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EDITORIALS

Editorial opinions expressed are those of the writers.

THE 1981 JOURNAL—A CONTINUING PERSPECTIVE

After the second full year of publication from Carville and at the beginning of the 50th year of publication of the JOURNAL, it again seems appropriate to review the progress that has been made in leprosy in the past year. As reflected in the pages of the JOURNAL, 1981 was a year of interesting developments, providing us with recollections of the origins of the International Leprosy Association, refinements in our thinking, and a number of new concepts.

The original articles of the March issue began with a careful histologic characterization of the Fernandez reaction across the leprosy spectrum by Thomas, *et al.* (1–8)*. While there was good clinical and histologic correlation between the early and late lepromin reaction in polar tuberculoid and polar lepromatous cases, there was marked variation in the two clinically (but not histologically) in borderline and indeterminate cases. The early or Fernandez reaction was as good an indicator of lepromin reactivity as the late or Mitsuda reaction if it was assessed histologically. Gupta, *et al.* (9–15) found that lymph node aspiration cytology smear patterns correlated with clinical and histopathologic classifications of leprosy patients. Stoner, *et al.* (16–20) described a case of BT leprosy in a four-year-old boy, which became clinically apparent 2 weeks after the child had been vaccinated with BCG. The suggestion was made that BT leprosy was precipitated by intradermal BCG and that this could be on the basis of the BCG overcoming a phase of primary immunosuppression in an individual who might have otherwise progressed to lepromatous leprosy. Reich, *et al.* (21–26) described a new blood test which utilizes a laser nephelometric measure of the interaction between serum and a suspension made from a leprosy biopsy. This relatively simple and rapid test identified high reactors five times more frequently in household contacts of leprosy patients than from persons in the surrounding community. Nuti, *et al.* (27–30) found that almost half of both tuberculoid and lepromatous leprosy patients had circulating immune complexes in their sera, as measured by Clq solid phase assays, and that the presence of circulating immune complexes was correlated with the presence of autoantibodies. Rolston, *et al.* (31–36) studied 11 male lepromatous patients and found elevated levels of prolactin, luteinizing hor-

* Numbers in parentheses refer to page numbers of the INTERNATIONAL JOURNAL OF LEPROSY, volume 49, 1981.

mone, and follicle stimulating hormone. Bajaj, *et al.* (37–41) reported evidence of impaired renal function in 84.1% of lepromatous patients with erythema nodosum leprosum (ENL), in 66.6% of patients with quiescent ENL, and in 54.4% of patients with uncomplicated lepromatous leprosy. The most common abnormalities noted were diminished endogenous creatinine clearance and proteinuria. Szabados, *et al.* (42–48) found that isolated platelets from leprosy patients had a diminished capacity to take up serotonin and that this was probably due to their low sialic acid content. In patients with active disease and those with lepra reactions, leprous plasma itself could correct this abnormality. Desoxyfructoserotonin raised serotonin uptake by platelets from lepromatous patients *in vitro*. Shetty, *et al.* (49–56) found γ-glutamyl transpeptidase activity in several mycobacteria, including *M. leprae*. Glycyl D-amino acids were active as acceptors for the γ-glutamyl group. Understanding the role of this enzyme in mycobacterial metabolism could provide the rationale for the development of new antibacterial chemotherapeutic agents. Dhople and Hanks (57–59) measured the ATP content of *M. leprae* using the fire fly bioluminescence method and found it to be about 1.24 pg per million organisms, about half that present in *M. lepraemurium*.

The editorial section of the March issue began with an eloquent editorial by Lechat (60–64) outlining the development of the International Leprosy Association, the agencies which have provided crucial support over the years, the recent problems which have arisen, and the challenges which lie ahead. We were fortunate to have a guest editorial by Cochrane (67–71) outlining the Leonard Wood Memorial Conference in Manila in January 1931, which led to the founding of the International Leprosy Association. Hastings (73–82) reviewed the contents of the 1980 JOURNAL.

In the March correspondence, Harboe and Closs (85–88) reported that they were unable to reproduce the lithium acetate extraction from *M. leprae* of an antigen with similar properties to the antigen extracted by Caldwell and Buchanan (Int. J. Lepr. **47** [1979] 469–476) and that antigenic material isolated and provided by Caldwell and Buchanan crossreacted with *M. avium* and BCG, as measured by precipitation by antisera to *M. avium* and BCG. Buchanan, *et al.* (88–89) responded that the antisera to *M. avium* and BCG could have been reacting with antigens in their extract other than those they had suggested were "specific" as measured by a pool of sera from lepromatous patients adsorbed by Abe, *et al.* (Int. J. Lepr. **48** [1980] 109–119). They further reported that they had found that Abe's adsorbed serum had shown shared reactivity between *M. leprae* and *M. lepraemurium*, *M. bovis* (BCG), *M. gordonnae*, *M. nonchromogenicum*, *M. flavescens*, and *M. gastri*. Bergel (89) pointed out his belief that the mechanism of action of sulfones in leprosy involves its anti-oxidant capacity, while Seydel (90) felt that the relevant antibacterial mode of action was on 7,8-hydropteroate synthetase with inhibition of bacterial growth occurring because of depletion of dihydrofolate. Ridel, *et al.* (91–92) reported findings suggesting that activated macrophages in lepromatous leprosy patients are responsible for suppressing the responses of lymphocytes to concanavalin A in the presence of *M. leprae* antigens. Kato (93–94) reported the cultivation of acid-fast bacilli, tentatively designated *Mycobacterium X*, from 5 of 13 lepromata, using a tetradecane-DMSO medium and incubating at 34°C. The five cultures were identical, none grew on Löwenstein or Dubos media, and four cultures tested gave growth patterns in the foot pads of mice similar to those of *M. leprae*. Malik, *et al.* (94) found significantly longer breath-holding times in leprosy patients compared to healthy controls and concluded that respiratory reflexes modulated by vagal nerves are affected in leprosy patients. Pettit (95–96) expressed concern over the lack of uniformity in defining indeterminate leprosy and urged that leprosy not be diagnosed unless there is proof of the disease.

The news and notes section of the March issue noted the new agreement between the Ministry of Health of the Ethiopian government and the All Africa Leprosy and Rehabilitation Training Centre (97–99). The Silver Jubilee of the Hemerijckx Government Leprosy Centre in Polambakkam in

India was noted (103). His Holiness Pope John Paul II granted a private audience to members of ILEP on the occasion of their 24th Working Session in Rome in December 1980 (104). Dr. R. J. W. Rees was awarded the Manson Medal for 1980 by the Royal Society of Tropical Medicine and Hygiene in recognition of his outstanding contributions to the fields of tropical medicine and hygiene (110).

