CURRENT LITERATURE

This department carries selected abstracts of articles published in current medical journals dealing with leprosy and other mycobacterial diseases.

General and Historical

Arnold, H. L. How "indeterminate" leprosy got its name. Int. J. Dermatol. **20** (1981) 393–395.

This is an interesting personal account of the background negotiations involving classification which took place during the Fifth International Congress of Leprosy in Havana in 1948. The Latin American proposal to use the term "incaracteristico (I)" had led to confusion since the English translation of "uncharacteristic" did not match the symbol "I." Dr. Arnold then suggested the English translation of "indeterminate." Surprisingly, the subsequent Spanish translation used the word "indeterminado (indifferenciado)." Although not accepted by that Congress, the term "indeterminate" stuck and was officially adopted at the Madrid Congress in 1953.—RCH

Zafarullah, M., Bano, Hasina and Vohora, S. B. Juzam (leprosy) and its treatment in Unani medicine. Am. J. Chinese Med. **8** (1980) 370–384.

Juzam (leprosy) is attributed to excessive accumulation, infiltration, and dispersal of *sauda* (burnt humors) throughout the body disturbing the normal temperament of the organs. A variety of causative factors responsible for excessive production or retention of *sauda* are enumerated. Unani plants, animals, minerals, and formations used for the treatment of leprosy are tabulated with recipes, methods of preparation, doses, and modes of administration.—Authors' Summary

Chemotherapy

Brasil, Secretaria da Saúde do Estado do Rio Grande do Sul. Erupções cutaneas graves causadas pela tioacetazona no tratamento da tuberculose, Estado do Rio Grande do Sul, Brasil. [Severe dermatitis induced by the use of thiacetazone in the treatment of tuberculosis in the State of Rio Grande do Sul, Brazil] Boletin de la Oficina Sanitaria Panamericana **90** (1981) 10–18. (in Portuguese)

Observations on 1890 inpatients receiving treatment for tuberculosis with streptomycin, INH and thioacetazone showed drug-induced dermatitis in 71 cases (incidence 37.6/1000) of which 18 (incidence 9.5/1000) were serious enough to have resulted in five deaths (mortality 2.6/1000). The data on the outpatients under treatment, although incomplete, indicated that the incidence of toxicity in the 1890 inpatients was comparable to that in the overall total of 12,434 patients under the same therapeutic scheme in the course of the observation period. In view of the high mortality rate encountered with the use of this scheme and considering that no such toxic effects were observed in prior schemes which included streptomycin and INH, thioacetazone was classified as unacceptable for routine application in the treatment of tuberculosis.—Authors' Summary

Farb, H., West, D. P. and Pedvis-Leftick, A. Clofazimine in pregnancy complicated

by leprosy. Obstet. Gynecol. **59** (1982) 122–123.

Little is known of the perinatal consequences of the use of clofazimine (B663, Lamprene) to treat leprosy. Two patients who were treated with the drug throughout pregnancy are presented and the literature is reviewed. Although the two current pregnancies ended successfully, three neonatal deaths in 15 pregnancies (20%) have been reported. These data suggest that patients taking clofazimine during pregnancy be managed at a perinatal center where adequate neonatal care can be given.—Authors' Summary

Gidoh, M., Tsutsumi, S. and Takitani, S. Determination of three main antileprosy drugs and their main metabolites in serum by high performance liquid chromatography. J. Chromatogr. **223** (1981) 379–392.

The simultaneous analysis of main antileprosy drugs such as 4,4′-diaminodiphenyl sulfone (DDS), clofazimine, rifampin and their main metabolites in serum was examined by high performance liquid chromatography using a μBondapak C_{18} column. When the drugs dissoluted from serum were developed by tetrahydrofuran–0.5% acetic acid (40:60), clofazimine and rifampin could be analyzed separately. Apart from the mutual separation of water-soluble conjugates of DDS, the individual analysis of DDS, its main liposoluble metabolite and a few related sulfone compounds is possible when the drugs are first developed by acetonitrile–water (20:80). By the use of tetrahydrofuran–water (50:50) containing PIC B5, the rapid measurement of clofazimine isolated from the other compounds is also possible.—Authors' Summary

Laing, A. B. G. The problem of dapsone-resistant leprosy: diagnosis and management. Int. J. Dermatol. **20** (1981) 275–277.

The prevention of sulfone resistance depends on improving the training and expertise of leprosy control workers so that relapsing and defaulting patients can be picked up much more quickly than at present. If all leprosy cases are properly surveilled, sulfone-resistant cases will be detected early and will have less chance of spreading their resistant infection to others.—Author's Summary

Nath, I., Prasad, H. K., Sathish, M., Sreevatsa, Desikan, K. V., Seshadri, P. S. and Iyer, C. G. S. Rapid, radiolabeled macrophage culture method for detection of dapsone-resistant *Mycobacterium leprae*. Antimicrob. Agents Chemother. **21** (1982) 26–32.

Mycobacterium leprae cells extracted from the skin biopsies of 14 bacilliferous lepromatous patients were maintained in human-murine macrophage cultures for three weeks in the presence of [^{3}H]thymidine and DDS (4,4′-diaminodiphenyl sulfone). All cultures except one containing freshly extracted viable bacilli showed significant incorporation of [^{3}H]thymidine as compared with control cultures containing heat-killed bacilli of the corresponding strain. Six susceptible strains of *M. leprae* obtained from untreated, freshly diagnosed patients showed significant inhibition of the uptake of the radiolabel in the presence of 3 ng and 10 ng of DDS per ml per culture. Eight strains of *M. leprae* obtained from patients clinically suspected of DDS resistance were tested in a similar manner. These strains were also concurrently inoculated in the foot pads of mice given orally 10^{-2}, 10^{-3}, and 10^{-4} g of DDS per 100 g of diet for nine months. Concordant results were obtained by both methods: five strains were found to be resistant, one was susceptible, and one was partially resistant. Strain VIII did not incorporate [^{3}H]thymidine in the macrophage cultures and proved to be resistant in the mouse foot pad. The macrophage culture system provides a sensitive, rapid screening method for the early diagnosis of DDS resistance.—Authors' Summary

Pattyn, S. R., Van Loo, G. and Sansarricq, H. Quatre cas de lèpre dapsone resistants en Haute-Volta. (Four cases of dapsone-resistant leprosy in Upper Volta.) Médecine d'Afrique Noire **28** (1981) 147–148. (in French)

In four out of five patients clinically suspected of dapsone resistance and observed

in Ouagadougou, the presence of DDS-resistant *Mycobacterium leprae* was proven by mouse foot pad inoculation. The same technique indicated an irregular intake of dapsone in the fifth patient.

In common with other documented cases from Mali, Senegal, and Burundi, these patients from Upper Volta had been treated for more than 20 years. It now remains to determine the extent of the problem at country level and to establish if cases of dapsone resistance arise earlier but escape attention, or if they do not in reality exist.—A. C. McDougall (*From* Trop. Dis. Bull.)

Rezaev, A. A. The influence of antileprosy drugs on glycolytic processes in rats infected with *M. leprae*. Vestnik Dermatologii i Venerologii **11** (1981) 32–34. (in Russian)

The effect of current antileprosy drugs on levels of lactic (LA) and pyruvic (PVA) acids in the blood, liver, and leproma in rats infected with adapted strains of *M. leprae* was studied. Rats were treated with solusulphone alone and with solusulphone-rifampin, solusulphone-prothionamide, solusulphone-prothionamide-rifampin combinations. The highest level of LA was noted in blood and liver from rats receiving solusulphone with rifampin and prothionamide and in leproma from untreated animals. The increased levels of PVA in blood and liver were observed in the animals without treatment. The level of PVA decreased in rats given solusulphone in combination with rifampin and rifampin and prothionamide during a month. Solusulphone-prothionamide combination did not change PVA level. The lowest level of PVA in blood and liver was noted in rats treated with solusulphone-rifampin-prothionamide combination. It was observed that with decrease in PVA level the levels of LA increased and vice versa. Thus the lowest PVA level corresponded to the highest level of LA in rats treated with solusulphone-prothionamide-rifampin combinations. The optimal balance between LA and PVA levels was achieved in animals treated with solusulphone alone.—A. A. Juscenko

Shepard, C. C. A brief review of experiences with short-term clinical trials monitored by mouse-foot-pad inoculation. Lepr. Rev. **52** (1981) 299–308.

Beginning in 1964 we used mouse foot pad inoculations to monitor the loss in numbers of viable *Mycobacterium leprae* that occurs when the patient begins antileprosy therapy. Our studies eventually involved patients at the U.S. Public Health Service Hospital in San Francisco and the Leonard Wood Memorial facilities in Cebu, Philippines, and mouse foot pad laboratories in San Francisco and Cebu, as well as Atlanta. We found that to monitor short-term therapeutic trials, the mouse foot pad method was the most efficient one available, in the sense that it required the smallest number of patients. All the results are compiled here in a standard form of presentation to facilitate comparisons between trials and regimens. A table is provided for statistical consideration of results such as these.—Author's Summary

Warndorff, J., Bourland, J. and Pattyn, S. R. Follow-up on short-course 2 months' rifampicin treatment of paucibacillary leprosy. Lepr. Rev. **53** (1982) 9–17.

The results of follow-up for between one and three and a half years of paucibacillary leprosy patients treated with eight weekly doses of 900 mg rifampin are presented.

In the pilot trial in Burundi, eight patients were followed for three years and more. All did well, including one patient who developed a reversal reaction.

In Addis Ababa, three patients on rifampin developed neuritis at 9 to 18 weeks after the start of therapy and were excluded from the trial. Three patients treated with rifampin were followed for three years and five for at least two years. All patients had their lesions healed or considerably improved; there were no relapses and no adverse effects due to the intermittent administration of the drug. Three patients in the dapsone-treated group were followed for three years and two for at least two years. In this group one patient developed severe neuritis and two others, who absconded for about two years, did not improve clinically or worsened.

