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EDITORIALS

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The 1982 JOURNAL—a Continuing Perspective

With the December 1982 issue, the JOURNAL completed its 50th year of publication, a formidable accomplishment attesting to our forebearers' dedication, perserverance, and hard work. More simply but perhaps more importantly, the JOURNAL's half-century of publication means that it has continuously had information to convey about leprosy to its readers. The progress that has been made in the past year, as reflected in the 1982 JOURNAL, has again been considerable.

The group of 14 excellent articles of the March issue began with an elegant demonstration by Mshana, *et al.* (1–10)* of mycobacterial antigens in skin biopsy specimens from leprosy patients throughout the spectrum. Mycobacterial antigens were demonstrable by a rabbit peroxidase anti-peroxidase system in a considerably higher proportion of patients than the proportion which were bacteriologically positive by conventional staining. Extracellular, and not intracellular, antigen was associated with tissue responses of both erythema nodosum leprosum (ENL) and reversal reactions. Ridley, *et al.* (11–19) using immunoperoxidase techniques, painstakingly studied a variety of immunological factors in the skin of leprosy patients across the spectrum. Complement components, IgG and IgM, lysozyme, and plasminogen peaked in both tuberculoid (TT) and active lepromatous (LL) cases. With the exception of TT cases, the generation of immunologic factors within the lesions seemed to be in proportion to the antigenic load. Seydel and Wempe (20–30) conducted sophisticated analyses of bacterial growth kinetics with a series of potential inhibitors of *Mycobacterium leprae* using "*M. lufu*" as a model strain. Rifampin, clofazimine, dapsone, prothionamide, isoniazid, in order of potency, were active as single drugs. At least partial resistance could be demonstrated to develop *in vitro* at low concentrations of the drugs. Each of the dihydrofolate reductase inhibitors, trimethoprim and pyrimethamine, while inactive alone, were synergistic in combination with dapsone. Duncan and Pearson (31–38) observed that nearly half of Ethiopian women with leprosy experienced deterioration of peripheral nerve function during a single pregnancy and/or lactation. Insidious silent neuritis was seen more frequently than overt neuritis. Warndorff-van Diepen (39–42) studied 244 long-treated lepromatous patients and found that skin smears

* Numbers in parentheses refer to page numbers in the INTERNATIONAL JOURNAL OF LEPROSY, Volume 50, 1982.

from the earlobe were more productive than those from the finger in demonstrating acid-fast bacilli. Gupta, *et al.* (43–46) found antispermatozoal antibodies in the sera of 30%–39% of lepromatous and 19%–33% of tuberculoid leprosy patients. These autoantibodies seemed to increase with the duration of the disease. Wangel, *et al.* (47–55) found subcutaneous amyloid deposits in 15 of 37 leprosy patients and in 3 of 18 unaffected family members. There was no association with the lepromatous form of the disease or with long standing trophic ulceration. Compared with unaffected family members, the leprosy patients had increased serum α-liproprotein and were more often hepatitis B surface antigen carriers. Date, *et al.* (56–57) reported an interesting case of tuberculoid leprosy with chronic renal failure. He was given a renal allograft after five months of dapsone treatment. The leprosy showed continued healing on dapsone despite high doses of immunosuppressive drugs given in conjunction with the renal allograft. Barton, *et al.* (58–67) studied 62 lepromatous patients treated with dapsone monotherapy for periods of three months to ten years. Of 52 who could produce nasal mucus (nose blow), 11 were positive for acid-fast bacilli but only 1 of the 52 patients had morphologically intact acid-fast bacilli in nasal mucus. This suggests that dapsone monotherapy greatly diminishes the infectivity of lepromatous patients and that this diminished infectivity often persists despite poor drug compliance and continuing disease activity. Fukunishi, *et al.* (68–75) studied the ultrastructural morphology of the peribacillary substances of *M. leprae* and *M. lepraemurium,* both grown in nude mice, and demonstrated that the spherical droplets (foamy structures) surrounding *M. leprae* are made up of a specific substance produced by the multiplication of *M. leprae* in any suitable host cell. Binkhuysen and Das (76–82) compared the ultrastructural characteristics of BCG and *M. leprae* and found few differences. Dhople and Storrs (83–89) found that *M. leprae* are different from *M. lepraemurium* in that they can withstand even the most severe purification procedures that are necessary in order for them to be used for biochemical and metabolic procedures (4% NaOH, trypsin, chymotrypsin, collagenase, Triton X-100, ATPase) and essentially totally retain their intracellular ATP and infectiousness. Seydel, *et al.* (90–95) applied a laser microbe mass analyzer method and obtained mass spectra from single bacterial cells, demonstrating that damaged cells can be identified and suggesting that this could possibly be applied to monitoring the effects of chemotherapy on *M. leprae.* Shepard (96–101) reviewed the methods used to study the effects of drugs on *M. leprae* using the mouse foot pad model and presented methods for the statistical analysis of the results of the kinetic method and the proportional bactericidal method.

In The Editorial section of the March issue, Hastings (102–116) reviewed the contents of the 1981 JOURNAL. The News and Notes section contained an interesting, brief account of leprosy in Albania (119). Professor Lechat, President of the ILA, requested news from national leprosy organizations for a new subsection of the JOURNAL (122).

The Current Literature section of the March issue contained an interesting report by Gangadharam, *et al.* (126) demonstrating the bactericidal activity of clofazimine against *M. intracellulare in vitro.* Twelve patients with dapsone-resistant leprosy were described by Li Wenzhong, *et al.* from the People's Republic of China (126–127). Sher, *et al.* (128–129) reported that lepromatous leprosy patients have significantly lower serum levels of zinc, iron, and vitamin A, and elevated levels of copper compared to tuberculoid patients. Sheskin, *et al.* (129 and 247–248) observed that soaking the hands of leprosy patients in warm water for 30 minutes does not result in the formation of wrinkles as it does in normal individuals. Bahr, *et al.* (129–130) found that indomethacin enhanced the *in vitro* response of peripheral blood mononuclear cells to soluble mycobacterial antigens in tuberculoid, but not lepromatous patients. A normal, prostaglandin-dependent, indomethacin-sensitive regulatory mechanism seems to be absent from the peripheral blood mononuclear cells of lepromatous leprosy patients. Deo, *et al.* (130) reported lepromin conversion in 50% of LL and 80% of BB/BL patients within four months after receiving gamma-irradiated ICRC bacilli as a vaccine. Greiner, *et al.* (130) found the his-

tocompatability antigen, HLA-B7, to be associated with lepromatous leprosy and HLA-B17 to be associated with tuberculoid leprosy among patients from northern Thailand. Fast bands of C4 were noted only among the borderline and lepromatous leprosy cases. Hunter and Brennan (132) described a glycosylphenolic phthiocerol diester of *M. leprae* closely related to "mycoside A" from *M. kansasii,* but differing in the composition of the attached trisaccharide. The distinct trisaccharide in *M. leprae* contains 2, 3-di-*O*-methylrhamnose, 3-*O*-methylrhamnose, and 3, 6-di-*O*-methylglucose. This phenolic glycolipid of *M. leprae* is present in large amounts in infected tissue and may be responsible for the electron-transparent "foam" which characteristically surrounds the organism in infected lepromatous tissue. Ishaque (132) confirmed the identity of *in vitro* and *in vivo* grown *M. lepraemurium* and their pathogenicity in animals. Prasad and Nath (132–133) described the incorporation of ^{3}H-thymidine by 54% of *M. leprae* strains from human biopsies maintained in human macrophage cultures over a 15-day period. Lefford, *et al.* (133) found that BCG protected mice against *M. lepraemurium* infection on the basis of crossreactive immunity rather than nonspecific immunity or immunopotentiation. Gatner and Rubenstein (134–135) observed a decrease in the prevalence of positive tuberculin reactions around the age of 13 and speculate that there may be a depression of delayed hypersensitivity reactions at puberty. Mahakrisnan, *et al.* (135) suggest that dapsone may be effective in cutaneous rhinosporidiosis. Satyanarayana, *et al.* (135) found that mild degrees of malnutrition had no effect on the immune response of children to BCG.