The current literature section of the March issue noted the complimentary article by Garfield (120–121), pointing out that the INTERNATIONAL JOURNAL OF LEPROSY is considered to be the leading journal in the leprosy field, ranking in the top third of journals covered in *Science Citation Index* in 1978 and in the top 20% in terms of how rapidly authors cite articles it publishes. Acocella and Conti (121) reviewed the interactions of rifampin with other drugs. Balakrishnan and Christian (122) reported that, as measured by dapsone/creatinine ratios in urine, irregularity of dapsone intake by leprosy patients ranged from 15–25%. de Bergeyck, *et al.* (122) reported the now rather well-known complication of prolonged high dose clofazimine therapy, gastro-intestinal symptoms and radiographic abnormalities in the small bowel. Dutta (123) reported two cases of tuberculoid leprosy who developed erythema multiforme bullosum due to dapsone. In a 24-week study, Girdhar, *et al.* (123) were unable to demonstrate a significant advantage of administering a single 1500 mg dose of rifampin along with dapsone 100 mg daily to previously untreated lepromatous patients compared to a control group treated with dapsone alone. Jayaraman, *et al.* (124) found that desoxyfructo-serotonin inhibited the *in vitro* uptake of DOPA by *M. leprae*. The Chinese herb, Lei-Gong-Teng was reported to be highly effective in the treatment of both erythema nodosum leprosum and reversal reactions. Side effects were mainly gastro-intestinal and were noted in 30–47% of treated patients. Krishna Murthy and Raja Babu (124) reported a case of toxic delirious psychosis in a 5-year-old child after accidental ingestion of dapsone. Lal and Garg (125) reported a 40-year-old woman with leprosy who developed exfoliative dermatitis and hepatitis 6 weeks after starting dapsone in a dosage of 100 mg daily. In the treatment of mouse foot pad infections with *M. leprae*, Pattyn and Van Loo (125) found evidence for synergism in the combination of dapsone and ethionamide and in drug combinations which included streptomycin. Ramu, *et al.* (126) found evidence suggesting that dapsone in a dose of 100 mg daily reduces the intensity of lepromin skin test reactivity in TT and BT leprosy patients. Ree and Taylor (126) measured dapsone/creatinine ratios in the urine of leprosy patients under treatment in Papua New Guinea and found that approximately 25% of outpatients attending the leprosy clinic were not taking medication. Tomecki, *et al.* (126) reported a 16-year-old female who developed fever, malaise, dermatitis, jaundice with hepatic dysfunction, lymphadenopathy, and hemolytic anemia after receiving dapsone 50 mg daily for one week for acne vulgaris. Akhtar, *et al.* (127) reported two patients with lepromatous leprosy presenting initially with lepromatous orchitis, and Albert, *et al.* (127–128) emphasized the rheumatic manifestations seen in their series of 21 leprosy patients. Gupta and Panda (129) found no amyloidosis in 1445 biopsied tissues from 1222 leprosy patients in India. They suggested that the consumption of a mainly vegetarian diet in India and that of meat in Western populations is the probable cause of the differences in the prevalence of amyloidosis among leprosy patients in these two groups of people. Kumar, *et al.* (129) found significantly reduced serum phospholipid levels and cholesterol levels in lepromatous leprosy patients compared to normals and tuberculoid patients. Kumar, *et al.* (129) reported two patients with lepromatous leprosy who developed transient jaundice during erythema nodosum leprosum. Kumar, *et al.* (129–130) found higher blood levels of serotonin in lepromatous leprosy patients compared to normal controls and that highly infective lepromatous patients had higher values than non-infective patients. Naik and Gurnani (130) measured serum lysozyme activity in the sera of leprosy patients and found significant elevations compared to normal controls. Values were highest in erythema nodosum leprosum patients, then lepromatous, borderline, and tuberculoid leprosy patients in that order. Smith (131) made the observation that tetanus appears to oc-

cur less often among leprosy patients than the general population, and Wahba, *et al.* (131) suggested that psoriasis is very rare among leprosy patients. Kotteeswaran, *et al.* (132) studied skin biopsies from leprosy patients and found that *M. leprae* are discharged and disseminated through sweat and sebaceous secretions, suggesting that infection through skin to skin contact can be one of the common modes of transmission of the disease. Kumar, *et al.* (132) found that leprosy patients, particularly lepromatous cases, showed reduced skin responses compared to normal controls to testing with PPD, Dharmendra lepromin, DNCB, histamine, and croton oil. Mathias, *et al.* (133) found a considerable reduction in lymphocytes in the thymus dependent white pulp of the spleen in eight autopsied lepromatous leprosy patients. Melsom, *et al.* (133) reported that 10 of 20 babies born of mothers with active lepromatous leprosy showed a slower decline in anti-*M. leprae* antigen 7 antibodies than that expected from the catabolism of maternal IgG. This indicates that these babies were stimulated by *M. leprae* antigen 7, either as free antigen or by viable *M. leprae* before birth, suggesting that leprosy can occur as a congenital infection. During the first 18 months of life, children of mothers with bacilliferous leprosy are frequently exposed to *M. leprae* to a sufficient extent for the baby to produce anti-*M. leprae* antibodies during this period. Nath and Singh (133–134) found that autoclaved whole *M. leprae* inhibited *in vitro* lymphocyte proliferation in response to concanavalin A in 80% of tuberculoid leprosy patients and in 35% of untreated lepromatous leprosy patients as measured on day 4. Healthy contacts and 53% of lepromatous leprosy patients showed enhanced responses in the presence of *M. leprae*. Nath, *et al.* (134) studied HLA-D-identical siblings suffering from leprosy. Tuberculoid patients had circulating lymphocytes which suppressed lymphoproliferative responses to antigen and mitogen while lepromatous patients had only weak suppressor lymphocyte activity. On the other hand, macrophages from responder individuals augmented, and those from lepromatous patients inhibited, *M. leprae* induced proliferation of lymphocytes. Shepard, *et al.* (135), in studies aimed at the development of an antileprosy vaccine for use in man, found that 2.5 megarads of gamma irradiation and two-phase separation of *M. leprae* using a dextran : polyethylene glycol system did not decrease immunogenicity as measured by foot pad enlargement in mice after challenge with heat-killed *M. leprae*. On the other hand, 0.1 N NaOH for 2 hr at room temperature and trypsin and chymotrypsin digestion for 24 hr at 37°C did decrease immunogenicity of the organisms. Sun Zhen De (135–136) reported a decrease in active E-rosettes in lepromatous leprosy patients and an increase in these cells after *in vitro* exposure to porcine thymosin. The suggestion was made that immunotherapy with thymosin might be helpful in leprosy patients. Touw, *et al.* (136) found that *M. leprae* suppressed the *in vitro* proliferation of human peripheral blood mononuclear cells to antigen and mitogen. The suggestion was made that some of the immunologic aberrations seen in lepromatous leprosy patients may be due to the suppressive effects of large numbers of *M. leprae*. Wahba, *et al.* (136–137) found plasma factors which depress the *in vitro* chemotaxis of neutrophils from highly bacilliferous lepromatous leprosy patients. Wideback, *et al.* (138) determined antigenic relatedness of mycobacterial and nocardial species serologically based on differences in antigen 21. The order of relatedness went from *M. leprae* to *M. tuberculosis* to *N. caviae* to *M. avium* to *M. fortuitum*. Resoagli, *et al.* (139) found an acid-fast infection in the spleen of a dead armadillo which had been found in northeastern Argentina. Shepard, *et al.* (139) studied *M. leprae, M. bovis,* (BCG), and 17 other cultures for possible protection of mice against challenge with viable *M. leprae*. Consistent protection was observed only with *M. leprae* and BCG. Welch, *et al.* (139) found that viable *M. leprae* decrease in the foot pads of mice after reaching the level of 10^6 bacilli per foot pad, and the half time of loss of viable *M. leprae* was 25 days. De Vries, *et al.* (140) confirmed an HLA-linked control of susceptibility to tuberculoid leprosy (but not other forms) and suggested a recessive inheritance of this trait for which HLA-DRw2 appears to be a genetic marker. Meesters (140–141) reported a marked decline in the number of registered cases and