Compared with standard dapsone therapy, rifampin treatment did not accelerate healing; neuritis was not more frequent but it occurred much earlier. Some points to be taken care of in similar future trials are discussed.—Authors' Summary

Clinical Sciences

Baranov, Y. N. and Podoplelov, I. I. Features of digital dermatoglyphics in leprosy patients. Vestnik Dermatologii i Venerologii **4** (1981) 64–67. (in Russian)

A comparative study of digital dermatoglyphics was performed in 438 patients with leprosy, 292 of their healthy blood relatives, and 500 healthy controls. Compared with healthy controls, leprosy patients and their relatives showed a significant increase in the frequency of whorls in the fingers, due mainly to a decrease in arcs and due less to a decrease in loops. Accordingly, they showed a tendency to an increase in the total ridge count, but such tendency was significant only for women. It was concluded that the fingerball patterns of the "whorl" type indicate an increased susceptibility to leprosy; whereas the patterns of the "arc" type are obviously associated with the factors of relative resistance to the disease. It is suggested that dermatoglyphic studies in leprosy endemic areas might be useful for revealing the factors of hereditary associated with a high risk of infection with leprosy.—A. A. Juscenko

Centro de Estudos "Reynaldo Quagliato." Hanseniase dimorfa com surtos de reacao hansenica e lesoes viscerais. (Dimorphous hanseniasis with outbreaks of hansenic reactions and visceral lesions. Hansen. Int. **4** (1979) 116–125. (in Portuguese)

The paper presents the case of a patient with borderline hanseniasis. After a long period of illness, he presented an outbreak with new lesions that showed reactional tuberculoid aspects; he later presented lesions with clinical and histological aspects of virchowian hanseniasis. This evolutional type is compatible with the pseudo-exacerbations outbreaks reported by Souza Lima. This patient also presented an erythema nodosum outbreak with clinical manifestations of icterus and hepatomegaly. The pathogenesis of the pseudo-exacerbations outbreaks is discussed, as well as the special situation of borderline patients, subject to neurologic injuries during the pseudo-exacerbations outbreaks, and cutaneous, neurological, and visceral lesions during the erythema nodosum Hansenicum outbreaks.—Authors' Summary

Kasili, E. G., Orinda, D. A. and Mudasia, J. Serum lysozyme (muramidase) levels in the normal and various pathological states in Kenyan Africans. E. Afr. Med. J. **58** (1981) 163–170.

Serum lysozyme was assayed spectrophotometrically in 186 Kenyan Africans. The sample composition comprised 95 normal controls and 91 patients with the following distribution of diseases: leukemia, 32; carcinoma of the esophagus, 29; malignant lymphoma, 14; Wilms' tumor, 6; lepromatous leprosy, 5; and others, 5. The enzyme activity was markedly raised in chronic granulocytic leukemia and acute myelomonocytic leukemia. Cases of acute lymphocytic leukemia and carcinoma of the esophagus had significantly reduced enzyme activity. Contrary to what has been previously reported, serum lysozyme levels in Wilms' tumor, malignant lymphoma, and chronic lymphocytic leukemia were found to be normal. Similarly, leprosy patients and one with multiple myeloma showed normal values. Serum lysozyme determinations are of value in the diagnosis of acute leukemias and chronic granulocytic leukemia.—Authors' Summary

Kaur, S., Kumar, B., Kataria, Y. P. and Chakravarti, R. N. Kveim test in leprosy: a clinical and histopathological evaluation. Lepr. Rev. **52** (1981) 329–335.

The gross appearances and microscopic features of Kveim tests were studied in 21 North Indian leprosy patients. Of six patients with tuberculoid leprosy, two showed positive reactions and a close correlation between nodule formation and granulomatous histology. Of 15 patients with lepromatous leprosy, only one patient (who showed no evidence of a papule or induration at the Kveim test site) yielded a positive response microscopically. These findings suggest the occurrence of a low level of Kveim reactivity in North Indian leprosy patients. However, it is suggested that further studies with proper controls should be carried out to eliminate the possibilities of chance inclusion of subclinical leprotic skin lesion at the site of Kveim antigen injection and needle trauma in triggering or accelerating granulomatous inflammation.—Authors' Summary

Reddy, S. C., Subrahmanyam, V. V. and Padmavathi, L. Ocular lesions in leprosy. Indian J. Dermatol. Venereol. Lepr. **47** (1981) 220–225.

Out of 100 cases of leprosy studied for ocular complications, 46 were suffering from lepromatous leprosy and 54 from non-lepromatous leprosy; 72 were males and 28 females. The patients were in the age group of 13 to 70 years, with the maximum incidence (45%) in the fifth decade of life. The mean duration of leprosy was 11.8 years, with a range between 4 and 36 years.

Single or multiple ocular lesions were found in 84% of patients. Impaired or absent corneal sensation (70%) was the most frequently seen ocular lesion in this study, followed by madarosis of eye brows and eye lids (56%), anterior uveitis (21%), lagophthalmos (19%), ectropion of lower lid (8%) and scleral lesions (4%), etc. Uniocular blindness was observed in 8% of patients. Periodical check up of all leprosy patients for any ocular involvement is essential in order to detect and treat the eye complications in early stages.—Authors' Summary

Saoji, A. M. and Kelkar, S. S. Qualitative studies of serum lactate dehydrogenase isoenzyme patterns in leprosy. Lepr. Rev. **52** (1981) 309–314.

Serum lactate dehydrogenase isoenzyme patterns were studied in polyacrylamide gel disc electrophoresis in 72 cases of leprosy to define correlation with clinical varieties and presence of specific pattern. The cases were classified on the basis of history, clinical examination, bacterial and morphological indices, lepromin test and biopsy according to Ridley and Jopling into 41 lepromatous (15 active, 23 regressing and 3 ENL); borderline lepromatous, 5 cases; borderline tuberculoid, 7 cases; tuberculoid, 18 cases and indeterminate, 1 case. Serum LDH zymograms showed a diversity of patterns but there was no correlation with the clinical form of the disease. The commonest abnormalities affected isozymes 4 and 5. Thus in 28 cases both isozymes were depressed or absent and in a further 18 cases one or other of these isozymes were depressed or absent. Four cases showed other abnormalities, and in 11 cases each the LDH zymogram was normal or showed a generalized increase in density of all five LDH bands. In 25 healthy controls, 23 showed a normal isozyme pattern and in 3, LDH 5 was absent.—Authors' Summary

Sheskin, J., Gorodetsky, R., Weinreb, A. and Loewinger, E. Iron content of skin before and after thalidomide treatment of lepra reaction. A preliminary report. Dermatologica **163** (1981) 145–150.

The concentration of copper, zinc, and iron in the skin of patients suffering from lepra reaction was measured by diagnostic x-ray spectrometry (DXS) at the sites of the lesions before and after treatment with thalidomide. The results were compared with the levels of these elements in the skin of healthy individuals. No significant changes in the copper level of leprous skin were found. The zinc levels showed significant elevations in some lesions with no apparent trend. The iron level in the affected areas had highly elevated values in all cases of lepra reaction. However, in contrast to the fast clinical improvement which followed the treatment with thalidomide, the iron levels did not decrease for prolonged periods.—Authors' Summary

Sheskin, J., Sabato, S. and Yosipovich, Z. La prueba de formación de arrugas pro-

vocadas por el agua tibia sobre las yemas de los dedos en el diagnóstico del mal de Hansen. (A test of wrinkle formation caused by soaking in warm water in diagnosing Hansen's disease.) Rev. Fontilles **13** (1981) 149–154. (in Spanish)

The following test was carried out with 22 leprosy patients and 20 healthy people participating. All immersed their hands in water at a temperature of 38°C to 40°C for a period of half an hour. At the end of that time it was observed that while 100% of the uninfected persons showed considerable puckering of the skin on their fingers, this manifestation was absent in 18 of 22 diseased participants.

Certainly the test group was small. However, if this experiment were to be carried out on a larger scale, and should the results confirm our findings, it would provide one more factor to consider in the diagnosis of leprosy.—Authors' Summary

Soni, N. K. and Chatterji, P. Disturbance of taste in leprosy. J. Laryngol. Otol. **95** (1981) 717–720.

The sense of taste was assessed in a group of 30 leprosy patients. The method used and the results are presented. Twelve patients (40%) showed some degree of impairment of taste sensation and this was shown to be related to the severity of the disease. The possible reasons for the loss of taste are discussed.*—Authors' Summary

Tokudome, S., Kono, S., Ikeda M., Kuratsune, M. and Kumamaru, S. Cancer and other causes of death among leprosy patients. J. Natl. Cancer Inst. **67** (1981) 285–290.

A follow-up study was done on the mortality from 1956 to 1975 among 2383 Japanese patients with leprosy who were admitted to a leprosarium in Japan. The leprosy was classified into two types: lepromatous and tuberculoid. Irrespective of the type of leprosy or the sex of the leprosy patient, mortalities were increased from tuberculosis, pneumonia and bronchitis, nephritis and nephrosis, and from total causes. The suicide rate was high among female patients. Deaths from total malignant neoplasms were higher than expected among patients with lepromatous leprosy for both sexes (49 observed vs. 44.02 expected); whereas they were lower than expected among patients with tuberculoid leprosy (35 observed vs. 36.83 expected). However, the differences were not statistically significant. Mortalities from cancers of the cervix and the esophagus among females with lepromatous leprosy were significantly high. The risk of lymphoreticular cancers was not increased.—Authors' Summary

Yoshimura, M., Sameshima, M., Fujita, S. and Ohba, N. Blood staining of the cornea in Hansen's disease: a light- and electron-microscopic study. Ophthalmologica (Basel) **181** (1980) 314–319.

Blood staining of the cornea was studied by light and electron microscopy: a 55-year-old male with Hansen's disease had blood staining of the cornea due to intracorneal hemorrhage; he received a partial-thickness keratoplasty following one year after the onset of the staining. The excised specimens revealed deposits of degraded erythrocytes in the stroma. Numerous dense granules, probably of erythrocytic breakdown products, were phagocytosed by macrophages as well as parenchymal cells. The presence of macrophages was limited to the middle part of the stroma in which newly formed vessels were remarkable.—Authors' Summary

* Editor's Note: One of 9 patients with BT-TT had impairment of taste sensation; 2 of 8 with BB, and 9 of 13 with BL-LL leprosy.—RCH

Immuno-Pathology

Cabrini, J. M., Botasso, O., Corona, C. and Morini, J. C. Lepra: Inmunologia. (Leprosy: Immunology). Leprologia **22** (1980) 91–103. (in Spanish)

The authors review the immunology of leprosy. They begin by describing the methodology used to study cell-mediated and humoral immunity. They review published results of such tests in leprosy patients and compare both types of immunity in the different forms of the disease. Various hypotheses are discussed as to the probable mechanisms of the deficient immune responses in patients with lepromatous leprosy: 1) a defect in macrophages in lysing the bacillus and/or processing antigens of the bacillus; 2) blockade of the afferent branch of the immune response in which antigen could not be recognized because it is masked by blocking antibodies; 3) blockade of the efferent limb of the immune response in which immunized cytotoxic T lymphocytes are present, but they are unable to function due to blockade by immune complexes; 4) genetic deficiency of the immune response in which there is a lack of the capacity to recognize certain antigens; 5) active suppression of cell-mediated immunity by the activation of suppressor lymphocytes.—Authors' Summary

Corona, C. J. J., Cauzzi, N., Cabrini, J. L., Poli, H. and Morini, J. C. Repuesta cutanea a la lepromina bacilar normalizada incubada con suero de enfermos de distintas formas clinicas de lepra. (Cutaneous response to normal bacillary lepromin incubated with sera from patients with distinct clinical forms of leprosy.) Leprologia **22** (1980) 143–144. (in Spanish)

The object of this study was to study the mechanisms responsible for the defective immune response of patients with lepromatous leprosy to *Mycobacterium leprae*. Bacillary lepromin was incubated with various sera and injected intradermally in the interscapular space into patients with tuberculoid leprosy. Lepromin preparations were separately incubated with: a) saline (control), b) normal human serum, c) serum from patients with tuberculoid leprosy, d) serum from patients with lepromatous leprosy, and e) serum from patients with reactional lepromatous leprosy. The cutaneous responses in the tuberculoid patients who received injections of these lepromin preparations were evaluated at 48 hr (early) and at 21 days (late). No changes were noted in the late responses. On the other hand, early cutaneous responses were reduced when normal bacillary lepromin was incubated with serum from reactional lepromatous leprosy patients. This could be due to the increased production and/or liberation of blocking elements in reactional lepromatous leprosy. These blocking elements could then act to coat the antigenic sites on the bacilli resulting in a weak immune response.—*Adapted from* Authors' Summary.