The June issue's original articles began with the case report of clofazimine-resistant leprosy by Warndorff-van Diepen (139–142). The 56-year-old Ethiopian male was diagnosed as having lepromatous leprosy in 1963, relapsed with clinically apparent sulfone-resistant disease in March 1973, and was treated with clofazimine 100 mg daily initially and later ranging from 200 mg daily to 100 mg three times weekly. Clinical relapse occurred in October–December 1979, and bacilli from a skin biopsy taken in November 1980 multiplied in mice fed clofazimine, beginning two months after inoculation, in concentrations as high as 0.003% w/w in the diet. Rifampin, 600 mg daily, resulted in a noticeable regression in the patient's nodules within two weeks, suggesting that these clofazimine-resistant bacilli were sensitive to rifampin. With this case, resistance has now been reported to all the commonly used antileprosy drugs. Phadnis, *et al.* (143–147) studied 50 Indian leprosy patients and found abnormal renal histology in 28 of them. Ten patients had interstitial nephritis probably resulting from opportunistic secondary infections and/or drug toxicity. Membranoproliferative glomerulonephritis was the next most common lesion being found in eight patients. One patient had renal amyloidosis. Kumar, *et al.* (148–151) studied the structural and functional status of the small bowel in ten lepromatous patients and found essentially no clinically significant changes. Murray (152–158) found that 10% of 630 leprosy patients had a reactive plasma reagin (RPR) test, a reactive fluorescent treponemal antibody absorption (FTA-ABS) test, and historical, clinical, and/or postmortem evidence of syphilis. Eight percent of these patients had a false-positive RPR. Sharma, *et al.* (159–163) studied sera from 20 ENL patients during the reaction and four weeks later after clinical remission. IgG increased after remission while IgM and IgA levels showed no significant changes. Autoantibodies (anti-thyroglobulin antibody, antinuclear antibody, and rheumatoid factor) were detected in nine patients and, of these, three patients developed them only after remission of the ENL. Turkel, *et al.* (164–171) studied the ultrastructure of the dermal microvasculature in leprosy and found endothelial swelling and hypertrophy, increased endothelial and pericytic cytoplasmic processes, and pronounced basal lamina reduplication. Phagocytized, membrane-bound intraendothelial organisms were demonstrated. Liu, *et al.* (172–176) studied the histopathology of skin biopsies from 20 patients with indeterminate leprosy. Neural infiltration was noted in 94% of the cases; 67% showed inflammatory infiltration of the sweat glands; 47%, changes in arrector pili muscles; and 45%, changes in pilosebaceous glands. Lesions were found in the epithelium in 25% of these indeter-

minate cases. Job, *et al.* (177–182) correlated the histopathology of the lepromin reaction in armadillos with their susceptibility to infection with *M. leprae.* Ten of 11 animals with a lepromatous lepromin reaction and the one animal with a borderline lepromin reaction developed disseminated disease. The two armadillos with a tuberculoid lepromin reaction and one of the 11 with a lepromatous lepromin reaction failed to develop leprosy. Kvach and Veras (183–192) reported an interesting fluorescent staining method utilizing fluorescein diacetate and ethidium bromide for determining the viability of mycobacterial cells. The technique is promising as an alternative means of determining the viability of *M. leprae.* Nakamura (193–199) described the growth-stimulating effect of DL-aspartic acid on cultures of *M. lepraemurium* in liquid media. Camargo, *et al.* (200–204) studied patterns of fatty acid oxidation by several mycobacteria, compared them with that of *M. lepraemurium,* and suggested that radiometric measurements of differential fatty acid metabolism may provide a basis for strain identification among mycobacteria.

In the Editorial section of the June issue, we were pleased to have the succinct review by Price (206–212) on the background, rationale, previous results, and implications of BCG vaccination in leprosy. This review was written while the author was a medical student, and it was first prize winner in the 1980 competition sponsored by the British Leprosy Relief Association for essays on leprosy.

We were saddened to note the passing of a giant in the leprosy field, Dr. Casimiro Lara (213).

A stimulating Correspondence section in the June issue began with a note by McDougall and Ross (214–215) on the simultaneous existence of two strains of *M. leprae* in the same patient bearing different drug sensitivities. Azulay (215–216) described reduced chemotaxis of monocytes from virchowian hanseniasis patients compared to normal controls and demonstrated an inhibitor of the chemotaxis of normal monocytes in the sera of virchowian hanseniasis patients. Nuti, *et al.* (217–218) found elevated IgE levels in the serum of both tuberculoid and lepromatous patients compared to matched healthy controls from the same area. Gupta, *et al.* (218–219) reported reduced salivary IgG and IgA in both tuberculoid and lepromatous patients compared to controls. Payne, *et al.* (220–221) demonstrated that the purified glycolipid of *M. leprae* identified by Hunter and Brennan (132) was serologically active when incorporated into liposomes. Browne (221–223) responded to an earlier question regarding the diagnosis of indeterminate leprosy, concluding that the clinical concept is both valid and valuable. Pettit (224) remained doubtful.

The News and Notes section of the June issue noted the founding of the College of Hansenology of the Endemic Countries (225); well-deserved honors to Professor G. P. Talwar (230), Dr. J. M. Mehta (230–231), and Professor A. J. Selvapandian (231); and the revival of the former PHILIPPINE JOURNAL OF LEPROSY under the new name of the PHILIPPINE JOURNAL OF DERMATOLOGY AND LEPOSY (233). The closing of the system of the United States Public Health Service Hospitals other than the National Hansen's Disease Center at Carville was noted (234). The apparent increase in the prevalence of leprosy caused by dapsone-resistant *M. leprae* was reviewed (234–236).

The Current Literature section of the June issue began with an account of how indeterminate leprosy got its name by Arnold (243). Thiacetazone was implicated as a cause of drug-induced dermatitis in approximately 4% of tuberculosis patients (243). Farb, *et al.* (243–244) pointed out that three neonatal deaths have been reported in 15 pregnancies in patients receiving clofazimine. Gidoh, *et al.* (244) described a high-pressure liquid chromatographic method capable of analyzing clofazimine, rifampin, dapsone, and their principal metabolites. Nath, *et al.* (244) found concordant results in testing 13 of 14 strains of *M. leprae* for dapsone sensitivity by standard mouse foot pad assays and by three-week ^{3}H-thymidine incorporation by the bacilli in murine macrophage cultures in the presence of dapsone. One strain did not incorporate thymidine *in vitro* but showed a dapsone-resistant growth pattern in the mouse foot pad assay. Warndorff, *et al.* (245–246) had favorable results in treating paucibacillary patients with eight weekly