in the estimated prevalence of leprosy in the Gambia. Navarrete, *et al.* (141) found a significantly higher frequency of the serum atypical pseudocholinesterase variant among lepromatous leprosy patients than among healthy contacts and suggested that this may be one of the possible genetic markers for susceptibility to leprosy. Grange, *et al.* (144) noted that 20% of patients with tuberculosis do not have measurable antibodies to any of the antigens of *M. tuberculosis*. They therefore argue that the availability of highly purified soluble antigens specific for *M. tuberculosis* would not permit more cases of tuberculosis to be diagnosed serologically. Grange, *et al.* (144) presented evidence that antimycobacterial antibodies of the IgG class gave maximum discrimination in the serodiagnosis of tuberculosis.

In the original articles of the June issue, Harboe, *et al.* (147–158) reported sophisticated studies with leprosy sera reacting with a purified preparation of *M. leprae* antigen 7. Antibodies in different patients are directed against different determinants on this antigen. Lepromatous leprosy patients particularly seem to recognize determinants other than arabinogalactan and arabinomannan. Sher, *et al.* (159–166) gave levamisole, 150 mg daily 2 consecutive days per week for 6 weeks, to treated lepromatous leprosy patients. Twenty percent of treated patients showed conversions of SKSD skin test reactions from negative to positive. Lepromatous patients without previous antileprosy chemotherapy showed increased lymphocyte counts. No clinical improvement, no lepromin conversions, and no histologic changes in skin biopsies were observed. Browne, *et al.* (167–176) reviewed their experience in treating 31 lepromatous and borderline lepromatous patients in the United Kingdom with clofazimine and reported that no other drug currently available for the treatment of leprosy could have achieved such good results in a comparable group of patients. Sharma, *et al.* (177–179) studied 35 adult female patients with bacillary positive leprosy and found that leprosy appeared to have no direct effect on menarche, menstruation, fertility, and menopause. Morrison and Collins (180–186) carried out antimycobacterial assays on 16 2-acetylpyridine thiosemicarbazones using a number of culturable mycobacteria *in vitro*. Lipophilicity, as measured by log p values, was related to antibacterial potency. Maximum antibacterial activity for slow-growing mycobacteria occurred with a log p value of approximately 4.0, for a rapid grower at a log p value of approximately 3.0, and for *M. leprae in vivo* at a log p value of approximately 2.0. These findings have considerable significance in the design of new antibacterial drugs of the thiosemicarbazone class. Sathish and Nath (187–193) reported details on the uptake of ^{3}H thymidine by *M. leprae in vitro* in mouse peritoneal macrophages. Approximately 60% of *M. leprae* strains showed significant uptakes over a 14-day period *in vitro*. Portaels and Pattyn (194–197) reported progress made in optimizing culture conditions for *M. lepraemurium*. Incubation of aerated tubes at 37°C in a humidified atmosphere was optimal. Glycerol was necessary at a concentration of 0.5–2.0%, and optimal growth occurred only between pH 5.8 and 6.3 on Ogawa egg yolk medium. Young (198–204) compared lipid extracts from lepromatous leprosy skin biopsies with those from normal skin and armadillo-derived *M. leprae* by thin layer chromatography. Mycolic acids, a 6-deoxyhexose-containing lipid, and a wax ester were found in infected skin, which corresponded to lipids present in purified *M. leprae*. Mycobacterial lipids were present in lepromatous skin biopsies in much higher concentrations than would be predicted from the number of acid-fast bacilli present. Accumulation of lipid debris from dead *M. leprae* could provide a protective environment in infected cells for remaining viable bacilli. Toman (205–217) provided an authoritative review of bacterial persistence in relation to the treatment of leprosy. The presence of persisters in lepromatous leprosy is not surprising, and it is unlikely that a new drug or new drug combination will be found which is capable of eradicating persisting *M. leprae*. Nevertheless, there exists a definite need to reexamine the justification for lifelong chemotherapy in lepromatous leprosy.

In the editorial section, we were honored to have the elegant overview of leprosy work in the last 30 years in the People's Republic of China by Ma Haide and Ye Gan-yun (218–223). The incidence and

prevalence of leprosy has decreased; approximately 300,000 patients have been cured clinically, and the total number of leprosy patients is now about 200,000. Hill-Smith (223–227) concisely reviewed the immunopathology of nerve damage in leprosy. This review was one of the prize winning British Leprosy Relief Association (LEPRA) essays for 1979. Huikeshoven (228–258) provided us with an extraordinarily useful and scholarly review of sulfone therapy in leprosy. The 257 references in this review cover virtually the entire literature on the subject and serve to put this central theme of leprosy therapy into invaluable perspective.

In the correspondence section of the June issue, Bergel (259) pointed out the biological antioxidant activity of serotonin and related this to the reported antileprosy activity of desoxyfructoserotonin.

In the news and notes section, the myriad accomplishments of Mr. Robert Watelet were described in connection with his receiving the 1980 Damien-Dutton Award (260–261). It was noted (262) that the UNESCO Science Prize for 1980 was awarded to Drs. Belton, Conalty, O'Sullivan, and Twomey from the Laboratories of the Medical Research Council of Ireland for the discovery of clofazimine. The historical visit of the President of the International Leprosy Association, Dr. Michel Lechat, to the People's Republic of China was reported (263). Dr. D. L. Leiker (264) was awarded a well-deserved honorary doctorate by the University of Amsterdam in recognition of his contributions in the fight against leprosy.