Dastur, D. K., Porwal, G. L., Shah, J. S. and Revankar, C. R. Immunological implications of necrotic, cellular and vascular changes in leprous neuritis: light and electron microscopy. Lepr. Rev. **53** (1982) 45–65.

The fine structural changes and, to a lesser extent, histochemical and histopathological features of biopsy specimens of nerves from patients with non-lepromatous leprosy (mainly very early cases), or lepromatous leprosy (mostly treated cases), have been studied from the point of view of possible immunological response of the host tissues. Using electronmicroscopy and acid phosphatase or β-glucuronidase as markers of lysosomal enzymes, the survival and degradation of *Mycobacterium leprae* by Schwann cells and macrophages in the nerves is compared; both these cells utilizing the lysosomal machinery for such degradation, the macrophages more strongly, once the individual bacillary space has been breached. Long-treated lepromatous patients show relatively fewer intact and more degenerating bacilli. Both live and killed *M. leprae* appear to provide antigenic material, and plasma cells as well as activated macrophages harboring considerable rough ER

probably produce antibodies and lysosomal enzymes.

Impressive, fine structural changes in clinically well-preserved nerves from patients with very early non-lepromatous leprosy, as well as those with overtly tuberculoid and untreated or treated lepromatous leprosy, included the appearance of products of breakdown of nerve fibers, particularly of myelin, vacuolated macrophages among the fibers; and changes in the intraneural blood vessels such as loosening of the endothelial-tight junctions, proliferation of basement membrane and exudation of plasmatous material perivascularly. On the basis of these findings three possible nonbacterial antigens producing damage to nerve parenchyma are considered: 1) myelinogenous proteins which are known to evoke allergic neuritis and further myelin destruction, as an autoimmune mechanism; 2) the vascular basement membrane material which is mainly a protein, like reticulin; and 3) plasma proteins, especially when containing high, circulating levels of antibodies.—Authors' Summary

Dharmendra. Resistance against leprosy in armadillos—intraspecies differences of. (Editorial) Lepr. India **53** (1981) 505–506.

Studies of the cellular mechanisms of resistance require a precise definition of resistance in terms of a standard challenging dose. Assuming a situation similar to that prevailing in man, Kirchheimer and Sanchez attempted to find a challenging dose the maximum number of *Mycobacterium leprae* which will not cause disseminated leprosy in 90% of intradermally infected armadillos within three to four years. To their surprise dose-response experiments with decreasing doses of leprosy bacilli have produced unexpected results. Even when infected with as few as 10^3 *M. leprae* (A), only a small proportion of armadillos will exhibit resistance. Therefore, resistance against leprosy in the human species and in nine-banded armadillos shows a reversed frequency distribution and therefore might not be based on identical mechanisms.

In a limited trial the same workers had shown that heat-killed *M. leprae* in an adjuvant provides protection against challenge with live *M. leprae* in armadillos but, in view of their recent observations, it is doubtful that the efficacy of vaccinating human beings against leprosy can actually be evaluated in armadillos.—(*Adapted from* the editorial)

Meghlaoui, A., Herbage, D., Huc, A. and Monier, J. C. Mise au point d'une technique immunoenzymatique (ELISA) pour la détection des anticorps anti-collagène de type I et II: recherche de ces anticorps au cours de la polyarthrite rhumatoïde, du lupus érythémateux disséminé et de la lèpre. (Detection of anti-collagen type I and II antibodies by an immunoenzymatic technique (ELISA): results in rheumatoid arthritis, systemic lupus erythematosus and leprosy.) Ann. Immunol. (Inst. Pasteur) **132** (1981) 287–305. (in French)

An attempt was made to detect antibodies against type I and/or II collagen in sera from patients with rheumatoid arthritis, systemic lupus erythematosus (SLE), and leprosy. This study was performed with an immunoenzymatic technique: ELISA (enzyme-linked immunosorbent assay).

The following steps were performed: bovine collagen type I or II was adsorbed on glass beads; possible free sites were saturated by incubating the beads with sheep serum; then the antibodies specifically bound to collagen were detected by a peroxidase-labelled anti-immunoglobulin; the immune complexes at the surface of the beads were revealed by a substrate specific for peroxidase and of great stability—Trinder's reactive.

Using conditions previously shown to be optimal, the prevalence of anti-collagen antibodies was as follows: In patients with lepromatous leprosy the percentages of positive sera against collagen type I and II were 40% and 44%, respectively; in patients with tuberculoid leprosy the percentages were lower, 10% and 30%, respectively. Ten percent of the SLE patients had antibodies against collagen type I, half of the prevalence noted for anti-collagen type II antibodies (20%). Finally, 13.6% of the patients with rheumatoid arthritis had antibodies against collagen type I, a percentage very similar to that of the patients with

anti-collagen type II antibodies (14.6%).—Authors' Summary

Mshana, R. N. Hypothesis: erythema nodosum leprosum is precipitated by an imbalance of T lymphocytes. Lepr. Rev. **53** (1982) 1–7.

Erythema nodosum leprosum (ENL) has so far been taken as an immune complex mediated disease. Failure to demonstrate these complexes in or around blood vessels showing perivasculitis in a substantial number of patients with ENL has never been clearly explained. It is proposed that initiation of ENL is mediated by an imbalance of T lymphocytes, especially suppressor T cells, leading to modulation of polymorphonuclear leukocyte function.—Author's Summary

Potts, R. C., Sherif, M. M., Robertson, A. J., Gibbs, J. H., Brown, R. A. and Beck, J. S. Serum inhibitory factor in lepromatous leprosy: its effect on the pre-S-phase cell cycle kinetics of mitogen-stimulated normal human lymphocytes. Scand. J. Immunol. **14** (1981) 269–280.

The sera of ten Egyptian men with long-standing lepromatous leprosy (LL) (mean duration 17.4 years) that had failed to respond to dapsone treatment were shown to inhibit mitogen stimulation responses of normal human lymphocytes. When first tested, the sera partly inhibited the response to phytohemagglutinin (PHA) and pokeweed mitogen and virtually abolished that to concanavalin A (Con A). After repeated freezing and thawing, the Con A inhibition had disappeared; whereas the PHA response was still partly inhibited. The inhibitory serum factor(s) had similar actions on lymphocytes from each of six normal donors. Although the sera varied in potency, they showed similar dose-response curves when tested against lymphocytes from a single donor. The principal action of the sera was to reduce the number of cells responding to mitogen, without modifying the kinetics of recruitment or rate of volume growth during G_1-phase in those cells that were unaffected by the inhibitory substances(s). Study of PHA dose-response curves and of the effect of delayed addition of LL serum suggested that the serum factor(s) act by diminishing the responsiveness of the cells, rather than by reducing the concentrations of free mitogen or by blocking cell membrane mitogen receptors. The serum from one apparently healthy attendant, who had nursed leprosy patients for 30 years but who did not have leprosy or other chronic infective disease, completely inhibited stimulation by all three mitogens in a manner different from that of LL sera. Serum from the other 13 control patients did not modify the response of normal lymphocytes to stimulation by any of the three mitogens studied. It was concluded that the inhibitory factor(s) in the serum of patients with LL were a consequence of the disease and not of the environment in which the patients lived. Microscopy confirmed that the techniques used for recovery of the cultured cells did not introduce bias into the volume spectroscopy measurements.—Authors' Summary

Pudifin, D. J. and Duursma, J. Circulating immune complexes in normal blood donors of three races. S. Afr. Med. J. **60** (1981) 886–887.

Circulating immune complexes were measured by means of a modified Raji cell assay in 50 blood donors from each of three race groups—Indian, Black, and White. The results ranged widely and were, on the average, higher in Blacks than in others. The difference is probably related to the hypergammaglobulinaemia commonly found in Blacks. For maximum clinical usefulness, results should be expressed so as to indicate the degree of variation from appropriate normal mean.

Because the finding of immune complexes in serum does not necessarily indicate disease, it is clearly vital that results be carefully interpreted in the light of the other laboratory and clinical features in each case.—(*Adapted from* Authors' Summary)

Qiang Nengxian, Ma Lin, Wang Donghuai, Gu Shenggui, Feng Bi and Shi Zhangying. Investigation of T lymphocytes and acid non-specific esterase activity in leprosy patients. Chinese J. Dermatol. **14** (1981) 142–146. (in Chinese)

Using the active E-rosette test, total E-rosette test and acid α-naphthyl acetate esterase (ANAE) cytochemical staining method, the percentage of Ea·RFC, Et·RFC, ANAE-positive lymphocytes, ANAE-positive Ea·RFC, and Et·RFC in peripheral blood were detected in 76 patients with active leprosy (lepromatous leprosy 46, tuberculoid leprosy 30). The results showed that the percentages of Ea·RFC and Et·RFC of both groups of leprosy patients were lower than that of the normal individuals. The decrease of ANAE-positive lymphocytes in L leprosy patients was more marked than in T leprosy patients. These findings suggest that active L and T leprosy patients lack mature T-lymphocytes and T-lymphocytic population with the receptor of sheep erythrocytes in peripheral blood, especially in L patients. Thus the ANAE staining method may be used as a useful approach to determine clinically the state of cell-mediated immunity of leprosy patients and to investigate the subpopulations of lymphocytes.—Authors' Summary

Ridley, D. S. The pathogenesis and classification of polar tuberculoid leprosy. Lepr. Rev. **53** (1982) 19–26.

Skin biopsies received from about 1500 patients of varied ethnic and geographical origins produced 26 cases that fell within the polar tuberculoid (TT) group on the strictest definition, and a further 18 cases that might be considered as TT on histological and immunological grounds.

The 44 cases were of two broad types. Nearly half were characterized by many lymphocytes but few other histological features, with no severe nerve involvement, no signs of reaction and good clinical-histological correlation. The remainder were characterized by severe nerve involvement or erosion of the epidermis and often by signs of reaction, all of which are associated with high lymphocyte transformation values; many of these cases were clinically BT.

There was a fairly sharp distinction between these two types, with an intermixing of features only in cases that were not truly polar. There was also a partial geographical separation of the two types. The first appeared to represent primary lesions with high cell-mediated immunity; the second, to have evolved through reactions associated with delayed hypersensitivity.—Author's Summary

Saha, K. and Lahiri, S. C. Pharmacologically active mediators of hypersensitivity reactions in the blood of lepromatous patients with erythema nodosum leprosum. Lepr. Rev. **52** (1981) 315–320.

