CURRENT LITERATURE

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General and Historical

Amaral, Afranio do. "Hanseníase," problema linguistico em medicina visto à luz da sociologia, da higiene e da filolǒgia. ["Hanseniasis," as a linguistical and medical problem, considered in its psychological, hygienic and philologic aspects.] Publ. Cent. Est. Leprol. **13** (1973) 16-29. (In Portuguese)

The author analyzes the proposal of the term *Hansenosis* (or Hanseniosis or Hanseniasis) as a substitute for the word *leprosy,* for the purpose of avoiding the stigmatizing connotation of the latter word.

Considering the etymologic aspects, the author feels that there is no linguistic support (generic "taxon") for the creation of the new term, as happened with the inclusion in medical terminology of the following terms: salmonellosis (salmon - salmonella - salmonellosis); Pasteurellosis (Pasteur - Pasteurella - Pasteurellosis); leishmaniosis (leishman - leishmania - leishmaniosis), etc.

That being the case, the author proposes as a solution for the time being and also to avoid the stigmatizing connotation of the word *leprosy,* admission of the name *Hansen's mycobacteriosis* with the creation of the new bacterionymous: mycobacteriosis. As a permanent solution, it would be necessary to create the anthroponymous Hansenia, as a new genus perfectly justified for the bacillus of Hansen. Thus, Hanseniosis (Hansenosis, Hanseniasis) would obey the following origin: Hansen - Hansenia - Hanseniosis. —(*Adapted and translated from* Portuguese summary)

Kirchheimer, Waldemar F. Leprosy. Am. J. Med. Technol. **40** (1974) 474-478.

We are at the beginning of a new era in leprosy. We know now that most human beings are resistant to the naturally encountered infectious hazards, that the different clinical types of leprosy are the result of individual differences in native resistance, and we have hypotheses about the reasons for these differences which we can hope to put eventually to the test. We can now distinguish the leprosy bacillus from other not culturable mycobacteria. We can determine whether or not the bacilli are viable, we can screen drugs for their efficacy and find out whether a patient's bacilli are sensitive to the drug he is receiving. If we can learn to breed armadillos at will and to devise a test to measure their susceptibility to *M. leprae* without infecting them, we can explore the following fundamental and applied aspects of leprosy as it occurs in man: the mechanism of susceptibility and resistance; studies of the modes of transmission; long-range chemotherapy; chemoprophylaxis; effect of dose-level on emergence of drug-resistant bacillary mutants; relationship between tissue temperature and bacterial load; mechanism of neural damage. From armadillos with lepromatous leprosy we can now obtain amounts of leprosy bacilli comparable to what ordinarily is provided from bacterial cultures. That this will enhance our knowledge of the recalcitrant leprosy bacillus and that we might force it to release eventually its secrets is no longer a vain expectation.

Perhaps this brings the day closer when there will no longer be 12 to 15 million victims of the activities of *M. leprae* in this world.—Author's Summary

Wood, S. R. A short history of leprosy in postage stamps. Proc. Roy. Soc. Med. **67** (1974) 717-719.

The emphasis of this paper is a brief summary of well-known aspects of the history of leprosy. This serves as a vehicle for noting that up to 1973 only Belgium (1964) and Cuba (1948) had issued stamps commemorating Hansen's discovery of the leprosy bacillus. The paper mentions other later related

stamps, in most instances not specifying their locale or time, and states that more than a dozen countries other than Norway produced leprosy commemorative stamps in 1973. These countries are not specified. The reviewer having seen a similar statement earlier has sought without success to find this many commemorations. To the philatelist the title of this paper will be misleading. —O. K. Skinsnes

Clinical Sciences

Saint-André, P., Feral, J., Bueno Numez, A. M., Giraudeau, P. and Cisse, B. Le traitement de l'érythème noueux lépreux (ENL) par le chloramphénicol. [The treatment of *erythema nodosum leprosum* with chloramphenicol.] Afr. Med. **12** (1973) 871-878. (In French)

The authors treated with chloramphenicol 31 African patients suffering from clinically severe (22) or moderate (8) grades of *erythema nodosum leprosum* (ENL), and one patient with an acute peripheral neuritis. After careful pathologic assessment, the patients were given one gram of the drug three times a day; three-quarters took the drug orally and the remainder received it intramuscularly.

In patients suffering from severe ENL, either long-standing or recurrent, the raised temperature returned to normal within a week, and the skin lesions disappeared within 12 days in all patients and within 8 days in a third. The level of C-reactive protein, which had been considerably raised in all patients, fell to zero within 18 days in all patients, and within 11 days in 60%.

In patients with less severe forms of ENL, a similar rapidity of disappearance of signs and pathologic accompaniments was noted in some, but not in those patients suffering from a persistence of fewer ENL lesions.

The authors consider that chloramphenicol must now be reckoned as inferior only to thalidomide in the control of ENL, although relapse occurred in 30% of patients between 15 days and 4 months.

The mode of action of the drug is discussed in some detail, and the intriguing possibility that, in some instances at least, reaction may be precipitated by the presence of staphylococci in the urinary tract or elsewhere. The authors suggest that chloramphenicol may act on the antibodies that represent one of the components of the immune complex responsible for the triggering of the "reaction." Whatever the explanation, the treatment of a notoriously refractory complication of lepromatous leprosy by means of chloramphenicol deserves further investigation.—S. G. Browne (*From* Trop. Dis. Bull.)

Sebille, A., Boisson, M. E. and Rougemont, A. Manifestations cliniques de la névrite lépreuse. [Clinical manifestations of leprosy of the nervous system.] Méd. Afr. Noire **21** (1974) 193-197. (In French)

The authors present an analysis of the gross clinical manifestations of peripheral nerve damage seen in a selected series of 90 patients suffering from various kinds of leprosy (61 lepromatous, 20 tuberculoid, 4 borderline, and 5 indeterminate). All were receiving treatment for leprosy at the Marchoux Institute, Bamako, Mali.

Their results, which disclose no novel findings, confirm the generally accepted views that the ulnar nerve trunk is more frequently affected than the median or radial, and the external popliteal more frequently than the posterior tibial. Despite modern antileprosy treatment, peripheral nerve lesions either appeared or became worse in about half the patients. Dissociation of sensory modalities is held to be early and transitory. The role of compression of the nerve trunk in osseous or fibrous canals is emphasized.