In the current literature section of the June issue, Balakrishnan and Seshadri (268) found that rifampin, but not clofazimine, enhanced the urinary output of concomitantly administered dapsone in leprosy patients. Baquillon, *et al.* (268) reported a 5.7% prevalence of dapsone resistance among multibacillary leprosy patients in Bamako, Mali. Boddingius and Stolz (269) suggested that antileprosy drugs may not penetrate into peripheral nerves and particularly into Schwann cells and that this may explain the persistence of drug-sensitive *M. leprae* in treated leprosy patients. Kasik and Monick (269) concluded that the immunosuppressive and antibacterial activities of the rifamycins are probably not related. Kritzinger (269–270) reviewed factors which influence patient compliance with taking of medications. A high level of education, and explanation by the physician regarding the medicine, and a minimum number of tablets and regimens all favored compliance. McConkey, *et al.* (270) studied the effects of dapsone in rheumatoid arthritis patients and suggested that it might be useful in the management of these patients. El-Beheiry, *et al.* (271) found testicular lesions in 35 of 148 male leprosy patients. There was good correlation between the results of semen analyses and histological and histochemical studies of testicular biopsies. Laja and Soyinka (271) described a rare case of isolated tuberculoid lesions involving the palms and soles. Pannikar and Arunthathi (272) reported a patient with complete albinism who had borderline lepromatous leprosy. Troy, *et al.* (272) reported a squamous-cell carcinoma arising in a neurotrophic ulcer in a leprosy patient. Bahr, *et al.* (273) found raised levels of IgM antibodies to β_2-microglobulin in sera from active lepromatous leprosy patients but not in sera from systemic lupus erythematosus patients. Raised levels of IgG and IgM antibodies to human thymocyte membranes were found in sera from the most active lepromatous patients. Izumi (275) found elevated levels of C3 activator and C3c in sera from active lepromatous leprosy patients with erythema nodosum leprosum compared to patients with active lepromatous leprosy without erythema nodosum leprosum, suggesting alternative pathway complement activation. Stanford, *et al.* (277) found a remarkable correlation between responses to *M. leprae* and *M. vaccae* in skin testing, lymphocyte transformation tests, and enzyme-linked immunosorbent assays of antibodies to mycobacterial antigens in leprosy patients and their healthy children in Iran. Stanford, *et al.* (277) proposed that there are two mechanisms of cell-mediated immune response to mycobacteria, the *Listeria*-type and the Koch-type of responses. Both produce positive tuberculin tests, but *Listeria*-type responses are more protective than Koch-type responses. Contact with environmental mycobacteria will induce one or the other type response and BCG vaccination will enhance it. In places

where environmental species prime for *Listeria*-type responses, BCG vaccination will afford good protection against both tuberculosis and leprosy. In places where environmental species induce Koch-type responses, BCG will be ineffective. A large contact with *M. scrofulaceum* appears to prejudice against BCG efficacy in Burma. Thomas, *et al.* (277–278) studied the histology of the Mitsuda reaction and concluded that histological evaluation of the lepromin reaction was an important assessment of the immunological status of leprosy patients. Kusunose, *et al.* (278 and 373) found that superoxide dismutase is one of the major proteins of *M. leprae*, as well as *M. lepraemurium*. The enzymes from *M. leprae* and *M. lepraemurium* share some common antigenic components. Superoxide dismutase may be very important in protecting obligate intracellular parasites against the killing effect of superoxide radicals produced by phagocytic cells. Young (279) described a simple method for the extraction and analysis of wall-bound mycolic acids from small samples of mycobacteria and showed that *M. leprae* had mycolic acid classes which differed from those of a number of other acid-fast bacilli. Navalkar (280) described IgM antibodies against *M. leprae* appearing in mice shortly after infection. IgG antibodies appear in the animals at the time when the growth of *M. leprae* enters the logarithmic phase. Ganapati, *et al.* (281) screened 11,505 adult inpatients admitted for complaints other than leprosy in various general hospitals in Bombay and found that 101 had leprosy and that 10 were smear positive. Kardjito and Grange (283) studied 90 patients with smear-positive pulmonary tuberculosis in East Java. Rheumatoid factor was detected in 21% of these patients and was significantly associated with high levels of IgM class antibodies to *M. tuberculosis*. It was not possible to place the cases into a spectrum of immunological responses similar to that occurring in leprosy. It was postulated that this could be due to differences in the relevance to protection of the various immunological mechanisms in the two diseases. Wendt, *et al.* (284) reported the existence of a natural mechanism for the transfer of significant numbers of mycobacteria from water to air and suggest that aerosolization of potentially pathogenic mycobacteria from water may be a major pathway for human infection.

The original articles of the September issue began with an extensive immunological comparison of 22 species of mycobacteria by Gillis, *et al.* (287–293). Lithium acetate antigenic extracts of the mycobacteria were tested by immunodiffusion precipitation for reactivity with a lepromatous leprosy serum pool which had been adsorbed to make it specific for *M. leprae* when used in an indirect fluorescence test. The serum pool recognized two components of *M. leprae* extract, one of which was shared with *M. lepraemurium* and BCG. The serum pool also recognized components of *M. flavescens*, *M. gastri*, *M. gordonnae*, and *M. nonchromogenicum*, but did not recognize 15 other species. Sehgal and Kumar (294–301) studied skin biopsies from lepromatous leprosy patients for immune complexes and their sera for autoantibodies and circulating immune complexes. A polyclonal rise in IgG, IgM, and IgA and increased frequency of positive Latex agglutination reactions and parietal cell antibodies, and in a large proportion of cases, evidence of circulating immune complexes were found in the patients. In about one-third of the patients, immunoglobulins and complement were found in dermal capillaries and small arterioles. Matsuo, *et al.* (302–306) studied the antibacterial activities of prothionamide and one of its metabolites, prothionamide-S-oxide. The S-oxide metabolite showed equivalent activity to the parent compound against *M. tuberculosis in vitro* and against *M. leprae* in the mouse foot pad, suggesting that the therapeutic activities of prothionamide *in vivo* result from a summation of action of both prothionamide and its S-oxide. Sritharan, *et al.* (307–310) found that dapsone, 100 mg daily for 14 days, caused a significant drop in hemoglobin, concomitant increases in serum bilirubin and in the urinary excretion of urobilingen, and a significant fall in serum haptoglobin in lepromatous leprosy patients, strongly suggesting that routine dapsone therapy results in mild intravascular hemolysis. Pavithran, *et al.* (311–314) reported measurements of porphyrins in leprosy patients. Curiously, leprosy patients, particularly untreated leprosy patients, have increased protoporphyrins and increased coproporphyrins in

their erythrocytes and excrete decreased amounts of uroporphyrins in their urine compared to normal individuals. Mascaro, *et al.* (315–316) reported an interesting patient with papular lepromatous leprosy lesions clinically localized to one-half of the face. Fieldsteel, *et al.* (317–323) studied neonatally thymectomized Lewis rats infected with *M. leprae* and found no close correlation between bacillary loads and residual T-lymphocytes. They suggested that, in addition to T-lymphocytes, another mechanism of resistance to *M. leprae* may be present in these animals, possibly involving activated macrophages. Shetty and Antia (324–330) reported electron-microscopic studies of sciatic nerves in immunologically intact mice during the course of foot pad infections with *M. leprae*, demonstrating selective intense involvement of unmyelinated fiber groups and their Schwann cells between the fourth and eighth month after inoculation.

In the editorial section of the September issue, we were fortunate to have an authoritative review and perspective on the chemotherapy of leprosy by Acocella (331–340), based on extensive experience with treating tuberculosis. Professor Acocella masterfully presented the rationale for combination chemotherapy in both diseases, the principles involved in choosing individual drugs, the controversy surrounding proposed "short course" chemotherapeutic regimens, and the problems of patient compliance and cost of treatment.