A bioassay technique was employed to study the mediators of hypersensitivity reactions (MHR) in the blood of 9 control subjects and 20 borderline and polar lepromatous patients, including 8 patients with erythema nodosum leprosum (ENL). MHR were isolated from blood and studied on virgin rat uterus following the technique originally described by Brocklehurst. The contractions of the uterus were recorded, compared with a stock bradykinin solution which was taken as the reference standard and the levels of MHR were expressed as ng bradykinin equivalent/ml blood. The mean level of MHR in lepromatous patients without ENL was 6.69 ng bradykinin equivalent/ml blood, but was significantly elevated in patients with ENL (18.09 ng bradykinin equivalent/ml). It was postulated that during the attack of ENL, *Mycobacterium leprae* or its broken products were released in the circulation containing high levels of antimycobacterial antibodies and thereby triggered the formation of circulatory immune complexes (CIC), activation of complement, deposition of CIC in various tissues, and release of pharmacologically active mediators of hypersensitivity reactions.—Authors' Summary

Saha, K., Sharma, V. and Siddiqui, M. A. Decreased cellular and humoral anti-infective factors in the breast secretions of lactating mothers with lepromatous leprosy. Lepr. Rev. **53** (1982) 35–44.

Breast secretions from 28 healthy lactating women and 12 lepromatous mothers feeding their children for a varying period (2 days to 2½ years) were studied for the total and differential cell counts and immunoglobulin concentrations. It was observed that the total leukocyte count in the milk of the lepromatous mothers was low

and also the macrophage count was significantly decreased. The mean secretory immunoglobulin-A level was significantly decreased in the colostrum as well as in the mature milk of the lepromatous mothers as compared with those from the healthy mothers. Acid-fast bacilli could be detected in 9 of the 12 leprosy patients' breast secretions by employing a new technique of coprecipitation of bacteria by 4% polyethylene glycol. The immunologic implications of these findings have been discussed.—Authors' Summary

Stanford, J. L., Nye, P. M., Rook, G. A. W., Samuel, N. and Fairbank, A. A preliminary investigation of the responsiveness or otherwise of patients and staff of a leprosy hospital to groups of shared or species specific antigens of mycobacteria. Lepr. Rev. **52** (1981) 321–327.

In an attempt to classify skin test responsiveness of leprosy patients according to the groups of antigens, rather than the individual mycobacterial species to which they respond, we have tested patients and staff members at Anandaban leprosy hospital in Nepal with Burulin (made from *Mycobacteria ulcerans*) and three specially mixed reagents. Ability to make a positive response to group i, common mycobacterial antigens, was almost absent and to group ii, antigens associated with slow growers, was markedly impaired in the patient groups. However, positive responses to group iv, species specific, antigens of slowly growing species were retained. Non-specific skin-test unresponsiveness (Category 2) due either to sequestration of the relevant cells outside the circulation or to circulating suppressor factors was present in 2 of 27 staff members, 9 of 24 TT/BT patients, 11 of 18 BL patients, and 10 of 22 LL patients. Evidence of a suppressor mechanism possibly triggered by group iv antigens of fast growers and operative on positive responses to slow growers, was demonstrable in 3 of 12 staff members, 8 of 14 TT/BT patients, 7 of 7 BL patients, and 6 of 12 LL patients.

It cannot at the moment be proved whether these observations are related to susceptibility to the disease or are consequences of it. However, the presence of the same, or similar, suppressory phenomena among staff members argues against the latter.—Authors' Summary

Stoner, G. L., Touw, J., Atlaw, T. and Belehu, A. Antigen-specific suppressor cells in subclinical leprosy infection. Lancet **2** (1981) 1372–1377.

A two-stage *in vitro* culture system was used to assay cells which suppress the lympho-proliferative response to *Mycobacterium leprae* (ML). Responses to ML, purified protein derivative of tuberculin, and streptokinase-streptodornase were preferentially suppressed by mitomycin-treated cells which had been primed with the same antigen in a seven-day primary culture. Healthy subjects exposed to leprosy for more than three years showed strong suppression of the response to ML antigens (11 of 12 showed more than 40% suppression); whereas those exposed for three months to three years showed much less suppression (12 of 15 showed less than 40% suppression). The *in vitro* generation of strong ML-specific suppression may reflect the maturation of a well-regulated and protective immune response. However, premature induction and *in vivo* activation of these suppressor cells could predispose to disseminated (lepromatous) forms of leprosy. With this assay, it would be possible to assess the ability of proposed leprosy vaccines to engage strongly the regulatory network controlling the immune response to ML in the same way as long-term exposure to the natural infection.—Authors' Summary

Tarabini-Castellani, G., Tarabini-Castellani, G. L., Dinle, Y. H., Mohamed, F. A., Yacub, A. H., Agib, A. M. and Mahamud, I. A. Investigaciones sobre la cicatriz post-leprominica. (Studies on the post-lepromin scar.) Rev. Fontilles **13** (1981) 155–190. (in Spanish)

The post-lepromin scar (p.l.s.) for the first time in 1977 was made the object of a broad-based study with human lepromin by J. Walter, *et al.* in leprosy sufferers mostly tuberculoid cases, in Burma, Mandalay, area: "the post-lepromin scar, subject to further studies, might be regarded as a re-

liable indicator of a stabilized immune situation and could be a means of identifying high resistant individuals in the population."

Our research on the p.l.s. using lepromin of armadillo was conducted on healthy subjects, some of whom were already vaccinated and others not vaccinated with BCG, in both endemic and non-endemic areas. Attention was focused on the influence of the BCG vaccine administered simultaneously with the lepromin test on immunodepressed cases.

Our findings have been as follows:

1) There is, percentagewise, a direct relation between the appearance of the p.l.s. and the size of the Mitsuda nodule. The p.l.s. occurs in all cases where there is an ulcerated nodule, and often also when the nodule is not ulcerated, including 1 mm to 2 mm nodules. Prior vaccination with BCG results in an increase in the overall percentage of cases showing the p.l.s. In non-endemic areas the percentage increase was 20.33 (ranging from 56.81 in 44 subjects not previously vaccinated with BCG to 77.14 in 70 subjects vaccinated with BCG). In the endemic areas the p.l.s. increased 41.17 (ranging respectively from 38.81% in 237 cases to 80.08% in 226).

2) In the screening in an agricultural village, 432 persons were subjected to a lepromin test; the p.l.s. reading was possible in 98% because there was no time limit. In the control village, the combined reading of Mitsuda nodule and of p.l.s. was possible only in 53.37% of 444 persons who had been equally subjected to the lepromin test*.

3) Following a second lepromin test administered to 52 lepromin-negative subjects, the p.l.s. developed in: a) 45% of cases (20 subjects) who had been injected with a single mixture of lepromin + BCG; b) 41.7% cases (17 subjects) injected with BCG alone; c) 6.66% of cases (15 subjects) injected with lepromin used as a vaccine. Only one subject, in the group treated with BCG alone, developed an ulcerated nodule.

4) Two young women who had responded negatively to three consecutive lepromin tests were administered lepromin + BCG mixture. In both cases there was a positive response to the lepromin test injected at the same time, an ulcerated nodule of 12 mm followed by the post-lepromin scar. Five months later, their response to a subsequent test was considerably weaker: both women developed a 4 mm to 5 mm nodule, but only one showed ulceration, and a small normochromic post-lepromin scar. The control subject, equally immune-depressed, developed a 4 mm nodule at the fourth and fifth lepromin test; the nodule was not ulcerated and did not evolve into the p.l.s. This finding, therefore, is not less than the results given by the second subject in the experiment.

The p.l.s. obtained in immunodepressed subjects as a result of a simultaneous vaccination cannot be taken as an indicator of a stabilized immune situation, as it could be in all other cases.

At the same time, it is considered to justify the hope to achieve a stabilized CMI even in these cases through further research and intensified vaccinations.

5) It is considered that the p.l.s.: a) Is the only lepromin reading which permits an easy and secure screening in the healthy immunodepressed persons of hansenian endemic regions, a research which constitutes the first step for the eradication of the leprosy; b) can be a practical system for the research of the C.M.I. against *M. leprae* in all the immunological studies of it.

6) The stability, specificity, and the possible reproduction of the p.l.s. in various successive lepromin controls are still under research, especially in the initially immunodepressed cases in which the p.l.s. was observed after the use of the vaccination.—Authors' Summary

Vishnevetsky, F. E. and Juscenko, A. A. The modern views of pathomorphology of leprosy. Proceedings of Leningrad Scientific Society of Pathologists **22** (1981) 289–294. (in Russian)

The latest data of pathological anatomy of leprosy are presented which are suggestive of the changes in sectional statistics in leprosy patients compared with the presulfone era. A significant decrease in lethal complications due to leprosy is noted with

* The percentage of p.l.s. rose from 4.54 in the earliest years to 66.66 in the subjects at the age of 41–50.

simultaneous increase in the frequency of cardiovascular diseases and tumors in leprosy patients. Specific lesions of the internal organs are characterized now by the absence of visible lepromas in the liver, spleen, lymph nodes, and testes. The data presented suggest significant changes in the course of the leprosy process during recent years which should be considered as the consequences of therapeutic pathomorphosis. The data on modern Ridley-Jopling classification of leprosy are presented.—A. A. Juscenko

Wall, J. R. and Walters, B. A. J. Immunoreactivity *in vitro* to human testis in patients with lepromatous leprosy. Aust. N.Z. J. Med. **11** (1981) 357–379.

Patients with lepromatous leprosy and tuberculoid leprosy, together with normal aged matched controls, were tested for *in vitro* immunoreactivity against a panel of soluble extracts prepared from normal human tissues. The panel consisted of a soluble homogenate of human testis as well as two partially purified fractions of this extract and control extracts from other human tissues. Immunoreactivity was assessed by extract-induced peripheral blood lymphocyte (PBL) transformation, leukocyte migration inhibition (LMI), and leukocyte adherence inhibition (LAI).

Although no difference in PBL transformation, LMI, or LAI was obtained between the groups with the control tissue extracts, significant reactivity was obtained for the patients with lepromatous leprosy in at least one of the *in vitro* tests, when one of the testis extracts was used (Mann-Whitney test). No such reactivity to the testis extracts was obtained in the patients with tuberculoid leprosy or the normal control subjects. Of the 22 patients studied with lepromatous leprosy, 13 had clinical evidence of testicular disease and 9 of these patients had raised PBL transformation and LAI reactivity to the testis extracts.

This finding of immunoreactivity against testicular extracts in a significant number of patients with lepromatous leprosy by at least one of the *in vitro* tests used suggests that the associated *in vivo* testicular atrophy that occurs in these patients may have an autoimmune basis.—Authors' Summary

Microbiology

Coates, A. R. M., Hewitt, J., Allen, B. W., Ivanyi, J. and Mitchison, D. A. Antigenic diversity of *Mycobacterium tuberculosis* and *Mycobacterium bovis* detected by means of monoclonal antibodies. Lancet **2** (1981) 167–169.