[The outstanding clinical sign in the nerve trunk itself, at the sites of predilection, is said to be "enlargement." No indication is given of the diameters of the trunks in relation to the pathologic changes within the nerve, and in its sheath, changes that are determined by the form of leprosy and its duration.]—S. G. Browne (*From* Trop. Dis. Bull.)

Sehgal, V. N. Significance of the local sweat response in the diagnosis of leprosy. Dermatologica **148** (1974) 217-223.

Sweat response to intradermal carbachol

injection was studied in hypopigmented skin lesions of 113 patients, comprising 88 with tuberculoid and 25 with dimorphous leprosy. The results were compared with contralateral controls. The sensory status of these patches prior to the test was carefully determined in each case and the patients were grouped accordingly. The sweat response was found to be significantly lowered in hypopigmented lesions. The cutaneous sensations and sweat functions were mostly corresponding. In a few cases, however, there was a demonstrable impairment of autonomic function, although the sensory functions were normal or equivocal. This method of assessment of autonomic functions, therefore, deserves a place as a diagnostic technic in leprosy.—Author's Abstract

Shields, J. A., Waring, G. O. III and Monte, L. G. Ocular findings in leprosy. Am. J. Ophthalmol. 77 (1974) 880-890.

One hundred patients with clinically proved leprosy were examined ophthalmologically and the findings were compared with previous reports. Although ocular or adnexal involvement was present in 72%, it was often mild and did not threaten vision. Only 10% of the patients were visually incapacitated as a result of ocular leprosy. The most common causes of visual loss were the complications of keratitis and iritis. In reporting the incidence of ocular complications of leprosy, we differentiated conditions that are benign, like madarosis, from those that may impair vision, like keratouveitis.—Authors' Summary

Chemotherapy

Banerjee, D. K., Ellard, G. A., Gammon, P. T. and Waters, M. F. R. Some observations on the pharmacology of clofazimine (B663). Am. J. Trop. Med. Hyg. **23** (1974) 1110-1115.

Chemical methods are described for the determination of clofazimine in the serum, urine, and feces, and in homogenates of liver and spleen. Feeding clofazimine to mice resulted in a large accumulation of crystalline drug in the liver and spleen. When dosage with clofazimine was terminated tissue and serum concentrations fell extremely slowly, at rates over a period of four months equivalent to a half-life of about 70 days. The concentrations of clofazimine were also measured in the serum, urine, or feces of leprosy patients and a healthy volunteer. Clofazimine appeared to be incompletely absorbed in man. The relevance of these findings to the treatment of leprosy with clofazimine is discussed.—Authors' Abstract

Gelber, R. H., Gooi, H. C., Waters, M. F. R. and Rees, R. J. W. The pharmacology of sulphetrone and its implications in sulfone resistance. Lepr. Rev. **45** (1974) 308-312.

Spectrofluorometric technics were utilized to quantitate dapsone and N^4-acetyldapsone (MADDS) contamination of a sulphetrone preparation used for leprosy in Malaysia between 1947 and 1951. Also plasma levels of DDS and MADDS following administration of a standard intramuscular dose of this preparation were studied. The preparation was contaminated with trace amounts of DDS but no MADDS. Following injection the plasma levels were substantial and suggested that sulphetrone was converted *in vivo* to DDS. The importance of these findings to the problem of sulfone resistance is discussed.—Authors' Summary

Grigor, R. R., Lang, W. R. and Nicholson, G. I. Gut amyloidosis in lepromatous leprosy regressing with therapy. Lepr. Rev. **45** (1974) 313-320.

Two Samoan patients with gut amyloidosis secondary to lepromatous leprosy were studied for five years. Intestinal "psuedo-obstruction" and malabsorption were prominent early features. Evidence suggesting regression of the amyloid deposits following control of the leprosy included clinical, biochemical, radiological and histological data. —Authors' Summary

Levy, Louis. Pharmacologic studies of clofazimine. Am. J. Trop. Med. Hyg. **23** (1974) 1097-1109.

A pharmacologic study of clofazimine (B663) was carried out in mice and human subjects to provide information needed for interpretation of data from studies of drug action in the two species. The quantities of B663 in mouse carcasses were measured to

determine the half-time of disappearance ($T_{½}$) of the drug and the absorption of the drug after oral administration. The antimicrobial activity of orally administered B663 was studied in mice infected with *Mycobacterium leprae* and correlated with the quantity of B663 in the carcass. Published studies of the effect of the drug in murine infections with *M. leprae* and *M. tuberculosis* were reinterpreted. The $T_{½}$ of B663 is about one week in male BALB/c mice. The antimicrobial effect of the drug appears to require a concentration in the mouse carcass smaller than 1 mg/kg for *M. leprae* and greater than 5 to 10 mg/kg for *M. tuberculosis*. The concentration of B663 was also measured in the plasma, urine and feces of volunteers and leprosy patients. The $T_{½}$ of the drug is at least 70 days in man. The disposition of the drug thus differs greatly between the two species, making difficult the transfer of information from laboratory to clinic—Author's Abstract

Mansfield, Richard E. Tissue concentrations of clofazimine (B663) in man. Am. J. Trop. Med. Hyg. **23** (1974) 1116-1119.

Clofazimine (B663) has been the subject of considerable study in the experimental animal because of its antimycobacterial activity. This is the first study of the tissue distribution of B663 in man. Three leprosy patients were studied at autopsy; a skin biopsy was studied in a fourth patient. Tissue concentrations were analyzed by a simple chemical method. Tissue coloration was observed in the internal organs. Initially, the subcutaneous tissues appeared gray to opaque, but within minutes of exposure to the air began turning a yellow-orange color; after some ten minutes, tissues high in fat content were orange-red. Highest concentrations of B663 were observed in tissues with high fat content and in the bile. Tissues with a reticuloendothelial component or high vascularity also showed relatively high concentrations. High levels were present also in the liver and in the gall bladder.—Author's Abstract

Mitchison, D. A. and Allen, B. W. Sensitive microbiological method for the detection of rifampicin in urine. Tubercle **55** (1974) 245-248.

