as compared to *E. coli*, can be solely attributed to the high affinity of their dihydropteroate synthetases for dapsone. Mester de Parajd, *et al.* (274) treated seven leprosy patients for an average period of six months with deoxyfructo-serotonin, demonstrating antibacterial activity with no side effects. Modlin, *et al.* (274–275 and 285–286) studied the distribution of T lymphocyte subsets in the skin lesions of leprosy patients. Two patterns were observed. In tuberculoid leprosy, helper-inducer cells were present among the epithelioid cells and suppressor-cytotoxic cells were predominantly in the lymphocytic mantle surrounding the epithelioid cell aggregates. In lepromatous tissue, the helper-inducer and the suppressor-cytotoxic cells were both distributed among the histiocytes. Appa Rao, *et al.* (275) described an effective technique for cleansing the nostrils in leprosy patients. Brazin (276) reviewed the ear, nose, and throat manifestations of leprosy. Hameedullah, *et al.* (278) studied 20 multibacillary leprosy patients and found 121 acid-fast bacilli from 930 sq cm of intact skin surface. Kruyt, *et al.* (278) reported an interesting case who developed borderline lepromatous leprosy in association with generally depressed cell-mediated immunity due to cytomegalovirus infection. Raval, *et al.* (280) found that bacillemia occurs in practically all untreated borderline and lepromatous patients. The numbers of bacilli were on the order of 4000/ml and bore no relationship with bacillary load as measured by skin and nasal smears. Sheskin (281) reported a case of diffuse lepromatosis of Lucio-Alvardo-Latapí with the Lucio phenomenon from the Near East. Das, *et al.* (282) studied subcellular fractions of BCG as antigens in leprosy patients. Different leprosy patients showed different patterns of antibody response to the antigens in the different fractions. Fleming and Rook (283) showed that soluble extracts of ultrasonically disrupted mycobacteria, including *M. leprae*, caused strong T cell-dependent polyclonal B cell activation in peripheral blood mononuclear cell preparations from normal humans. Cells from lepromatous leprosy patients showed no polyclonal B cell activation in the presence of extracts of *M. leprae*, although they responded normally to the other mycobacterial species. Jaswaney, *et al.* (284) suggested that the decreased erythrocyte rosette-forming cells of lepromatous leprosy patients are due to serum factors which specifically interact with a subset of T lympho-

cytes. Lad and Mahadevan (284–285) found that macrophages have receptors for the carbohydrate moieties of the cell wall of *M. leprae* and that adherence of *M. leprae* to macrophages was reduced in the active stage of leprosy but was restored after effective treatment of the patient or after trypsin treatment of the macrophages. Mshana, *et al.* (286) showed that both borderline lepromatous and lepromatous leprosy patients had increased circulating suppressor T cells, while the total number of T cells was normal. The suppressor cell population decreased with the duration of treatment, the change being evident as early as 21 days after treatment had started. In five patients who developed ENL, the number of suppressor cells decreased prior to the onset of ENL and increased to original values with clinical recovery. Mshana, *et al.* (286–287) found immunoglobulin or complement deposits in six of 26 biopsies from active ENL lesions. These deposits were found in the dermo-epidermal junction, within foam cells and, in one patient, around a blood vessel. Five of 20 patients with lepromatous leprosy without ENL showed similar deposits in the dermo-epidermal junction and within foam cells, but not around blood vessels. The presence of acute inflammatory infiltrates was not correlated with immunoglobulin or complement deposits. These deposits were not a constant feature of ENL lesions and may be secondary rather than primary in these lesions. Narayanan, *et al.* (287) studied T cell subsets in leprosy lesions and found that activated T cells (OKT3+ and Ia^+) were maximal in TT and were markedly reduced in LL. The helper/suppressor ratio (OKT4+/OKT8+) ranged from 1.2–5.0 in TT and from 0.2–1.0 in LL lesions. Nye, *et al.* (287) showed that reagents from fast-growing mycobacterial species, when mixed with reagents prepared from slow-growing mycobacteria, are capable of suppressing skin test responses to the latter. Opromolla, *et al.* (287) showed that 55% of active lepromatous leprosy patients have a positive Rubino reaction, while only 6% of clinically inactive patients are positive. Rea and Yoshida (288) described a serum migration inhibitory activity present in 48% of untreated leprosy patients. The activity was present in all forms of the disease but particularly in patients with active reactional states. Saha, *et al.* (288) found that the concentration of factor B breakdown product (Ba) and its ratio to factor B increased with the bacterial density in lepromatous leprosy patients and more so in patients with ENL. The alternative pathway may be the mechanism of complement activation in lepromatous leprosy. Van Voorhis, *et al.* (288–289) found that lepromatous leprosy lesions were devoid of helper T cells (OKT4+,Leu 3a+) and contained almost exclusively suppressor T (OKT8+,Leu 2a+) populations. Tuberculoid infiltrates contained predominately helper T cells. Vazquez-Escobosa, *et al.* (289) found that nonreactional nodular lepromatous leprosy patients have large quantities of circulating immune complexes consisting of IgG. Das and Tulp (289–290) described a method of purifying *M. leprae* from infected tissues consisting of homogenization, two-phase partition in dextran-polyethylene glycol and finally sedimentation in a sucrose gradient using unit gravity. Imaeda, *et al.* (290) found that *M. avium* and *M. lepraemurium* had 74.2%–92.9% DNA homology, suggesting a close genetic relatedness. Based on the immunological characteristics of its catalase, Katoch, *et al.* (290) found that *M. lepraemurium* was taxonomically uniquely positioned between *M. tuberculosis* and *M. avium*. Nakamura (290 and 290–291) found that DL-aspartic acid and dextran stimulated the *in vitro* growth of *M. lepraemurium*. Ridell (291) studied the β-antigen of *M. leprae*, concluding that it was a ribosomal antigen corresponding to antigen 5 of *M. leprae* and antigen 1 of *M. smegmatis* as defined by crossed immunoelectrophoresis. Silva, *et al.* (291) studied the ultrastructural alterations observed in *M. leprae* cells during treatment and concluded that the cell wall of *M. leprae* is the last bacterial structure to disappear during the degenerative process. Wheeler, *et al.* (291) described *n*-acetyl-β-glucosaminidase, β-glucuronidase and acid phosphatase activities in cell-free extracts of *M. leprae* from armadillo liver. Young (292) analyzed lipid extracts from lepromatous leprosy skin biopsies and showed the presence of several mycobacterial lipids including *M. leprae*-specific glycolipid, phthiocerol dimycocertosate, and mycolic acids. The amount of mycobacterial lipids present in lepromatous