Although *Mycobacterium tuberculosis* and *M. bovis* can be separated by morphological, biochemical, and animal pathogenicity tests, they are conventionally regarded as serologically homogeneous. However, murine monoclonal antibodies can distinguish between strains of *M. tuberculosis* and *M. bovis* strain Vallée, between *M. bovis* strain Vallée and *M. bovis* strain BCG, and even between certain different strains of *M. tuberculosis*. These antibodies will be used to explore the antigenic structure of mycobacteria. They will be of value for taxonomic and epidemiological studies as well as for improving the specificity of serological tests for tuberculosis.—Authors' Summary

Dhople, A. M. and Hanks, J. H. *In vitro* growth of *Mycobacterium lepraemurium*: transition from *in vivo* grown to *in vitro* adaptation. Kurume Med. J. **27** (1980) 149–155.

For successful *in vitro* growth of any host-dependent organism the most important thing is the ability of *in vivo* grown cells to synthesize *in vitro*-type cell membranes. In case of *Mycobacterium lepraemurium* factors responsible for such conversion are α-ketogluterate, hemin reduced oxygen tension, and lecithin-cholesterol liposomes.—Authors' Summary

Danhaive, P., Hoet, P. and Cocito, C. Base compositions and homologies of deoxyribonucleic acids of corynebacteria isolated from human leprosy lesions and of related microorganisms. Int. J. System. Bacteriol. **32** (1982) 70–76.

The deoxyribonucleic acids (DNAs) of 25 strains of leprosy-derived corynebacteria (LDC)—non-acid-fast, gram-positive bacteria independently isolated from human leprosy lesions and propagated in axenic culture—were purified and analyzed. The guanine plus cytosine content, by buoyant density determination, was 54 mol % to 59 mol % for most LDC strains, a range that corresponds to that (50 mol % to 60 mol %) of corynebacteria which multiply in animal cells. These values were checked by chromatographic analyses of acid digests of the DNAs. The taxonomic position of the LDC as determined by DNA base composition was confirmed by the results of the corynomycolic acid determinations of the cell walls of the LDC. The results of the hybridization of the DNAs from the LDC strains suggest the occurrence of two high-homology groups, in which most of the strains were accommodated. In contrast, little homology was observed between the DNAs of the LDC and the reference corynebacteria employed. From these data, it can be inferred that the LDC represent a homogeneous and unique cluster of organisms within the genus *Corynebacterium*, more specifically within the group of corynebacteria pathogenic for humans.—Authors' Summary

Pattyn, S. R. and Portaels, F. Growth of *Mycobacterium leprae* in experimental animals and on artifical media. Bull. Inst. Pasteur **79** (1981) 233–250.

The authors review the multiplication of *Mycobacterium leprae* in experimental animals. Approaches to the *in vitro* cultivation of *M. leprae* are discussed. A number of "difficult to grow" mycobacteria are discussed and the article concludes with some generalities and specific characteristics of *M. leprae* which are now known and which will have to be taken into account in attempts at *in vitro* cultivation. Among the approaches which may be advisable are: 1) inocula containing high numbers of *M. leprae* with a high percentage of them viable; 2) prolonged observation times since *M. leprae* has a generation time of about 13 days; 3) an incubation temperature of between 30°C and 35°C or perhaps even lower; 4) a wide range of pH values; 5) testing different sources of carbohydrates, of mycobactins, and other possible growth factors and pretreatment procedures, and 6) monitoring the experiments with bacterial counts and mouse foot pad inoculations.—(*Adapted from* the article)

Experimental Infection

Curtis, J., Adu, H. O. and Turk, J. L. A lack of correlation between antigen-specific cellular reactions and resistance to *Mycobacterium lepraemurium* infection in mice. Immunol. **43** (1981) 293–301.

C57BL mice are moderately resistant to subcutaneous infection with *Mycobacterium lepraemurium*, limiting the multiplication of organisms at the site of infection and preventing spread to the draining lymph nodes. BALB/c mice, on the other hand, are highly susceptible to infection with *M. lepraemurium*; bacilli multiply at the site of infection and spread in large numbers to the draining lymph node by six months. The authors suggest that "In spite of this difference in local immunity the changes in cellular reactivitiy to specific antigen as assessed by the node cells were similar in the two strains over the time studied." They point out, however, that there is a difference in the kinetics of the delayed-hypersensitivity response between the two mouse strains: BALB/c delayed foot pad responses peak at 24 hr and disappear by 48 hr; whereas C57BL foot pad responses persist for several days. It is suggested that

this difference is not significant as infection with non-pathogenic BCG to which both strains of mice are equally and highly resistant produce similar skin test responses.—James Alexander (From Trop. Dis. Bull.)

Vishnevetsky, F. E. and Juscenko, A. A. Pathomorphological changes in the internal organs of intact and *M. leprae* infected nine-banded armadillos. Bull. Exp. Biol. Med. **8** (1981) 105–109. (in Russian)

The histological examination of the internal organs of intact armadillos and armadillos with early *Mycobacterium leprae* infection was performed. Four months after inoculation with *M. leprae* obtained from an untreated lepromatous patient, autopsy of two animals showed tuberculoid structures in the lungs, liver, and skin. The extensive areas of nodular and diffuse tuberculoid structures with abundant multinuclear giant cells of different form, including Langhans' cells, were observed in the lungs. In the skin of abdomen and limbs epithelioid cell nodules with lymphocytes were revealed. In the liver there were granulomas with lymphoid, epithelioid, and giant (Langhans' type) cells, some granulomas being in the state of fibrosis. A conclusion is made that experimental leprosy infection in nine-banded armadillos may run its course not only in the lepromatous but also in the tuberculoid form of the disease.—A. A. Juscenko

Epidemiology and Prevention

Abe, M., Ozawa, T., Minagawa, F. and Yoshino, Y. Subclinical infection in leprosy—its detection and control by fluorescent leprosy antibody absorption (FLA-ABS) test. Lepr. Rev. **52** Suppl. (1981) 263–273.

The fluorescent leprosy antibody absorption (FLA-ABS) test was used for detecting subclinical leprosy infection in the inhabitants in the Miyako Islands which were known as leprosy hyperendemic areas in Japan. One hundred twenty-six of 1559 schoolchildren and 68 of 571 adults had suspicious neural signs, such as the enlargement of auricular and/or ulnar nerve(s) without sensory loss. The FLA-ABS test was positive in 90 (71.4%) of 126 schoolchildren with the enlargement of peripheral nerve and in 13 (14.1%) of 92 children without any clinical signs. In adults similar percentages, 66.2% (45/68) and 16.9% (23/136) were obtained. Therefore, a correlation between the FLA-ABS test and the neural sign is significant statistically in both schoolchildren and adults. Serological specificity of these positive reactions was checked by testing for cross-reactivity with the other mycobacteria. Only 16 out of 183 positive sera showed some cross-reactions. After additional absorption of the sera with the cross-reacting bacteria, positive reactions against *M. leprae* were not affected at all. On the other hand, the FLA-ABS test was negative in all of the healthy blood donors and the students of a nursery school and in 23 of 24 patients with the other skin diseases in leprosy non-endemic areas. Therefore the percentage of positive FLA-ABS test is considered to represent the rate of subclinical leprosy infection. The lepromin test with the Dharmendra's antigen was conducted on the schoolchildren for selecting the individuals with low or no resistance against leprosy. Among 217 schoolchildren examined simultaneously with this and FLA-ABS tests, 58 showed positive reactions in both. Enlargement of peripheral nerves was found in 36 of these cases. The other 30 children showed a positive FLA-ABS test, with a negative or doubtful Fernandez' reaction. The neural sign was found in half of these cases. It was suggested that these children should receive priority for vaccination for the prophylaxis of leprosy.—Authors' Summary

Belda, W. and Lombardi, C. A. Incidência da Hanseníase no Estado de São Paulo em 1978. (Incidence of Hansen's disease in the state of São Paulo in 1978) Hansen. Int. **4** (1979) 98–112. (in Portuguese)

The authors describe and evaluate the distribution of 2081 new cases of Hanseniasis, recorded in the State of Sao Paulo (Brazil) in 1978, according to the following personal characteristics of the patient: sex, age, place of birth, education level, and housing.

The distribution of the cases according to some characteristics related to the disease and to health care are also described and discussed: clinical types of the disease, duration of the disease, occasion and manner in which the patient sought health care (spontaneous or not).

The geographic distribution of cases and the secular trend of new cases recorded in the last ten years are also presented and discussed.—Authors' Summary

Bjune, G. The lymphocyte transformation test in leprosy with special reference to its use in epidemiology. Lepr. Rev. **52** Suppl. (1981) 241–250.

LTT is cumbersome, expensive, and prone to a lot of technical pitfalls and variance. Great variance according to stage of clinical/subclinical infection, concurrent diseases, nutritional status, phase of menstrual cycle and even the time of day must be kept in mind. The optimal dose of antigen and the time for the responses to peak show individual variation. The lymphocytes should be prepared on the spot as soon as possible after blood collection, or carefully shipped as whole blood at ambient temperature for no longer than 12 hours. Acceptability in study populations is dependent upon local attitudes to blood sampling. The test is clearly not a good one for screening a large number of individuals.

The most severe drawback in the present situation is, however, that the relevance of a positive response in a healthy individual is not established. The explanations for a positive LTT response to *Mycobacterium leprae* antigens could be:

1) crossreaction due to contact with other mycobacteria,
2) specific sensitization to *M. leprae* causing immune protection,
3) contact with *M. leprae* causing a subclinical infection which in the future will become overt leprosy,
4) contact with *M. leprae* leading to an immune response entirely irrelevant for protection of later disease,
5) "non specific" effect of factors in the test serum, antigen preparation or test conditions.

Some of these shortcomings can only be met by being fully aware of all the pitfalls while applying the test. Other problems must be solved by the purification and characterization of the *M. leprae* antigens for use in the test.—Author's Summary

Bryceson, A. The relative importance of specific immunity in protecting against leprosy. Lepr. Rev. **52** Suppl. (1981) 93–107.

The studies of Godal, and Negassie and Abe demand a revision of present concepts of the epidemiology of leprosy. Subclinical infection is the rule and provides a weak measure of specific protection but also provides a latent reservoir of infection in the community. Other forms of specific protection may also exist. The pattern of disease and resistance will be affected by other factors, notably genetic susceptibility, intensity of transmission, and exposure to other mycobacteria, both wild and BCG. The relative importance of these factors is different when leprosy is epidemic, endemic, or waning.—Author's Summary

Cap, J. A. The epidemiological situation in Africa. Lepr. Rev. **52** Suppl. (1981) 53–60.

The estimated prevalence rate for Africa is very high, but relatively little information is available at least on the spot.

Leprosy is mainly concentrated in the western, central, and eastern parts and is characterized by a low proportion of lepromatous cases and a relatively low proportion of disabilities.

The occurrence of dapsone resistance is of the same magnitude as in other parts of the world and if no measures are taken, there is a great risk in producing primary resistant multibacillary and paucibacillary cases.—Author's Summary

Centers for Disease Control, U.S. Department of Health and Human Services/Pub-

lic Health Service. Morbidity and Mortality Weekly Report **29** (1981) 128 pp.