A sensitive, specific and simple test for rifampicin in urine is described, based on the bactericidal activity of the drug on *Staphylococcus aureus*. The method has been used to monitor the taking of daily doses of 75 mg rifampicin during a clinical study in Hong Kong (see table below).

Urine test: *Staph. aureus*, NCTC 10702, sensitive to RMP (S strain), but resistant to many other antibiotics including streptomycin, and its RMP-resistant variant NCTC 10703 (R strain) were used as test organisms. They have been described previously for use in the plate diffusion method (Mitchison, Allen and Miller, 1970). Each strain was grown in nutrient broth (Oxoid No. 2) overnight and a viable count set up. The culture was then dispensed into batches of polypropylene ampoules which were quick frozen in liquid nitrogen (-196°C). For use, an ampoule was thawed and diluted approximately 1 in 1000 in sterile water, the exact dilution being calculated from the initial viable counts, so that finally there were equal concentrations of viable S and R organisms.

To each of two 76 × 12 mm tubes was added 1.0 ml of urine, neat or diluted in nutrient broth, and 0.1 ml of the diluted S or R culture. The tubes were incubated in a water

Detection of RMP in timed urine collections after supplement dose of RMP or placebo.

Supplement	Urine specimens	Interval between taking supplement and end of 2-hour urine collection (hours) 0	2	22	24	26	28	48
Placebo	No. tested	6	7	7	7	6	7	7
	positive	1	2	1	1	1	0	0
RMP 75 mg	No. tested	13	13	13	12	13	13	13
	positive	7	11	12	10	11	10	6

bath at 37°C for three hours and, from each tube, one loopful (platinum/iridium loop 4.5 mm dia., holding 0.01 ml) was spread on the surface of a quarter of a plate of nutrient agar (Oxoid broth No. 2 with 1% agar No. 3) containing 1000 μg/ml streptomycin. A control test with normal urine was set up with each batch. The results were read after overnight incubation of the plates. Plates from the control urine and from the test urines incubated with the R strain yielded 100–200 colonies. A result was considered positive if the colony count on the S plate was less than ten percent of the count on the R plate. Rarely, the R strain was inhibited, for instance because of antibacterial drugs to which the strain was sensitive in the urine; no result could then be obtained.—(*Adapted from* authors' paper)

Murray, J. F., Jr., Gordon, G. R. and Peters, J. H. Tissue levels of dapsone and monoacetyldapsone in Lewis rats receiving dietary dapsone. Proc. West. Pharmacol. Soc. **17** (1974) 150-154.

Today, the most widely used and most thoroughly studied drug for the treatment of human leprosy is dapsone (DDS). It is extremely active—the estimated minimal inhibitory concentration (MIC) against *M. leprae* in the mouse foot pad is ≤ 10 ng/ml of plasma; in the rat foot pad, the MIC is 2 to 4 ng/ml of plasma. From therapeutic studies in leprosy patients using very low doses of DDS or its repository form, N, N¹-diacetyl DDS, we can estimate that the MIC of DDS for *M. leprae* in man is less than 20 to 30 ng/ml of plasma.

This report extends an earlier study by us of this drug in normal and *M. leprae* infected rats to measurements of tissue levels. These initial investigations have been performed to test our analytical systems for their ultimate application to the determination of tissue levels of DDS in leprosy patients.—*(Adapted from article, p 150)*

Peters, J. H., Gordon, G. R., Biggs, J. T. and Levy, L. The disposition of dapsone and monoacetyldapsone in the dog. Proc. Soc. Exp. Biol. Med. **148** (1975) 251-255.

Four female dogs receiving 1.0 mg dapsone (DDS)/kg iv exhibited logarithmic decline of plasma levels of DDS with a mean half-time of disappearance ($T_{½}$) of 11.7 hours. No evidence of acetylation of DDS to monoacetyl DDS (MADDS) was found. An equimolar dose of MADDS was deacetylated slowly to DDS by the same dogs. The mean $T_{½}$ of MADDS was 6.5 hours, significantly less than that of DDS. In two-hour plasma samples after these doses of drugs, protein-binding of DDS and MADDS averaged 71% and 84%, respectively. Tests of protein-binding of the two drugs *in vitro* confirmed the observations *in vivo*.—Authors' Summary

Sharma, C. S. Gangadhar. Effect of broxyquinoline and broxaldine in leprosy. Lancet **1** (1975) 405. (Letter to Editor)

My experience in treating leprosy patients with a combination of broxyquinoline and broxaldine seems to indicate that this combination might have some specific effect in leprosy. Throughout the period of therapy no serious adverse reactions were encountered. These patients did not receive any specific antileprosy treatment.

This possibility should be further investigated.—(*Adapted from* author's Letter to Ed.)

Shepard, C. C., Levy, L. and Fasal, P. Further experience with the rapid bactericidal effect of rifampin on *Mycobacterium leprae*. Am. J. Trop. Med. Hyg. **23** (1974) 1120-1124.

The effect of rifampin therapy in leprosy was studied in two clinical short-term trials in which skin punch biopsy specimens were taken at regular intervals for the innoculation of mice in order to monitor the decrease in proportion of viable *Mycobacterium leprae* in the patients' lesions. In a trial of rifampin in a dosage of 600 mg daily, the bacterial viability fell to undetectable levels in the first specimen taken after the start of therapy (at 3-4 days in four patients, 7-8 days in nine, and 14 days in two). Dapsone-treated controls required 20 to more than 112 days for the same change. In a trial of single dose of 1,500 mg rifampin, the viability fell to undetectable levels in the first specimen taken after the start of therapy also (at 3-5 days in all 14 patients).—Authors' Abstract

Terencio de las Aguas, Jose and Richeri, Daniel. Tratamiento de la lepra con Rifampicina. [Treatment of leprosy with rifampicin.] Rev. Leprol. **9** (1974) 365-373. (In Spanish)

Eleven lepromatous leprosy cases treated with rifampicin, ten male and one female, were studied. Seven of the lepromatous leprosy patients had advanced disease, having been treated with sulfone for many years and suffering relapses because they were intermittent in treatment. Four patients were not treated and the disease evolution period was very short. All of them were highly positive bacteriologically.

They were given 600 mg daily and observation time was from 8 to 33 months. In general, they tolerated treatment very well and the presence of leprosy reaction was less frequent than with the sulfone.