lesions is much greater than that expected on the basis of the number of acid-fast bacilli present, and the incorporation of ^{14}C-acetate into cell wall mycolic acids can be used to monitor the growth of intracellular mycobacteria. Bhat and Vaidya (292) studied the sciatic nerves of immunosuppressed mice with *M. leprae* infections and showed an early segmental demyelination and late axonal degeneration. Lancaster, *et al.* (293–294) demonstrated the growth and dissemination of *M. leprae* in congenitally athymic, nude mice. Venkataramaniah, *et al.* (295) found no significant differences in the mouse foot pad growth patterns of *M. leprae* from leprosy patients with low, high, and intermediate Morphological Indexes. Alemayehu and Naafs (295) found that the age at onset of leprosy in Ethiopia was between 15 and 20 years of age in all classifications with the age at onset being earlier in areas with high endemicity compared to areas with low endemicity. Fekete and Tedla (295) reported two cases of BT leprosy in children aged 18 months. Saikawa (296–297) found no noticeable benefit from BCG vaccination in contact children in preventing leprosy in Okinawa. Goode (299) studied the phage types of 100 strains of *M. tuberculosis* from Nepal and compared them with those of bacilli from different geographical regions. The findings provided further evidence for the existence of geographical differences in the types of tubercle bacilli. Soo Duk Lim, *et al.* (302) showed that suppressor T cells were increased, helper T cells were decreased, and that the mean percentage of T cells was significantly decreased in Behçet's syndrome. Sutherland, *et al.* (302–303) estimated the risks of developing tuberculosis following infection or reinfection. For those with a recent primary infection the risk of developing progressive primary tuberculosis was estimated to be 5.1%–5.9% annually for five years following the primary infection. For those with a distant (i.e., not recent) primary infection and a recent reinfection with *M. tuberculosis,* the risk of developing exogenous tuberculosis was estimated to be 1.9%–1.1% annually (for five years) following reinfection. For those with a distant primary infection but no recent reinfection, the risk of developing endogenous tuberculosis was estimated to be 0.03%–0.002% annually, after the first five years following primary infection, in the absence of reinfection.

The original articles of the September issue began with the careful study by Touw Langendijk, *et al.* (305–311) on anti-*M. leprae* antibodies in patients with borderline tuberculoid leprosy. High antibody activity was significantly correlated with active skin lesions, new skin lesions, and neuritis, despite dapsone treatment of long duration. The study pointed out that there is not always an inverse relationship between cell-mediated and humoral immune responses to *M. leprae* and that increased inflammatory activity in skin lesions and nerves is associated with high antibody levels in patients with persisting BT leprosy. Dahle, *et al.* (312–320) demonstrated a strong correlation between clinical activity in BT patients and anti-*M. leprae* antigen 7 antibody activity. A characteristic pattern of rapid and marked increase in antibody activity occurred shortly after the initiation of treatment in newly diagnosed BT cases. Sasiain, *et al.* (321–327) studied ConA-induced suppressor activity in patients with lepromatous leprosy during and after ENL reactions. Compared to normal controls. ConA-induced suppressor responses were markedly reduced during ENL, and the reduction was even more marked after the ENL episode had passed. Kyriakidis, *et al.* (331–335) presented evidence that patients with long-standing lepromatous leprosy have defective autonomic control of the heart. Dawson, *et al.* (336–346) presented details of the growth of *M. leprae* in congenitally athymic rats. The animals are highly susceptible to *M. leprae* but despite their lack of thymic-dependent T cell function, they seem to possess defense mechanisms capable of limiting the infection. Job, *et al.* (347–353) described tuberculoid, borderline, and lepromatous patterns of tissue responses after lepromin skin testing in armadillos, all of which were resistant to infection with *M. leprae.* The interesting possibility is raised that animals with an innate resistance to infection may not need to develop a cell-mediated immune response to *M. leprae.* Sehgal, *et al.* (354–358) described 1327 new leprosy cases diagnosed from 1977 to 1982 who were attending a large Delhi hospital for other ailments. Modderman, *et al.* (359–365) described striking sex differences after