In the correspondence section of the September issue, Skinsnes (341–342) reported information obtained during a visit to the People's Republic of China showing a significant and progressive decline in the incidence of leprosy over the last 21 years in Kwangtung Province. Paul and Rose (342–343) reported their favorable experience in treating 73 long-standing active lepromatous patients for 4 months with the combination of dapsone 100 mg daily, clofazimine 200 mg daily for 2–3 weeks followed by 100 mg daily, and rifampin 1200 mg as a single dose once monthly. Other than continuing erythema nodosum leprosum reactions, only two patients had side effects (presumably excluding skin pigmentation from clofazimine). One had joint pains and an ulnar neuritis, and one patient had attacks of fever lasting 1–2 days each time after taking the monthly dose of rifampin. Devi, *et al.* (344–345) studied lipoprotein profiles in 82 leprosy patients and found that high percentages of leprosy patients have hyperlipoproteinemia, particularly Type IV hyperlipidemia, compared to healthy contacts. Kazda (345–346) shared a number of practical points regarding the maintenance of nine-banded armadillos in captivity, particularly with regard to treating parasitic diseases and maintaining them free of mycobacterial contamination.

The news and notes section of the September issue noted the well-deserved 1981 Damien-Dutton Award to the American Leprosy Missions in recognition of 75 years of service to leprosy victims. Secours au Lépreux was accepted as a full member of the International Federation of Anti-Leprosy Associations (ILEP) (349). ALERT was designated as a WHO Collaborating Centre for Training in Leprosy (349). Wilhelm Dewald was named as the General Manager of the German Leprosy Relief Association (GLRA) (349). The Schieffelin Leprosy Research and Training Centre celebrated its Silver Jubilee on completion of 25 years of leprosy service (351). Prime Minister Indira Gandhi of India launched a Leprosy Eradication Program designed to ". . . rid the country of this dreaded affliction in 20 years" (352 and 355–356). A WHO Technical Visiting Group visited the People's Republic of China to discuss further cooperation on leprosy control programs between WHO and China (353). The Silver Medal of the Order of St. Lazarus of Jerusalem was conferred on Stanley Browne in recognition of his distinguished services on behalf of leprosy sufferers (357).

In the current literature section of the September issue, Anderson and Gatner (360) found that dapsone stimulates the motility of normal neutrophils *in vitro* and the neutrophils of leprosy patients *in vivo*. Anderson, *et al.* (360) reported further details indicating that dapsone causes slight inhibition of peroxidase-mediated protein iodination *in vitro* and *in vivo* and hexose monophosphate shunt activity *in vivo*. The drug decreased the inhibitory activity of serum from lepromatous leprosy patients on normal neutrophil migration. The stimula-

tion of neutrophil motility by dapsone was related to its inhibition of the peroxidase-H_2O_2-halide system *in vitro*. Cates (360–361) studied compliance with dapsone self-administration among leprosy patients in South India by measuring urinary dapsone/creatinine ratios and found that 37% of 189 patients were judged to be taking dapsone regularly. Davies and Ng (361) in patients in Northeast India found that about 50% had taken dapsone within a 24-hr-period preceding measurements or urinary dapsone/creatinine ratios. Homeida, *et al.* (361) described a case of optic atrophy and motor neuropathy occurring in a 20-year-old Sudanese man who took dapsone 600 mg daily for 10 days. Huikeshoven, *et al.* (361) described an enzyme-linked immunosorbent assay (ELISA) for sulfones in urine and showed its greater sensitivity than the urinary dapsone/creatinine ratio determinations currently used. Ko (362) found that 41% of Korean leprosy patients were not taking dapsone as prescribed. Lal, *et al.* (362) reported three (of 300) leprosy patients treated with clofazimine 100 mg daily who developed severe gastrointestinal side effects 1–8 months after starting therapy. One of the patients died. Levy (362) studied four clofazimine analogs which were active in mouse foot pad infections with *M. leprae* and suggested the importance of the two p-chloro-substituents in the structure of clofazimine for its antibacterial activity. Ramu, *et al.* (363) found that rifampin combined with dapsone was more efficient in clearing acid-fast bacilli from the blood of lepromatous leprosy patients than combinations of dapsone plus clofazimine, dapsone plus thiacetazone, or dapsone alone. Bajaj, *et al.* (363) found acute impairments of renal function in patients with erythema nodosum leprosum, which improved after the reactions subsided. ffytche (365 and 365–366) found that lepromatous leprosy patients had severe visual impairment mainly because of the combined effects of corneal and lens opacities associated with small, non-reacting pupils and iris atrophy. The cause of the "chronic iritis" leading to the iris atrophy is believed to be neuroparalytic from early involvement of the small nerves of the iris, particularly the autonomic supply. The progressive atrophy of the iris preferentially affects the dilator muscle and leads to a non-reacting, meiosed pupil. Cataract surgery with broad iridectomy and inferior sphincterotomy offers these patients with chronic lepromatous complications the best chance of preserving vision. Kaur, *et al.* (366) found that skin smears from the earlobes gave maximum bacteriological and morphological indexes in most lepromatous leprosy patients, although a few cases gave higher values at elbows, fingers, and toes. Ness, *et al.* (366) reported two leprosy patients with a lupus-like inhibitor directed against coagulation factor X. Sun and Chou (367) analyzed 320 Chinese leprosy patients for their earliest symptoms and found that anesthetic macules with dermal color were the most common initial symptoms (46.9% of cases) followed by erythema (18.7%) and hypopigmented macules (14.4%). Yao-De (368) found that 42% of inactive lepromatous leprosy patients with no demonstrable acid-fast bacilli by Wade-Fite staining of skin biopsies were positive by Harada's staining method. Positive findings were most frequent in specimens with degenerated foam cells. Dastur and Porwal (369) reported extensive studies of the light microscopic pathology, histochemistry of lysosomal enzymes, and fine structural changes in the nerves of lepromatous leprosy patients. Gupta, *et al.* (369) found that 75% of 21 lepromatous leprosy patients had histologic lesions in percutaneous renal biopsy specimens. A proliferative type of glomerulonephritis was the most common abnormality noted. Han, *et al.* (370) reported that two injections of transfer factor prepared from lymphocytes from lepromin-positive tuberculoid patients could convert the early, but not the late, lepromin reactions in lepromatous leprosy patients. Kano, *et al.* (370) examined lepromatous leprosy sera for the presence of various antibodies and immune complexes. Circulating immune complexes were demonstrated in 43–54% of patients; these contained predominantly IgG in patients with lepra reactions and predominantly IgM without reactions. Nath, *et al.* (370–371) made the interesting observation that patients with primary neuritic leprosy show a selective, uniform lack of *M. leprae* induced lymphocyte transformation. Ridley

(371) described the ultrastructure of mononuclear phagocytic cells and found a continuous spectrum of macrophage development throughout the spectrum of leprosy. Ridley, *et al.* (371) described variations in the histology of erythema nodosum leprosum lesions which were related to the ethnic background of the patients. Erythema nodosum leprosum may be a complex of reactions whose form may be modified by ethnic factors as well as by the immune status of the patient within the leprosy spectrum. Stoner (372) hypothesize that phases of immunosuppression during infection with *M. leprae* could determine the leprosy spectrum. Asselineau, *et al.* (372) studied the lipid constituents of *M. leprae*. Cholesterol (from the infected host) and the main fatty acids were identified. Mycolic acids were identified and the absence, or at least very low levels, of tuberculosterate was noted. David, *et al.* (372) described the neuropathy and organization of paracrystalline inclusions in *M. leprae*. Janczura, *et al.* (372–373) reported the primary structure of the wall peptidoglycan of leprosy-derived corynebacteria. Wheeler and Gregory (374) also identified superoxide dismutase in *M. leprae* and reported that the bacilli also contained peroxidatic activity. Chaudhary (375) reported a leprosy prevalence rate of 0.5 per thousand in Western Rajasthan in India. Kim (375) estimated the current leprosy prevalence rate in Korea to be approximately 1.3 per thousand. Behere (376) reported the distressing finding that 14 of 24 leprosy patients verbalized suicidal ideas and two had had suicidal attempts. Crovato and Levi (377–378) found that clofazimine 100 mg daily was effective in treating two patients with annular lupus erythematosus.