Clinical improvement was eminent in all of them and bacteriologic improvement was fair. A longer treatment period is necessary so that these results can be validated.—(*Adapted from* English summary)

Waters, M. F. R. and Helmy, H. S. The relationship of dapsone (DDS) therapy to *erythema nodosum leprosum*. Is it direct or indirect? Lepr. Rev. **45** (1974) 299-307.

A double-blind, internally controlled clinical trial is reported of the effect of dapsone on the severity of *erythema nodosum leprosum* (ENL) in 17 sulfone-resistant lepromatous patients, 16 of whom were suffering from ENL of varying severity. During the ten weeks of the trial, alternative antileprosy treatment was continued unchanged. Dapsone, 100 mg daily in a colored capsule, was prescribed for 14 consecutive days between the third and seventh week, the timing being allocated by random distribution, and on the remaining 56 days an identical placebo capsule was given. The clinical severity of the ENL was measured by a number of parameters, and the intake of all reaction-suppressing drugs was recorded. No evidence was obtained that dapsone either immediately or after an interval, exacerbated or precipitated episodes of ENL. It is concluded that dapsone has no direct ENL-stimulating action per se, but that ENL results indirectly, consequent on the drug's chemotherapeutic activity against *Mycobacterium leprae*.—Authors' Summary

Waters, M. F. R., Rees, R. J. W., McDougall, A. C. and Weddell, A. G. M. Ten years of dapsone in leprosy; clinical, bacteriological and histological assessment and the finding of viable leprosy bacilli. Lepr. Rev. **45** (1974) 288-298.

Twelve lepromatous patients who had completed 10 to 12.5 years of continuous chemotherapy, principally or entirely with dapsone, were assessed clinically, bacteriologically and histologically. In all 12, the disease showed full clinical response to therapy, although three patients remained smear positive, and two of these still suffered from mild *erythema nodosum leprosum*. However, by mouse foot pad inoculation it was shown that 7 of 12 patients still harbored viable *M. leprae*. Thus bacterial multiplication was obtained in mice inoculated with 10 of 37 tissue suspensions prepared from extensor skin, striated muscle, peripheral nerve and smooth muscle; although the numbers of positive foot pads in each group of mice were small, in keeping with the minute numbers of leprosy bacilli, of variable viability, inoculated. No bacterial enhancement was obtained in thymectomized-irradiated mice, and three of six strains died out on passage; these findings recalling the difficulties encountered by McCune *et al* in culturing *M. tuberculosis in vitro* from tuberculous mice subjected to effective chemotherapy. Three of these strains of *M. leprae* (two from skin and one from nerve) from separate patients, were shown to be fully sensitive to dapsone. The importance of these findings is discussed, especially with regard to clinical relapse of leprosy after premature stopping of treatment and to the total duration of dapsone therapy required in lepromatous leprosy.—Authors' Abstract

Immuno-Pathology

Balakrishnan, S., Ramanujam, K. and Ramu, G. Adreno-cortical function tests in lepra reaction. Indian J. Med. Res. **62** (1974) 1166-1170.

Adrenocortical function tests were carried out in 27 cases of lepromatous leprosy in the reactive and subsided phases of lepra reaction. The results show a significant lowering

of total 17-ketogenic steroids excretion in urine in the patient group particularly in the reactive phase. The response to ACTH administration (carried out in three cases) also indicates a subnormal response. A relative increase in serum potassium level and a lowering of the serum sodium/potassium ratio in the reactive phase is associated with a marked lowering in the urinary excretion of potassium. A mild lowering in blood sugar levels and a flat type of glucose tolerance test are also seen in some patients with lepra reaction. These findings indicate the possible existence of a certain degree of adrenocortical insufficiency in lepra reaction and to a lesser extent in its subsided phase as well. The possible factors responsible for these findings are discussed—Authors' Abstract

Bechelli, L. M., Kyaw Lwin, Gallego Garbajosa, P., Gyi, M. M., Uemura, K., Sundaresan, T., Tamondong, C., Matejka, M., Sansarricq, H. and Walter, J. BCG vaccination of children against leprosy: nine-year findings of the controlled WHO trial in Burma. Bull. WHO **51** (1974) 93-99.

The leprosy incidence rates so far in the vaccinated and unvaccinated children aged 5-9 and 10-14 years are similar. The BCG-vaccinated children aged 0-4 years at intake had an incidence rate lower than that of children in the control group. BCG vaccination did not protect household contacts or children aged 5-14 years not exposed in the household, and did not influence the distribution of the forms of leprosy in the cases detected. The lepromin reaction in relation to the age at intake was consistently stronger in the vaccinated children than in those of the control group; the younger the age group the more pronounced was the difference, which was only slight in the age group 10-14 years at intake. If the results of the late lepromin reaction are related to the age at onset (when the children are older than at intake), the differences between the BCG and the control groups tend to decrease. It does not seem that the BCG-vaccinated children suffer from a less serious form of leprosy than the nonvaccinated children (most of them nonreactors to tuberculin).—Authors' Abstract

Bernard, J. C., Guaraz, R. and Bensadon, J. Estudio anatomoclínico de algunos aspectos gastroenterológicos en la patología reaccional del lepromatoso. [Anatomoclinico study of several aspects of gastrointestinal lesions in cases of active leprosy patients in reaction.] Leprologia **18** (1973) 290-302. (In Spanish)

We have studied clinically and pathologically the gastrointestinal lesions in 21 cases of active leprosy patients in reaction at the Sommer Sanatorium.

We observed that the more intense the leprosy reaction was, the more evident were the digestive lesions.

During clinical observations we saw vomiting, abdominal pains, abdominal distention, nausea, diarrhea and digestive hemorrhages in the most intensive reactional cases.

We did not observe any anatomical pathologic alterations in the light and medium intensity reaction cases, but in the intense reactions we observed simple gastritis, simple colitis, erosive gastritis and erosive colitis. This is the order in which we noticed the lesions, while the lepromatous reactions were more intensive.—(*Adapted from* English summary)

Bullock, Ward E. Immunodeficiency in leprosy. *In:* Progress in Immunology II, vol. 5, L. Brent and J. Holborow, eds., North-Holland Publishing Co., 1974, pp 193-202.

