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The 1987 JOURNAL—a Continuing Perspective

Nineteen eighty-seven was another year of steady progress in leprosy research. Multidrug therapy is being applied more and more widely. New antibacterial drugs are being developed. The basis for this generation of field trials of antileprosy vaccines has been set and the groundwork for the next generation vaccines is being laid. The upcoming XIII International Leprosy Congress in September at The Hague promises to be an exciting demonstration of the remarkable progress we have made in the last 5 years. It again seems appropriate to review the new information available to us as reflected in the pages of the 1987 JOURNAL.

The Original Articles of the March issue began with Katoch, *et al.* (1–8)* who found that dapsone 100 mg daily for 1 year plus rifampin 600 mg monthly for the first 6 months was superior to dapsone and rifampin in the same doses for 6 months in the treatment of paucibacillary leprosy patients. Schaad-Lanyi, *et al.* (9–15) studied the pharmacokinetics of clofazimine in healthy volunteers. Absorption was enhanced when the drug was taken with food; clofazimine is eliminated slowly with a half-life of approximately 10.5 days. To rapidly reach a steady state concentration, higher daily loading doses followed by a daily maintenance dose are recommended. Sebille, *et al.* (16–22) presented neurophysiologic evidence that at least 25% of tuberculoid leprosy patients treated with dapsone monotherapy developed a dapsone-induced neuropathy which compounded the nerve damage due to leprosy. Sirsat, *et al.* (23–29) presented three cases who developed, subacutely, progressive motor neuropathy following excessive doses of dapsone for several months. Gill, *et al.* (30–35) followed the lymphocyte transformation test in healthy, tuberculin-positive volunteers following immunization with armadillo-derived, heat-killed *Mycobacterium leprae* intradermally. At the highest doses of the vaccine, 1.5×10^8 and 5.0×10^8 bacilli, strong lymphoproliferation in response to *M. leprae* antigens developed 3 months after vaccination and persisted for 12 months. Rao and Rao (36–41) showed statistically significant reductions in leukocyte migration *in vitro* in the presence of whole *M. leprae,* but not *M. leprae* sonicate, in erythema nodosum leprosum (ENL) patients compared to uncomplicated lepromatous patients. Sinha, *et al.* (42–53) sensitized guinea pigs and mice with autoclaved and unautoclaved integral preparations of *M. leprae, M. tuberculosis, M. vaccae,* and BCG, and challenged the animals by skin testing 4 weeks later with a variety of antigens and antigenic fractions from these mycobacteria. Autoclaved *M. leprae* and *M. vaccae* were better sensitizers than their native counterparts. Two *M. leprae* antigens, a 12 kD protein designated MY1, prepared by affinity chromatographic purification of soluble *M. leprae* antigens with the monoclonal antibody designated ML06, and a 35 kD protein, designated MY2, prepared similarly with a monoclonal antibody designated ML04, were not active. The soluble *M. leprae* antigen preparation from which the 12 kD and 35 kD proteins had been removed was active. Gillis and Job (54–62) purified the 65 kD cell-wall-associated protein of *M. gordonae* and showed that it was capable of eliciting delayed-type hypersensitivity (DTH) skin-test responses in guinea pigs immunized with *M. leprae, M. gordonae,* and BCG. Richard, *et al.* (63–69) studied specific suppressor cells in the spleens of C3H mice 4 months after intravenous (i.v.) infection with *M. lepraemurium* by adoptive transfer experiments. The radio-sensitive Lyt 1+, 2+ cell suppressed the induction of DTH reactions and a radio-resistant Lyt 1+, 2− cell suppressed the expression of the DTH cutaneous reaction. Guelpa-Lauras, *et al.* (70–77) demonstrated the activity of pefloxacin against *M. leprae* in mouse foot pad infections, pointing out the need for controlled clinical trials of pefloxacin or other fluoroquinolones in lepromatous patients. Gelber (78–82) demonstrated the activity of streptomycin and kanamycin in mouse foot pad infections with

* Numbers in parentheses refer to page numbers in the INTERNATIONAL JOURNAL OF LEPROSY, Volume 55, 1987.

M. leprae using the proportional bactericidal method. Luderschmidt (83–87) applied a methylene blue-borax and basic fuchsin technique to demonstrate *M. leprae* in plastic-embedded, semithin sections allowing an exact demarcation of the subsequent ultrathin area for electron microscopic study. McDougall, *et al.* (88–98) described histopathologic findings in 686 biopsies in a total population survey for leprosy in Northern Malawi together with clinical findings and correlations. Ridley, *et al.* (99–108) undertook detailed histopathologic and immunocytochemical studies of peripheral nerves across the leprosy spectrum in untreated, nonreacting patients. Microreactions were frequent, except in lepromatous leprosy (LL), and were thought to be local responses to the recognition of mycobacterial antigen. Baskin, *et al.* (109–115) presented necropsy findings from a rhesus monkey with generalized lepromatous leprosy. The animal was inoculated with *M. leprae* from a naturally infected mangabey monkey 56 months before sacrifice.

In the Editorial section of the March issue, Maier (116–139) comprehensively reviewed allergy or DTH and cell-mediated immunity (CMI) in leprosy. Hastings (140–156) reviewed the contents of the 1986 JOURNAL.

In the Correspondence section of the March issue, Kato (157–159) highlighted several early European monographs on leprosy. Srinivas, *et al.* (159–160) reported a patient with a hypopigmented tuberculoid lesion which repigmented satisfactorily following treatment with photoactivated 8-methoxypsoralen. Chevallard (160–162) described a simplified surgical technique for patients with a flexible claw-hand deformity. Kumar, *et al.* (162–164) studied the lipid composition of skin biopsies from untreated leprosy patients across the spectrum and found that phospholipids and triglycerides were elevated in borderline lepromatous and lepromatous leprosy biopsies.

In the Current Literature section of the March issue, Bhate, *et al.* (172) compared two regimens of multidrug therapy (MDT) in paucibacillary patients. Many cases required more than 6 months of treatment. Dhople and Green (172) used ATP measurements and ^{3}H-thymidine uptake by *M. leprae in vitro* to demonstrate the sensitivity of the bacilli to dapsone. Chattopadhyay and Gupta (173) reported interesting improvements in 30 patients varying from lepromatous to borderline tuberculoid (BT) following 12 weeks of immunotherapy with preparations of autologous skin. George, *et al.* (174) found thyroglobulin antibodies in 6 of 182 sera from LL patients and 5 of 24 sera from LL patients with ENL. Gupta, *et al.* (174) showed that antispermatozoal antibodies were higher in lepromatous patients than in tuberculoid patients and increased in proportion to the duration of the disease in both types of disease. Jain, *et al.* (175) found a variety of autoantibodies in LL patients and in ENL patients. None of these had any corresponding clinical expression. Jain, *et al.* (175) applied histamine in dimethyl sulfoxide to leprosy lesions and showed a transient improvement in pain and touch sensation. Rohatgi, *et al.* (175–176) reviewed uveal tract involvement which was found in 11.2% of the eyes in a series of 424 leprosy patients. Singh (176) described a retinal lesion occurring in a lepromatous patient. Ashworth, *et al.* (176) found that 6% of healthy household contacts of known leprosy patients were antibody positive using a monoclonal-antibody-based competition radioimmunoassy. Gumaraes Proenca, *et al.* (177) found that the Mitsuda test was negative in 86% of sarcoidosis patients compared to 15% of controls. Kumar, *et al.* (178) described a visual dipstick dot enzyme immunoassay for the detection of IgM antibodies against phenolic glycolipid-I (PGL-I) in sera. Modlin, *et al.* (179) developed T8-positive lymphocyte cell lines from skin biopsy specimens of patients with leprosy. Dhople (179) found that counts of *M. leprae* increased if the bacterial smear was treated with periodic acid prior to staining with the Ziehl-Neelsen (ZN) technique, and speculated that there were chromophobic *M. leprae* which are not stained by the routine ZN technique which may exist in treated leprosy patients. Hunter, *et al.* (179–180) isolated a family of major arabinose- and mannose-containing phosphorylated lipopolysaccharides from *M. leprae* and *M. tuberculosis.* The only antigenic member of the family, lipoarabinomannan-B (LAM-B), was recovered in large quantities. LAM-B was found to be one of the dominant immu-