injections of a long-acting dapsone preparation. They concluded that the sex difference can probably be explained on the basis of differences in the thicknesses of gluteal fat between men and women, i.e., that men received intramuscular injections and women received the same injections subcutaneously in most cases. Almeida, *et al.* (366–373) reported that the prevalence of dapsone-resistant infection among lepromatous and borderline lepromatous leprosy patients treated for a minimum of three years was 3.3% with an average annual incidence of 0.28% per year. No association was found between the incidence of dapsone-resistant infection on the one hand and either the regularity or the initial dosage of dapsone on the other. Mouse foot pad tests detected bacilli resistant to dapsone not only among patients deteriorating despite dapsone monotherapy but also among patients improving on dapsone monotherapy. Almeida, *et al.* (374–377) performed mouse foot pad studies to detect dapsone-resistant *M. leprae* in 18 newly diagnosed and previously untreated leprosy patients. Of 12 successful tests, five detected dapsone-resistant *M. leprae.* Known contact with a treated patient did not increase the risk of dapsone-resistant *M. leprae* occurring in this group. The authors question the hypothesis that treated patients are likely to be the only source, or even the major source, of resistant *M. leprae* in untreated patients. Almeida, *et al.* (378–381) found that the efficacy of dapsone monotherapy did not diminish between groups of BL and LL patients initiating chemotherapy in 1964–1966, on the one hand, and in 1971–1973 on the other. Almeida, *et al.* (382–384) found that relapse rates decreased steadily with the time elapsed after the attainment of smear negativity in LL and BL patients receiving dapsone monotherapy. Almeida, *et al.* (385–386) followed up 58 living lepromatous leprosy patients who had received dapsone monotherapy for more than 20 years. Fifty-one of the 58 patients were currently smear negative and clinically inactive.

The September issue contained a brilliant review of the outstanding work on the phthiocerol-containing surface lipids of *M. leprae* by Brennan (387–396). Baker (397–403) thoughtfully reviewed the problem of cultivation of the leprosy bacillus.

The tragic death of Ayele Belehu (404) was noted in the Obituary section. The passing of the distinguished Dr. Frank Davey was noted with sadness (405–406).

The lively Correspondence section of the September issue began with an explanation of the value of rifampin + Isoprodian® by Freerksen (407–408). Sengupta, *et al.* (409–410) presented interesting data showing the presence of light chains and immunoglobulins in the urine of leprosy patients. Mathur and Bumb (410–411) drew attention to the beneficial effects of oral zinc sulfate in the healing of uncomplicated trophic ulcers in leprosy. Rotberg (411–413) reviewed the hypothesis that about 20% of humans are genetically incapable of becoming Mitsuda positive after infection by Hansen's bacillus, and pointed out that it would be advisable to demonstrate in advance that any new vaccines and techniques are capable of eliminating or at least significantly reducing this "Hansen-anergic fringe" before undertaking extensive, costly, and time-consuming preventative field studies. Clezy (413) reported three interesting cases who apparently had simultaneous Type I and Type II reactions and made remarkable bacteriologic recoveries. Nelson and Schauf (413–415) thoughtfully commented on the work of Mathai, *et al.* regarding the risks of developing leprosy among workers in a general hospital caring for leprosy patients. Lynch and Lopez (416–417) commented on the observations of Nuti, *et al.* on serum IgE levels in leprosy patients. Rabello, *et al.* (418–420) reviewed the importance of indeterminate leprosy. Jopling (420) and Pettit (420–421) clarified their positions.

The News and Notes section of the September issue noted the well-deserved receipt of the 1982 Damien-Dutton Award by Dr. Ma Haide of the People's Republic of China (422–423). Dr. Jacinto Convit was unanimously elected an honorary member of the American Society of Tropical Medicine and Hygiene (430).

In the Current Literature section of the September issue Balakrishnan, *et al.* (436–437) noted that a higher percentage of dapsone resistance was detected among institutionalized leprosy patients as compared to patients treated in the field. Goihman-Yahr (437) pointed out that current problems in leprosy research are basically similar to those of autoimmune disorders and