In summary, evidence for a direct suppression of cellular immune function by infection with obligate intracellular parasites has been reviewed. Utilizing murine leprosy as a prototype of such infection, we have demonstrated that the recirculation of infused thoracic duct lymphocytes is markedly disturbed. The mechanism of this perturbation appears to be a hindrance to exit of lymphocytes from lymphoid organs. This hindrance in turn may be secondary to an increased resistance to the passage of lymphocytes caused by granulomatous involvement of critical trafficking areas. We hypothesize that in certain infections characterized by extensive granulomatous invasion of lymphoid organs, a disturbance in traffic of T lymphocytes may contribute to the complex of factors acting to compromise immune function of the host.—Author's Summary

Bullock, W. E., Jr., Ho, M. F. and Chen, M. J. Quantitative and qualitative studies

of the local cellular exudative response in leprosy. J. Reticuloendothel. Soc. **16** (1974) 259-268.

Qualitative and quantitative analyses of the local exudative response to skin abrasion were performed on patients with tuberculoid and lepromatous leprosy and compared with control subjects. The inflammatory response of leprosy patients was qualitatively normal as measured by serial coverslip preparations over a period of 28 hours. Migratory sequences and proportions of polymorphonuclear leukocytes (PMN), lymphocytes and macrophages did not differ from controls throughout the 28 hour period of study. Application of *M. leprae* Ags to abrasion sites at 12 hours induced a transient PMN migration into the exudates of all subjects. The response was greatest in patients with tuberculoid leprosy and minimal among patients with lepromatous disease.

Mobilization of leukocytes into cell collection chambers from skin abrasions was significantly decreased ($p < 0.05$) among patients with lepromatous leprosy (24.9 ± 16.6 cells/24 hours) as compared with controls (45.6 ± 26.9 cells/24 hours).

It is suggested that humoral or tissue factors may be present in patients with lepromatous leprosy that may alter the kinetics of PMN responses to inflammatory stimuli.—Authors' Abstract

Cezar, P. C., Mizusaki, K., Pinto, W. Jr., Opromolla, D. W. A. and Beiguelman, B. Hemoglobina S e lepra. [S hemoglobin and leprosy.] Rev. Bras. Pesqui. Med. Biol. 7 (1974) 151-167. (In Portuguese)

A sample of 489 leprosy patients, almost all lepromatous type, and another one of 518 individuals nonaffected by leprosy, were submitted to screening tests for S hemoglobin. Among the leprosy patients, 401 were Caucasoid (272 male and 129 female) and 88 were Negroid (61 male and 27 female), while the control group was composed of 354 Caucasoid (112 male and 242 female) and 164 Negroid (52 male and 112 female).

Screening tests were performed by means of *Sickledex* (Ortho Diagnostics, Raritan, N.J., U.S.A.; Johnson & Johnson, Brazil), using half of recommended volumes of both the test solution and the total blood. These tests allowed the authors to demonstrate positive reactions among 9.09% of the Negroid leprosy patients (5 male and 3 female), 7.32% of the Negroid controls (4 male and 8 female), and 0.75% of the Caucasoid leprosy cases (2 male and 1 female). Complete agreement between these positive reactions and the results of the standard sickling test with 2% sodium metabisulphite solution, after 30 minutes at room temperature, was found. The starch gel electrophoretic examination of the hemolysates of the 23 ascertained *Sickledex*-positive individuals have demonstrated that they exhibited the sickle cell trait (AS heterozygotes). The same investigation applied to the hemolysates of 58 *Sickledex*-negative Negroid leprosy patients has shown that all were homozygous for the normal adult hemoglobin gene.

All the leprosy patients with the sickle cell trait, as well as 10 of the 12 AS heterozygous individuals of the control sample, have been submitted to detailed clinical examination and most of them also to radiologic and electrocardiographic investigation. Laboratory proof included complete hemogram, protein electrophoresis, investigation of bilirubins and transaminases (SGOT and SGPT) levels, serologic reactions for Chagas disease and syphilis, as well as urine and protoparasitologic examinations.

The sensitivity and specificity of *Sickledex* for screening individuals with S hemoglobin, even when the recommended volumes of both the test solution and blood are reduced, were confirmed. It was also concluded that:

1. The frequency of individuals exhibiting the sickle cell trait in the analyzed samples have not supported the hypothesis that leprosy might have contributed to maintain high frequencies of that allele by preferential selection of AA homozygotes, in spite of the similar geographic distribution of both leprosy and the gene for S hemoglobin in Africa and Asia.

2. The data obtained are also not consistent with a secondary hypothesis that the gene for S hemoglobin might have a pleiotropic effect on susceptibility to leprosy infection.

3. The sickle cell trait does not seem to affect the clinical evolution of leprosy or to intensify the signs and symptoms manifested by AS heterozygous leprosy cases.—(*Adapted from* English abstract)

Dutta, L. C., Das, N. C., Chatterjee, B. C. and Bujarbarua, D. N. Ocular lesions in leprosy. J. Indian Med. Assoc. **61** (1973) 385-388.

Eyes of 45 leprosy patients were examined. The incidence of eye lesions of both lepromatous and nonlepromatous types was almost equal. Madarosis and corneal involvement were found to be more common in the lepromatous group than in nonlepromatous cases. The incidence of neural lesions and uveal tract involvement was more in nonlepromatous than in the lepromatous group. Excessive pigmentation of the skin around the eye and conjunctiva were found in three cases. Seven cases of choroidoretinal lesions and two cases of facial nerve paralysis were observed.—(*Adapted from* authors' summary)

Dutta, R. N. and Saha, K. Cold antibodies in leprosy and their characteristics. Indian J. Med. Res. **62** (1974) 869-876.