nogens of the leprosy bacillus reacting readily with antibodies from lepromatous patients. It is immunologically crossreactive with a like product from *M. tuberculosis.* Lee and Colston (180) used the adenylate energy charge (AEC) (ratio of the mole fraction of ATP plus half the mole fraction of ADP in the total adenine nucleotide pool) to monitor the effects of culture conditions on *M. leprae.* Portaels, *et al.* (180) extensively studied 17 strains of mycobacteria recovered from six armadillos experimentally infected with *M. leprae.* These armadillo-derived mycobacteria fell into five groups and were clearly different from *M. leprae.* Prabhakaran, *et al.* (181) speculate that dapsone resistance in *M. leprae* must represent a genetic change since the bacilli retain full dapsone resistance when passaged for nearly 2 years in mice that are not fed the drug. Walsh, *et al.* (181–182) reviewed the status of naturally acquired leprosy in the nine-banded armadillo in Louisiana and Texas in the U.S.A. Wang, *et al.* (182) found that hibernating hedgehogs were more susceptible to infection with *M. leprae* intravenously than nonhibernating animals. Job, *et al.* (182–183) studied ear and nose specimens from a large number of wild nine-banded armadillos. In one armadillo there was evidence to suggest that *M. leprae* entered the tissue through a thorn prick. Kim, *et al.* (183) typed leprosy patients and healthy controls for HLA antigens. Neelan, *et al.* (183) found that three injections of acedapsone at 10-week intervals was 57% effective in preventing leprosy among household child contacts of multibacillary cases. Ponnighaus and Boerrigter (183) presented data indicating a decline in leprosy incidence, a trend toward higher lepromatous rates, and a shift in the age distribution of new leprosy patients toward older age groups in Malawi. Smith and Parkhe (184) suggest that the most relevant method of assessing progress in leprosy control programs may not be changes in the prevalence of the disease but rather the prevalence of disability. Birke and Sims (184) identified the level of protective sensation for the plantar aspects of the feet in leprosy patients using Semmes-Weinstein monofilaments. Jagirdar (185) suggested that acupuncture might be useful in the management of certain aspects of leprosy. Collins and Uttley (185) tested 276 strains of mycobacteria for susceptibility to ciprofloxacin and found that many strains were sensitive to low concentrations of the drug. Douvas, *et al.* (186) found that recombinant gamma-interferon enhanced the replication of *M. tuberculosis* in macrophage cultures *in vitro.* Mustafa and Godal (187) found that *in vitro* activation of T cells from healthy individuals vaccinated with BCG by BCG leads to the induction of suppressor cells that suppress the proliferation of fresh T cells in response to BCG. van Eden, *et al.* (188) produced a T-lymphocyte clone from rats induced by immunization to *M. tuberculosis* which recognized both *M. tuberculosis* antigens and the proteoglycan component of cartilage. Wallis, *et al.* (188–189) found that mycobacterial protein antigens directly stimulate monocytes to release interleukin-1 (IL-1). This phenomenon may be central to the response of the naive host to mycobacterial infection. Young and Lamb (189) described a technique to separate complex antigen mixtures by polyacrylamide gel electrophoresis followed by transfer to a nitrocellulose membrane, fractions of which are used to directly screen individual polypeptides in T-cell proliferation assays.

In the Original Articles of the June issue, Locniskar, *et al.* (249–260) studied the responsiveness of peripheral blood mononuclear cells (PBMC) from leprosy patients to *M. leprae* antigens *in vitro.* Cells from tuberculoid patients showed a robust response to *M. leprae* and lepromin but were unresponsive to PGL-I delivered in liposomes. Cells from lepromatous patients did not respond to any of the three antigens. Recombinant IL-2 caused antigen nonspecific augmentations of proliferation over a wide range of doses. Neither sonicated *M. leprae,* Dharmendra lepromin, nor PGL-I suppressed the concanavalin A (ConA)-induced proliferation of PMBC from patients. Ottenhoff, *et al.* (261–266) found that there were no significant differences in distribution of HLA class I and class II antigens among BT patients with a history of reversal reactions, BT patients with no history of reversal reactions, and healthy individuals. These findings do not support the hypothesis that HLA Ir genes might control the development of reversal reactions. Schuller-Levis, *et al.* (267–272) studied monocyte chemo-

taxis in leprosy patients and found that chemotaxis was inversely correlated with bacterial index and with serum levels of anti-PGL-I IgM antibodies. Naik, *et al.* (273–276) tested leprosy sera for the presence of cold-reacting lymphocytotoxic antibodies. Although 32% of the leprosy sera and 67% of the control sera showed reactivity, the strength of the reactivity of the leprosy sera was significantly higher than that of the control group. These cold-reacting lymphocytotoxic antibodies could play an immunoregulatory role in leprosy. Rawlinson, *et al.* (277–285) studied serologic changes in inactive Australian aboriginal leprosy patients, aboriginal family contacts of leprosy patients, and European sporadic contacts. Levels of acute-phase reactants such as C-reactive protein, serum globulins, and autoantibodies were comparable between leprosy patients and their family contacts. Amezcua, *et al.* (286–292) tested a variety of sera for antibodies to *M. leprae* by the FLA-ABS test of Abe. Ninety-nine of 100 sera from LL patients and 108 of 123 household contacts of leprosy patients were positive while none of 215 of various controls were positive. Orme (293–298) studied the generation of acquired immunity to BCG in mice compared to that generated in animals receiving a mixture of BCG and killed *M. leprae.* No significant qualitative differences were observed. Job, *et al.* (299–304) found that 100 μg of PGL-I in 0.1 ml of normal saline produced a positive DTH granuloma at 21 days in lepromin-positive armadillos and negative responses in lepromin-negative animals. Hoffenbach, *et al.* (305–315) studied anti-*M. lepraemurium* IgG and IgM antibody production in C57BL/6 mice inoculated intravenously or subcutaneously (s.c.) with *M. lepraemurium.* Mice inoculated i.v. developed high and predominantly IgM antibody responses with heavily disseminated infections while s.c. inoculated mice developed relatively higher IgG antibodies and a more controlled infection. Harshan, *et al.* (316–321) correlated the ability of *M. leprae* to take up the ^{3}H-thymidine inside murine peritoneal macrophages in culture and the proportion of the bacilli which stained green (including those which showed dual fluorescence) with the fluorescein diacetate/ethidium bromide method. Significant linear correlations were found when comparing the ^{3}H-thymidine uptake with either the absolute numbers per ml or the percent of green bacilli. Shepard, *et al.* (322–327) evaluated a number of beta-lactam antibiotics against *M. leprae* infections in the mouse foot pad by the kinetic method and found that 7-aminocephalosporanic acid, cefuroxime, and cefoxitin showed activity. Bharadwaj, *et al.* (328–332) studied the ultrastructural morphology of lysosomes in skin biopsies from leprosy patients using acid phosphatase as the marker enzyme. Lysosomal morphology was well maintained in the macrophages of tuberculoid, borderline tuberculoid, and borderline tuberculoid leprosy in reaction, but their morphology and membrane integrity was lost in lepromatous leprosy and in lepromatous leprosy in reaction. Gibbels, *et al.* (333–337) enumerated myelinated nerve fibers and unmyelinated fibers in a sural nerve biopsy from a LL patient. The findings suggested a combination of segmental demyelination with Wallerian degeneration of myelinated fibers and a loss of genuine unmyelinated fibers together with considerable regenerative activity of both fiber populations. Fleury and Bacchi (338–344) showed that the use of the immunoperoxidase technique for the detection of S-100 protein to visualize peripheral nerves represents an efficient auxiliary aid in the diagnosis of tuberculoid leprosy.

In the Editorial section of the June issue, Ell (345–350) reviewed the course of plague and leprosy in the Middle Ages in Europe and concluded that the disappearance of leprosy from Western Europe was not due directly to the plague epidemics which began in 1347. Plague probably hastened the decline of leprosy in other ways, especially through the neglect of hospitalized patients.

In the Correspondence section of the June issue, Rada S., *et al.* (351–353) showed that in their LL patients IL-1 and IL-2 were not able to restore lymphocyte proliferation in response to *M. leprae.* In some LL patients, IL-2 had a nonspecific mitogenic effect. Gelber and Mohagheghpour (353–354) reported that a previously described patient with untreated nodular lepromatous leprosy with rare *M. leprae* in the lesions showed marked lymphoproliferative response to *M. leprae in vitro.* Srinivas, *et al.* (355–357) found that topical corticosteroids under occlusive

dressings are effective in suppressing the manifestations of reversal reactions in skin lesions. Asensio, *et al.* (357–358) showed that the slow isoniazid (INH)-acetylator phenotype predominated among 47 diabetic leprosy patients and was significantly higher than that seen among nondiabetic leprosy patients, diabetic patients without leprosy, or patients with pulmonary tuberculosis. The authors propose that dapsone may have an undescribed diabetogenic effect manifesting itself in slow INH-acetylator leprosy patients. Kaur, *et al.* (358–361) administered preformed immune complexes of sonicated *M. leprae* and rabbit anti-*M. leprae* antibodies intravenously to mice with foot pad infections with *M. leprae.* When given simultaneously with the *M. leprae* inoculation in the foot pad, these immune complexes resulted in more dissemination of the infection. Kato (361–362) obtained growth of an acid-fast organism with some of the characteristics of *M. leprae* from *M. leprae*-infected armadillo tissue inoculated onto agar slants prepared with a multifactorial culture medium which included sonicated and autoclaved *M. phlei.*

In the News and Notes section of the June issue, the initiation in India of the mass vaccination studies of the Cancer Research Institute antileprosy vaccine was noted (364). The retirement of Dr. Paul W. Brand from his position as Chief, Rehabilitation Branch at Carville and his being awarded the U.S. Surgeon General's Medallion were noted (368).