doses of 900 mg of rifampin. Baranov and Podoplelov (246) suggested that dermatoglyphic studies in leprosy endemic areas might be useful in revealing hereditary factors associated with susceptibility to the disease. Sheskin, *et al.* (247) found highly elevated levels of iron in the skin of patients with ENL and that these levels remained elevated after the reactions had been controlled with thalidomide. Soni and Chatterji (248) made the interesting observation that leprosy patients, particularly BL-LL cases, have impaired taste sensation. Tokudome, *et al.* (248) found no evidence that 2383 Japanese leprosy patients experienced higher than expected mortality rates due to cancer. Cabrini, *et al.* (249) reviewed the immunology of leprosy. Corona, *et al.* (249) found that pre-incubating integral lepromin with serum from reactional lepromatous patients reduced the subsequent early (Fernandez) response in tuberculoid patients. Meghlaoui, *et al.* (250–251) found that leprosy patients, particularly lepromatous cases, have serum antibodies directed against collagen. Potts, *et al.* (251) described serum factor(s) in lepromatous leprosy patients which reduced the number of normal human lymphocytes responding to PHA, PWM and Con-A *in vitro*. Pudifin and Duursma (251) measured circulating immune complexes in sera from healthy blood donors of various racial groups and found widely ranging results. The finding of immune complexes in serum does not necessarily indicate disease. Ridley (252) studied skin biopsies from approximately 1500 leprosy patients and found 44 which could be classified as polar tuberculoid; approximately half of these seemed to represent primary lesions and half seemed to have resulted from upgrading from BT. Saha and Lahiri (252) bioassayed mediators of inflammation in the sera of leprosy patients and found that ENL patients had elevated levels compared to lepromatous patients without ENL. Saha, *et al.* (252–253) reported that, compared to those of healthy lactating women, the breast secretions from mothers with lepromatous leprosy had decreased numbers of leukocytes, macrophages, and secretory IgA; 9 of the 12 leprosy patients had demonstrable acid-fast bacilli in their breast secretions. Stanford, *et al.* (253) found that leprosy patients had impaired or absent skin test responses to the common mycobacterial antigens (Group i) and to antigens associated with slow growers (Group ii). Positive responses to the species specific antigens (Group iv) were retained. Evidence of a suppressor mechanism, possibly triggered by Group iv antigens of fast growers and operative on positive responses to slow growers, was demonstrable in healthy hospital staff members, in TT/BT patients, BL patients, and LL patients. Stoner, *et al.* (253) assayed suppressor cells in healthy subjects exposed to leprosy and found that the *in vitro* generation of strong *M. leprae*-specific suppression was associated with exposure to the disease for more than three years. Tarabini-Castellani, *et al.* (253–254) emphasized the value of the post-lepromin scar in evaluating effective cell-mediated immunity against *M. leprae*. BCG increased the proportion of subjects subsequently developing a post-lepromin scar while lepromin alone was essentially ineffective. In two individuals who had three consecutive negative lepromin tests, lepromin plus BCG resulted in conversion of the lepromin into positive, but five months later their responses to subsequent lepromins were considerably weaker. In *in vitro* tests of lymphocyte blast transformation, leukocyte migration inhibition, and leukocyte adherence inhibition in response to tissue antigens, Wall and Walters (255) found evidence of autoimmunity (delayed hypersensitivity) among lepromatous leprosy patients directed against testes. This correlated with clinical evidence of testicular disease. Coates, *et al.* (255) could distinguish between various strains of mycobacteria, even of the same species, using murine monoclonal antibodies. Danhaive, *et al.* (256) studied the DNAs of leprosy-derived corynebacteria and found that these organisms form two high-homology groups, showing little homology with the reference corynebacteria. Pattyn and Portaels (256) presented a sophisticated review of the multiplication of *M. leprae* in experimental animals and approaches to *in vitro* cultivation. Curtis, *et al.* (256–257) found a lack of correlation between antigen-specific lymph node cell responses and resistance to *M. lepraemurium* infection in C57BL (relatively resistant) and BALB/c (highly susceptible) mice. Vishnevetsky and

Juscenko (257) demonstrated tuberculoid histopathology in two armadillos inoculated four months earlier with human *M. leprae*. Abe, *et al.* (257) screened school children and adults in the Miyako Islands with the fluorescent leprosy antibody absorption (FLA-ABS) test, and found a correlation between positive FLA-ABS tests and peripheral nerve enlargements. The percentage of positive FLA-ABS tests was considered to represent the prevalence of subclinical leprosy infection. Among 217 school children tested with both the Dharmendra skin test and the FLA-ABS test, 88 were positive in FLA-ABS, 58 of whom also had positive Dharmendra skin tests (36 of the 58 with enlarged peripheral nerves) and 30 of whom had negative or doubtful skin tests (15 of the 30 with enlarged peripheral nerves). Among these children, therefore, 88 of 217 or 41% had presumably been infected with *M. leprae,* and 30 of 88 or 34% of the infected children were presumably incubating multibacillary leprosy. Patarroyo, *et al.* (264) reported a particular multiparous serum which reacted with B cell subpopulations and a minor T cell population of 60% of lepromatous leprosy patients and 16% of normal controls with no particular reactivity with tuberculoid leprosy or other diseases. This genetic marker was not related to any one of the defined HLA-A, -B, or -D markers, showed autosomal dominant segregation patterns, and was highly associated with susceptibility to lepromatous leprosy. Stanley, *et al.* (265–266) made a final report on the effects of BCG vaccination of children against leprosy in Uganda, indicating a continuing protective effect of BCG up to 12–13 years after vaccination. Goodfellow and Minnikin (267) were able to identify *M. chelonei* by characteristic patterns of two non-polar, mycolic acid methyl esters using two-dimensional, thin-layer chromatography of whole-organism acid methanolysates. Ouaissi, *et al.* (267–268) demonstrated circulating *Onchocerca volvulus* antigens in a high proportion of infected patients using sophisticated immunologic techniques. Sparks and Ross (268) distinguished between various species of mycobacteria using analytical isoelectric focusing techniques and examining the pattern of bands produced by the beta-lactamases.

The September issue's original articles began with a demonstration by Melsom, *et al.* (271–281) of falling IgG and IgA anti-*M. leprae* antibodies and a decrease in antibodies against *M. leprae* antigen 7 in lepromatous patients being treated with dapsone. The decrease in IgM-anti-*M. leprae* antibodies was smaller. Wallach, *et al.* (282–290), enumerating circulating T cell subsets with murine monoclonal antibodies, found increased suppressor and decreased helper cells in uncomplicated lepromatous leprosy correlated with bacteriologic load. During ENL reactions there was a transient fall in circulating suppressor cells, suggesting that insufficient T cell mediated suppression results in the well-known exaggeration of B cell responses as well as increased general (but not *M. leprae* specific) T cell responses during ENL. Mshana, *et al.* (291–296), using similar methodology, found a normal distribution of helper and suppressor T cells in BT cases, reduced helper and increased suppressor T cells in BL-LL cases, and transiently increased helper and reduced suppressor T cells in ENL patients, compared to normal controls. Gupta, *et al.* (297–305) studied the *in situ* nature of mononuclear cell infiltrates in the dermal lesions of untreated leprosy patients. The quantity of T lymphocyte infiltration correlated with the leprosy spectrum showing maximum density in tuberculoid lesions. Rojas-Espinosa, *et al.* (306–315) found elevated lysosomal enzyme activities in peritoneal cells from *M. lepraemurium*-infected mice at four months after infection, which tended to decrease by six months after infection. *M. lepraemurium*-infected mice seemed to have macrophages in a high state of biochemical activation but were unable to destroy the infecting bacilli. Liu Jihe, *et al.* (316–318) found decreased numbers of Langerhans' cells in the skin lesions of borderline and tuberculoid leprosy patients compared to normal appearing skin from the same patients. Khuller, *et al.* (319–321) demonstrated antibodies to sulfolipids from *M. tuberculosis* in lepromatous leprosy patients' sera. Sen and Sarin (322–324) found reduced concentrations of lysozyme in the tears of lepromatous leprosy patients compared to healthy controls. Haddad, *et al.* (325–329) presented evidence that BCG enhances lepromin reactiv-

ity and that antigens of *M. borstelense* and either *M. avium* or *M. gallinarum* may impair lepromin reactivity. Koticha, *et al.* (330–334) analyzed the factors affecting the time required to attain bacteriologic negativity in 922 initially bacteriologically positive leprosy patients treated with dapsone monotherapy. As expected, irregular treatment and advanced lepromatous disease delayed the attainment of bacteriologic negativity. Age and sex had no affect. Repeated reactions, during which dapsone was routinely discontinued, delayed the attainment of negativity in all types of disease except in reactional tuberculoid cases. Single episodes of ENL reactions were associated with more rapid negativity in lepromatous leprosy patients than no reactions or repeated reactions. Worth and Bomgaars (335–341) reviewed the epidemiology of leprosy in Hawaii over the past 21 years; there has been a continued decline in incidence among ethnic Hawaiian people; the vast majority of new cases are immigrants; and the new immigrant cases have not resulted in a significant secondary outbreak among Hawaiians.