of cancer immunology. Katoch, *et al.* (437) reported a case of toxic epidermal necrolysis possibly due to dapsone. Ramu and Sengupta (438) reported beneficial effects of levamisole in persistently bacteriologically positive lepromatous cases, consisting of a temporary conversion of the early lepromin reaction in a majority of the patients and a corresponding improvement in clinical and bacteriological status. Revankar, *et al.* (438) found that 68% of patients in an urban field project were regular in consuming dapsone and that 28% were irregular as judged by urine examination. Vellut, *et al.* (438–439) studied the reasons for absenteeism during leprosy treatment and found that anxiety for loss of income while attending the medical clinic and the erroneous impression of cure as soon as skin lesions improved were of first importance. Yagnik, *et al.* (439) found that levamisole-treated lepromatous leprosy patients more commonly experienced ENL reactions than did control patients receiving standard dapsone treatment and placebo. Donde, *et al.* (440) studied sensory and mixed nerve conduction velocities in leprosy patients and found that all the clinically involved nerves, and about 30% of clinically normal nerves, showed a delayed conduction velocity. Jain, *et al.* (440–441) found that serum fibrinolytic activity was significantly decreased in patients with ENL compared to those with uncomplicated lepromatous leprosy who, in turn, showed lower activity compared to patients with tuberculoid leprosy and to controls. Kher, *et al.* (441) found decreased serum cholesterol and α-lipoprotein fractions in lepromatous leprosy patients compared with age-matched controls. Yemul, *et al.* (441) found increased serum α-1-antitrypsin levels in lepromatous leprosy patients and in patients with lepra reaction compared to healthy controls. Bach, *et al.* (442) studied the *in vitro* proliferative response to *M. leprae* of T cell subsets in leprosy patients. In tuberculoid patients, *M. leprae* induced proliferation in T cells which predominantly involved OKT4+ cells but to a smaller extent also involved OKT8+ cells. In a majority of lepromatous patients neither OKT4+ nor OKT8+ enriched cells developed a proliferative response to *M. leprae.* In four *M. leprae* unreactive patients, however, treatment of unfractionated cells with complement alone restored a strong proliferative response to *M. leprae.* These results suggest that the *in vitro* unresponsiveness to *M. leprae* results, at least in some patients, from an active suppressor mechanism but that the effector phase of such suppression does not directly involve OKT8+ T cells. Chakrabarty, *et al.* (442) identified immunoglobulins, complement components, and C-reactive protein in immune complexes isolated from sera of lepromatous patients. One mycobacterial antigen was directly identified in these immune complexes, while two other components of possible *M. leprae* origin were also found. Mathur, *et al.* (443) found significant reductions in Langerhans' cell populations in LL and BL patients compared to TT, BT, and normal individuals. Miller, *et al.* (443) described an ELISA utilizing an arabinomannan from *M. smegmatis* to detect anti-mycobacterial antibodies in sera from lepromatous patients and contacts. Mustafa and Godal (443–444) induced suppressor T cells *in vitro* by exposing peripheral blood mononuclear cells from BCG-vaccinated healthy donors to BCG. The suppressor cells could inhibit the proliferation of fresh cells to other mycobacterial antigens, including *M. leprae.* The suppressor T cells which were induced were in the OKT4+ class of T cells. Wadee, *et al.* (444) presented evidence indicating that when macrophages ingest mycobacteria, they release phosphatidylethanolamine and phosphatidylinositol of bacterial origin into their culture supernatants, which are responsible for activating suppressor T cells. Wadee and Rabson (445) demonstrated that phosphatidylethanolamine and phosphatidylinositol bound to OKT8+ cells in a specific manner and with significantly greater affinity than they did to other cell types. The receptors for these two phospholipids were trypsin and heat sensitive, and the receptor sites could be regenerated after a 24 hr incubation after trypsinization. Andersen, *et al.* (445) found that mycobacterial species could be identified by their gas chromatographic patterns for cellular fatty acids. David, *et al.* (445–446) studied *M. leprae* by fluorescent microscopy on smears stained by auramine, o-ethidium bromide, fine structural observation of ultrathin sections, reduction of potassium tellurite as observed under the electron microscope, and ATP content. There was no correlation between the quantitative data from these procedures

and the Morphological Index. Draper, *et al.* (446) described a characteristic mycobacterial wax, phthiocerol dimycocerosate, from livers of armadillos experimentally infected with *M. leprae.* Mittal, *et al.* (446) described a rapid microculture assay using radiolabeling and mouse macrophages to determine the viability and drug susceptibility of *M. leprae.* Portaels and Pattyn (447) described the characteristics of *M. leprae* and *M. lepraemurium. M. leprae* has predominantly glycine in its cell wall peptidoglycans rather than alanine. *M. leprae* lacks dicarboxymycolates which are present in most other mycobacteria and also either lacks or has very low levels of tuberculostearic acid. Rastogi, *et al.* (447–448) studied the ultrastructural characteristics of *M. leprae* and *M. avium,* both grown in animal host tissues. Both bacilli contained an outer electron-transparent zone, had the same location of an α-1-2-glycol bond containing polysaccharide, had the same organization of the peptidoglycan layer and, finally, contained a deposit of polysaccharides at the outer surface of their respective electron-transparent zones. Thus, at least some of the ultrastructural features characteristic of *M. leprae* seemed to be partially determined by the growth of these bacteria in animal host tissues. Lagrange, *et al.* (450) found that large doses of armadillo-derived, irradiated *M. leprae* could induce a state of CMI in high-responder strains of mice but that in low-responder strains no such immunity developed at all after immunization with *M. leprae.*

In the Original Articles of the December issue, Cartel, *et al.* (461–465) found a 13% incidence of hepatitis among multibacillary leprosy patients treated daily with the three-drug combination of dapsone, rifampin, and either ethionamide or prothionamide. No cases of hepatitis were observed among paucibacillary leprosy patients treated with the two-drug combination of dapsone and rifampin. The hepatotoxicity associated with ethionamide or prothionamide seems to have been potentiated by the concurrent administration of rifampin. Bhatki, *et al.* (466–472) described the clinico-pathological features of five cases of lepromatous leprosy who developed reversal reactions following vaccination with the ICRC bacillus vaccine. Desikan, *et al.* (473–480) described the sequence of histopathological changes occurring in the skin of patients across the leprosy spectrum in response to Dharmendra antigen. Neutrophils were predominant during the first 48 hr, particularly in the LL, BL, and BT types. A tendency for lymphocytes to cluster around nerve twigs was seen in the TT and BT cases. Collins, *et al.* (481–489) sensitized guinea pigs with heat-killed mycobacteria and measured subsequent Fernandez and Mitsuda reactions to whole-cell antigens of these mycobacteria. *M. leprae* induced a highly persistent state of lepromin hypersensitivity which was quantitatively superior to that observed in animals sensitized with the three other mycobacteria tested. Hall, *et al.* (490–494) demonstrated the uptake of iron chelated to the exochelins from *M. neoaurum* by suspensions of *M. leprae.* No uptake occurred when the iron was chelated with exochelins from BCG, *M. smegmatis,* or *M. vaccae.* Greco and Galanti (495–499) described the epidemiology of leprosy in Italy.