In the Current Literature section of the June issue, Shu, *et al.* (370) discuss leprosy control from the interesting point of view of cost benefit ratios. Gonzalez, *et al.* (371) found partial dapsone resistance (at 0.0001% dapsone in the mouse diet) in approximately 7% of new leprosy patients surveyed for primary dapsone resistance in Cuba. Gopalakrishnan (371–372) analyzed the reasons for dropouts during the treatment of leprosy in South India. Krishna, *et al.* (372) found that blood levels, half-lives, and areas under the plasma concentration curves of dapsone were significantly reduced when it was administered along with daily rifampin. Pattyn (373) showed in mouse foot pad infections that single doses of rifabutin and rifapentine are eight times more active against *M. leprae* than rifampin. Venkatesan, *et al.* (373) studied the effect of clofazimine on the pharmacokinetics of rifampin and dapsone and found no significant effects in leprosy patients. Zuidema, *et al.* (374–375) reviewed the clinical pharmacokinetics of dapsone. Anandaraj (375) studied the psychosocial aspects of drug default in leprosy and concluded that improved health education can yield considerable benefits in this area. Chattopadhyay, *et al.* (376) found a modified pilocarpine test to be simple and useful in the early diagnosis of leprosy. Rao, *et al.* (377) concluded that the moderate undernutrition observed in LL patients was associated with poverty and deprivation of food and not with the disease itself. Rao and Saha (377) found that LL patients have significantly low serum levels of zinc, calcium, and magnesium and increased copper in comparison with healthy control subjects. Singh, *et al.* (377–378) studied untreated leprosy patients of various types and found various urinary tract abnormalities. Ye, *et al.* (378) showed that over half of untreated multibacillary leprosy patients had demonstrable bacteremia in the range of 3–10 $\times$ 10^4 bacilli per ml. Arruda, *et al.* (378) found no effect of thalidomide on serum levels of immunoglobulins IgM and IgA, rheumatoid factor or isohemagglutinins anti-A and anti-B when administered to a group of 45 LL patients at a dose of 100 mg daily for 18 days. Barnass, *et al.* (379) showed an enhancement of the lymphoproliferative response to mycobacterial antigens by IL-2 using cells from LL patients, but this effect was found in a minority of the patients; it was not specific to *M. leprae* and it could occur with cells from normal donors. Britton, *et al.* (379) studied a cell-wall fraction of *M. leprae* which was potent in activating immune T cells. Utilizing a panel of monoclonal antibodies, the dominant immunogen in this preparation was shown to be a complex of proteins with apparent molecular weights of 50–65 kD. Chatterjee, *et al.* (380) described the synthesis of the natural disaccharide-octyl-bovine serum albumin and showed excellent sensitivity and specificity, making this neoglycoprotein highly suited to replace the native PGL-I antigen for studies of the serology of leprosy. Chiplunkar, *et al.* (380) prepared T-cell clones from mice immunized intradermally with *M. leprae.* T-cell

clones as well as native Lyt 2+ T cells from *M. leprae*-immunized mice were capable of lysing bone marrow macrophages expressing *M. leprae* antigens. These findings suggest that specific Lyt 2+ T cells participate in the immune response to *M. leprae* and further suggest that cytolysis of *M. leprae*-infected host cells may play a role in the immunology of leprosy. Cree and Beck (381) showed that killed *M. leprae* reduced the chemiluminescence of both neutrophils and monocytes phagocytizing opsonized zymosan *in vitro*. Itty, *et al.* (381) studied the adherence of *M. leprae* to mouse Schwann cells in culture and found evidence that the receptors involved in adherence may be lipid. Levis, *et al.* (381–382) found in general that serum levels of IgM antibodies to PGL-I, IgG antibodies to PGL-I, the number of *M. leprae* antigens detected by Western blots by IgG antibodies, and levels of antibody to the 65 kD antigen of *M. leprae* were all positively correlated with the bacterial index (BI) of skin biopsies in leprosy patients. Lindh, *et al.* (382) showed that *M. leprae* do not induce peripheral blood cells from lepromatous patients to produce gamma-interferon but do so with cells from borderline tuberculoid patients. Liu, *et al.* (382) described ultrastructural changes and reduced numbers of Langerhans' cells in the skin lesions of borderline patients. Mehra, *et al.* (382–383) described the recombinant DNA expression strategy used to deduce the amino-acid sequences of six different antigenic determinants on the 65 kD antigen of *M. leprae*. A peptide containing the amino-acid sequence to the *M. leprae*-specific determinant was synthesized and shown to bind the corresponding monoclonal antibody. Millikan, *et al.* (383) found that 1.5×10^8 killed, purified armadillo-derived *M. leprae* were safe and had acceptable local reactions in normal volunteers when injected intradermally. Mohagheghpour, *et al.* (383) found that helper T cells (CD4+ cells) from most lepromatous patients' peripheral blood would respond to *M. leprae* after having been cultured for 48 hr but that these cells from most lepromatous patients would not respond when they were fresh. Nelson, *et al.* (384) studied peripheral blood lepromin-induced suppression of the ConA response across the leprosy spectrum. Significant suppressor activity was seen in 15 of 15 untreated or recently treated lepromatous patients, 3 of 5 borderline lepromatous, 10 of 14 treated lepromatous, only 2 of 27 patients with active or thalidomide-controlled ENL, 5 of 29 tuberculoid, 1 of 6 patient contacts, and 0 of 11 normal controls. Olcen, *et al.* (384) followed the urinary excretion of *M. leprae* antigens during treatment in lepromatous patients. Ottenhoff, *et al.* (384–385) studied the HLA class II restriction determinants' repertoire of 36 *M. leprae*-reactive, helper T-cell clones. The majority of the restriction determinants for *M. leprae* were on DR and not on DP or DQ molecules. This suggests that DR molecules are the main products of *M. leprae*-specific Ir genes. Prasad, *et al.* (385) found that the PGL-I antigen of *M. leprae* markedly suppressed the ConA responses of peripheral blood mononuclear cells in both lepromatous and tuberculoid patients. Sibley and Krahenbuhl (386) showed that *M. leprae*-burdened macrophages isolated from the foot pad granulomas of infected nude mice are refractory to activation with gamma-interferon. Uyemura, *et al.* (386) studied *M. leprae*-induced suppressor cell activity in patients with ENL and found a loss in suppressor cell function. In 24 of 25 patients, cyclosporine A (CsA) restored this activity *in vitro*. Dhariwal, *et al.* (387) detected trehalose-6-monomycolate (TMM), but not trehalose dimycolate or cord factor, from armadillo-derived *M. leprae*. Hall and Ratledge (387) isolated exochelins from cultures of *M. neoaurum* and an armadillo-derived mycobacteria grown in iron-deficient media and showed that they could transport iron into suspensions of *M. leprae*. Since no iron uptake occurred into iron-sufficient armadillo-derived mycobacterial cells, this may mean that the *M. leprae* were growing in an iron-deficient environment *in vivo* prior to isolation and testing *in vitro*. Kusaka and Mori (387–388) discussed the applicability of the pyrolysis gas chromatography-mass spectrometry of mycobacterial mycolic acid methyl esters for identifying *M. leprae*. Lygren, *et al.* (388) studied five mycobacteria for catalases, peroxidases, and superoxide dismutases. No catalase or peroxidase activity was detected in *M. leprae* with the methods used. Superoxide dismutase activity was detected and in crossed immunoelectrophoresis was as-

sociated with *M. leprae* antigen 4. Talati and Mahadevan (389) detected a lipase in *M. leprae* as demonstrated by the ability of the bacteria to hydrolyze tributyrin. Vasanthakumari, *et al.* (389) described a method for staining for AFB which does not involve heating and which might be suitable for laboratories in developing countries where a reliable source of heat is not available. Brett and Butler (389–390) found a correlation between resistance to the spread of *M. lepraemurium* and the capacity to generate macrophage-activating factors in response to *M. lepraemurium* antigens *in vitro* in two strains of mice. Hoffenbach and Bach (390) infected different strains of mice s.c. with *M. lepraemurium.* Different genetic factors were associated with bacillary growth, a defect in IL-2 production, and the generation of specific antibody in these animals. Job, *et al.* (391) demonstrated that *M. leprae* could infect the placenta and fetuses in lepromatous nine-banded armadillos. Rojas-Espinosa, *et al.* (391) found antimycobacterial antibodies and elevations in lactate dehydrogenase in the sera of *M. leprae*-infected armadillos as the disease progresses. Cartel, *et al.* (392) described the epidemiology of leprosy in Guadeloupe, pointing out the high proportion of relapsed patients who had been treated by dapsone monotherapy for 5 years or more. Cai and Hong (392), Lei (392), Lu (392–393), Ren and Xie (393), Yang (393–394), and Zhou (394) described the decline in leprosy in different parts of China. Paties, *et al.* (393) pointed out that leprosy is still being transmitted in Italy. Lu (394–395) discussed leprophobia from the Chinese perspective. Masur, *et al.* (396) reported disappointing results with a combination of rifabutin and clofazimine in AIDS patients infected with *M. avium-M. intracellulare.*

The June issue contained the abstracts of the Second U.S. HD Research Conference held in Baton Rouge, Louisiana, in December 1986. Dhople (402) found that *in vitro*-grown *M. lepraemurium, M. "lufu,"* and *M. leprae* all have the ability to take up ^{3}H-thymidine, possess thymidine kinase, but not thymidine phosphorylase. For a given culture medium for *M. leprae* there were excellent correlations among intracellular ATP, bacterial DNA, ^{3}H-thymidine uptake, and viability of *M. leprae* as measured by the mouse foot pad technique. Franzblau and Harris (402–403) and Harris, *et. al* (403) described a number of metabolic analyses, a number of potential cultivation media, and the effect of several antileprosy drugs on *M. leprae.* Foster, *et al.* (403–404) found that feeding mice diets containing high amounts of fats enhanced the growth of *M. leprae* in the foot pads compared to mice receiving low-fat diets. Ohashi (404) extensively characterized two strains of mycobacteria, Molokai-75 (MO-75) and Hawaii-75 (HI-75) cultured from tissues of leprosy patients and at one time alleged to be *M. leprae.* The strains appeared to be *M. intracellulare* and *M. scrofulaceum,* respectively. Khera and Mahadevan (405) described 65 mycobacterial isolates harvested from nodules of lepromatous leprosy patients. Williams and Gillis (405) described efforts to obtain expression of the recombinant 65 kD protein of *M. leprae* using the cloning vector pKK223-3. Clark-Curtiss (405–406) performed restriction fragment length polymorphism analyses using human *M. leprae* from two experimentally infected armadillos, *M. vaccae, M. "lufu,"* several armadillo-derived mycobacterial strains, and *M. leprae* purified from a naturally infected armadillo. The probes utilized hybridize to the same size fragment from human *M. leprae* strains and from the naturally infected armadillo *M. leprae,* but not to the other mycobacterial species tested. Anderson, *et al.* (406–407) described the synthesis of peptides which correspond to the epitopes of the 65 kD protein of *M. leprae* recognized by monoclonal antibodies. Mshana and Nilsen (407) showed the presence of HLA-DR and HLA-DQ antigens on Schwann cells, lymphocytes, macrophages, and endothelial cells in leprosy neuropathy lesions. Mshana, *et al.* (407–408) found that mouse peritoneal macrophages failed to express Ia antigen after stimulation with lymphokines if infected *in vitro* with live mycobacteria. Levis, *et al.* (408–409) measured antibodies to PGL-I, *M. tuberculosis* lipoarabinomannan, against *M. leprae* proteins by Western immunoblots and against an epitope in the 65 kD protein of *M. leprae* recognized by a murine monoclonal antibody designated IVD8 by competitive antibody binding assay. Leprosy patients with higher bacterial loads showed higher levels