As Guest Editorials in the September issue, we were honored to have a definitive review of antibody studies in leprosy by Harboe (342–350), a succinct review of the immunological basis for renal glomerular disease in leprosy by Date (351–354), and a thoughtful consideration of the factors influencing the quality of service to leprosy patients by McDougall (355–358).

The September issue noted the premature death of the brilliant Benty Karat, a loss to leprosy workers throughout the world (359–360).

The Correspondence section of the September issue contained a wealth of information. Modlin, *et al.* (361–362) studied T lymphocyte subsets in skin lesions across the spectrum of leprosy. Two immunohistologic patterns were observed. In tuberculoid patients suppressor/cytotoxic T cells were largely confined to the mantle of the lesions and helper/inducer T cells were scattered throughout the granuloma. In non-tuberculoid lesions, helper/inducer and suppressor/cytotoxic T cells were admixed throughout the granuloma among the histiocytes. Ridley (363–364) thoughtfully and carefully considered the clinical and histopathologic evidence for the dissociation of delayed hypersensitivity and cell-mediated immunity in non-lepromatous leprosy. Pfaltzgraff (365–367) outlined his view that rifampin treatment increases the risk of deformity and disability due to Type 1 reactions in borderline leprosy. Mshana, *et al.* (367–368) outlined their view that there are two completely different mechanisms involved in leprous neuropathy. One involves an auto-immune mechanism leading to loss of pigment and hair as well as sensory loss, and the other is a consequence of delayed hypersensitivity to intraneural *M. leprae* antigens affecting motor or major peripheral nerve trunks. Kato (368–370) pointed out the need for continued priority to be given to the cultivation of *M. leprae.* Portaels and Pattyn (370–374) cultivated three slightly different scotochromogenic strains of mycobacteria from two of four *M. leprae*-infected armadillo livers on Ogawa medium at pH 5.5–6.0 containing suspensions of autoclaved "*M. lufu,*" *M. lepraemurium,* or *M. leprae.* Three factors influenced the *in vitro* growth of these armadillo-derived mycobacteria—low pH (5.4–5.7), large inocula, and pretreatment of the organ suspensions with acid or alkali.

In the Book Reviews of the September issue, Yoshie's authoritative and definitive book, *Leprosy of the Upper Respiratory Tract. Atlas of Clinical Pictures and Notes on the Research (1938–1943),* is noted (384).

In the Current Literature section, Feng, *et al.* (385–386) identified two metabolites of clofazimine. Gatner, *et al.* (386) showed that clofazimine inhibits neutrophilic motility and lymphocyte blast transformation *in vitro* and *in vivo.* Kim (386) reported both primary and secondary dapsone-resistant *M. leprae* from Korea. Miyachi and Ozaki (387) found that thalidomide-treated guinea pigs did not have neutrophils which were inhibited in their chemotaxis. Modderman, *et al.* (387) reported that IM injections of suspensions of dapsone particles in aqueous vehicles could maintain therapeutic serum levels for up to 25 days. Pattyn, *et al.* (387) found no additive effect on inhibiting the growth of *M. leprae* from adding isoniazid to either dapsone or prothionamide. Castro-Coto and Hidalgo-Hidalgo (388) reported that one third of the new leprosy cases in Costa Rica have the diffuse lepromatous

form. Dutta and Murthy (389) studied 52 children with undiagnosable hypo-pigmented skin patches in Bangalore, India. Dapsone for one year was followed by improvement or clearing in 22 of 25 cases. In the control group who were not treated, 9 of 24 improved or cleared within one year but 3 of the 24 control children developed diagnosable indeterminate leprosy. Kim (391) studied the Bacteriologic Index in skin smears from nine anatomical sites in 39 treated lepromatous leprosy patients and found that the values were from highest to lowest: the eyebrow, ear lobe, lower leg, chin or dorsal surface of the terminal phalanx of the middle finger, dorsal surface of the middle phalanx of the middle finger, dorsal surface of the terminal phalanx of the second finger, and dorsal surface of the middle phalanx of the second finger. Malaviya and Ramu (391) reported an interesting case of leprous facial paralysis with complete loss of taste and somatic sensation of the tongue on the paralyzed side. The involvement of the glossopharyngeal nerve is discussed. Ng, *et al.* (391) pointed out that there is no association between glomerulonephritis and a history of ENL and that the incidence of glomerulonephritis is similar in lepromatous and non-lepromatous cases. Panayi (392) proposed that rheumatoid arthritis has a clinicopathologic and immunologic spectrum similar to leprosy. Penchenier, *et al.* (392) pointed out a clinical association between onchocerciasis and leprosy in Mali, and speculated that one may predispose to the other. Rea (392) speculated that proliferation of *M. leprae* in vascular endothelial cells may be important in the pathogenesis of both pure primitive diffuse lepromatous leprosy and Lucio's phenomenon. Saha, *et al.* (392–393) found that higher proportions of unimmunized leprosy patients had protective serum tetanus antitoxin levels than did unimmunized controls. Venkatesan, *et al.* (393) reported higher levels of protein-bound fucose in the sera of untreated lepromatous leprosy patients than in normal controls. Ghei, *et al.* (395) found that dapsone inhibits *in vitro* lymphocyte blast transformation in response to PHA. Jagannath and Sengupta described an indirect hemagglutination test (395) and a counter current electrophoresis technique (396) for measuring specific antibodies against *M. leprae*. Kim (396) reported upgrading of the histopathology of lepromatous nodules to borderline following local injections of BCG or levamisole. Kirchheimer and Sanchez (396) reported that, regardless of the infecting dose of *M. leprae,* only about 20% of armadillos are resistant to the infection. In contrast, the great majority of humans are resistant to leprosy. Results of antileprosy vaccination in armadillos may not apply to vaccination in humans, since the mechanisms of susceptibility to leprosy may differ in the two species. Løvik and Closs (397) induced repeated, strong, local delayed-hypersensitivity reactions to *M. lepraemurium* antigens in pre-sensitized C3H/TifBom mice and found no measurable inhibition of the multiplication of *M. lepraemurium* at the same site, demonstrating a clear dissociation between delayed-type hypersensitivity to soluble mycobacterial antigens and protective immunity against mycobacteria. Melsom, *et al.* (397) found IgA and IgM anti-*M. leprae* antibodies in cord sera of babies of mothers with leprosy, indicating intrauterine infection. Melsom, *et al.* (397–398) studied IgA-, IgM-, and IgG-anti-*M. leprae* antibody levels in a variety of leprosy patients. IgM antibodies were clearly increased in indeterminate cases compared to controls, and IgM antibody levels did not fall significantly after more than ten years of treatment in active cases. Stanford (398–399) reviewed the immunology of leprosy. Leprosy patients lack effective cell-mediated immunity against common (Group i) mycobacterial antigens. Protective immunity stimulated by BCG involves recognition of these Group i antigens. Lepromatous patients lack the ability to recognize species-specific (Group iv) mycobacterial antigens, and thus are unable to recognize *M. leprae* and some of the nonpathogenic environmental mycobacteria. This immunologic unresponsiveness allows antigenically related organisms such as some corynebacteria and some scotochromogenic mycobacteria to survive in some lepromatous patients. Immunotherapy and immunoprophylaxis may lie in the induction of cellular reactivity to the Group i or common mycobacterial antigens. Valentijn, *et al.* (399) found circulating immune complexes in leprosy patients with and without ENL. On the other hand, there was a significant