Patients suffering from lepromatous leprosy are known to have raised levels of immunoglobulins with marked increase of various autoantibodies. In this study we are reporting the occurrence of raised titers of cold isoantibodies against human group O red cells in 88 of 142 unselected cases of leprosy patients which were found to be harmless to the host. Thirty-eight of 88 had a titer of 1:64 and above but not exceeding 1:512. From normal individuals 200 sera were also included as controls. The characteristics of the immunoproteins present in the cold isoantibodies had been studied by indirect Coomb's test in 18 selected leprosy cases. In ten patients, these were of IgM class, in four of IgA class, two cases IgG and one case showed only IgE. This is the first time cold antibody of IgE class has been reported. Moreover, in five cases cold antibodies had immunoglobulins which had no light chains. Six cases had kappa light chains, five cases had lambda chains, and nine cases had neither kappa nor lambda chains. The present work in contrast to the normal cold isoagglutinins, showed the heterogeneity and inconsistency of the immunoglobulin classes of the cold antibodies present in the sera of leprosy patients. The disparity of the distributions of the light chains has also been seen in this work.—Authors' Summary

Finlayson, M. H., Bilbao, J. M. and Lough, J. O. The pathogenesis of the neuropathy in dimorphous leprosy: electron microscopic and cytochemical studies. J. Neuropathol. Exp. Neurol. **33** (1974) 446-455.

The lesions and distribution of mycobacteria were studied in sural nerve biopsies from patients with dimorphous (borderline) leprosy. Schwann cell infection led to extensive focal myelin breakdown and fibrosis, which occurred while patients were as yet relatively asymptomatic. Axonal loss was gradual, and accompanied by more severe fibrosis, until replacement of nerve by densely packed, poorly cellular collagen made regeneration impossible. The bacteria tended to proliferate at one site within the nerve and there was no evidence of significant bacterial transport within nerve fibers or in the extracellular space. The distribution of intraneural bacteria in early lesions was compatible with blood-borne dissemination of the infection.—Authors' Abstract

Job, C. K. and Verghese, R. Electron microscopic demonstration of *M. leprae* in axons. Lepr. Rev. **45** (1974) 235-239.

Biopsies from 14 lepromatous nerves were examined. Unequivocal evidence for the presence of *M. leprae* in axonal cytoplasm was found in four biopsies. In the nerves the organisms are present much more frequently and in large numbers in Schwann cells, macrophages and perineurial cells and, therefore, the intra-axonal bacilli may not have much part to play in the destructive process of the nerve. However it is suggested that axons are very likely sites for bacilli to remain protected from the bodily defense mechanisms and drugs resulting in relapse of the disease.—Authors' Abstract

Kelkar, S. S., Niphadkar, K. B., Khare, P. M. and Gharpuray, M. B. Environment and carriage of hepatitis B antigen in leprosy. Indian J. Med. Res. **62** (1974) 1794-1799.

Hepatitis B antigen carriage was studied in 152 patients of leprosy attending the outpatient department of the Sassoon General Hospitals, Poona. This group consisted of 37 cases of lepromatous leprosy and 115 of tuberculoid leprosy. Sera from the patients were studied for presence of hepatitis B antigen by both immuno-electroosmophoresis

and agar-gel diffusion. Agar-gel diffusion was much less sensitive than immuno-electroosmophoresis. The carriage rates for hepatitis B antigen were 13.5% in the lepromatous leprosy patients (5 positive in 37) and 4.3% in the tuberculoid leprosy patients (5 positive in 115). The accommodation, sanitation and source of water of each patient was established by careful interrogation. The environment, in terms of these three parameters was best with tuberculoid leprosy patients, less so in the lepromatous leprosy patients not carrying hepatitis B antigen and the worst in the five patients with lepromatous leprosy carrying the hepatitis B antigen. Carriage of hepatitis B antigen appears to be related to poor environmental circumstances which seem to favor transmission of the hepatitis B virus.—Authors' Abstract

Kelkar, S. S., Niphadkar, K. B., Khare, P. M. and Kasbekar, P. V. SGOT, SGPT and hepatitis B antigen in leprosy. Lepr. Rev. **45** (1974) 321-325.

Serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) levels were determined in seven cases of tuberculoid leprosy carrying hepatitis B antigen (HB-Ag) and compared with the levels in 50 HB Ag-negative cases of tuberculoid leprosy. The mean value for SGPT and SGOT in the former group was 7.86 and 8.86 IU/L respectively, while in the latter it was 9.08 and 11.48 respectively. Similarly the mean values for SGPT and SGOT in eight HB Ag-positive cases of lepromatous leprosy were 8.88 and 13.75 IU/L respectively, while the mean figures for 50 HB Ag-negative cases of lepromatous leprosy were 7.96 and 12.48 IU/L respectively. The differences obtained in lepromatous leprosy were statistically insignificant. There was no difference in the serum enzyme levels of HB Ag-positive and negative cases and the range of values obtained were comparable. The absence of liver damage as indicated by enzyme studies suggests the host-parasite relationship of the hepatitis B virus in leprosy to be one of symptomless carriage.—Authors' Summary

Languillon, J., Rucher, H. and Sarrat, H. La lèpre lépromateuse nodulaire à cellules fusiformes chez l'Africain. Aspect "histoid" de Wade. [Nodular lepromatous leprosy with spindle-shaped cells in the African. The "histoid" leprosy of Wade.] Med. Trop. **33** (1973) 595-604. (English Summary)

The authors, from Dakar, record five examples of the histoid variety of leprosy first described by Wade (Trop. Dis. Bull. **61** [1964] 673). Despite adequate treatment for several years, four patients presented characteristic skin lesions that showed a typical histopathologic picture of classical histoid leprosy and numerous leprosy bacilli (presumably drug-resistant). In the fifth patient, the lesions appeared before any treatment had been given.

A brief review of the relevant literature is included.—S. G. Browne (*From* Trop. Dis. Bull.)

Mudd, Stuart and Shayengani, Mehdi. Delayed-type hypersensitivity to *S. aureus* and its uses. Ann. NY Acad. Sci. **236** (1974) 244-251.

This study was elicited by observation of the frequent concurrence of staphylococcal infection and leprosy in leprosaria in New Guinea. Since some beneficial effects of staphylococcal phage lysate (SPL) had been seen in tuberculosis, it was natural to study the antigen in leprosy. The double-blind study was suggested by Dr. L. N. Magnussen in Masanga.

Twenty-four lower-grade students were studied, aged from 7 to 13, in a boarding school at Masanga Leprosarium. All were leprosy patients. Their conditions covered the immunological spectrum from tuberculoid leprosy through the intermediate grades to lepromatous leprosy.