of antibody in these tests. Meeker, *et al.* (409–410) monitored leprosy patients sequentially for antibody levels to PGL-I antigen of *M. leprae.* Chehl, *et al.* (410–411) were unsuccessful in attempting to induce ENL in *M. leprae*-infected nude mice using IgG and IgM monoclonal antibodies to either PGL-I or the 65 kD protein of *M. leprae.* Sibley and Krahenbuhl (411–412) showed that in normal macrophages, a majority of phagosomes containing freshly isolated live *M. leprae* resisted fusion with Thorotrast-labeled lysosomes. In contrast, a majority of phagosomes containing gamma-irradiated *M. leprae* underwent lysosome fusion in normal macrophages. Ramasesh, *et al.* (412–413) compared fluorescein diacetate : ethidium bromide staining, the rate of PGL-I synthesis, and ATP content of *M. leprae* as means of measuring the *in vitro* microbicidal effects of activated macrophages on *M. leprae.* Collins, *et al.* (413–414) described a series of experiments involving chronic *M. avium*-complex infections in athymic and T-cell-depleted mice. Breger (414) presented results and correlations between Semmes-Weinstein monofilament sensory nerve mappings and sensory nerve conduction velocities in leprosy patients. Bell-Krotoski (414–415) monitored the neural status of leprosy patients during various drug therapies. Look (415) outlined his approach to the successful treatment of plantar ulcers in leprosy patients. Nawoczenski, *et al.* (415–416) compared the effectiveness of several rocker shoe designs, differing in the placement, radius of curvature, and the angle of the rocker, in reducing pressure on the forefoot in walking. Theriot, *et al.* (416) presented data on the reliability of the biothesiometer in measuring plantar vibratory thresholds in normal subjects and in leprosy patients. Mukherjee, *et al.* (416–417) presented evidence for an active involvement of the microvasculature, particularly endothelial cells, in the movement of bacilli and in the development of the granulomas in leprosy skin lesions. Gormus, *et al.* (417) reported a second sooty mangabey monkey with naturally acquired leprosy. The animal had been housed in direct contact with the first mangabey monkey found to have the disease. Ohkawa, *et al.* (417–418) studied the immune responses of 23 mangabey monkeys experimentally inoculated with mangabey-origin *M. leprae in vitro.* An immunologic spectrum could be seen with regard to the proliferation of peripheral blood mononuclear cells *in vitro* in response to Dharmendra-type human *M. leprae.* Walsh, *et al.* (418) inoculated three adult African green monkeys with *M. leprae* isolated from the sooty mangabey monkey with naturally acquired leprosy. For 2 years after inoculation, all three animals appeared to have progressive lepromatous disease. In two of the animals the skin lesions regressed and were histopathologically compatible with regressing borderline leprosy. All three animals were necropsied 5 years after inoculation and all three had extensive lesions in all the major peripheral nerve trunks of the upper and lower extremities. Malaty, *et al.* (418–419) described the use of trigeminal ganglia of adult rabbits as an *in vitro* model system for studying the invasion and reaction of trigeminal neurons to leprosy bacilli. Vadiee, *et al.* (419) studied antibodies to PGL-I in armadillos inoculated with *M. leprae* and found that there was an inverse relationship between bacterial load and IgG anti-PGL-I antibodies. Truman, *et al.* (419–420) found an average antibody prevalence rate of 11.1% using an ELISA for IgM class antibodies against the PGL-I antigen of *M. leprae* among Louisiana armadillos. These antibody prevalence rates were five times higher than rates based on histopathological examination.

The Original Articles of the September issue began with the report by Radhakrishna and Nair (425–434) which presented evidence of an association between regularity of dapsone intake and the development of deformities in a longitudinal study of a large number of leprosy patients in South India. Andrade, *et al.* (435–440) described their experience in implementing MDT in an urban population. Miller, *et al.* (441–449) treated three leprosy patients with chronic, steroid-dependent ENL with cyclosporine A. Excellent results were obtained in two patients and a partial response in the third. Azulay (450–453) presented a case of primary visceral Virchowian hanseniasis. Ponnighaus, *et al.* (454–462) described a procedure for grading the degree of confidence that a diagnosis of leprosy is correct after considering all available clinical, historical, bacteriological, and histopathological infor-

mation. Koumantaki, *et al.* (463–467) studied the sibship size and birth order distribution of 187 leprosy patients and appropriate controls in Greece. There was a tendency for tuberculoid leprosy patients to belong to the later birth order, suggesting that early exposure in life predisposes to the tuberculoid form of leprosy. Lieber and Lieber (468–480) report results of field research on a leprosy epidemic among the Kapingamarangi people living in two communities in the Federated States of Micronesia. Inoculation of *M. leprae* through the frayed fibers of pandanus-leaf floor mats and sleeping mats is presented as a likely means of spreading the leprosy infection. Laal, *et al.* (481–493) studied the *in vitro* immunologic responses of patients undergoing type 1 reactions. In control nonreactional leprosy patients, BT patients showed integrity of T-cell functions as compared to multibacillary BB-BL nonreactional patients. In the BT reactional group, *M. leprae* antigen-induced lymphoproliferation was reduced in 80–90% of the patients. Leukocyte migration inhibition was reduced in 40% and suppressor cell activity was also reduced in a majority of the reactional BT patients. The bacilliferous BB and BL patients in reaction showed significant general improvement in leukocyte migration inhibition and in antigen-induced lymphoproliferation as compared to uncomplicated BB-BL patients. Suppressor cell activity also increased during the reactional phase in BB-BL patients. The 48 hr DTH skin test responses to *M. leprae* antigens continued to reflect the background leprosy type, i.e., being positive in BT reactional individuals and negative in BB-BL reactional patients. Shen, *et al.* (494–498) identified activated T lymphocytes in leprosy skin lesions using a monoclonal antibody, anti-Ta1, which identifies antigen-activated T lymphocytes *in vitro*. Greater numbers of Ta1+ lymphocytes were observed in tuberculoid leprosy lesions, lepromin skin tests, and reversal reactions as compared to lepromatous leprosy or ENL. Bansal, *et al.* (499–506) found vascular abnormalities by venography in 96.3% and by histopathological studies in 76.6% of leprosy patients. Zhou, *et al.* (507–509) demonstrated microgranulomas in the retina in a pathologic study of an eye from a leprosy patient. Jayalakshmi, *et al.* (510–514) reported findings of 35 autopsies on leprosy subjects from Sungai Buluh, Malaysia. Generalized amyloidosis was found in six (17%) of these patients. Chandi and Chacko (515–520) examined skin biopsies from cutaneous lesions of early leprosy patients by light and electron microscopy. The patterns were consistent with *M. leprae* being extruded from the circulation into the epineurium where they then may be carried in inflammatory cells across the perineurium.

In the Editorial section of the September issue, the elegant review of HLA class II immune response and suppression genes in leprosy by Ottenhoff and de Vries (521–534) was reprinted with the kind permission of *Health Cooperation Papers,* Prof. Enrico Nunzi, Editor. Johnstone (535–547) reviewed the long search for animal models for leprosy.

In the Correspondence section of the September issue, Converse, *et al.* (548–551) presented *in vitro* data that show that cimetidine inhibits the production of a suppressor factor from peripheral blood mononuclear cells from LL patients in response to *M. leprae.* On the other hand, cimetidine caused no changes in lymphocyte transformation tests in response to *M. leprae* in either lepromatous (BL-LL) or tuberculoid (BT) patients. Nelson, *et al.* (551–553) pointed out the differences between the studies done by Converse, *et al. in vitro* and the *in vivo* studies done by their group. Pfaltzgraff (553–554) suggested that clofazimine would have been useful in the management of the patient described by Gelber and Zacharia with bilateral ulnar nerve abscesses [IJL 54 (1986) 480–482]. Gelber and Zacharia (554–555) felt that clofazimine would not have altered the course in this patient. Pankajam, *et al.* (555–556) presented a patient with juvenile pityriasis rubra pilaris who had been the object of leprophobia for many years. Li, *et al.* (556–559) presented two cases of osteoarticular chronic hypertropic neuritis, both of whom had been diagnosed as having leprosy. Srinivas, *et al.* (559–560) described a dental surgeon who developed numbness in an area habitually in contact with an air rotor and a clinical micromotor used in his practice. Jaled (560–561) outlined the modified Bratton-Marshall method for detecting sulfones in the urine. Prabhakar (561–562) described

attempts at cultivation of *M. leprae* using a medium based on healthy human nasal mucus and bovine serum albumin. Pandya (562–563) questioned the use of the word "phagocytosis" to describe the interactions between Schwann cells and *M. leprae in vitro*. Band and Talwar (563–565) felt that the term was appropriate. Grange, *et al.* (565–566) raised the possibility that *M. leprae* may replicate within certain species or strains of amoebae. Islas-Rodriguez, *et al.* (566–569) studied the *in vitro* reactivity of peripheral blood mononuclear cells from active lepromatous patients and found that they produced diminished amounts of IL-2 in response to ConA but that they responded normally to exogenous IL-2.