From data primarily submitted by state and territorial health departments to the Centers for Disease Control and the National Office of Vital Statistics, there were 223 new leprosy cases reported in the United States in 1980. One hundred ninety-two were imported cases, 90 were reported from California and 17 from Texas. Thirty-one cases were classified as endemic, with Texas, Louisiana, and Hawaii accounting for 24 of them. Since 1957, the reported number of new leprosy cases has continued to increase, but this represents primarily an increase in imported cases rather than an increase in indigenous transmission of the disease.—RCH

Christian, M. The epidemiological situation of leprosy in India. Lepr. Rev. **52** Suppl. (1981) 35–42.

Leprosy today continues to remain an important public health problem in the Indian sub-continent. Lack of accurate knowledge regarding its epidemiology and limited resources to investigate and combat the disease are some of the factors hindering progress in our efforts at containment of disease transmission. The geographical distribution of the disease shows great variation in pattern with a tendency to focalization. It seems to have reached the long drawn out plateau phase in most of the states in this sub-continent.—Author's Summary

Closs, O. and Reitan, L. J. *In vitro* lymphocyte stimulation using a purified antigen of *M. leprae* and tuberculin PPD. Lepr. Rev. **52** Suppl. (1981) 251–262.

An immunological test which is to be used in epidemiological studies of leprosy should fulfill as many of the following criteria as possible:

1) It should be specific enough to obtain complete discrimination between those who have been and those who have not been exposed to the infection.
2) It should be sensitive enough to detect a high proportion of the individuals who have been exposed to an infectious case of leprosy without developing clinical signs of the disease (subclinical cases).
3) It should be easy enough to perform to be used in large-scale population studies.
4) It should give an estimate of protective immunity and thus be an instrument for the evaluation of the need for and the effect of vaccination.

It is clear that a test that fulfills all these criteria does not exist today and, moreover, we cannot be certain that such an ideal test will ever become available.

An immunological test may be based either on humoral or on cell-mediated immune responses. There is some evidence indicating that an individual may develop delayed type hypersensitivity (DTH) to *Mycobacterium leprae* within a few months after being exposed to the infection. Specific DTH may therefore develop early enough to be an indicator of subclinical infection.

Specific DTH can be estimated either by skin testing or by stimulating lymphocytes *in vitro*, the so-called lymphocyte stimulation test (LST). The latter test is far too labor-intensive to be used in large-scale population studies. However, LST has certain advantages compared to a skin test:

1) Various concentrations of several antigen preparations may be tested simultaneously in the same individual without any chance of the reactions interfering with one another.
2) Less strict precautions are necessary with regard to sterility of the antigen preparations since no ethical considerations have to be made.
3) The test does not interfere with the immune response of the test subject, and thus a relatively small test population may be used repeatedly over an extended time period.

In a situation where a number of different antigen preparations may have to be tested with regard to specificity and potency, the importance of these advantages is significant.

At present lepromin is the only antigen which is in general use for testing of specific DTH in leprosy. This antigen has several obvious disadvantages, and it would be de-

sirable to have preparations which are more well defined, are easier to standardize with regard to potency, and have a more restricted specificity.

Several workers claim to have identified species-specific antigenic components of *M. leprae*, but so far the species-specific nature of such components has not been confirmed in other laboratories. Kronvall, *et al.* have demonstrated that *M. leprae* specific determinants are present in at least one component of the bacillus, and the results of Harboe, *et al.* likewise indicate that species-specific determinants may be present in a number of components. Thus at the moment the best alternative would seem to be to explore the use of components containing some species-specific determinants as reagents in tests for DTH. One should remember, also, that to be a suitable reagent for testing of DTH an antigen should both contain *M. leprae* specific determinants and be capable of sensitizing a high proportion of individuals to these determinants as a result of subclinical infection.

There follows a description of the production and evaluation of a cell wall fraction of *M. leprae* which by certain criteria is similar in composition to tuberculin PPD.—Authors' Summary

de Vries, R. R. P., van Eden, W. and van Rood, J. J. HLA-linked control of the course of *M. leprae* infections. Lepr. Rev. **52** Suppl. (1981) 109–119.

The genetic factors controlling the course of *Mycobacterium leprae* infections are not simple, not confined to HLA, and probably different and/or differently modulated by environmental factors in different populations.

As far as HLA-linked factors are concerned, most evidence exists regarding the development of tuberculoid leprosy. This means that individuals prone to develop tuberculoid leprosy may be genetically different from those who stay healthy after exposure to the bacillus. We realize that this is not in keeping with the ideas many epidemiologists have on tuberculoid leprosy.

It seems that the HLA-linked factor(s) do not confer susceptibility to infection, but rather modulate the type of immune response to *M. leprae*. This is similar to observations in mice for other intracellular growing bacteria, such as *Listeria* and *Leishmania*, where the susceptibility to infection is not, but the development of specific immunity is linked to H-2, the equivalent of the HLA system in the mouse.—Authors' Summary

Fine, P. E. M. Problems in the collection and analysis of data in leprosy studies. Lepr. Rev. **52** Suppl. (1981) 197–206.

Leprosy is sometimes defined as a chronic disease affecting skin and nerves and attributable to *Mycobacterium leprae*. It might also be described as a rare disease of varied and controversial manifestations, found mainly in poor and distant populations, and characterized by ostracism of cases, fear in contacts, neglect by administrators, hyperbole in fund-raisers, a blind eye in the medical establishment, and dogma among its committed workers. Therein lie many of the problems in its study. The following suggestions may help us to surmount some of them:

1) A major international collaborative study should be encouraged to assess comparability of diagnosis and classification between different clinicians and histopathologists.
2) Publications should be fully explicit on procedures for diagnosis and classification of cases.
3) Greater emphasis should be placed upon improving and documenting field ascertainment methods than on institutionalizing poor routine data.
4) Immunological measures of infection should be applied in population-based studies of the epidemiology of *M. leprae* infection.
5) Case control methods should be applied to studies of risk factors for infection and for disease.—(*From* the article)

González Alfonso, N. and Apolinaire Pennin, J. J. Caracteristicas epidemiológicas de la lepra. Estudio de la prevalencia en la ciudad de Santa Clara. (Epidemiologic characteristics of leprosy. A study of the prevalence in the city of Santa Clara.)

Rev. Cub. Hig. Epid. **18** (1980) 55–68. (in Spanish)

The epidemiologic characteristics of leprosy and its prevalence in the Santa Clara City were studied. Among other points, the knowledge of infection sources and the deepening within some heredofamilial aspects are emphasized. Conclusions are made.—Authors' Summary

Harboe, M. *Mycobacterium leprae* and the host response. Lepr. Rev. **52** Suppl. (1981) 1–14.

Under standard conditions of inoculation of *Mycobacterium leprae* in the foot pads of normal or thymectomized mice, the same pattern of multiplication has been obtained by several hundred strains of *M. leprae* from patients with active disease, irrespective of the clinical type of leprosy, race, or region of the world from which they came. These observations indicate strongly that the extent of multiplication *in vivo* is determined by the host response and not by variation in virulence or pathogenicity of the parasite. The evidence for strain variation in *M. leprae* is meager, although existent.

Variation in host response is profound and responsible for most of the variation in clinical course after infection. Our knowledge of the basis of this variation is only fragmentary. Most studies have been concerned with patients with persisting disease, i.e., late in the process; whereas the events crucial for determination of the subsequent course may occur close to the infection with *M. leprae* several years earlier. To a great extent, we do not even know how to study the early events after infection on the individual level.

Epidemiological studies may provide information on variation in events associated with the initial infection and on the probability and extent of superinfection. This information needs to be correlated with determination of clinical course and careful immunological studies at different stages in humans and in experimental models. I expect that collaborative and long term studies of this kind will be mutually rewarding and required to obtain an understanding of leprosy comparable to that of other important infectious diseases.—Author's Summary

Harboe, M. Radioimmunoassay and other serological tests and their application in epidemiological work. Lepr. Rev. **52** Suppl. (1981) 275–288.

Various types of radioimmunoassay (RIA) have been developed for demonstration and quantification of antibodies against *Mycobacterium leprae*. They may be classified as follows: a) RIA for antibodies against one cross-reacting component of *M. leprae*; b) RIA for antibodies against *M. leprae* specific antigenic determinants; c) RIA demonstrating antibodies of a particular immunoglobulin class against *M. leprae*.

The purpose of this paper is to present our current knowledge on these various radioimmunoassays and their informative value in human leprosy and in monitoring the development of systemic mycobacterial infection after experimental inoculation of armadillos. Finally, the plans for further development and tests of these assays in our laboratory are discussed.—Author's Summary

Irgens, L. M. Epidemiological aspects and implications of the disappearance of leprosy from Norway; some factors contributing to the decline. Lepr. Rev. **52** Suppl. (1981) 147–165.

First of all, the Norwegian experience demonstrates the need for and benefits from an adequate system for acquisition of information on leprosy patients. Such a system is important from a practical preventive as well as from a general epidemiological point of view. Thus the Norwegian experience supports the initiative taken by WHO in establishing information systems in countries where leprosy is prevalent today.

Furthermore, taking into consideration the often highly insufficient nutrition found in endemic areas today, the Norwegian experience suggests a systematic approach towards improved nutritional conditions in such areas, evaluating its effects in the perspective of leprosy control.

Finally, the possible epidemiological implications of the finding of *M. leprae*-like organisms in the environment should be further pursued.

Both in the evaluation of nutritional pro-

grams and in the analyses of the epidemiological significance of environmental mycobacteria, there is a great need for immunological tools. The implementation of such tools in epidemiological settings seems necessary to clarify most of the problems challenging leprology today.—Author's Summary

Kazda, J. Occurrence of non-cultivable acid-fast bacilli in the environment and their relationship to *M. leprae*. Lepr. Rev. **52** Suppl. (1981) 85–91.

Using the mouse foot pad technique devised by Shepard for cultivation of *Mycobacterium leprae*, we have been able to isolate non-cultivable acid-fast bacilli (NC AFB) from environmental samples. NC AFB could first be demonstrated in samples originating from former leprosy-endemic regions in Norway. Samples collected in present leprosy-endemic areas (Ivory Coast, India, Peru, Portugal) also yielded NC AFB.

The isolated NC AFB were shown to be polymorphous acid-fast rods which, similar to *M. leprae*, multiply to a limited extent in the foot pads of mice, even after passage. All attempts to culture them on the common culture media such as Löwenstein-Jensen, and Middlebrook medium failed. On the basis of their morphological properties and pronounced acid fastness the isolants have tenatively been classed with the genus *Mycobacterium*.—Author's Summary

Kidson, C. Population studies: Potential and limitations for analysis of genetic and non-genetic factors in leprosy. Lepr. Rev. **52** Suppl. (1981) 177–185.

Given that susceptibility to leprosy has a genetic basis, at least in part, does this affect proposals for intervention in the natural history of the disease in human populations? If genetic susceptibility exists in population groups in Europe, this has not precluded the disappearance of leprosy from most countries in that region. Clearly the environmental and socioeconomic factors are of great importance in determining the outcome. Despite the problem of drug resistance, chemotherapy is relatively successful, although not always in those populations at greatest risk, for logistic or socio-cultural reasons.