Each of the 24 starters was given an intradermal injection of 0.1 ml lepromin (kindly supplied by Dr. John Hanks) in the left forearm. One week later they were subcutaneously given the first dose of SPL or a placebo of similar appearance, at 0.1 ml. These were followed weekly by subcutaneous injections of 0.1 ml. The physician did not know which was SPL and which placebo, but gauged the dose in accordance with the severity of the reaction. After 12 weeks of these injections, the second dose of lepromin was given intradermally in the right forearm. Readings were taken after 24 hours for the antigen-placebo injections and after 24 and 48 hours for lepromin (Fernandez reactions).

Measurements were of induration, along two diameters.

The results were tabulated. When the code was opened at the end it was found that the reactions of delayed-type hypersensitivity to staphylococcal antigens were significantly greater in those who had been elicited with SPL, as were reversions from lepromin negativity to lepromin positivity. The clinical aspects of this investigation are still under study, and will be reported later.

The use of induction and elicitation to evoke cell-mediated resistance in leprosy is by no means entirely an exercise of faith. There is clear evidence that the interactions of the cells of the reticuloendothelial system and *Mycobacterium leprae* are critical. Evocation of cell-mediated immunity with BCG has been on trial for many years as a preventive against leprosy; three very large field trials have been conducted, however, with results that are not consistent. New insights are being gained regarding the immunology of this ancient disease. Much, however, remains unclear and is still in need for rational understanding.

Reconnaissance of the practical possibilities of induction and elicitation under other conditions with *S. aureus*-SPL system is in progress.—(*From* text, p 249)

Myrvang, Bjorn. Immune responses to *Mycobacterium leprae* in man. J. Oslo City Hosp. **25** (1975) 3-24.

Application of immunological *in vitro* methods to the detection of people exposed to *M. leprae* has provided evidence that leprosy bacilli are frequently transmitted from leprosy patients to healthy contacts. The findings suggest that the mounting of a cell-mediated immune response to *M. leprae* antigens prevent disease manifestations from developing in most people infected. Hence it may be that leprosy develops in individuals who after infection fail to rapidly generate the immune mechanism necessary to create an environment which inhibits microbial growth. The realities of this postulate can only be proven by long-term follow-up studies but may be supported by findings that patients in the indeterminate early stages of leprosy do not show any immune response to *M. leprae* detectable in the peripheral blood.

In the classifiable forms of leprosy the diversity of clinical and histopathological manifestations appear to reflect the cell-mediated immune response mounted after *M. leprae* has been allowed to proliferate for various lengths of time. Thus cell-mediated immune responsiveness to *M. leprae* antigens underlies the defined clinical and histological spectrum of disease, which ranges from the high resistant tuberculoid type, through various borderline forms, to the disseminated lepromatous type.

The cell-mediated immune response evoked, involving lymphocytes and macrophages and substances released from these cells, is likely to be the main factor in producing the structural and functional disturbances of skin and peripheral nerves characterizing tuberculoid and borderline leprosy. Moreover, a rapid increase in the cell-mediated immune response to *M. leprae* antigens may give rise to the acute exacerbations of the disease called reversal reactions.

In lepromatous leprosy patients, whose cell-mediated immune responsiveness to *M. leprae* is completely lacking, the innocuous nature of *M. leprae* is clearly demonstrated. Despite the inability of the patients to restrict bacillary growth, overt damage to host cells only occurs after many years of extensive microbial proliferation. The vast number of bacilli stimulate abundant formation of antibodies, which together with soluble *M. leprae*-antigens released upon treatment, may give rise to tissue destruction with an immune complex genesis.—Authors' Conclusions

Nagai, S., Matsumoto, J. and Kohda, K. Delayed-type skin reactivity of enzyme proteins from mycobacteria. Am. Rev. Respir. Dis. **110** (1974) 362-365.

Five highly purified enzymes (aminoacylases, lactate oxygenase, and fumarases), isolated from the cells of *Mycobacterium phlei* or *Mycobacterium smegmatis,* were tested for their delayed-type skin reactivity on guinea pigs sensitized with the cells of one of these two species or with those of *Mycobacterium tuberculosis.* All of these enzyme proteins were reactive in the skin test with a marked species-specificity. Fumarase from pig heart muscle did not react at all. One approach is suggested in this paper to study the relationship between the structure of the skin-reactive antigen and the delayed-type reaction. The antigenic

proteins were purified from the cells of mycobacteria using their enzymatic activities as indicators for isolation. As lactate oxygenase can be easily obtained in a crystalline form with a high yield, effects of some modifications of the enzyme protein on skin reactivity were studied.—Authors' Summary

Quismorio, F. P., Rea, T. H., Levan, N. E. and Friou, G. J. Immunoglobulin deposits in lepromatous leprosy skin. Arch. Dermatol. **111** (1975) 331-334.

Immunoglobulin deposits were detected in 10 of 13 biopsy specimens from apparently uninvolved skin of patients with lepromatous leprosy. There were deposits of IgM at the dermo-epidermal junction in the skin of five patients, and deposits of IgM along the dermal collagen and elastic fibers in the skin of the other five. The deposits were eluted with acid buffers and high molarity salt solution. Circulating IgG antibodies to intercellular substance of epithelial cells, similar to those present in pemphigus vulgaris, were found in 25% of patients with lepromatous leprosy who were studied. These antibodies appeared to be different from the skin-bound immunoglobulin deposits.—Authors' Abstract

Reich, Claude V. Rapid effective measure of a humoral substance(s) reacting specifically with *Mycobacterium leprae* antigens. Infect. Immun. **10** (1974) 963-965.

Leprosy-specific humoral reactants were demonstrated by light scatter. Of 132 lepromatous leprosy sera, 70% gave more extensive reactions than 99% of 100 normal sera. —Authors' Abstract

Reichart, Peter. Pathologic changes in the soft palate in lepromatous leprosy. An evaluation of ten patients. Oral. Surg. **38** (1974) 898-904.