In the Current Literature section of the September issue, Alvarenga (576–577) reviewed the excellent experience to date with Isoprodian-rifampin as combined chemotherapy for both tuberculosis and leprosy. Baciewicz, *et al.* (577) reviewed the clinically important drug interactions when rifampin is combined with other drugs. Becx-Bleumink (578) presented operational aspects of implementation of multidrug therapy (MDT) in Ethiopia. Over 5500 patients have been released from treatment. These patients are instructed to attend clinics regularly for follow-up examinations but only 25–30% do so. About 3500 patients who have been released from chemotherapy continue to need care because of disabilities. Chapon, *et al.* (579) reviewed four patients with thalidomide-induced neuropathy developing during treatment of discoid lupus erythematosus. Signs and symptoms were limited for a long period of time to distal paresthesiae with altered sensory conduction velocities. Depasquale (579) reported that practically no patients had relapsed in Malta 5–10 years following the discontinuation of Isoprodian-rifampin. Dhir, *et al.* (579) found that 55% of paucibacillary patients treated with MDT had active disease at the end of 6 months' treatment. Dietrich and Wabitsch (579–580) saw no detectable differences in the initial responses of lepromatous and borderline lepromatous patients to treatment with dapsone alone, dapsone plus rifampin daily, or rifampin daily plus Isoprodian daily. Grosset (581) reviewed the rationale for the WHO recommendations regarding MDT and pointed out the remaining unanswered questions regarding the duration of treatment, persisters, and risk of relapse after stopping treatment. Kartikeyan and Bhalerao (582–583) found a 47% defaulter rate among registered leprosy patients in a slum area in the suburbs of Greater Bombay. The typical defaulter was male, diagnosed during mass surveys, and 15–44 years old. The principal reasons for dropout were unsuitable clinic timings and the lack of knowledge about the need for continued and regular treatment. Leiker (583) treated 400 leprosy patients, one third lepromatous and borderline lepromatous, with daily rifampin and dapsone, and with clofazimine on alternating days. Most of the patients had been pretreated with a single drug. They were treated for 1 year with the combination and thereafter released from treatment and kept on observation. So far, 3–5 years after treatment was discontinued, no relapses have been found. Mahadevan, *et al.* (583–584) described three *in vitro* assay systems to rapidly determine drug activity against *M. leprae*. Mehta, *et al.* (584) studied the pharmacokinetics of rifampin in combination with dapsone and/or clofazimine. Millan, *et al.* (584–585) reported studies of different MDT regimens in multibacillary patients in Senegal. They propose a diphasic regimen in which an initial treatment phase of 2 months consists of daily administration of three antibacterial drugs among which are rifampin and ethionamide. The second phase uses two drugs, clofazimine combined with either dapsone or ethionamide, self-administered until smear negativity. Pattyn (586) reported that ofloxacin, and to a lesser extent pefloxacin, was active against *M. leprae* infections in mice. Prabhakaran, *et al.* (587) found beta-lactamase in *M. leprae* from armadillos which had been treated with penicillin G benzathine but not in *M. leprae* from tissues of armadillos which had not received penicillin. Schaper, *et al.* (587–588) synthesized and screened a series of thiosemicarbazones for activity against "*M. lufu*." One of these, designated PH22, appeared to act as an inhibitor of ribonucleotide reductase and to show promise. Seydel, *et al.* (588) discussed approaches to the development of antibacterial drugs in leprosy. Newer quinolone derivatives and combinations of new inhibitors of bacterial folate

synthesis are promising compounds. Waters, *et al.* (589) discussed some of the clinical problems in MDT, such as difficulty in accurately classifying patients as multibacillary or paucibacillary and the difficulty in distinguishing between bacterial relapse and reversal reactions in the treatment of paucibacillary leprosy. Wheeler (589) discussed those metabolic activities of *M. leprae* which may be potential targets for antileprosy agents. Gupta, *et al.* (590) found significantly increased palmar ridge malformations in multibacillary leprosy patients. Miller, *et al.* (590–591) analyzed leprosy sera for antinuclear antibodies and found that they were present in 16% of the patients. The titer was uniformly low and there was no consistent fluorescence pattern. Nigam, *et al.* (591) found that renal involvement in the form of inflammatory lesions and nonspecific changes in the glomeruli and tubules are very common in lepromatous leprosy, particularly during the reactive phase. Sheriff (592) found that tuberculoid patients under treatment generally had low sperm counts and low spermatozoal motility with a greater number of abnormal forms compared with healthy controls. Singh (592) described a 45-year-old male patient with BL leprosy in reaction who developed large bullae on existing leprosy lesions. Wallach, *et al.* (592–593) reported that four patients with severe ENL were treated successfully by plasma exchange and/or fresh-frozen plasma infusions after failure of classical therapy. Improvement was rapid with no clinical relapse after 4–7 years of follow-up. Buchanan, *et al.* (594) studied the reactivity of different monoclonal antibodies to the 65 kD protein of *M. leprae.* Fourteen of the monoclonal antibodies recognized different epitopes; one recognized an epitope found only on *M. leprae* and the others recognized epitopes present on as few as 8 or as many as all 23 of the mycobacterial species studied. Drosos, *et al.* (594) demonstrated that the cryoglobulins of a patient with Lucio phenomenon contained PGL-I antigen and a specific antibody to that antigen. Emmrich, *et al.* (594–595) showed that a recombinant 65 kD protein of BCG was capable of stimulating T4 clones established from a patient with tuberculoid leprosy. Harboe and Ivanyi (595) characterized monoclonal antibodies to *M. leprae* in crossed immunoelectrophoresis and showed different patterns of reactivity with *M. leprae* antigens 2, 7, and 11. Hussein, *et al.* (595) isolated T-cell clones from *M. lepraemurium*-infected mice. By adoptive transfer experiments, it was shown that four clones transferred DTH responses locally but had no effect on local resistance. One clone (Lyt-2+) transferred increased resistance locally but did not transfer DTH. Husson and Young (595–596) presented evidence that the 65 kD proteins of *M. tuberculosis* and *M. leprae* play a role in the humoral and cell-mediated immune responses to these pathogens. Kaldany, *et al.* (596) described two methods for detecting the PGL-I antigen of *M. leprae* in the urine of lepromatous patients. Kaplan, *et al.* (596) found that *M. leprae* antigens suppressed T-cell proliferation in response to mitogens and antigens in both lepromatous and tuberculoid patients as well as in controls never exposed to *M. leprae* or *M. leprae*-endemic areas. Both soluble and particulate fractions of *M. leprae* suppressed proliferation in a dose-dependent fashion. One suppressive antigen was lipoarabinomannan-B. Koster, *et al.* (597) found that circulating T cells from some leprosy patients proliferate in the presence of PGL-I *in vitro* but that the response is weak, occurs in patients with both lepromatous and tuberculoid disease, and is unrelated to lepromin responsiveness. Lee, *et al.* (597–598) studied BT skin lesions and found that in the active border of the lesions the number of T cells, the proportion of helper T cells, the number of cells positive for HLA-DR staining, and the expression of DR antigen on the surface of keratinocytes in the epidermis were all increased compared to biopsies taken inside the annular lesions. Maeda and Narita (598) reported that a Lewis rat schwannoma cell line exhibited an *in vitro* affinity for live *M. leprae.* Narayanan, *et al.* (598–599) studied the immunological characteristics of dermal infiltrates in the human skin reactions induced by armadillo-derived leprosin coupled to liposomes and standard Dharmendra lepromin and found them to be identical. Sengupta, *et al.* (600) studied delayed hypersensitivity skin reactions to tuberculin alone or in mixtures with antigens of *M. leprae.* The tuberculin reaction was significantly inhibited in more than one half of both LL and BT patients by leprosin, the

leprosin-derived 12 kD protein, or leprosin depleted of the 12 kD antigen. No such suppression was found in healthy controls from a leprosy-endemic area. Cocito and Delville (600–601) reviewed the properties of leprosy-derived corynebacteria (LDC) and suggested that leprosy is a disease produced by *M. leprae,* possibly helped by LDC. Dhople and Green (601–602) reported definitive multiplication of *M. leprae in vitro* in Dhople-Hanks medium and Mahadevan's conditioned medium using supernates of dorsal root ganglia cultures. The multiplication occurred in primary cultures but subcultures could not be achieved. Franzblau, *et al.* (602) found 16 of 31 *M. avium/M. intracellulare* clinical isolates from Hiroshima to contain plasmids. Kato (602–603) obtained positive growth and subcultures from 3 out of 4 specimens of host-grown *M. leprae* inoculated in exochelin-mycobactin-enriched media. Kazda, *et al.* (603) isolated a strain of *M. leprae* from soil in Bombay by the mouse foot pad technique. A direct inoculation of a suspension from the same soil sample also yielded a *M. intracellulare,* serotype Darden. Ramasesh, *et al.* (603) found that *M. leprae* in a murine macrophage system incorporated radiolabeled palmitic acid into PGL-I *in vitro.* Seydel and Lindner (603–604) described mass spectrometric analysis of single *M. leprae* cells. Bona, *et al.* (605) found numerous acid-fast bacilli in about 90% of *Culex fatigans* caught in homes of normal individuals as well as leprosy patients. Shields, *et al.* (606) conducted a genetic epidemiologic investigation on 269 leprosy kindreds containing 552 affected individuals in Papua New Guinea. The composite kindred data suggest a genetic hypothesis for the nonimmunologically induced susceptibility to leprosy per se. Ahrens, *et al.* (607) described a patient with dermatitis herpetiformis who developed a combined motor and sensory peripheral neuropathy some 4 years after he began oral dapsone. The neuropathy improved after cessation of dapsone therapy. Ottenhoff, *et al.* (609) skin tested leprosy patients with antigens of *M. tuberculosis, M. leprae, M. scrofulaceum,* and *M. vaccae.* Results were analyzed in relation to HLA class II phenotypes. HLA-DR4 was associated with high responsiveness to antigens specific to *M. tuberculosis* but not to antigens shared with other mycobacteria. Resnick, *et al.* (609) found that *M. lepraemurium* die in the course of systemic infection of mice, including nude mice.