In the December issue, we were fortunate to have a series of 11 articles which were the results of the SEARO/WPRO/IMMLEP/THELEP Joint Scientific Meeting on Leprosy, Rangoon, Burma, 18–19 November 1981 and the Joint Indian and IMMLEP Scientific Meeting on Immunoepidemiology of Leprosy, New Delhi, India, 14–16 February 1983. Following an introduction and summary (500–504), Bloom (505–509) succinctly summarized the rationales for vaccines for leprosy, vaccine strategies, inherent problems, and present prospects. Godal, *et al.* (510–514) presented impressive data suggesting that the cell-mediated immunological unresponsiveness in lepromatous leprosy commonly is due to a deficiency in the production of interleukin 2 and related factors, and is not due to a lack of *M. leprae*-reactive T cells. These findings provide strong evidence that the specific immunological unresponsiveness in lepromatous leprosy is due to active suppression. Rees (515–518) reviewed the progress that has been made in the preparation of *M. leprae* for human vaccine studies. Shepard (519–523) presented the experimental animal systems which have been used to study potential *M. leprae* vaccines. Buchanan

(524–530) reviewed the serodiagnostic methods reported to be specific for infection with the leprosy bacillus, or to methods of potential serodiagnostic value that have utilized chemically defined and pure antigens of *M. leprae*. Convit, *et al.* (531–539) presented their results with a mixture of heat-killed *M. leprae* and viable BCG as immunotherapy in leprosy patients and contacts. Deo, *et al.* (540–549) reviewed their results with ICRC bacilli as an immunotherapy for various types of leprosy patients and lepromin-negative residents in an endemic area. Talwar and Fotedar (550–552) described results obtained with two prospective antileprosy vaccines, "*Mycobacterium w*" and acetoacetylated *M. leprae*. Fine (553–555) reviewed the natural history of leprosy in light of the problems it may create in the interpretation of vaccine trials. Noordeen (556–558) discussed epidemiological considerations in vaccine trials. Guld (559–562) presented a number of operational problems which will need to be addressed in vaccine trials.

We were fortunate to have obtained permission to reprint the excellent review on the bacteriology of *M. leprae* by Draper (563–575) which originally appeared in *Tubercle*. Charosky, *et al.* (576–586) succinctly outlined the pathogenesis of neuropathies in leprosy, proposed a classification of these neuropathies, and outlined their management in a Guest Editorial.

The loss of the eminent leprologist Ricardo S. Guinto was noted in the Obituary section of the December issue (587–591). In the Correspondence section Winsley, *et al.* (592–594) proposed "bubble" or "calendar" packs for the administration of antileprosy drugs in an effort to increase compliance.

In the Current Literature section of the December issue, Anderson (609) pointed out that commonly used antileprosy drugs were capable of producing adverse immunological reactions. Guelpa-Lauras, *et al.* (610) reported high prevalences of resistance of *M. leprae* to dapsone and rifampin in recurrences of lepromatous leprosy in Martinique and Guadeloupe. Pattyn, *et al.* (610–611) described a patient whose disease remained active one year after receiving 1200 mg of rifampin and despite 19 years of treatment with dapsone. The patient's bacilli showed intermediate resistance to dapsone and no resistance to rifampin by mouse foot pad drug sensitivity testing. Saint-André, *et al.* (611) described the beneficial effects of chloramphenicol in ENL. Saint-André, *et al.* (611) described beneficial effects from isoprinosine in multibacillary leprosy patients. Chawhan, *et al.* (614) found significantly elevated serum levels of α-1-antitrypsin in patients undergoing ENL. Selliah and Ayasamy (614) reported an interesting case of tuberculoid leprosy simulating squamous cell carcinoma involving the cheek, right lower mandibular alveolus, the buccal mucosa of the right retromolar area, and extending posteriorly to involve the pharynx. The lesion involved the right floor of the mouth, the right ventral surface of the tongue, and the posterior aspect of the right hard and soft palate. This very large ulcerative lesion healed within two months on rifampin and dapsone. Birdi, *et al.* (616) presented evidence that *M. leprae* induced alterations in the membranes of lepromatous macrophages but not macrophages from tuberculoid or normal individuals. This altered membrane in lepromatous macrophages could prevent effective macrophage-lymphocyte interaction and thereby be one of the mechanisms by which CMI is suppressed in lepromatous leprosy. Haregewoin, *et al.* (618) showed that although lepromatous T cells failed to produce interleukin 2 after exposure to *M. leprae in vitro*, they can respond by proliferation to *M. leprae* in the presence of T cell conditioned medium containing interleukin 2. This suggests that the unresponsiveness in lepromatous leprosy to *M. leprae* antigens results from a deficiency in the production of interleukin 2 or related factors and is not due to a lack of *M. leprae*-reactive T cells. Modlin, *et al.* (619) studied the distribution of T lymphocyte subsets in the tissue of reactional states in leprosy. Segregation of these suppressor/cytotoxic phenotypes at the periphery of the granuloma was found in both nonreactional tuberculoid lesions and in reversal reactions, but was better developed in the nonreactional tuberculoid lesions. In ENL and Lucio's reaction, the helper/inducer and suppressor/cytotoxic phenotypes were both admixed with the ag-