The original articles in the December issue began with the definitive descriptions of Ridley and Radia (383–392) on the histological course of reactions in borderline leprosy. These reactions appear to represent episodes of delayed hypersensitivity whose eventual outcome cannot be predicted clinically or histologically at the onset. Opromolla, *et al.* (393–397) reported a controlled trial of adding rifampin 450 mg daily or 1200 mg once a month to dapsone 50 mg daily in 35 patients with lepromatous leprosy. The results were practically identical, and no adverse effects were attributable to the once monthly rifampin schedule. Pandya and Chulawala (398–405) reported an interesting *in vitro* electrophysiologic and light microscopic study of segments of sural nerves from patients with leprosy and patients with non-leprous neuropathy. In leprous neuropathy, there appears to be an indiscriminate involvement of all three major nerve fiber groups, the large, fast conducting myelinated fibers, the slower conducting, small myelinated fibers, and the very slow conducting unmyelinated fibers. Kusaka, *et al.* (406–416) reported elegant studies in which mycolic acids from *M. leprae* were isolated and identified by high performance liquid chromatography and mass spectrometry. *M. leprae* characteristically contain α (dicycloprophyl) mycolic acids with an α branch which is 20 carbons in length, suggesting that this microorganism has a special position in mycobacterial phylogeny. α Mycolic acids with the same structure were found in a skin leproma from a leprosy patient, from an *M. leprae*-infected nude mouse foot pad, from the liver of armadillos experimentally infected with *M. leprae*, and from the liver of an armadillo with naturally acquired leprosy-like disease. Four articles appeared by special arrangement with the Scientific Working Group of THELEP in the December issue. Pearson (417–420) reviewed the problem of dapsone resistant leprosy. The THELEP approach to dapsone resistant leprosy was outlined (421–426). Guinto, *et al.* (427–430) reported a survey of the prevalence of primary dapsone resistance in Cebu in the Philippines. Of 58 strains of *M. leprae* from consecutive previously untreated BL-LL patients, one showed partial dapsone resistance, and one showed intermediate resistance by standard mouse foot pad testing, leading to an estimated prevalence of 3.6 per 100 patients at risk. The fourth article in the series was the report of the third meeting of the Scientific Working Group of THELEP in October 1980 (431–436).

In the editorial section of the December issue, we were privileged to have the critical and provocative review of the literature on the genetic regulation of susceptibility in leprosy, tuberculosis, and leishmaniasis

by Fine (437–454). This carefully reasoned reassessment of available evidence provides each of us with an opportunity to reexamine our biases in this traditionally controversial area.

In the correspondence section, Wright and Ranjarajan (455–457) described an interesting technique for *in vitro* priming of human lymphocytes with antigen which results in selection and expansion of clones reactive to the priming antigen. Exciting possibilities for the application of the technique to leprosy were outlined. The view that dapsone 100 mg daily is more responsible for improvement in the peripheral neuritis of reversal reactions than concomitantly administered prednisone was put forward by van der Meulen and Mock (457–458). Naafs (459) remained unconvinced that their retrospective study was definitive, suggested that steroids were indicated in patients with reversal reactions whose nerves deteriorate despite effective antileprosy treatment, and called for a prospective controlled trial.

The news and notes section reported the first Australia-wide meeting on leprosy, attended by a distinguished group of speakers, including Dr. Trevor Smith from Thailand and Dr. Ma Haide from the People's Republic of China (460). The first announcement and call for abstracts for the XII International Leprosy Congress to be held 21–26 November 1983 in New Delhi was noted (460–461). Much deserved honors went to Dr. (Miss) C. Vellut, Dr. K. V. Desikan, and Dr. C. K. Job for their outstanding work in leprosy in India (462). Mr. Ryoichi Sasakawa, President of the Nihon Kensho-Kai Foundation in Japan, gave a plaque of appreciation to Dr. W. F. Kirchheimer for his research with the armadillo in leprosy (464). Dr. Paul Brand and Mr. Philip Pepper received well-deserved awards from the U.S. government (465).

In the current literature section, Browne (468) concluded that leprosy was most convincingly first described in India in the sixth century B. C. Ellard, *et al.* (469) found that only about 60% of Ethiopian leprosy outpatients took their prescribed dapsone regularly. Frey, *et al.* (469) report a fatal "DDS syndrome" in a lepromatous leprosy patient 3 weeks after starting treatment at 100 mg daily. Imkamp (470) reported 10 patients with Type I reactions who did not respond to clofazimine. Sreevasta, *et al.* (470) found viable *M. leprae* by mouse foot pad inoculation 2 years after treating lepromatous leprosy patients with rifampin 300 mg daily for the initial 3 months followed by dapsone 50–100 mg daily for another 21 months (2 years total). Duncan, *et al.* (471) and Duncan, *et al.* (471) in a prospective study pointed out the very substantial risks leprosy patients experience during pregnancy and lactation. Relapses of "cured" tuberculoid patients, increased disease activity, and the development of dapsone resistant disease were markedly more frequent, particularly during the third trimester. Moleres (472) published detailed studies of osteoarticular changes due to leprosy, including cystic osteitis due to specific infection of the bone with *M. leprae*. Gharpuray, *et al.* (472) found reactional granulomatous lesions in the livers of 20 of 21 patients with leprosy in acute reaction. Girdhar, *et al.* (472) reported the disturbing finding that 4.3×10^3 to 4.3×10^4 acid-fast bacilli per ml were present in the milk of untreated lactating female leprosy patients. Nigam, *et al.* (473) made the interesting observation that diabetes mellitus was more common among their leprosy patients, particularly their lepromatous leprosy patients, than in a control population, and that effective antileprosy chemotherapy improved the diabetic status of the patients. Rée, et al. (473–474) found that male lepromatous leprosy patients without obvious testicular atrophy or gynecomastia had significantly elevated FSH and LH in their plasma and significantly lowered plasma testosterone compared to tuberculoid patients. On the other hand, Shilo, *et al.* (474) studied male lepromatous leprosy patients with obvious testicular atrophy and gynecomastia and found increased FSH, a mixed pattern of basal LH levels, and normal testosterone levels, although estradiol 17β and estrone levels were elevated. Singhal, *et al.* (474) found elevated levels of serum alpha-1-antitrypsin in leprosy patients, particularly lepromatous leprosy patients with erythema nodosum leprosum. Sritharan, *et al.* (474–475) noted that untreated lepromatous leprosy patients, and