In the Original Articles of the December issue, Menzel, *et al.* (617–625) examined household contacts of leprosy patients with an enzyme-linked immunosorbent assay for antibody to the terminal disaccharide portion of the PGL-I antigen of *M. leprae.* Household contacts with more than 1 year of exposure to a lepromatous patient had antibodies more often than did household contacts with less than 1 year of exposure to a lepromatous patient or household contacts of tuberculoid patients or persons without known exposure to leprosy in the household. One third of persons without household exposure to leprosy were antibody positive in this area of Ethiopia. Chanteau, *et al.* (626–632) conducted a seroepidemiological surveillance of a leprosy contact population in French Polynesia. Using an enzyme-linked immunosorbent assay to detect IgM antibody against the terminal disaccharide of the PGL-I antigen of *M. leprae,* it was found that specific antibody levels were higher in healthy Polynesians than in normal individuals living in a nonendemic country. In a population of household contacts observed for 2 years, 12.8% were seropositive and one developed lepromatous leprosy. Eighty-seven percent of these household contacts were seronegative, and three developed paucibacillary disease. Miller, *et al.* (633–636) measured IgM antibody to PGL-I in serial serum specimens from patients during the course of therapy and found that these levels declined rapidly and consistently with treatment in multibacillary patients. Lyons and Naafs (637–645) measured antibody levels to 16 environmental mycobacteria in leprosy patients and healthy controls from two different areas of Zimbabwe, one with predominantly lepromatous leprosy and the other with predominantly tuberculoid cases. Significant differences were found between the two areas, suggesting that exposure to environmental mycobacteria could influence the type of leprosy developed by a susceptible individual. Rada, *et al.* (646–650) measured *in vitro* suppressor reactivity in a group of leprosy patients before and after immunotherapy with a mixture of *M. leprae*

and BCG. Immunotherapy was found to increase the responses in lymphocyte transformation tests in BL-LL patients to levels comparable to those observed in BT-TT patients. Gonzalez-Amaro, *et al.* (651–656) presented findings suggesting that LL patients might have abnormalities in the contrasuppressor immune circuit. Chaturvedi, *et al.* (657–666) presented the effects of administration of the ICRC antileprosy vaccine in healthy household contacts of leprosy patients and in healthy noncontacts. Lepromin conversion occurred which was stable for at least 3 years. Lamba, *et al.* (667–671) studied corneal involvement in leprosy. Corneal disease was most frequently among lepromatous patients; most of the corneal involvement was secondary to pathology of the lid; tear film abnormalities in association with lagophthalmos and abnormal corneal sensation contributed to the corneal morbidity. Guelpa-Lauras, *et al.* (672–679) reported mouse foot pad studies of *M. leprae* from biopsies of multibacillary leprosy patients. From 101 biopsies from relapsed cases, 18% were sensitive to dapsone, 14% showed low-level, 22% showed intermediate-level, and 47% showed high-level resistance to dapsone. From 133 biopsies from new cases, 61% were sensitive to dapsone, 28% showed low-level, 6% intermediate-level, and 5% high-level dapsone resistance in mice. Datta, *et al.* (680–684) demonstrated alpha-, keto-, and methoxy mycolates in the acid methanolysate products of purified *M. leprae.* Job, *et al.* (685–688) lepromin skin tested wild caught armadillos. The histopathological appearance of the Mitsuda reaction in these animals covered the entire spectrum of leprosy from tuberculoid to lepromatous. Only 8.8% of the animals showed a positive Mitsuda reaction.

In the Editorial section of the December issue we were fortunate to have a scholarly review of experimental murine leprosy and its relevance for the study of mycobacterial resistance in man by Lovik (689–701). We were also pleased to have a review guest editorial by Klenerman (702–712) on etiological factors in DTH reactions in leprosy.

In the Obituary section of the December issue, we were saddened to learn of the deaths of Fr. Dr. Joseph Ambrosoli (713) and Prof. Walter Büngeler (714–715).

In the Correspondence section of the December issue, Quesada-Pascual, *et al.* (716–718) decribed the establishment and maintenance of an armadillo (*Dasypus novemcinctus*) colony for leprosy research in Mexico City. Douglas, *et al.* (718–721) measured antibodies to the terminal disaccharide portion of the PGL-I antigen of *M. leprae* in the sera of household contacts of new lepromatous patients and among a noncontact control population in Cebu, The Philippines. The seropositive rate was 11.2% for contacts and 1.7% for the control group. Three of 36 seropositive contacts have developed leprosy over the course of 2 years. Ramanathan (721–722) recommended that a standard be included in tests for anti-*M. leprae* antibodies to minimize and eventually eliminate variability when these assays are performed in various parts of the world. Job, *et al.* (722–725) smeared 10^7 viable *M. leprae* on the skin of nude mice and serially sacrificed the animals and examined the site of exposure to *M. leprae* by light microscopy. There was evidence that *M. leprae* can enter the epidermis of unbroken skin especially through hair follicles and sebaceous glands. Almeida (726–727) disagreed with the conclusions reached by Shepard, *et al.* [IJL 54 (1986) 11–15] that primary dapsone resistance has increased since 1977.

In the News and Notes section of the December issue, further details of the upcoming XIII International Leprosy Congress were provided (728–730).

In the Current Literature section of the December issue, Naudin, *et al.* (738) outlined the practical problems in implementation of multidrug regimens in Senegal. Reich (738) postulated that in endemic areas the majority of the population incubates subclinical leprosy infections at various levels and that clinical leprosy arises from within the pool of subclinical infection in the endemic population rather than by transmission from an index case. Dousset-Faure, *et al.* (739) evaluated the long-term results of 30 patients treated with rifampin, prothionamide, and dapsone for 6 or 12 months between 1974 and 1976. The patients were treated with dapsone alone after the period of three-drug treatment. Twelve of the 30 patients were evaluated in 1983. Six of the patients were considered to have had clinical relapses. Seven of the 12 pa-

tients did not take dapsone regularly and the six relapses belonged to this group. Grillone and Pattyn (739) treated paucibacillary leprosy patients with 10 weekly doses of rifampin 600 mg and found an 88% cure rate at 3 years as judged by histopathology. In multibacillary leprosy, daily rifampin, ethionamide, and dapsone for 2 months was followed by 10 months of daily ethionamide and dapsone with weekly rifampin and excellent clinical and bacteriological results were obtained. There were no relapses for 2–3 years after the end of therapy among 111 patients. Husser, *et al.* (739–740) treated paucibacillary leprosy patients with dapsone daily for 3 years, rifampin 900 mg weekly for 8 doses, or rifampin 900 mg daily for 12 doses. Patients have been followed for periods of 24–56 months and no differences could be seen among the three regimens. Pattyn, *et al.* (740) treated 10 patients with dapsone-resistant multibacillary leprosy with rifampin twice weekly for 6 months, ethionamide daily for 6 months, and dapsone daily for 12 months. Follow-up for 27–54 months has shown no relapses to date. Yang and Swarbrick (741 and 741–742) described the development of sustained-release delivery systems for dapsone and its derivatives. Balybin (742) found that levels of organic iodine in the body were reduced in the active stage of lepromatous leprosy. Abe, *et al.* (742–743) measured antimycobacterial antibodies in the sera and saliva from leprosy patients, household contacts, and inhabitants of leprosy-endemic areas. The fluorescent leprosy antibody absorption test (FLA-ABS) with saliva was positive in 59% of household contacts, 39% of school children in an endemic area, and 38% of adults with social contacts with leprosy, but negative in 23 patients with pulmonary tuberculosis. The percentages of positive reactions in saliva were comparable using the FLA-ABS test or the ELISA testing for antibodies against the PGL-I antigen of *M. leprae.* Brett, *et al.* (743–744) estimated the number of peripheral blood T lymphocytes responding to soluble antigens from tuberculin and *M. leprae* by limiting dilution analysis. In the peripheral blood of BCG-vaccinated individuals, frequencies between 1/1970 and 1/13,982 were observed in response to tuberculin and between 1/4097 and 1/24,717 in response to soluble antigens of *M. leprae.* In peripheral blood T lymphocytes from tuberculoid leprosy patients, the frequency of T lymphocytes responding to *M. leprae* antigens was either greater or similar to the frequency of T cells responding to tuberculin. Britton, *et al.* (744) characterized a 70 kD protein antigen common to *M. leprae* and BCG. Brown, *et al.* (744–745) determined the 15 amino acid sequence of the 65 kD antigen of *M. leprae* which binds to the *M. leprae*-specific monoclonal antibody designated IIIE9. de Vries, *et al.* (745) presented data on restriction and antigen specificity of *M. leprae*-reactive helper and suppressor T-cell clones. Fine, *et al.* (745) challenged the belief that tuberculin skin test results are informative with regard to the protective action of BCG against tuberculosis and leprosy. Gill, *et al.* (746) found that antibody responses to *M. leprae* increased in healthy human volunteers who received 1.5×10^8 or more heat-killed, armadillo-derived bacilli intradermally. The detectable increase in the antibody levels was first seen 6 months after vaccination and increased even further 1 year after vaccination in these individuals. Hokama, *et al.* (746–747) found significantly higher superoxide anion production with liposomes in monocytes from LL patients. Significant reductions in superoxide anion production occurred when C-reactive protein was incorporated into the liposomes. Hussein, *et al.* (747) described a leprosy serum factor that inhibits the growth of mitogen-stimulated normal human lymphocytes. The inhibitor was an IgG and acted by blocking the recruitment of lymphocytes into growth. Ivanyi and Praputpittaya (747) raised rabbit antisera against 12 mouse monoclonal antibodies to mycobacterial antigens and showed idiotype-specificity following cross-absorption with normal mouse globulin. Kaldany and Nurlign (747) detected PGL-I in LL patients' urine for up to 2 months after the initiation of therapy. Kaufman, *et al.* (748) showed that T cells of both the CD4 and CD8 phenotype were generated after immunization with *M. leprae* and *M. tuberculosis.* In functional studies mycobacteria-reactive T-cell clones of CD4 and CD8 phenotypes seemed to function similarly and to differ primarily in their antigen reactivity pattern. Klatser, *et al.* (749) utilized a monoclonal antibody, des-