gregated histiocytes similar to the case in nonreactional lepromatous tissue. The helper/suppressor ratio in ENL was significantly higher than that in nonreactional lepromatous tissue, however. The reversal of the helper/suppressor ratio in ENL as compared to nonreactional lepromatous disease may suggest that there is some role for cell-mediated immunity in the pathogenesis of ENL. Ridley, *et al.* (620) complexed BCG with homologous anti-BCG serum IgM at antigen/antibody equivalence and at twofold and fourfold antibody excess. These preparations were injected subcutaneously into rats. At equivalence the mixtures provoked rapidly developing necrotic destructive lesions containing many bacilli; while the mixtures at antibody excess caused the rapid formation of epithelioid cell granulomas without necrosis and containing few bacilli. Delayed-type skin reactions to PPD took longer to develop if BCG were complexed with antibody, the delay varying directly with the degree of antibody excess. Circulating immunoglobulin, perhaps IgM in particular, may play a significant role in the pathogenesis of mycobacterial disease. Ridley and Ridley (620) demonstrated that at the center of ENL lesions there was always disintegration of macrophages and release of bacterial antigen. These products combined first with IgM, later with IgG, and were found together with complement components of the classical pathway. The results support the view that ENL is an extravascular immune complex phenomenon occurring at the site of breakdown of small lepromatous granulomas. Salgame, *et al.* (620–621) showed that human peripheral blood mononuclear cell proliferation induced by *M. leprae* could be inhibited by suppressor factors in the lysate of macrophages from lepromatous leprosy patients but not from macrophages from normal subjects or tuberculoid patients. Spector, *et al.* (621) described a three-stage local reaction to primary subcutaneous infection of rats with BCG. There is a short-lived simple granuloma corresponding with high levels of CMI initially. This is followed by an explosive phase of necrosis and local mycobacterial multiplication corresponding to low levels of CMI and high levels of circulating anti-BCG antibody. Finally, the lesion resolves via an epithelioid cell granuloma with reductions in bacterial loads and a return of CMI. Williams (621–622 and 622) studied isolated epithelioid cells from disaggregated BCG granulomas ultrastructurally and functionally. A full spectrum of epithelioid cell morphology was present as early as four days after subcutaneous injection of BCG vaccine. Young and Buchanan (622) described results of an enzyme-linked immunosorbent assay utilizing the specific phenolic glycolipid from *M. leprae.* Gueur, *et al.* (623) studied immunological relationships among leprosy-derived corynebacteria and reference mycobacteria. A major crossreactive component, antigen M, was present in all of the leprosy-derived corynebacterial isolates and crossreacted with antigen 7 of *M. leprae* and antigen 60 of BCG. Hunter and Brennan (623) described additional extracellular lipids in *M. leprae*-infected armadillo tissue. The principle component consisted of a mixture of two diacylphthiocerols. In addition to the previously reported *M. leprae*-specific phenolic glycolipid I, these extracellular products also contained small amounts of two other phenolic glycolipids designated phenolic glycolipid II and phenolic glycolipid III. Kusaka and Izumi (624) described the fatty acid patterns of mycobacteria as detected by gas chromatography and suggested the possibility of simple detection of *M. leprae* by its characteristic gas chromatographic patterns. Wheeler (624–625) found that glycolysis and the hexose monophosphate pathway were used for glucose catabolism by suspensions of *M. leprae.* Key enzymes of glycolysis, the hexose monophosphate pathway, and glycerol catabolism were detected in cell-free extracts from purified *M. leprae.* Løvik and Closs (625–626) demonstrated a clear dissociation between delayed-type hypersensitivity to ultrasonicated *M. lepraemurium* and protective immunity to *M. lepraemurium* in mice. Schiefer and Middleton (626) described interesting experiments with the acid-fast bacteria from spontaneous cases of feline leprosy. The bacilli were transmitted to rats in which a general mycobacteriosis occurred, and to cats. On the other hand the infection of cats with *M. lepraemurium* did not produce any lesions. Collier (627) studied case holding in leprosy patients in Asia. Among patients who lived near the leprosy control

areas 32% were lost within the first year, while 63% of patients who lived outside the vicinity of the leprosy control area were lost within the first year. After five years, 66% of the local patients had been lost and 88% of the "non-local" patients had been lost. McDougall and Cologlu (628) measured the depth of the cellular infiltrate and bacillary mass in the skin of untreated lepromatous leprosy patients and related this to the depth of penetration of the mouth parts of some species of arthropods. The results showed that large numbers of bacilli are readily available to the biting apparatus of several species of arthropods. Brandsma and Lijftogt (630–631) reported 35 leprosy patients who had tendon-transfer surgery and who postoperatively recovered nerve function. None of the patients had been operated on within six months after the onset of nerve damage. Allen, *et al.* (631–632) concluded that amikacin has no role in the treatment of tuberculosis because of crossresistance with kanamycin and capreomycin and its expense. Barrière (632) reported that thalidomide was beneficial in two patients with pulmonary and cutaneous sarcoidosis.