and specific correlation between elevated serum C3d levels and ENL. Bhide, *et al.* (400) reported that vaccination of mice with a non-acid-fast coccoid organism of leprous origin inhibited the multiplication of *M. leprae* in these animals. Splenic cells from vaccinated mice could passively transfer delayed hypersensitivity to *M. leprae* to recipient mice. Chatterjee (400) found skin test responses to the cytoplasmic fraction of one of the leprosy-derived, non-acid-fast coccoid organisms were highly correlated to responses to standard lepromin. Daffe, *et al.* (400) found analogies between *M. gordonae* and *M. leprae* based on analyses of mycolic acids and lipids. Imaeda, *et al.* (400) found the highest degree of DNA homology between *M. leprae* and *Corynebacterium* sp. 2628 LB, isolated from a human leprosy patient, among the mycobacterial, nocardial, and corynebacterial species tested. Janczura, *et al.* (401) analyzed the cell walls of 24 coryneform, non-acid-fast, Gram-positive organisms isolated from human leprosy lesions and concluded that these strains represent a homogeneous group within the genus *Corynebacterium.* van Eden, *et al.* (405) found no heterogeneity for HLA antigens between sporadic (non-familial) tuberculoid leprosy and controls in Maharashtra, India, suggesting that tuberculoid leprosy is a heterogeneous disease with regard to genetic background.

The excellent group of original articles in the December issue began with an authoritative communication by Convit, *et al.* (415–424) on results of vaccinating 529 weak or non-reactors to *M. leprae* with a mixture of *M. leprae* and BCG. Evidence of clinical changes, histopathologic changes, and skin test responses to a soluble antigen from purified *M. leprae,* point to the efficacy of this combination immunotherapy and its potential value in immunoprophylaxis. Duncan, *et al.* (425–435) followed 114 Ethiopian women with leprosy during pregnancy and lactation. Fifty-five showed worsening of their leprosy status and in 31 this occurred during the third trimester of pregnancy; 40 developed Type 1 reactions and 28 had Type 2 reactions. Shield, *et al.* (436–445) tested a cell-free extract of armadillo *M. leprae* (LRA6) as a skin test reagent in 334 leprosy and 30 tuberculosis patients. It appears that LRA6 may detect a particular form of response to *M. leprae* which accounts for positivity only in a selective group of TT patients. Shield and Stanford (446–454) studied responses to LRA6 in contacts and non-contacts of leprosy, and found evidence suggesting that the degree of contact with *M. leprae* affects the level of positivity and the strength of response to LRA6. Anergy to the leprosy bacillus may occur even in the clinically unaffected person. Reitan, *et al.* (455–467) found that lymphocytes from patients with untreated lepromatous leprosy failed to respond to *M. leprae* antigens and the median response to PPD was significantly lower than in healthy controls. After dapsone treatment, the failure to respond to *M. leprae* antigens remained in LL patients, but the depression of the PPD response returned to normal. Evidence was presented suggesting that an antigen-induced suppressor mechanism may be operating *in vitro* with cells from patients with borderline tuberculoid leprosy. Sinha, *et al.* (468–470) found that untreated tuberculoid and lepromatous leprosy patients both had elevated levels of blood lactic and pyruvic acids. Liu, *et al.* (471–476) performed electron microscopic studies of histoid leprosy and found that cells containing bacilli could be divided into three types: ordinary macrophages, fusiform or elongated macrophages, and foamy macrophages. Girdhar and McDougall (477–479) made the interesting observation that bacilli from the more superficial part of the granuloma and the subepidermal free zone in the skin of untreated lepromatous leprosy patients showed a significantly higher Morphological Index compared to the mid and lower zones. Nakamura, *et al.* (480–487) found no evidence indicating that multiplication of *M. leprae* takes place on M-Y 14b agar medium. Job, *et al.* (488–493) presented an armadillo infected with *M. leprae* which showed histopathologic features characteristic of borderline leprosy. Turcotte and Lemieux (494–500) vaccinated C3H mice with a single dose of live BCG, whole extracts of mechanically disrupted *M. lepraemurium,* or a mixture of both of these antigens, and then infected them with *M. lepraemurium.* Vaccination was able to temporarily limit the growth and dissemination of the bacilli, but was unable to stop the fatal progression of murine leprosy.

The Editorial section of the December issue contained the editorial by Beiguelman (501–507) explaining the lysing threshold hypothesis, which considers the primary defect in lepromatous leprosy as inherited and located within the macrophages.

In the December issue the passing of Professor Felix Sagher (508) was noted with deep sadness.

The Correspondence section contained an interesting case report of Gilbert's syndrome occurring in a patient with dimorphous leprosy by Banerjee (509). Matsuo, *et al.* (510) reported three patients with primary dapsone-resistant leprosy in the Republic of Korea, including one patient whose bacilli multiplied in mice administered 0.01% dietary dapsone.

The News and Notes section noted the round-the-world investigative tour of eight countries by the eminent Chinese leprologist delegation consisting of Dr. Ma Haide, Dr. Ye Gan-yun, and Dr. Su Junrui (512–513). The resumption of publication of the *Leprosy Scientific Memoranda* under the sponsorship of the Leonard Wood Memorial was noted (522).

The Book Review section of the December issue contained an excellent account of leprosy research activities in India in the *Annual Report of the Director-General 1980–81, Indian Council of Medical Research* by Ramalingaswami (527–533).

In the Current Literature section of the December issue, Crawshaw (534) provided a moving account of the personal impact of his first encounter with leprosy. Balakrishnan, *et al.* (535) reported that desoxy fructoserotonin inhibits the multiplication of *M. leprae* in the foot pads of mice. Bharadwaj, *et al.* (535) found that patients treated with clofazimine showed an increase in clofazimine and a decrease in vitamin A in their skin. Plasma levels of vitamin A also decreased with an increase in the duration of treatment with clofazimine. Bourland, *et al.* (535) reported 28 strains of *M. leprae* secondarily resistant to dapsone from Burundi. The recommendations of the Study Group convened by WHO in Geneva on the chemotherapy of leprosy control programs appeared (535–536). For paucibacillary cases the recommendations are rifampin, 600 mg supervised once monthly, together with dapsone, 100 mg daily unsupervised for six months and then discontinuing. For multibacillary cases rifampin, 600 mg monthly supervised; dapsone, 100 mg daily unsupervised; and clofazimine, 300 mg monthly supervised, with 50 mg daily unsupervised, are recommended. The regimen for multibacillary cases is recommended for at least two years and ideally until slit-skin smears are negative. The duration of follow up is not yet defined but a minimum of four years for paucibacillary and eight years for multibacillary patients is recommended as reasonable. Feng, *et al.* (536) reported a quantitatively minor third urinary metabolite of clofazimine which was characterized as a hydrated clofazimine glucuronide. Janssens (537) reported two patients with primary dapsone-resistant BT leprosy. Ji (537) found that methyl formylrifamycin had therapeutic effects similar to rifampin in ten lepromatous patients. Smith (538–539) questioned the wisdom of universal implementation of the recommendations of the WHO Study Group advocating multi-drug regimens for leprosy. Questions were raised as to how these new drug regimens were to be funded and as to whether or not these short courses have been well-enough evaluated over a long-enough period to justify their being recommended worldwide. If these regimens were implemented in developing countries without a large injection of resources, they could have disastrous consequences with the development of multiple-drug-resistant organisms and the already restricted leprosy services able to treat only a few cases. Valles, *et al.* (539) reported IgA nephropathy occurring in lepromatous leprosy. van Rensburg, *et al.* (539–540) found that clofazimine inhibits neutrophil motility and lymphocyte transformation *in vitro* and *in vivo*. Venkatesan, *et al.* (540) found that hypoproteinemic mice had elevated concentrations of free dapsone in blood and tissues which could be because of diminished binding of dapsone to plasma albumin. Yawalkar, *et al.* (540) reported satisfactory clinical responses and safety after treating 93 previously untreated lepromatous leprosy patients with rifampin 450 mg daily or 1200 mg once monthly combined with dapsone 50 mg daily. Dabholkar and Gaitonde (541) reported that the adrenergic system is hypo-functional as compared to the cholinergic system in leprosy