ignated F47-9, which recognizes an *M. leprae*-specific epitope on the 36 kD protein of *M. leprae* to develop an ELISA competition test for serological investigation. This antigen is recognized by several T-cell clones from tuberculoid leprosy patients. Longley, *et al.* (750) found Langerhans' cells, IL-2-producing cells, and IL-2-receptor-bearing cells in LL patients in response to lepromin A. These cells fail to persist in skin-test sites and the patients failed to form tuberculoid granulomas. Modlin, *et al.* (750) cloned both suppressor and helper T cells from LL skin lesions. The unresponsiveness of LL patients to *M. leprae* may be related to the presence of these suppressor T cells within the lesions, acting perhaps by inhibiting IL-2 production. Mustafa, *et al.* (750–751) generated over 200 human T-cell clones from 19 individuals vaccinated with BCG, vaccinated with *M. leprae,* or patients with tuberculosis. All of the proliferating clones were of the CD4+ CD8− phenotype. Five clones from *M. leprae*-vaccinated subjects recognized an epitope on the 18 kD protein of *M. leprae* and 1 recognized the 65 kD protein of *M. leprae.* Nath (751) showed transient, but definite evidence of circulating functional T cells which produced lymphokines during ENL reactions in many LL patients. Nilsen, *et al.* (751) reported a series of immunohistochemical studies of leprous neuritis. Paucibacillary skin lesions were associated with multibacillary nerve lesions in 8 of 11 patients. Samuel, *et al.* (753) studied the interaction of human Schwann cells, human fibroblastic cells, and *M. leprae in vitro.* Evidence suggests that Schwann cells may be able to present *M. leprae* antigens to T cells and thus initiate immune responses against the organism. Tung, *et al.* (753–754) measured soluble IL-2 receptors in the sera of leprosy patients and found that these levels were significantly reduced in untreated tuberculoid or borderline tuberculoid patients, highly increased in patients with ongoing reversal reactions, and elevated to a lesser extent in patients with ENL. Xie and Dong (754) suggested that a variety of pre-oxidized Ziehl-Neelsen (ZN) stains, particularly those that utilize various periodic acid-oxidized ZN stains, result in a loss of specificity. Chakrabarty, *et al.* (755) isolated a nocardia-like organism from 22 multibacillary leprosy patients. Draper (755–756) reviewed the biochemistry of *M. leprae* and suggested that more information is needed on the transport of nutrients and the uptake of phosphorylated intermediates into the organism. The phosphatase associated with isolated *M. leprae* is derived from the host. *M. leprae* seems unable to synthesize its own purines. Juscenko and Visnevetsky (757) described the histochemical characteristics of reversal reactions in *M. leprae*-infected armadillos. Blake, *et al.* (758) reviewed the evidence for the existence of an environmental, nonhuman source of *M. leprae* capable of causing some human infections. Wang, *et al.* (759) compared a population in which all leprosy patients were treated at home as outpatients with another population in which all leprosy patients were isolated in leprosy hospitals for treatment. After 30 years, the control effects on leprosy were very similar. Xiong, *et al.* (760) pointed out that the cost of outpatient treatment is only 8% of the cost of hospitalization in treating leprosy patients. Shu, *et al.* (761) calculated the extremely large economic loss to society caused by the disability of leprosy patients through leprosy deformities. Doga, *et al.* (761–762) successfully treated 40 of 50 patients with cutaneous leishmaniasis with dapsone in a dosage of approximately 2 mg per kg per day for 21 days. Khor, *et al.* (763) studied experimental murine tuberculosis and found little evidence that interferon-gamma would increase the efficacy of the early stages of chemotherapy of tuberculosis. Levi, *et al.* (763–764) reported an interesting method of tuberculin testing by means of an ointment contained in an aluminum chamber. Ridley and Ridley (764) and Ridley and Ridley (764–765) presented evidence for the existence of a continuous spectrum of tissue responses in untreated tuberculosis, correlating with evidence of resistance to bacterial multiplication, the degree of necrosis, and the form, localization, and persistence of mycobacterial antigen.

The December issue contained the abstracts for the Twenty-Second Joint Leprosy Research Conference held at the National Institutes of Health in Bethesda, Maryland, on 20–22 July 1987. Abe (774) discussed strategies for serodiagnosis. *M. leprae*-specific antigens are now becoming available. Tests with high sensitivity tend to have low

specificity and vice versa. It may be possible to develop a simple rapid test suitable for large-scale survey use in the field using passive agglutination of particles coated with *M. leprae*-specific carbohydrate or peptide epitopes. Levis, *et al.* (775–776) found that multibacillary leprosy patients had higher levels of IgM and IgG antibody to the lipoarabinomannan of *M. tuberculosis* than paucibacillary leprosy patients. Gelber, *et al.* (776–778) treated *M. leprae*-infected neonatally thymectomized Lewis rats with a variety of chemotherapeutic regimens. Clofazimine plus rifampin and rifampin plus ethionamide appeared superior to dapsone plus rifampin, rifampin alone, or dapsone plus ethionamide. Ito, *et al.* (778) showed that ofloxacin suppressed the growth of *M. leprae* in nude mice. Dhople, *et al.* (778–779) reported limited but definite *in vitro* multiplication of *M. leprae* in a cell-free medium using ATP, DNA, and ^{3}H-thymidine as measurements of growth. This system was used to evaluate the action of drugs on *M. leprae.* A trimethoprim derivative, designated K-130, showed good activity *in vitro* and was also bactericidal in mouse foot pad infections. Another trimethoprim derivative, brodimoprim, and two N-alkylbenzylamines also showed activity. Converse, *et al.* (779) found that peripheral T cells of healthy leprosy patient contacts respond preferentially to regions of 11–16 kD of both BCG and *M. leprae* and to the 22–26 kD region of *M. leprae.* The 18 kD region was also found to be relevant in responses by individuals immunized with *M. leprae.* Ottenhoff and de Vries (779–781) presented findings that HLA-DR3 was associated with the TT but not the BL-LL type of leprosy in a Surinam population. A DR3-associated immune response gene predisposes to TT leprosy by regulating helper T-cell activity against *M. leprae.* Mshana, *et al.* (781) showed that interferon-gamma can induce MHC class I antigens on virtually all Schwann cells and MHC class II (Ia) antigens on 10–15% of Schwann cells *in vitro.* Draper (781–782) reviewed what is known and what remains to be learned about mycobacterial wall lipopolysaccharide. Brennan, *et al.* (782) isolated anatomically distinct cell walls of *M. leprae* and found unexpectedly large amounts of cell-wall proteins. Further purification resulted in a cell-wall protein-peptidoglycan complex which contained significant immunological reactivity. Krahenbuhl, *et al.* (782–783) found that *M. leprae*-burdened foot pad macrophages from nude mice but not peritoneal macrophages from the same animals were refractory to macrophage-activating factor or murine recombinant interferon-gamma. Sibley, *et al.* (783–784) showed that *in vitro* infection with viable *M. leprae* appears to partially restrict macrophage activation by early induction of prostaglandin E2 (PGE2). High levels of PGE2 were produced *in vitro* by biopsies from LL patients, suggesting that a similar suppression of interferon-gamma activity may occur in humans. Holzer, *et al.* (784–785) found increased phorbol myristate acetate-stimulated superoxide anion release from human monocytes *in vitro* treated with PGL-I compared to monocytes not treated with the lipid. Kaplan and Cohn (785–786) administered interferon-gamma into the skin of LL patients and evaluated the local response. The responses resemble those seen with the DTH reaction to tuberculin. Rea and Modlin (786) studied leprosy granulomas by identifying T-suppressor/inducer (CD4+ 2H4+) and T-helper/inducer (CD4+ 2H4−). Helper/inducer cells were four times greater in tuberculoid than in lepromatous lesions. In distribution, the suppressor/inducers were admixed with the macrophages in lepromatous leprosy but were restricted to the lymphocytic mantle in borderline tuberculoid granulomas. Mori (786–787) described detection of acid-fast bacilli from 27% of skin specimens and 15% of umbilical cord specimens collected from cesarean sections. Nakamura and Yogi (787–788) reported that CD-1 nude mice were relatively resistant to the growth of *M. leprae* compared with NOD hybrid nude mice. Portaels, *et al.* (788) reported that 96% of the mesenteric lymph nodes, 4% of the livers, and 31% of the spleens from nonleprous armadillos contained cultivable mycobacteria. The most frequently isolated species from both leprosy-infected and nonleprosy-infected animals belonged to the *M. avium-intracellulare-scrofulaceum* complex. Clark-Curtiss, *et al.* (788–789) used restriction fragment length polymorphism analysis to establish specific patterns for chromosomal DNA of *M. leprae* from different sources in