The December issue contained the abstracts of the Eighteenth Joint Leprosy Research Conference of the U.S.-Japan Cooperative Medical Science Program which was held 3–4 August 1983 in Bethesda, Maryland. Stoner (645) compared the similarities and differences between tuberculosis and leprosy and concluded that the two diseases are so different immunologically that the leprosy vaccine should be tested and judged on its own merits, independently of the apparent lack of efficacy of BCG against tuberculosis in the Madras trial. Ridel, *et al.* (645–646) injected *M. leprae* and *M. leprae*-burdened macrophages into the foot pads of mice and measured local immune responses in draining popliteal lymph nodes. Macrophages containing bacilli were clearly superior to *M. leprae* alone in causing local increases in the natural killer cell activity, blast transformation to ConA and lymphocyte blast transformation to *M. leprae* antigen by lymphocytes from the spleen of these animals. Shepard (646–647) compared the immunogenicity of BCG and *M. leprae* in normal and in *M. leprae*-tolerant mice. Intravenous injection of *M. leprae* induced good tolerance to the bacilli as measured by skin testing. The tolerant mice that received BCG or BCG+*M. leprae* were moderately sensitized to the *M. leprae* challenge. On the other hand, the *M. leprae*-tolerant mice were poorly protected against infection with all three vaccines although normal mice were well protected. The results indicated an association between immunity to infection and Mitsuda-type skin reactivity in these *M. leprae*-tolerant mice. Rea, *et al.* (647–648) studied T lymphocyte subsets in peripheral blood and tissues of leprosy patients across the spectrum. It was evident that there was no relationship between the tissue helper/suppressor ratio and the blood helper/suppressor ratio. Higher tissue helper/suppressor ratios were found in ENL patients than in lepromatous patients without ENL, suggesting an important role for cell-mediated immunity in the pathogenesis of ENL. Chehl, *et al.* (649) studied the induction of reversal reactions in a quantitative fashion in *M. leprae*-infected nude mice by infusing allogeneic splenic leukocytes from naive and *M. leprae*-immunized heterozygote donors. Watson, *et al.* (649–650) studied the *in vitro* production of interleukin 1 by macrophages in response to a variety of inducing agents. Three of five tuberculoid patients and one of two borderline patients produced interleukin 1 spontaneously. Cells from all seven tuberculoid and borderline patients produced interleukin 1 in a normal fashion after stimulation. On the other hand, three of ten borderline lepromatous to lepromatous patients did not produce detectable interleukin 1 in response to interleukin 1-inducing agents. Kaplan, *et al.* (650–651) described the infiltrating cells in the cutaneous lesions of leprosy across the spectrum. Antigen and mitogen-induced γ-interferon was studied in the peripheral blood mononuclear cells from lepromatous and tuberculoid patients. Nine out of nine lepromatous patients had cells with failed to release γ-interferon in response to stimulation by *M. leprae* or ConA. The responsiveness of the cells from lepromatous patients for γ-interferon release could be restored by the addition of partially purified interleukin 2 and *M. leprae* antigen, but not by interleukin 2 alone. Lefford, *et al.* (651–652) described a demyelinating peripheral neuropathy involving the hind quarters of CBA/J mice

infected with *M. lepraemurium*. The syndrome has never been observed in many other mouse strains. Dhople (653) described excellent correlations between the viability of *M. leprae* as measured by the growth in mouse foot pads and their ATP content as measured from skin biopsy specimens from leprosy patients. Nakagawa and Kashiwabara (653–654) found four phospholipid biosynthetic enzymes in cell-free extracts of host-grown *M. lepraemurium*. Nakamura (654–655) found a cord factor from *in vitro*-grown *M. lepaemurium* which was identical to that from *in vivo* bacilli. Ozawa, *et al.* (655) reported that T lymphocytes from tuberculoid patients showed strong responses to *M. leprae* antigen in the presence of HLA-DR identical or haploidentical lepromatous patients' macrophages. On the other hand, T lymphocytes from lepromatous patients failed to respond to this antigen in the presence of HLA-DR identical or haploidentical tuberculoid patients' macrophages. Miller, *et al.* (655–656) described the characteristics of a number of murine monoclonal antibodies against *M. leprae*. Two of these monoclonal antibodies appear specific for *M. leprae*. Atlaw and Roder (656–657) reported the development of human monoclonal antibodies against *M. leprae* antigens. Six of these appear to be specific for *M. leprae* protein antigens. The major immunoglobulin produced by the *M. leprae*-reactive clones was found to be IgM. Abe, *et al.* (657–658) found IgA antibodies against *M. leprae* in saliva from a significant number of leprosy patients. The percentage of positive reactions caused by salivary IgA antibodies was higher in tuberculoid and borderline patients than in lepromatous cases. Buchanan, *et al.* (658–659) evaluated a large number of sera from leprosy patients, normal controls, and household contacts of leprosy patients by an ELISA technique employing deacylated phenolic glycolipid of *M. leprae*. Among 112 household contacts of leprosy patients, 18 were consistently seropositive over a 2½ year period. Two of these 112 contacts developed tuberculoid leprosy during the period of observation and both of these patients were within a group of 18 contacts with consistently elevated antibody levels. Cho, *et al.* (659–660) found high anti-phenolic glycolipid I IgM antibodies in 96% of lepromatous patients and 62% of tuberculoid patients. The trisaccharide determinant of the phenolic glycolipid I is specific in its structure, serological activity and, to a lesser extent, the antibody class it evokes. Young and Buchanan (660–662) described the development of an ELISA to measure antibodies to phenolic glycolipid I of *M. leprae*, utilizing deacylated antigen and conjugate capable of detecting IgM antibodies. Khanolkar, *et al.* (662–663) developed murine monoclonal antibodies to phenolic glycolipid I of *M. leprae*. All of the antibodies produced were of the IgM class. Eight recognized only the *M. leprae* glycolipid with the relevant specificity directed toward the terminal 3, 6-di-*O*-methylglucose. In testing against whole organisms, there was strong specificity for *M. leprae* but some weak reactions were evident with *M. terrae*, *M. nonchromogenicum*, and one strain of *M. bovis*. Smith, *et al.* (663–664) found that 17 of 451 wild armadillos captured along the Texas Gulf Coast were infected with *M. leprae*. Wolf, *et al.* (664–665) described the experimental transmission of leprosy in mangabey monkeys, African green monkeys, and rhesus monkeys. In one of the rhesus monkeys a subpolar lepromatous disease developed 19 months after inoculation with *M. leprae*; an apparent reversal reaction then developed over the next four months; the animal then appeared to downgrade to essentially polar lepromatous status. Martin, *et al.* (665–666) reported reduced lymphocyte blast transformations in response to PHA, ConA, and pokeweed mitogens in mangabey monkeys with disseminated, progressive leprosy. Fukunishi, *et al.* (666–667) reported the ultrastructural features of the growth of *M. leprae* in a naturally infected mangabey monkey and found that they were identical to those in humans, armadillos, and nude mice inoculated with human *M. leprae*. Jacobs, *et al.* (667–668) described work using recombinant DNA techniques to construct genomic libraries of *M. leprae* in cosmid cloning vectors and the introduction of these recombinant molecules into strains of *E. coli* K-12 for further characterization. Fukunishi, *et al.* (668–669) studied the biochemical characteristics of the peribacillary substance of *M. leprae*.