patients. Dong, *et al.* (541–542) reported an interesting case of Type 1 lepra reaction occurring in a borderline tuberculoid patient after the intradermal injection of 0.1 ml of standard Mitsuda lepromin. Malaviya, *et al.* (543) reported six cases of nerve abscesses developing in patients with lepromatous leprosy. Ramanujam (545) pointed out the difficulties in differentiating tuberculoid leprosy and sarcoidosis. Sahasranam, *et al.* (546) found that cardiac autonomic functions are significantly affected in lepromatous leprosy patients. Terencio and Rubio (546) described three lepromatous patients who, after more than 15 years of disease and after various years of bacteriologic negativity, relapsed with clinical and histologic features of the borderline form of the disease. Bechelli, *et al.* (547) found that a positive Fernandez reaction to human or armadillo lepromin was always followed by a positive Mitsuda reaction. The correlation overall between the two reactions was poor. Negative or doubtful Fernandez reactions are almost always followed by positive Mitsuda reactions in children and adolescent noncontacts. Closs, *et al.* (547) studied *in vitro* lymphocyte stimulation in response to tuberculin and an antigen fraction, MLW 1, prepared from *M. leprae.* MLW 1 induced strong lymphocyte responses in patients with tuberculoid leprosy and healthy contacts of leprosy patients, but only weak or no responses in lepromatous leprosy patients and non-exposed controls. Fotedar, *et al.* (547) found that leukocyte migration inhibition responses of lepromatous leprosy patients were enhanced with acetoacetylated derivatives of *M. leprae.* Gillis and Buchanan (547–548) characterized 11 monoclonal antibodies as to their reactivity with *M. leprae* and 18 other mycobacterial species. Two monoclonal antibodies reacted only with *M. leprae.* Hua (549–550) found morphological abnormalities in capillary loops and relatively obvious changes in patterns of blood flow in leprosy patients. These changes were most marked in patients with the lepromatous form of the disease. Kano, *et al.* (550) found circulating immune complexes in 54% of lepromatous leprosy sera by the Raji-cell test and in 43% by the antibody inhibition test. The immune complexes showed predominately IgG in patients with lepra reactions and predominately IgM in patients without lepra reactions. Karazawa, *et al.* (550) studied responses of normal individuals to whole and sonicated lepromin. Both types of lepromin induced good Fernandez reactions but the sonicated lepromin gave weaker late (Mitsuda) reactions. Ridley and Russell (551–552) used immunoperoxidase techniques to demonstrate immunological factors in the granulomas of tuberculoid and lepromatous patients. Saha, *et al.* (552) gave seven lepromatous leprosy patients repeated transfusions of fresh blood donated by healthy, but tuberculin and lepromin positive subjects; the results were encouraging. Sengupta, *et al.* (552) found that only an anionic component of Dharmendra antigen sonicates produced specific skin reactions in tuberculoid leprosy patients. Shannon, *et al.* (552–553) found evidence of suppressor cells in lepromin skin test positive healthy subjects, inactive leprosy patients, and in active tuberculoid leprosy patients, but not in healthy naive subjects or in leprosy patients with borderline or uncomplicated lepromatous disease. Srinivasan, *et al.* (553) found discrepancies in 21 of 36 cases in the histopathological features of leprosy lesions in the skin compared to those in the peripheral nerve. In 19 of these cases, the lesions in the nerve were found to be immunologically more deficient than those in the skin. Stoner, *et al.* (553) studied cell-mediated immunity in lepromatous leprosy patients using HLA-D-identical siblings. Sixteen healthy siblings had peripheral blood mononuclear cells which showed a lymphoproliferative response to *M. leprae* antigens while those from 12 borderline lepromatous or polar lepromatous patients did not. Co-culture experiments did not reveal suppressor cells in lepromatous peripheral blood mononuclear cells which were capable of suppressing the lymphoproliferative responses to *M. leprae.* Lepromatous cells could respond to *M. leprae* antigens if the sensitized lymphocytes were provided by mitomycin-C-treated normal cells. Other recombination experiments failed to reveal a defect in the *M. leprae* antigen-presenting function of lepromatous adherent cells. The authors concluded that lepromatous patients simply lack sufficient numbers of antigen-specific T lymphocytes to initiate a lymphoproliferative response to *M. leprae* antigens. Touw, *et al.* (553–554) found that

IgG class anti-*M. leprae* antibody levels were high in lepromatous leprosy patients and varied from negative to strongly positive in tuberculoid patients. A significant increase in IgG-anti-*M. leprae* antibody levels was observed among tuberculoid patients with more widespread forms of the disease. Lepromatous patients generally had high levels of both IgG- and IgM-anti-*M. leprae* antibodies but no relation was found between the antibody responses and bacillary load or other clinical parameters. Marked decreases in specific IgG and IgM antibody levels were observed in lepromatous patients during their first year of treatment. Delville, *et al.* (554) reviewed the finding of diphtheroids or leprosy-derived corynebacteria isolated from leprosy lesions. Their antigenic structure is more closely related to *M. leprae* and other mycobacteria than to classical corynebacteria. Dutta, *et al.* (554–555) carried out biochemical tests of mycobacteria and found that *M. vaccae* showed closest relationships with *M. leprae.* Ketomycolate was found in the cell wall structure of both *M. vaccae* and *M. leprae.* Ishaque (555) isolated scotochromogenic mycobacteria from rat or mouse lepromata. These cultivable strains did not produce murine leprosy disease in susceptible mice while other mycobacteria isolated on Ogawa egg yolk medium did so. Kaur, *et al.* (555) found that *M. leprae* could survive ultraviolet radiation for 30 min, direct sunlight for 2 hr, and room temperature for 7 days. Khanolkar, *et al.* (555–556) found that *M. leprae* separated from armadillo tissues stored at −80°C had an active uptake system for DOPA. Lancaster, *et al.* (556) maintained mutant mice at a body temperature similar to that of armadillos and found that they do not become heavily infected with *M. leprae.* Thus, low body temperature alone is not sufficient to produce an overwhelming infection, suggesting that there is an additional lack of cell-mediated immunity in armadillos. Matsuo and Tatsukawa (556) were unsuccessful in cultivating *M. leprae* in cell culture under conditions of lowered redox potential. Nakamura (556) found that pantoyl lactone stimulated the growth of *M. lepraemurium* in a cell-free medium. Saoji and Kelkar (557) reported detectable LDH isoenzymes originating from *M. leprae* in the sera of leprosy cases. Wheeler and Gregory (557) demonstrated superoxide dismutase and peroxidatic activity in *M. leprae.* Bhat and Vaidya (557) showed early segmental demyelination and later axonal degeneration in the sciatic nerves of mice with experimental leprosy in teased single fiber preparations. Krahenbuhl, *et al.* (558–559) found that local injections, but not systemic treatments, with *Propionibacterium acnes* (formerly designated *Corynebacterium parvum*) inhibited the growth of leprosy bacilli in mice. Venkataramaniah, *et al.* (560) found comparable percentages of "takes" in mouse foot pad infections with bacilli isolated from patients by skin scrapings and regular skin biopsies. Bharadwaj, *et al.* (561) found that 52% of children in contact with leprosy patients were Dharmendra lepromin negative. Seventy-eight percent of these lepromin negative contact children were FLA-ABS positive, suggesting that they were at high risk of developing overt leprosy. Subclinical infection was found to be more common among contacts of multibacillary cases than among contacts of paucibacillary cases. Dominguez, *et al.* (561) reported definitive data on the epidemiology of leprosy in the Singu area of upper Burma. The incidence rate among contacts of already known cases was 9.8/1000 person-years; while the estimated yearly incidence among non-contacts was 5.9/1000. Hogerzeil and Reddy (561–562) found that leprosy control in an integrated community health project was superior to that obtained in a conventional survey, education, treatment program in regard to the number of new patients and in regard to case holding. Izumi, *et al.* (562) reported that HLA-B7 was found at a significantly higher frequency and Bw54 at a significantly lower frequency in lepromatous leprosy patients compared to healthy controls. Both lepromatous and tuberculoid patients showed a marked increase in HLA-DR2 frequency. Levis, *et al.* (562) provided an epidemiological evaluation of leprosy in New York City, emphasizing that the leprosy problem in New York City is almost exclusively a reflection of immigration patterns. Rao, *et al.* (563) found leprosy prevalence rates of approximately 23/1000 among school children in Andhra Pradesh, India. Saikawa (563) presented data on the decreasing leprosy incidence rates in Okinawa.