comparison to chromosomal DNA from cultivable mycobacteria. No polymorphisms were detected among the chromosomes of *M. leprae* from human leprosy patients, from a naturally infected armadillo, or from a naturally infected mangabey monkey. Sathish, *et al.* (789–790) screened the λgt11 recombinant DNA library and found 20 clones which react with a pool of sera from LL patients. Izumi, *et al.* (790) coated gelatin particles with the chemically synthesized trisaccharide moiety of the PGL-I antigen of *M. leprae* conjugated with bovine serum albumin via parahydroxyphenyl proprionate. This new agglutination reagent compared favorably with an indirect ELISA.

As a Supplement to the December issue, we were pleased to have the proceedings of the Workshop on Experimental Chemotherapy of Leprosy held in Osaka, Japan, 11–20 November 1986. The Supplement was generously supported by the Sasakawa Memorial Health Foundation and was dedicated to the memory of Dr. Charles C. Shepard. The Supplement began with an overview of the Workshop by Grosset, *et al.* (807–813). Levy (814–818) reviewed the multiplication of *M. leprae* in normal mice. Colston and Levy (819–822) outlined the breeding and husbandry of mice. Levy (823–829) reviewed the application of the mouse foot pad technique to clinical drug trials. Ji (830–835) discussed drug susceptibility testing of *M. leprae* using the mouse foot pad technique. Ji, *et al.* (836–842) outlined the techniques for drug screening using the continuous method, kinetic method, and proportional bactericide method. Levy (843–846) discussed the utility of the *M. leprae*-infected immunologically normal mouse in experimental chemotherapy. Grosset and Guelpa-Lauras (847–851) presented studies on the activity of rifampin in *M. leprae*-infected mice. Grosset (852–856) emphasized the importance of considering pharmacokinetics in drug screening in the mouse. Colston (859–863) discussed the preparation, husbandry, and utilization of thymectomized-irradiated mice in detecting persisting *M. leprae*. The Subcommittee on Clinical Trials of the Chemotherapy of Leprosy (THELEP) (864–871) presented an overview of the THELEP-controlled clinical drug trials, emphasizing the characteristics of the patients, primary resistance to dapsone, and detection of persistence of *M. leprae* among the treated patients. Gelber and Levy (872–878) reported studies of the frequency of detecting persisting *M. leprae* utilizing the neonatally thymectomized rat. Gelber (879–881) described the utilization of the neonatally thymectomized rat as a model of the human lepromatous patient for studies of chemotherapy and immunotherapy. McDermott-Lancaster, *et al.* (885–888) presented the characteristics, breeding, and husbandry of nude mice. McDermott-Lancaster, *et al.* (889–895) characterized the multiplication of *M. leprae* in nude mice and the utilization of *M. leprae*-infected nude mice as models of lepromatous leprosy. Colston and Levy (896–898) reviewed the use of other experimental animals in infections with *M. leprae*. The Supplement concluded with a summary of the Workshop by Grosset, *et al.* (899–900).

From a personal perspective, quite a number of significant advances in our knowledge have occurred over the last year. In the field of chemotherapy, there are more reports that at least 1 year of treatment is necessary for a significant number of paucibacillary (PB) patients. Ofloxacin and pefloxacin have been shown to be active against *M. leprae* in mouse foot pad infections. Dapsone seems capable of producing a peripheral neuropathy. Several beta-lactam antibiotics have shown activity in mouse foot pad infections with *M. leprae*. There is a disturbing report that regularity in dapsone intake may be associated with the development of deformities in leprosy patients. In one study the development of relapse after MDT in multibacillary (MB) patients appeared to be determined by whether or not they took dapsone monotherapy after the period of MDT. On the other hand, a number of studies have shown no relapses to date after discontinuing treatment altogether following MDT regimens in MB and PB patients. Most of these studies have a follow-up to date of 2–5 years.

In clinical sciences it was shown that over half of untreated MB patients have a bacteremia in the range of $3–10 \times 10^4$ acid-fast bacilli per ml. Cyclosporine A was shown to be active in ENL. A very high proportion of leprosy patients were shown to have ab-

normalities of the venous system. ENL patients were successfully treated with plasma exchange and/or fresh-frozen plasma infusions with long-term freedom from recurrence.

A great deal of work has been done in the immunology of leprosy. Antigens of *M. leprae* which are capable of eliciting DTH reactions *in vitro* and *in vivo* are being identified, frequently on the basis of recombinant DNA technology. There is increasing emphasis on the distinction between DTH and protective immunity in leprosy. There has been the development and field application of various tests to date of anti-*M. leprae* antibodies, most based on the PGL-I antigen of the bacillus. Generally these showed that infection is relatively common compared to overt disease. Agglutination tests for leprosy serology seem promising. Lipoarabinomannan B has been shown to be a major immunogen of *M. leprae.* There was a report that in *in vitro* macrophage cultures, recombinant gamma-interferon enhanced the growth of *M. tuberculosis.* Active LL patients' monocytes seem to have an intrinsic abnormality in chemotaxis. The ability of PGL-I to induce DTH is controversial. Suppressor/cytotoxic T cells reactive with *M. leprae* may produce cytolysis of host cells for the organism. Amino acid sequences of epitopes on the 65 kD protein of *M. leprae* are now known and synthetic peptides based on these sequences have been shown to be immunologically active. The ability of peripheral blood mononuclear cells from LL patients to respond to *M. leprae* antigens *in vitro* and the role of suppressor cells in the pathogenesis of LL remain controversial. HLA-DR molecules are the main products of *M. leprae*-specific Ir genes. The immunogenetics of leprosy is becoming clearer. *M. leprae*-burdened macrophages are refractory to activation with gamma-interferon. Schwann cells seem able to present antigens. Macrophages infected *in vitro* with live mycobacteria failed to express Ia antigen after stimulation with lymphokines. Type 1 reactions in BT patients show reduced *in vitro* immunologic responses to *M. leprae,* while type 1 reactions in BB-BL patients show increases in *in vitro* reactivity. The 65 kD protein of *M. leprae* has been shown to have 14 different epitopes as measured by monoclonal antibodies. Tuberculin reactions in the skin are significantly inhibited in more than one half of both LL and BT patients by the admixture of leprosin. The FLA-ABS test can be applied to saliva.

In microbiology, a number of *M. leprae in vitro* systems are reportedly inhibited by antileprosy drugs. A variety of mycobacteria have been identified in armadillos, both wild and inoculated with *M. leprae.* Exochelins from *M. neoaurum* and an armadillo-derived mycobacterium could transport iron into *M. leprae.* The possibility was raised that *M. leprae* may replicate within certain amoebae. After *in vivo* exposure to penicillin in armadillos, *M. leprae* seem to develop a beta-lactamase. Limited multiplication of *M. leprae* was reported by Dhople and Green. Alpha-, keto-, and methoxy mycolates have been demonstrated in *M. leprae.*

In experimental infections, *M. leprae* has been shown to infect the placenta and fetuses in lepromatous nine-banded armadillos. A second sooty mangabey monkey was reported with naturally acquired leprosy. Three African green monkeys exhibited progressive disease after inoculation with *M. leprae,* followed by spontaneous regression of the external lesions. However, extensive peripheral nerve lesions were present on necropsy. Only 9% of armadillos are lepromin positive.

In the field of epidemiology, it may be relevant that in armadillos leprosy may be transmitted by thorn pricks. Leprosy appears to be declining in Malawi and this may be relevant for vaccine trials. As many as 88% of household contacts of lepromatous patients may be positive for anti-*M. leprae* antibodies using the FLA-ABS test. Anti-PGL-I antibody prevalences are five times the prevalences based on histopathological examination for leprosy in Louisiana armadillos. Evidence has been presented that leprosy may be transmitted in Micronesia by means of inoculation of *M. leprae* through frayed fibers of pandanus-leaf floor and sleeping mats. Experimental evidence was presented that *M. leprae* can penetrate intact skin.

As is clear from the perspective of the 1987 JOURNAL, there continues to be an ex-

plosion of information occurring in the field of leprosy. A great many talented individuals are now applying their knowledge and skills to unravel various pieces of the puzzle presented by this disease. In many fields leprosy research now seems to be at the forefront. Hopefully, we can exploit these opportunities and rapidly devise better means of caring for today's leprosy victims and preventing tomorrow's. I look forward with impatient optimism to 1988.—RCH