particularly those with lepra reactions, showed a decreased ability to acidify urine and to excrete foreign dye as well as a drop in glomerular filtration rate. Artz, *et al.* (475) presented experimental evidence that either dysfunction or a reduction of the Con A-inducible T-suppressor cell subpopulation in peripheral blood is frequent in patients with disseminated mycotic or mycobacterial infections. Bach, *et al.* (475–476), in elegant work, studied T-cell subsets and T cell functions in leprosy patients and found that lepromatous patients with recent erythema nodosum leprosum had decreased percentages of suppressor T cells and increased proportions of helper T cells compared to lepromatous patients without erythema nodosum leprosum. It was suggested that this imbalance between T cell subsets contributes to the occurrence of erythema nodosum leprosum in lepromatous patients. Løvik and Closs (477–478) pointed out the marked discrepancy between delayed type hypersensitivity to soluble bacillary antigens and resistance to infection in murine leprosy, an observation of considerable potential relevance in mycobacterial vaccine development. Shannon, *et al.* (478) presented evidence suggesting that inhibition of IgM antibody synthesis by thalidomide might be a relevant mechanism of action of the drug in erythema nodosum leprosum. Smelt, *et al.* (478–479) found that essentially bacteriologically negative lepromatous leprosy patients could not be sensitized by killed armadillo-derived *M. leprae*. When immunized with a mixture of live BCG and killed *M. leprae*, delayed hypersensitivity to only PPD developed. They concluded that the immunologic unresponsiveness of lepromatous leprosy patients is antigen-specific and non-reversible. Smelt, *et al.* (479) successfully immunized healthy volunteers with 2×10^8 killed armadillo-derived *M. leprae* and found no better sensitization was obtained with a mixture of live BCG and killed *M. leprae*. It was suggested that killed armadillo-derived *M. leprae* may be a candidate for an effective antileprosy vaccine. Tarabini-Castellani, *et al.* (479) demonstrated that BCG vaccination results in a higher proportion of positive Mitsuda reactions than in unvaccinated individuals. Tarabini-Castellani, *et al.* reported the interesting finding that, in two young women who had had three successive negative lepromin skin tests, administration of a mixture of BCG and lepromin was followed by conversion of the lepromin test to highly positive. Lepromatous leprosy patients were treated with BCG by Villa, *et al.* (480–481) and the Mitsuda test became positive in six of the seven patients treated. Impressive biochemical studies of the energy coupling mechanisms of *in vivo* grown *M. lepraemurium* were reported by Ishaque, *et al.* (481). Portaels (481–482) described three new groups of mycobacteria isolated from the environment in Zaire; five of these strains were very sensitive to dapsone and may be useful in studies concerning the mechanism of action of dapsone. Curtis, *et al.* (482) pointed out the discrepancy between equivalent tests of delayed hypersensitivity and marked differences in the ability to limit the spread of *M. lepraemurium* in C57BL and BALB/c mice. Nsanzumuhive, *et al.* (483–484) made an interesting comparison of five methods of case-finding in tuberculosis in Kenya which could possibly be useful in leprosy. Approximately 5% of the suspected cases identified by Community Elders actually were cultured as positive cases. Brand, *et al.* (484) prepared a list of the relative tension capacities of forearm and hand muscles which should be of practical use in planning tendon transfer operations. Chauhan and Dhar (484–485) studied the personality characteristics of children with leprosy and found that they have high anxiety levels and a general need for affection, security, affiliation, and cooperation. Frimodt-Moller, *et al.* (486–487) made the discouraging observation that a domicilliary treatment program failed to have an impact on the prevalence of tuberculosis in a rural community in South India. Patra, *et al.* (488) suggested that a serum albumin/alpha$_2$ globulin ratio of less than 2 should arouse suspicion of amyloidosis in pulmonary tuberculosis patients. Seth and Srinivas (488) recommended a simple and rapid test for the detection of circulating immune complexes based on the selective precipitation of antigen-antibody complexes by polyethylene glycol 6000.

The December issue contained the ab-

stracts of the U.S.-Japan Cooperative Medical Science Program's Sixteenth Joint Leprosy Research Conference held in July in Bethesda, Maryland. Fukunishi, *et al.* (499) analyzed the spherical droplets associated with *M. leprae* in infected macrophages *in vivo* and found lipid components with estimated molecular weights of 1600, 1150, 500, and 300. Fieldsteel and Colston (499–500) showed that intact mice can be injected with small numbers of viable *M. leprae* mixed with large numbers of dead organisms, and 6 months later the bacilli passaged from their foot pads will show multiplication in new intact mice. Further experiments suggested that *M. leprae* might multiply in the foot pads of neonatally thymectomized Lewis rats after the inoculation of a single organism. Myers, *et al.* (500–502) reported further details of *M. leprae* infections in mangabey monkeys. There was progressive disease with peripheral neuropathy in the first animal which had spontaneously developed the disease. The bacilli from this index animal have been passaged to other mangabey monkeys, mice, and armadillos. Nakamura (502) found that vitamins B_6, B_{12}, K_3, and PABA stimulated the *in vitro* growth of *M. lepraemurium*. Kvach and Veras (502) described an interesting fluorescent staining technique which may be useful in determining the viability of mycobacterial cells, including *M. leprae*. Dhople, *et al.* (502–503) measured the ATP content of *M. leprae* from a variety of host tissues and found 1.2–1.4 picograms of ATP per 10^6 bacterial cells. *M. lepraemurium* from infected mouse liver contained twice this amount of ATP. *M. leprae*, in contrast to *M. lepraemurium*, did not appear to acutely lose ATP *in vitro*. Abe, *et al.* (503–504) reported additional studies of the epidemiology of leprosy utilizing the fluorescent leprosy antibody absorption (FLA-ABS) tests and lepromin tests. Early signs compatible with leprosy, such as enlargement of a peripheral nerve, were significantly related to positive FLA-ABS tests in asymptomatic school children in Okinawa. Gillis and Buchanan (506) reported the development of 12 separate clones of hybridomas producing monoclonal antibodies reacting with *M. leprae*, two of which did not react with 15 other mycobacterial species. Hunter and Brennan (504–506) isolated a pure glycolipid from serologically active *M. leprae* extracts which was found to be a phenolic glycolipid closely related to the mycosides A, B, G, from other mycobacteria but whose sugar composition is unique and probably exclusive to *M. leprae*. This glycolipid represented a high proportion of the mass of *M. leprae*, was excreted in large amounts into infected host liver tissue, and may be responsible for the electron-transparent "foam" which characteristically surrounds *M. leprae* in infected tissue. Quesada-Pascual, *et al.* (506) developed methods to identify and quantitate contaminating armadillo liver tissue in purified preparations of *M. leprae* from that source. Miller and Buchanan (506–507) developed an enzyme-linked immunosorbent assay (ELISA) to detect antibodies directed against a carbohydrate antigen of *M. smegmatis* composed predominantly of arabinomannan and found that 67% of leprosy patients and 7.2% of their household contacts had abnormally elevated titres. Katoh and Matsuo (507) found that *in vitro* infection of mouse peritoneal macrophages with *M. leprae* was followed by a significant decrease in lysosomal enzyme activities in these cells, in contrast to the effects of other mycobacteria tested. Kohsaka, *et al.* (508–509) found data suggesting that dapsone was ineffective in preventive and therapeutic studies of the chemotherapy of leprosy in infected nude mice. Additional studies have shown that the *M. leprae* strain used in the therapeutic study was sensitive to dapsone but that the strain used in the preventive study was resistant to dapsone. Jacobson (510) reviewed his experience with clofazimine in the management of leprosy patients and warned of the possibility that current trends toward the use of low doses of the drug may favor the development of clofazimine resistant *M. leprae*. Morrison (510–511) reported that one of a series of new 2-acetyl-pyridine thiosemicarbazones, compound 2P, was bactericidal for *M. leprae* in mouse foot pad infections. A small number of methylene blue positive rods were found to occur when multiplication of acid-fast bacilli was occurring in thiosemicarbazone treated an-