Kumar and Anbalagan (564) reviewed the behavior of 225 adult leprosy patients in South India. The majority of the patients did not know how they had contracted the disease and 10%–11% did not reveal the disease to their families. Almost half the cases delayed seeking medical consultation for one year or longer after their first suspicion that they had the disease. As an average, the patients admitted to taking only 62% of their expected treatment and 41% were not aware of the name of the drug they were taking. Malaviya and Ramu (565) reported results of surgical decompression in ulnar neuritis in leprosy and found that, in addition to relief from acute pain, sensory recovery was appreciable. Sebille, *et al.* (565–566) reported that isaxonine significantly improved nerve function and muscle reinnervation in cases with leprosy neuropathy. Gatner and Anderson (566–567) suggested that there is a disease spectrum in tuberculosis analogous to that of leprosy. Kadival, *et al.* (567) reported a radioimmunoassay to detect mycobacterial antigens in biologic samples. Mirza (567) found that adults with untreated pulmonary tuberculosis frequently failed to become sensitized to DNCB and had lower total peripheral blood T lymphocytes than other groups. Reich, *et al.* (567) fractionated culture filtrates of *M. tuberculosis* H37Ra and found a single protein, designated P2, which was the most immunologically reactive antigen. In an interesting review of tuberculosis control (568), it was pointed out that when the risk of infection declines sharply the risk of tuberculous disease in persons already infected also declines. This finding led to the conclusion that unless the risk of infection is low, new cases of tuberculosis arise predominately as the result of reinfection even of those already infected.

The December issue contained abstracts of the Seventeenth Joint Leprosy Research Conference held in Sendai, Japan, 25–27 July 1982. Hirata (577) described ultrastructural characteristics of *M. leprae.* Koseki, *et al.* (577–578) described changes in Ogawa egg yolk media inoculated with infected tissues from humans and mice. These egg yolk reactions seemed to be due to elevated activities of lysosomal enzymes in these tissues and were detrimental to the growth of *M. lepraemurium* on primary isolation. Nakamura (578) described the composition of a new medium (NDLASU) which permits the quantitative multiplication of *M. lepraemurium* to take place for up to four weeks of incubation. Matsuo (578) described the advantages of cycloheximide treatment of cell cultures for the cultivation of *M. lepraemurium* and its possible application to the growth of *M. leprae.* Nomaguchi, *et al.* (578–579) reported that smooth colonies of *M. lepraemurium* in Ogawa egg yolk medium did not produce lepromas in CBA mice, while rough colonies did. Hastings and Morales (579–582) speculated that viable *M. leprae,* considered alone, may be able to divide at a rate of about once a day. Yoneda, *et al.* (582–583) studied the effect of dapsone on nude mice experimentally infected with *M. leprae.* The multiplication of two strains of *M. leprae* was completely inhibited by dapsone in immunologically intact, normal mice. Full inhibition could not be achieved in nude mice inoculated with these strains and fed identical concentrations of dietary DDS. Kohsaka, *et al.* (583–584) found that "rhino" mice will support the multiplication of *M. leprae* in the foot pads but that yields were lower than with nude mice. Meyers, *et al.* (584–585) described disseminated leprosy in two species of monkey—sooty mangabey and rhesus. The rhesus monkey developed infiltrated lesions of the skin of the ears and face at inoculated sites, and of the skin of the scrotum, arms, legs, and tail at uninoculated sites, 15 months after inoculation with *M. leprae* from a naturally infected mangabey monkey. Nakamura and Yogi (585–586) reported that the development of lepromatoid lesions following inoculation with *M. leprae* in nude mice was influenced by the genetic background of the animals. Nakamura and Yogi (586–587) compared the growth of *M. leprae* in hereditarily athymic asplenic mice and in splenectomized nude mice, and concluded that lack of a spleen enhanced the development of lepromatoid lesions in the early stages after infection. Nakamura and Yogi (587–588) reported that carrageenan treatment and splenectomy enhanced the multiplication of *M. leprae* in nude rats, and that heterozygous thymus cells caused swelling in the infected right hind foot and a 10- to 100-fold reduction in bacillary counts in these ani-