The main uncertainty surely lies in the realm of the possible relevance of the type of genetics concerned to the response to a vaccine of those individuals at greatest genetic risk. If, indeed, genetic susceptibility is related to genes controlling immunodifferentiation and immune function then, especially in lepromatous leprosy, response to vaccination may also be under the control of those same genes. It is thus possible that a vaccine would not protect the most important susceptibles, namely those likely to provide a continuing reservoir of infection. While this suggestion is purely conjectural, it does have important practical, including economic, implications.

This is perhaps the most compelling argument in a pragmatic world for further selected population studies on leprosy, since those areas at highest risk are least likely to be fortunate enough to experience economic development of sufficient rapidity to render a potential vaccine irrelevant. Such studies, carried out prospectively, could most usefully be done in populations at high risk which are being considered for vaccine trials. Quite apart from genetic analysis, the other useful output from population studies is the simple one of selection of population groups in which vaccines might be best tested. Here the clear evidence of differing leprosy incidence in contiguous isolated populations is salutory.—Author's Summary

Kogan, V. R., Shubin, V. F., Davlekamova, F. A. and Semichenko, Z. I. Incidence of leprosy in family members of patients (according to the materials of the Astrakhan Zone). Vestnik Dermatologii I Venerologii (Moskva) **8** (1980) 69–71. (in Russian)

The incidence of leprosy among family members of the patients in the Astrakhan zone is analyzed. Along with a marked reduction of the general incidence there is a decrease in the incidence resulting from familial contacts with the source of infection from 11.08% in the period prior to 1952 to 1.53% in 1961–1977. Under the current conditions, successful detection of patients developing leprosy and follow-up observations of good quality are possible only with the participation of physicians of the entire

public health system which necessitates improvement of their knowledge of leprosy.—Authors' Summary

Kronvall, G. The potential of immunological tests as tools in the epidemiology of leprosy. Lepr. Rev. **52** Suppl. (1981) 207–219.

A review of some previous applications of immunological tests in leprosy and for comparative purposes also in tuberculosis has shown that specificity of the tests constitutes the major constraint on their use on a larger scale for epidemiological purposes. The main factor of importance for specificity is the quality of the antigen used in the test. As cell surface antigens seem particularly promising in terms of specificity, a better definition and separation of these components might open new avenues for continued progress in the field of leprosy research.—Author's Summary

Lechat, M. F. The torments and blessings of the leprosy epidemiometric model. Lepr. Rev. **52** Suppl. (1981) 187–196.

The major difference in the model approach to tuberculosis and leprosy is that in leprosy we cannot identify infection from disease. This black box, which can be called latency or incubation period or by whatever term, cannot be recognized. This, from a methodological point of view, has revealed a major difficulty.

The development of an appropriate test to recognize leprosy infection would drastically alter the prospects of epidemiological research in leprosy. It would then become possible to study how the disease is transmitted in the population, who get it, when, and under what circumstances.

This, if necessary, confirms once more that epidemiology cannot be dissociated from basic research, and that its achievements are closely dependent on progress in other fields—in this case, immunology. (*From* the article)

Loretti, A. and Garbellini, D. Leprosy in the Cape Verde Islands. Lepr. Rev. **52** (1981) 337–348.

After a general profile of the country, information is given concerning the history of leprosy in the Cape Verde Islands, with data related to the control activities of the years 1950–77. Finally the authors present the data collected during the first two years of activities under the new National Leprosy Control Project.—Authors' Summary

Magnusson, M. The control of specificity of skin test reagents. Lepr. Rev. **52** Suppl. (1981) 231–239.

While the term "specificity of skin tests" frequently is defined as the percentage of false positive reactions to the tests, there seems to be no generally used definition of the term "specificity of skin test reagents." At present, "difference in specificity" or "specificity difference" of two skin test reagents is used for the characterization of two such reagents that possess varying relative potencies when used or studied in different biological systems. A method (known for 25 years) for the measurement of specificity differences of mycobacterial sensitins by comparative reciprocal intradermal testing on guinea-pigs, is described in some detail. Other methods, which may be used for the same purpose, are only touched upon. Some prerequisites for using these same methods for the study of the specificity differences of a pair of lepromins are not complied with. The particular problems encountered in the study of specificity differences of preparations of lepromin are therefore dealt with separately. The definitions of "ideal preparations" of tuberculin and of lepromin and the definition of the specificities of these hypothetic preparations will depend on the specific purpose(s) of the use of these reagents.—Author's Summary

Motta, C. P. The epidemiological situation in the Americas. Lepr. Rev. **52** Suppl. (1981) 61–68.

The outstanding epidemiological characteristic of leprosy in the Americas is as follows:

1) With the exception of a few countries or territories, half the diagnosed cases are multibacillary forms.

2) The prevalence in children (age group 0 to 14 years) is less than 10% of the total cases.

3) Up to the 1950s most of the cases de-

tected came from rural areas (communities with fewer than 2500 inhabitants or dispersed population). At the present time, there is a reversal of the situation because of the phenomenon of "accelerated urbanization" in Latin America.

4) In general, the frequency of the disease is higher in areas of warm climate and high precipitation, but there are exceptions: for instance, the Colombian and north Ecuadorian Pacific coasts. Some areas of the Andean Cordillera (Colombia, Venezuela) with cool and medium humid climate have relatively high prevalence rates.

5) The leprosy endemicity in the Americas is low when compared with the African or Asian foci. There is a patchy distribution of the cases. Some limited foci (Paraguay, Colombia, Brazil) have prevalence rates up to 24 per 1000 and, in some situations, this pattern cannot be due to factors of land settlement or migratory movements of the population.

6) In most of the countries/territories the endemicity is not declining, even when the recommended policies of control are applied.—Author's Summary

Patarroyo, M. E., Molina, E., Londono, F., Bernal, D., Caro, L., Velasques, A., Silva, Y., Moya, R., Guevara, J., Meness, A. and Gonzalez, M. Identification of a particular B cell alloantigen associated with susceptibility to lepromatous leprosy. Lepr. Rev. **52** Suppl. (1981) 121–135.

The screening of a large group of multiparous sera against peripheral blood mononuclear cell subpopulations of patients with lepromatous leprosy resulted in the obtainment of a group of them recognizing the different HLA-DR specificities and some of the ones not yet defined and, at the same time, confirmed the results where no predominance in the frequency of any one of the alleles of the HLA-DR locus was found. A particular serum was found that reacted with 60% of lepromatous leprosy patients and 16% of the normal controls, and did not show any particular reactivity with tuberculoid leprosy or other diseases, giving a Relative Risk of 7.87; hence showing a high selectivity for a genetic marker associated with susceptibility to lepromatous leprosy. This particular serum did not show reactivity with any one of the HLA-D homozygous cell lines with all the D markers and did not show association with any HLA-A or B alloantigen. It is a genetic marker that shows autosomal dominant segregation pattern expressed on B cell subpopulations and on a minor T cell population, and it is highly associated with susceptibility to lepromatous leprosy.—Authors' Summary

Risso, H. I. Lepra en el Noreste (Zona I). (Leprosy in the Northeast (Zone I)) Leprologia **22** (1980) 133–137. (in Spanish)

The National Program of Leprosy Control in Argentina was begun in the Northeast (Zone I) in 1978. The teams are gradually being completed and all are not yet operational, but progress has been satisfactory. We have been able to bring 47.8% of the total estimated number of patients under control. In 1979, 329 new patients were discovered in a total population of 1,807,855. Of these new patients, 24% had the uncharacteristic or indeterminate form of the disease.—Author's Summary

Saikawa, K. The effect of rapid socioeconomic development on the frequency of leprosy in a population. Lepr. Rev. **52** Suppl. (1981) 167–175.

In Japan the possibility of leprosy transmissions in the community appeared to have been successfully minimized by the rather strict segregation policy started 50 years ago by the national government. This whole process took place before Japan achieved rapid economic growth and also before the start of chemotherapy. Okinawa and Taiwan, on the contrary, achieved reduction of incidence of leprosy after the start of chemotherapy, mostly on outpatient basis, and also at the time of rapid socioeconomic improvements.

Rapid socioeconomic development brought improvements in standard of living and the social environment, particularly the housing situation. These, together with a decrease in family size, greatly contributed toward removing overcrowded living conditions. As a result, the chances of household contact in rural areas, where the prevalence rate was high, was reduced which, in turn, possibly contributed considerably

to reduce the number of new leprosy patients.

In summary, it may be reasonable to assume when there is an active leprosy control program to prevent the infection in the community, socioeconomic development makes a notable contribution to reduce the chances of infection, thus reducing leprosy in the community.—Author's Summary

Sansarricq, H. Leprosy in the world today. Lepr. Rev. **52** Suppl. (1981) 15–31.

The constraints for leprosy control result mainly at present from inadequate infrastructure, from inadequate methodologies for case detection, and the severe shortcomings of dapsone monotherapy.

Possibilities for improving treatment methods already exist by means of combined chemotherapy, but there has been difficulty in putting them into practice. It might be possible, however, to solve these difficulties by intermittent administration of drugs. At the same time, by increasing the number of drugs in the regimens, their efficacy could be increased.

On the whole, based on presently available concepts, the development of an effective antileprosy vaccine remains an essential requirement for an effective strategy for leprosy control.

As for what WHO intends to do, in close collaboration with its member states during the next decade, this can be summarized as follows.

Improved technologies for case detection, especially early detection, treatment with chemotherapy, case holding and contact follow-up will be promoted through the development of more effective control planning, program management and training. Field application of significantly more effective control methods expected from the increased efforts in leprosy research will be encouraged. Curricula incorporating proven approaches will be constructed for the training of all levels of health workers—from the medical undergraduates to the primary health care personnel. The participation of national experts will be promoted in management and evaluation. Collaboration with international, bilateral, and voluntary agencies will be encouraged. According to the progress made, operational studies on vaccination will be initiated.—Author's Summary

Stanley, S. J., Howland, C., Stone, M. M. and Sutherland, I. BCG vaccination of children against leprosy in Uganda: final results. J. Hyg. Camb. **87** (1981) 233–248.

A total of 19,200 children, all contacts or relatives of known leprosy patients and all free of visible leprosy lesions, were included in a controlled trial of BCG vaccination against leprosy in Uganda between 1960 and 1964. They were followed for an average of eight years, during which time 261 developed early leprosy lesions. A less comprehensive follow-up was carried out for a further five years, when eight more cases of leprosy were identified.