imals. This loss of acid-fastness may result from inhibition of mycolic acid synthesis in the bacilli.

Piper, *et al.* (511–512) and Agrawal, *et al.* (512) reviewed results of screening thalidomide analogs for anti-inflammatory and immunosuppressive activities and presented structure-activity relationships for these compounds. Krahenbuhl and Humphres (512–514) studied natural killer (NK) cell activity in mice infected in the foot pads with *M. marinum* or *M. leprae* and in mice vaccinated in the foot pads with killed *M. leprae*. NK cell activity was increased in draining popliteal lymph node cells 10 or 17 days after food pad infections with *M. marinum* but not in the same cell population in other animals 136–138 days after foot pad infections with *M. leprae*. Foot pad immunization with 10^7 heat killed armadillo-derived *M. leprae* caused marked elevations in NK cell activities in draining popliteal lymph nodes 28 days later. Humphres, *et al.* (514) found that natural killer (NK) cell activities in peripheral blood mononuclear cells were significantly reduced in lepromatous leprosy patients with erythema nodosum leprosum compared to normal subjects or uncomplicated lepromatous leprosy patients. Bullock, *et al.* (515) found that more peripheral blood leukocytes from lepromatous leprosy patients produced immunoglobulin than did cells from normal donors when stimulated *in vitro* with pokeweed mitogen. This B lymphocyte hyperactivity in patients with lepromatous leprosy appears to be due to a deficiency of T-suppressor regulation over helper T cell activity and/or B cell function. Mehra, *et al.* (515–516) extended their studies of antigen-specific suppressor cells in lepromatous and borderline leprosy patients. The suppressor T cells belonged to a TH_2 +, Ia^+ subset. Measurements of Ia-like determinants on the TH_2 + subset of T cells may be an index of the degree of *in situ* activation of suppressor cells. Rea and Yoshida (516–517) studied migration inhibitory activity in the serum of leprosy patients. Inhibitory activity was heat stable, not dialyzable, and had a molecular weight of between 10,000 and 30,000 Daltons. It was significantly more common in all types of leprosy patients than in healthy controls and was particularly common in patients with reactions, both erythema nodosum leprosum and reversal reactions.

Clearly, once again in 1981, a great deal of information has appeared in the pages of the JOURNAL, and again, much of it has immediate relevance to our work. From a personal perspective, a number of general trends appear to be continuing and newer directions appear to be emerging.

The history of the development of the International Leprosy Association on the occasion of the 50th Anniversary of the Leonard Wood Memorial Conference on Leprosy in Manila in January 1931 was brilliantly reviewed in 1981. The Prime Minister of India, Mrs. Indira Ghandi, launched a campaign to eradicate leprosy from India by the year 2000.

In leprosy chemotherapy, numerous reports have appeared from all over the world of poor patient compliance with prescribed dapsone treatment. Dapsone resistant *M. leprae*, both secondary resistance and primary resistance, continue to be reported from many parts of the world. Emphasis continues on multi-drug regimens for multibacillary disease, usually involving dapsone plus various schedules of rifampin. A number of rare side effects of dapsone have been reported in 1981.

In the clinical sciences, there have been a number of excellent clinical descriptions and observations. Sometimes subtle renal damage in lepromatous patients, particularly those with erythema nodosum leprosum, seems more common than previously thought. Emphasis has been placed on studies of hormonal changes in male lepromatous patients. Pregnancy seems to pose a greater risk to female leprosy patients than was previously thought. There may be a neuroparalytic etiology of the iris atrophy which is unfortunately so commonly seen in long-standing lepromatous leprosy patients. Erythema nodosum leprosum may be associated with alternate pathway complement activation. Lepromatous patients have serum factors which inhibit the migration of both neutrophils and monocytes. Excellent studies of the neuropathy of leprosy in mice and humans have been reported this year.

Further refinements have been made in

the search for a leprosy vaccine as to the immunogenicity of *M. leprae* for mice and humans. Combinations of BCG plus *M. leprae* may immunize, or at least sensitize, normal individuals with persistently negative lepromin skin tests, although apparently this combination will not sensitize inactive lepromatous leprosy patients to *M. leprae*. Distinctions between delayed type hypersensitivity and resistance to infection in murine leprosy have been emphasized and could be relevant to vaccine development. The possibility that two types of delayed type hypersensitivity to mycobacteria exist, and only one may be related to protective immunity, has been put forward. Controversy continues as to suppressor phenomena in leprosy. Evidence has been put forward that macrophages are suppressive in lepromatous leprosy; that suppressor T cells are decreased in lepromatous patients compared to tuberculoid patients; and that lepromatous patients with erythema nodosum leprosum seem to have decreased suppressor T cells compared to uncomplicated lepromatous cases. Lepromatous patients seem to have decreased T-suppressor cells acting on helper T cells and/or B cells in *in vitro* immunoglobulin synthesis. Others continue to find increased suppressor T cell activities in lepromatous leprosy patients compared to tuberculoid patients. Excellent work continues in a number of centers on the antigenic analysis of *M. leprae*, applying more and more sophisticated serologic techniques. Several groups are applying serologic tests for field epidemiologic studies with a continuing pattern of relatively high frequencies of infections with *M. leprae* resulting in relatively few overt clinical cases.

In microbiology, there has been an enormous amount of progress by a number of groups in isolating, analyzing, and identifying lipid components of *M. leprae*. A variety of additional enzymatic activities of the bacillus have been identified as well as further studies of its ATP content. *M. leprae* have been shown to be present in large quantities in human milk from lactating women with active lepromatous leprosy, to be shed from intact skin, and to provide an antigenic stimulus to fetuses of lepromatous mothers *in utero*.

In the perspective of the JOURNAL, 1981 offered considerable progress in many areas in leprosy, continuing frustrations in others. In virtually all areas, however, the pace of the work seems to be quickening. How much longer can *M. leprae* withhold its secrets? I look forward with impatient optimism to 1982.—RCH