From the perspective of the JOURNAL, 1983 has again been a year of considerable progress in providing new information for

leprosy workers. From a personal perspective, a number of trends seem to have developed.

In the field of chemotherapy, there is a better understanding of the mechanism of action of dapsone on the dihydropteroate synthetase of *M. leprae*. The combination of rifampin with either ethionamide or prothionamide seems to be clearly hepatotoxic. Problems with compliance with chemotherapy continue to be reported. Questions have been raised regarding the degrees of correlation between drug sensitivity tested by mouse foot pad and clinical responses to dapsone monotherapy.

Clinical descriptions of leprous phlebitis have pointed out that it may be very common in lepromatous leprosy. Lepromatous patients seem to have exhausted adrenal cortical function. Synovial involvement in lepromatous leprosy has been emphasized. Suggestions have been made that leprosy affects the autonomic control of the heart and that leprosy patients have an increased risk of diabetes mellitus.

In immunopathology work is advancing at a rapid pace. Further characterizations of suppressor phenomena occurring in leprosy have appeared. The concepts have been put forth that suppressor cells may be a part of the normal immune response to *M. leprae* and that their demonstration in lepromatous leprosy does not prove that they are important in its pathogenesis. Possibilities have been raised in animal models that resistance to infection may exist which does not involve the development of competent cell-mediated immunity. Considerable effort continues on vaccine development and further information has been presented regarding the immunogenicity of various candidate vaccines in animals and humans. Considerable advances have been made in our understanding of the process of degradation of *M. leprae* in tissues as well as the patterns of cellular response in tissues to the bacillus. Clarifications on the distribution of T cell subsets in tissues and peripheral blood in various phases of the disease are emerging. Serologic techniques are becoming more and more refined, leading to better and better understanding of antibody responses to *M. leprae* in various forms of the disease. The importance of antibodies to *M. leprae* of the IgM class seems to be emerging. Antigenic analysis of *M. leprae* is continuing at a rapid pace. The ability of interleukin 2 to cause the *in vitro* proliferation of lepromatous mononuclear cells in response to *M. leprae* has had a major impact on theories of the pathogenesis of lepromatous leprosy.

In microbiology further characterizations of leprosy-derived corynebacteria have appeared. "*Mycobacterium X*" has been cultivated in a novel medium from *M. leprae*-infected tissues. A number of indirect measurements of the viability of *M. leprae* have been reported as not correlating well with the conventional Morphological Index. Considerable advances are being made in defining the biochemical pathways of *M. leprae* and the structure of its cell wall. Elegant work is underway characterizing the phthiocerol-containing surface lipids of the bacillus.

In the field of experimental infections, *M. leprae*-tolerant mice have been produced by the intravenous inoculation of the animals with leprosy bacilli. More reports have appeared of natural infections of armadillos with *M. leprae*. Exciting work continues with non-human primate models.

In epidemiology, strong evidence has been presented for the possibility of placental transmission of leprosy from lepromatous mothers to their babies.

As reflected in these pages, 1983 was again a year of rapid progress in many areas of leprosy and a year of continuing frustrations in others. Major advances are occurring in a number of basic areas of research in leprosy. In some of these, major advances have occurred right up to the current state-of-the-art. It seems likely that more and more the increase in our knowledge of leprosy will both depend upon, and make major contributions to, advances in basic sciences and other diseases. The whole process is at the same time both awesome and exhilarating. I look forward with impatient optimism to 1984.—RCH