In the main intake, between 1960 and 1962, 16,150 tuberculin-negative or weakly tuberculin-positive (Heaf Grades 0–II) children were allocated by an effectively random process to either a BCG-vaccinated or an unvaccinated control group. Both groups were seen and examined in an identical fashion for leprosy at approximately two-year intervals, and precautions were taken to ensure unbiased assessment of new cases of leprosy. After eight years, 41 cases of leprosy had been identified in the BCG-vaccinated group, and 201 in the control group, a percentage reduction in the BCG-vaccinated group compared with the control group of 80%. The percentage reduction was similar for those initially tuberculin-negative, and for those initially weakly positive, and did not depend upon the age at vaccination. It was also similar for both sexes, for contacts of lepromatous and contacts of non-lepromatous leprosy, for children having contact with one or more patient, and for differing grades of physical contact and genetic relationship with a patient. The protective effect of BCG vaccination continued over the eight-year period, although it may have fallen off slightly at the end.

In a group of 1074 strongly tuberculin-positive (Heaf Grades III–IV) children followed in parallel with the other two groups, a total of 16 cases of leprosy were identified. When adjusted for age, this incidence is 58% lower than that in the unvaccinated control children who were initially tuberculin-negative, indicating a protective ef-

fect against leprosy of naturally acquired strong tuberculin sensitivity.

Between 1970 and 1975, 1 new case of leprosy was identified in a child who had initially been strongly tuberculin-positive and had therefore not been vaccinated, 1 in a BCG-vaccinated child, and 6 in control children. Although the follow-up in this period was less comprehensive than that in the main part of the trial, the ascertainment of cases was unlikely to have been biased towards either vaccinated or control children. These results indicate a continuing protective effect of BCG up to 12 to 13 years after vaccination.—Authors' Summary

ten Dam, H. G. and Sansarricq, H. The use of immunological tests in epidemiological work. Lepr. Rev. **52** Suppl. (1981) 289–298.

A simple immunological test could be profitably utilized in a variety of epidemiological work in leprosy. The epidemiologist will be able to handle almost any test, even if it may seem to lack sensitivity and specificity. In this respect the viewpoint of clinicians might be quite different.

Progress in this field will probably be achieved more rapidly if experienced epidemiologists are given the opportunity to participate in the development of the test. The relevant activities of the Scientific Working Group on Immunology of Leprosy (IMMLEP) are being developed according to this requirement.—Authors' Summary

Van Praag, E. and Mwankemwa, S. A. A prevalence survey on leprosy and the possible role of village 10-cell leaders in control in Muheza District, Tanzania. Lepr. Rev. **53** (1982) 27–34.

A total population of 15,029 people in 12 villages was screened for leprosy. The selection of the villages in two divisions of Muheza District was based on a proportional cluster sampling method. An overall prevalence estimate of 7.9 per 1000 was found. Prevalence per village ranged from 0 to 25.8 per 1000. The prevalence was related to age and sex and a strong male preponderance was found. The type of leprosy was determined and 55% were new cases.

Community participation via village 10-cell leaders is assessed with regard to their ability to assist in leprosy control. Their use in promoting drug compliance of the patients and in diminishing the pool of as yet unidentified and possibly infectious cases is discussed.—Authors' Summary

Walsh, G. P., Meyers, W. M., Binford, C. H., Gerone, P. J., Wolf, R. H. and Leininger, J. R. Leprosy—a zoonosis. Lepr. Rev. **52** Suppl. (1981) 77–83.

We have observed naturally acquired leprosy in three animal species: nine-banded armadillos, a chimpanzee, and a mangabey monkey. The frequency of the infection in armadillos in the southern United States provides sufficient evidence to allow designation of the armadillo as a reservoir for the disease in this area. Although the prevalence of the infection of chimpanzees and mangabey monkeys in the wild is not known, the existence of spontaneous leprosy in these species requires that they be given consideration in the epidemiology of leprosy in geographic areas inhabited by these animals. The infection found in all three species has been of the lepromatous or near-lepromatous type and therefore highly bacilliferous and contagious. The role that these species play in the transmission of leprosy to man must now be ascertained.—Authors' Summary

Rehabilitation

Abraham, J. C. Rehabilitacion en lepra: Neuritis leprosa. (Rehabilitation in leprosy: Leprous neuritis.) Leprologia **22** (1980) 115–117. (in Spanish)

Microsurgery is a technical resource which is now recognized in the surgical treatment of neuritis in leprosy. The technique helps to overcome pain and to im-

prove tactile and stereognostics sensibility as has been proved clinically and electrophysiologically. It is difficult to perform a definitive evaluation, not only because of the number of cases necessary for statistical validity, but also because of the evolution of the lesions themselves.—(*Adapted from* Author's Summary)

Charosky, C. B. Clasificacion y tratamento de las neuropatias Hansenianas. (Classification and treatment of neuropathy in Hansen's disease.) Leprologia **22** (1980) 105–114. (in Spanish)

A six-year experience in the treatment of peripheral nerve pathology in leprosy patients assisted by a multidisciplinary team at the Hospital Muniz of Buenos Aires is presented. Different types of neuritis of leprotic origin are outlined, and their therapeutic approach is discussed. A series of 204 acute neuropathies in several nerve trunks, upon which a total of 54 operations were performed, is analyzed.—Author's Summary

Dong Li-Wen, *et al.* Surgical treatment of plantar ulcer with free skin flap in leprosy patients: a case report. J. Clin. Dermatol. **10** (1981) 188–189. (in Chinese)

Plantar ulcer is a common complication in leprosy patients. Its occurrence usually causes much difficulty in walking. A 49-year-old patient with a plantar ulcer (14.5×5.4 cm^2) for more than ten years was successfully repaired with transplanting a free skin flap from the right lower quadrant of the abdomen.

The donor area of the lower quadrant of the abdomen is wide enough to offer a huge skin flap with a good vascular supply. The diameter of the vessels of the skin flap is adequate for performing vascular microanastomosis. The vessel of the flap is rather short. Therefore, during the transplantation usually some small vein grafts are bridged between the vessels of the flaps and the recipient area.

The authors suggest that this kind of flap is indicated for huge plantar ulcers when ordinary skin flaps, such as cross-leg and abdominal tubed flaps, are difficult to perform.—(*Adapted from* Authors' Summary

Harahap, M. Augumentation of muscular wasting in the hand from leprosy. J. Dermatol. Surg. Oncol. **7** (1981) 582–585.

One of the stigmata of leprosy in the hand is muscular wasting between the metacarpals of the thumb and index finger. Such a deformity, which may rarely arise for other neuropathic reasons, may pass unnoticed in places where leprosy is not endemic, but is obvious to all in places where leprosy is still common and undesirably stamps afflicted persons as "lepers" even if the disease is arrested. A surgical technique is described in which a buried dermal graft is used for augumentation of the depression of that muscular wasting between thumb and index finger.—Author's Summary

Other Mycobacterial Diseases and Related Entities

Goodfellow, M. and Minnikin, D. E. Identification of *Mycobacterium chelonei* by thin-layer chromatographic analysis of whole-organism methanolysates. Tubercle **62** (1981) 285–287.

Two-dimensional, thin-layer chromatography of whole-organism acid methanolysates of *Mycobacterium chelonei* gives a characteristic pattern of two, non-polar mycolic acid methyl esters. All other mycobacteria examined so far contain mycolic acids with polar oxygen functions in addition to the 3-hydroxy acid unit.—Authors' Summary

Ouaissi, A., Kouemeni, L.-E., Haque, A., Ridel, P.-R., Saint Andre, P. and Capron, A. Detection of circulating antigens in onchocerciasis. Am. J. Trop. Med. Hyg. **30** (1981) 1211–1218.

This report describes the presence of circulating *Onchocerca volvulus* antigens (COA) in sera of patients with onchocerciasis. By using a double diffusion immunoelectrophoresis method, COA could be detected in 24 of 77 sera analyzed (31%). In contrast, when more sensitive assays such as the radioimmunoprecipitation-PEG assay or sandwich radioimmunoassay were used to detect COA, about 75% of the sera from *O. volvulus*-infected patients were found positive; moreover, a highly significant correlation between the two assays was observed. The parasite specificity of the COA was demonstrated directly by identity reaction with a component of *O. volvulus* somatic antigens. COA was never found when hyperimmune antisera against other parasite antigenic extracts were used instead of anti-*O. volvulus* hyperimmune serum. However, when anti-*O. volvulus* hyperimmune serum was used against sera obtained from patients infected with various other helminths we found a cross-reactivity between COA and the circulating antigens of other human filarids (*Wuchereria bancrofti, Loa loa, Brugia malayi*), but not with other nematode or trematode parasites (*Ascaris lumbricoides, Schistosoma mansoni, Fasciola hepatica*). Further immunoelectrophoretic studies demonstrated one precipitin arc localized in the cathodic region which seemed specific for COA, which raises the possibility of preparing a monospecific hyperimmune serum to circumvent cross-reactivities.—Authors' Summary

Seth, V., Kukreja, N., Sundaram, K. R. and Malaviya, A. N. Delayed hypersensitivity after BCG in preschool children in relation to their nutritional status. Indian J. Med. Res. **74** (1981) 392–398.

Cell-mediated immune response was studied by Mantoux test in 154 preschool children after BCG, in relation to their nutritional status. A significantly higher percentage of children showed Mantoux test positivity with 5 TU than with 1 TU. Overall skin positivity with 5 TU was elicited in 68.8% of children with normal nutrition in comparison to only 37.5% in children with severe PEM, i.e., protein energy malnutrition ($p < 0.02$). Mantoux conversion rate after BCG in children with mild to moderate degree of PEM was comparable to that in the normally nourished group. Percentage of children with varying extent of induration (5–<10 mm, 10–<15 mm and ≥15 mm) was comparable in normal and severely malnourished groups. There was no relationship between Mantoux conversion and age in the case of normally nourished children. However, in the undernourished group, a significantly higher proportion ($p < 0.05$) in the 1–<3 yr age group had Mantoux positive as compared to 3 yr to 6 yr age group. There was no significant difference in the mean value of the area of induration in Mantoux positive cases between these two age groups.—Authors' Summary

Sparks, J. and Ross, G. W. Isolectric focusing studies on *Mycobacterium chelonei*. Tubercle **62** (1981) 289–293.

Analytical IEF has been used to give a direct visual comparison of β-lactamases, down to extremely low levels, from very crude intracellular preparations. Identity and non-identity of strains could be proved by the pattern of bands produced by the β-lactamases.

Mycobacterial species gave a variety of β-lactamase patterns.

Identity was established between some strains of *M. chelonei*. IEF distinguished between enzymes within both the *chelonei* and *abscessus* sub-species that could not be differentiated by other methods. This technique could provide a means of identifying the source of a *M. chelonei* infection.—Authors' Summary

Tageldin, M. H., El Hassan, A. M. and Mustafa, I. E. Spontaneous release of mycophages from lysogenic bovine strains. Tubercle **62** (1981) 263–269.

Mycophages were successfully isolated from lysogenic bovine strains without previous exposure to physical or chemical agents. These mycophages were exposed to 53 mycobacterial strains using ATCC 607 as an indicator stain. These strains included rapidly growing strains, human, bovine, avian, murine, and BCG strains of different geographical origin. Mycophages PM/90/69 produced lysis of human, bovine, murine,

BCG strains and most of the rapidly growing strains, whereas mycophage V24 was sensitive to some rapidly growing strains only. Avian strains were resistant to both mycophages.—Authors' Summary