mals. Kashiwabara and Nakagawa (588–589) found that the particulate fraction of murine leprosy bacilli grown in host tissues contained phospholipid deacylating activities with acidic pH optima. Phospholipid deacylating activities with similar acidic pH optima were also detected in the particulate fraction of cultivated murine leprosy bacilli. Fukunishi, *et al.* (589) performed HPLC of acetone-soluble lipids of experimental armadillo leprosy lesions and found characteristic patterns of peaks and retention volumes. Nishiura and Fukunishi (589) studied peripheral nerve lesions of nude mice inoculated with *M. leprae* and found bacilli in perineurial cells, endothelial cells, Schwann cells, and axons of the myelinated nerve fibers inside the lepromas of the foot pads. Tsutsumi and Gidoh (589–590) studied a number of compounds for their immunopotentiative and immunosuppressive activities. Tsutsumi and Gidoh (590–591) reported a variety of biologic activities in derivatives of acidic anti-inflammatory drugs and discussed the possibility of using these types of derivatives in the treatment of peripheral neuritis. Hunter, *et al.* (591–592) reported the primary structure of the oligosaccharide of a specific phenolic glycolipid (Phenolic-Glycolipid-I) of *M. leprae* as well as its phenolic phthiocerol "core." A second phenolic glycolipid (Phenolic-Glycolipid-II) was found to be identical to Phenolic-Glycolipid-I except that the terminal sugar is 6-O-Me-glucopyranose instead of 3, 6-di-O-Me-glucopyranose. Large quantities of two diacyl phthiocerols were found in *M. leprae*-infected armadillo tissues and were presumably secreted by the bacilli. The Phenolic-Glycolipids-I and -II were immunologically reactive serologically. There is strong circumstantial evidence that these phenolic glycolipds in combination with the diacyl phthiocerols are the "peribacillary substance," "small spherical droplets," "foamy structures," "capsular material," "electron transparent zone," associated with *M. leprae.* Umland, *et al.* (592–593) described a solid-phase radioimmunoassay for IgG class antibodies against *M. leprae* glycolipid-I (Phenolic-Glycolipid-I). Antibody levels to *M. leprae* glycolipid-I fell sharply in one patient during an ENL reaction. Miller, *et al.* (593–594) reported that benzamidine inhibited the degradation of the surface proteins of purified *M. leprae* during purification. Using an ELISA assay, an arabinomannan antigen was detected on the surface of purified whole *M. leprae,* but more than 90% of this antigen remained in fractions that did not contain bacilli, following the Draper 1979 purification procedure. Approximately 30 murine monoclonal antibodies have been prepared which react with *M. leprae.* Eleven were directed at intracellular antigens; while several of the remainder appeared to have recognized surface components. Of the 11 antibodies directed at intracellular or non-exposed cell-wall antigens, 8 were IgG and 3 were IgM. Of the 19 antibodies that react against whole organisms and presumably recognize surface antigens, all were IgM. Sengupta, *et al.* (594–595) electophoresed Dharmendra antigen and found that the skin delayed-type hypersensitivity inducing antigen(s) reside(s) in the anionic region. Sera from lepromatous leprosy patients recognized an antigen near the well in immunoelectrophoresis of Dharmendra antigen. Akiyama, *et al.* (595) found evidence of both suppressor T cells and suppressor macrophages in the spleens of mice infected with *M. lepraemurium.* Izumi, *et al.* (595–596) reported results indicating that macrophages play an important role in prostaglandin-mediated regulation of cell-mediated immune responses to *M. leprae,* both in healthy individuals and in leprosy patients. Scollard and Gardner (596) found that phagosome-lyosome fusion occurred in 91% of instances following phagocytosis of *M. leprae* by cultured human mononuclear phagocytes. Modlin, *et al.* (596–599) found a deficiency in the T helper/inducer subset of lymphocytes in all active leprosy patients, but particularly well developed in the tuberculoid and lepromatous without ENL groupings. The helper/inducer deficiency was not present in active lepromatous patients with ENL, nor in inactive patients with prolonged dapsone therapy. There was no apparent relationship between the ratio of helper and suppressor phenotypes in the blood and their comparative numbers in tissue specimens. T suppressor/cytotoxic antigen-bearing lymphocytes were predominantly in the mantle of the lesions in tuberculoid leprosy. In tuberculoid leprosy, the helper/inducer cells were among the ag-

gregated epithelioid cells. The lepromatous and reversal reaction tissues did not show this architectural separation of T lymphocyte subsets. Matsuo, *et al.* (599) studied β-glucuronidase and lysozyme in the skin lesions of tuberculoid, borderline, and lepromatous leprosy patients. Heavy accumulation of lysozyme was noted in epithelioid and Langhans' giant cells, but not in lepra cells. Heavy accumulation of β-glucuronidase was noted in the spindle or oval cells in tuberculoid and borderline lesions. Naka and Douglas (600) described the development of ELISA techniques to detect antibody responses to antigens of *M. leprae.* Optimum coating of the antigens to the wells in microtiter plates was accomplished with a volatile ammonium acetate/carbonate buffer. Autoclaving *M. smegmatis* increased its reactivity in this system. *M. leprae* was found to be twice as reactive as *M. smegmatis* and autoclaving *M. leprae* similarly increased its reactivity. Abe, *et al.* (600), using the FLA-ABS test, found evidence that the ratio of the prevalence of subclinical infection to new cases with leprosy in an area ranged from 836–2329. There seemed to be a localization of positive responders in the FLA-ABS test surrounding houses in which a leprosy case had recently been found. Positive responders were also found where no case of leprosy had been recently reported, and the suggestion was made that a possible source of infection to these positive responders might be from the environment rather than from direct contact with leprosy patients. Bharadwaj, *et al.* (600–601) found higher proportions of positive FLA-ABS tests among contacts of multibacillary cases of leprosy than among contacts of paucibacillary cases. Many of the cases showing FLA-ABS positivity and lepromin negativity progressed to clinical disease in comparison to other groups. Vithayasai, *et al.* (601–602) described detailed clinical and epidemiological features of leprosy in two resettlement villages in northern Thailand. The leprosy attack rate among children between the ages of five and 16 in these resettlement villages was 21/1000; while the prevalence in children aged five through 14 years living in a leprosy endemic area of rural northeast Thailand in 1972 was 3.2/1000.

Clearly, 1982 has again provided a great deal of new information for leprosy workers. From a personal perspective, a number of general trends are apparent.

In the field of chemotherapy, more and more sophisticated *in vitro* studies of drugs with antibacterial activity have appeared. The surprising efficacy of dapsone in reducing nasal excretion of *M. leprae* in treated lepromatous leprosy patients was reported. Dapsone resistance continues to be reported from many parts of the world. Multidrug regimens have been recommended by a WHO Study Group and objections to these regimens have been raised. The first case of clofazimine-resistant disease has been reported.

Clinical observations have continued to provide new information. The considerable dangers of pregnancy and lactation to women with leprosy have been pointed out. The practical sites for skin scrapings have received attention. A number of studies have focused on the renal pathology in leprosy. Decreased taste sensation has been reported in the disease, and strong evidence now exists for the possibility of intrauterine infection.

In immunopathology a variety of serologic studies are becoming more and more definitive. The significance of circulating immune complexes in leprosy is being questioned. More detailed, classical histopathological observations are being made. The antigenic mosaics of mycobacteria are being clarified and exciting relationships with corynebacteria and other mycobacteria are being reported for *M. leprae.* Work proceeds in vaccine development with no agreement as yet on the optimum candidate for an antileprosy vaccine. New techniques are being applied to demonstrate mycobacterial antigens in leprosy tissues and the immunologic responses occurring locally, opening up new areas of understanding of the disease. Testicular damage due to autoimmunity has been reported. A number of studies are unable to find suppressor T cells in lepromatous leprosy patients, which are apparently acting on cell-mediated immune or delayed hypersensitivity systems, but report them in tuberculoid patients. Suppressor T cells and helper T cells have been enumerated in patients across the leprosy spectrum and acute changes have been noted in ENL patients, implying that sup-

pressor T cells may function in humoral immune responses in leprosy.

In microbiology, evidence is accumulating that the characteristic foamy substance surrounding *M. leprae* in tissues is due to a unique, humorally immunogenic, phenolic glycolipid of the organism. Refinements are being made in the cultivation of *M. lepraemurium* and efforts continue on the cultivation of *M. leprae.* Difficult-to-grow mycobacteria have been cultivated from specimens of armadillo livers containing *M. leprae.*

In experimental infections, more and more refined studies of *M. leprae* infections in immunodepressed rodents have appeared. New non-human primate models of infection with *M. leprae* are providing exciting possibilities for future studies.

In the field of epidemiology, more studies have appeared seeking a genetic marker for the disease. Populations are being studied with sophisticated serological techniques and suggest that infection with *M. leprae* is common, but that the disease is considerably more rare, in populations from endemic areas.

Once again in the perspective of the JOURNAL, 1982 showed considerable progress in most areas of leprosy with continuing frustrations in some. Exciting work is continuing to provide a steady stream of new information and major advances seem to be around every corner. I look forward with impatient optimism to 1983.—RCH