Sixty-two patients with lepromatous leprosy were examined for changes in the uvula and the soft palate. Ten patients had definite gross pathologic changes in this area. Loss of the uvula and part of the soft palate due to granulomatous infiltration, leproma formation, ulceration, and fibrosis were found. Absence of these structures was observed in a very marked degree only in patients in whom lepromatous leprosy had been present for many years or who had not undergone any kind of specific treatment. The histologic and functional features, such as difficulty in swallowing, regurgitation, and rhinolalia aperta, with their possible consequences are described.—Author's Summary

Rollier, Rene. Quelques aspects immunologiques en Dermatologie. [Some immunologic aspects in dermatology.] Maroc Med. **54** (1974) 372-375. (In French)

This overview of certain immunologic features of leprosy, superficial mycoses, and collagen and bullous diseases is intended for the nonspecialist. Leprosy has the broadest coverage. The author states, without giving data or citing references, that the leukemias and visceral cancers occur more frequently in lepromatous than in tuberculoid leprosy patients. Renal amyloidosis in leprosy is classified as an autoimmune disease.—W. M. Meyers

Ruscher, H., Faye, I., Languillon, J., Sarrat, H., Oudart, J. L. and Carnus, H. Intérêt d'une stimulation immunitaire par BCG itératif dans le traitement de la lèpre lépromateuse. Nouveau bilan chez treize malades. [Interesting immunity stimulation by repeated BCG dosage in lepromatous leprosy. New data in 13 patients.] Bull. Soc. Med. Afr. Noire Lang. Fr. **18** (1973) 470-476. (In French)

The clinical and histological changes observed in 13 cases of leprosy treated by repetitive doses of BCG given separately or in conjunction with standard treatment argue in favor of an efficient immunizing stimulant, by means of this vaccine. Nine patients showed a transitory regression towards an interpolar form with positive results from cutaneous tests for lepromin and intrication of tuberculoid and lepromatous histologic structures. Six patients have been declared noncontagious after 22 to 30 months of treatment.—English Summary

Shao, J. Affinity of *M. leprae* to lymphocytes of leprosy patients *in vitro*. Dar es Salaam Med. J. **5** (1973) 27-28.

The adherence of *Mycobacterium leprae* to lymphocytes from patients with tuberculoid and lepromatous leprosy has been studied. The two groups were studied simultaneously.

While lymphocytes from nine tuberculoid patients showed very high adherence property to *Mycobacterium leprae,* there was an obvious diminished affinity for the *leprae* among the lymphocytes from nine lepromatous patients.

It is concluded that lepromatous patients have a diminished number of circulating lymphocytes that have antigenic receptors for *Mycobacterium leprae.*—(*From* Trop. Dis. Bull.)

Stojaković, M., Macanovic, K. and Salamon, T. Über die Sensibilisierung lepröser Patienten auf DNCB. [Sensitization of leprosy patients using DNCB.] Dermatol. Monatsschr. **160** (1974) 570-572. (In German)

Sensitivity to DNCB in six patients with lepromatous leprosy and in one patient with tuberculoid leprosy was investigated. Simultaneously, the intradermal testing with PPD and trichophytin was performed. Immunoelectrophoretic pattern of serum proteins in five patients was studied. Five of six patients with lepromatous leprosy and one patient with tuberculoid leprosy were sensitized to DNCB. There was excellent correlation between sensitivity to DNCB and PPD, but not between DNCB and trichophytin.—Authors' English Summary

Swift, Thomas R. Peripheral nerve involvement in leprosy: quantitative histologic aspects. Acta Neuropathol. (Berl.) **29** (1974) 1-8.

Nerve biopsies in three lepromatous and three dimorphous leprosy patients are reported. Bacilli were found in all three lepromatous nerves, and in one dimorphous nerve. Bacilli were present in cutaneous nerve twigs in all six patients.

Myelinated fiber counts were severely reduced in four patients. Large fibers were affected to a greater extent than small fibers. Evidence of widespread segmental demyelination with remyelination was present. Wallerian degeneration was not found. Schwann cell involvement with subsequent segmental demyelination appears to be an important event in the pathogenesis of leprous neuritis. —Authors' Summary

Terencio de las Aguas, J., Hierro, J. del and Alemany, A. M. Transaminasas y antígeno Australia en la lepra. [Transaminase and Australia antigen in leprosy.] Rev. Leprol. **9** (1973) 239-243. (In Spanish)

High transaminase levels occur quite frequently in leprosy, the rate in leprosy patients being 45.5%, and it appears mainly in patients with a very long leprosy process who have visceral disturbances, especially of the liver. These levels reflect the visceral disturbance. We believe that transaminase is a very sensitive indicator of lesions from the different organs affected by leprosy, first of all the liver.

In reactional phases, we have observed a frequency of 50% of high transaminase levels, which denote the production of visceral lesions and affectation of the reticuloendothelial system. In acute episodes they will produce more and more visceral involvement.

Patients with nephrosclerosis and amyloidosis, these being the worst complications in lepromatous patients and very often being the cause of death, also showed high transaminase levels at a rate of 30%.

In general, it is remarkable that SGOT levels are quite often the highest, also producing the highest figures in hepatic and reactional patients.

We believe that these enzymes in leprosy are a clear exponent of toxic effects from the Hansen bacillus in the different organs, and that they are, as well, a very important test for the clinical control of visceral complications.—(*Adapted from* English summary)

Terencio de las Aguas, J., Richeri, D. and Alemany, A. M. Estudio de la immunidad humoral en la lepra. [Humoral immunity in leprosy.] Rev. Leprol. **9** (1974) 355-360. (In Spanish)

Leprosy humoral immunity was studied in 93 patients (82 lepromatous and 11 tuberculoid). The immunoglobulins, antibodies to muscle, antimitochondrials, antithyroid and antinuclears, the rheumatic factor, C-reactive protein and the rate of antistreptolysines were considered.

It was concluded that when humoral immunity is conserved or even elevated, it fails, in the lepromatous leprosy patient, to cause destruction of the mycobacterium.—(*Adapted from* English summary)

Microbiology

Bergel, Meny. Cultivo e inoculación del *Mycobacterium leprae* en tejidos y órganos en estado de necrobiosis y necrosis. [Culture and inoculation of *M. leprae* in necrotic tissues.] Rev. Lat. Am. Microbiol. **15** (1973) 181-186. (In Spanish)

Culture of *M. leprae* in necrotic tissues is proposed as a new possibility *in vivo* and *in vitro*. The culture in mouse foot pad and rat testis was necrotized by cadmium chloride. The author presents a long list of possible technics to achieve the same purpose.—English Abstract

Camargo, E. E., Larson, S. M., Tepper, B. S. and Wagner, H. N. Jr. Radiometric measurement of metabolic activity of *Mycobacterium lepraemurium*. Appl. Microbiol. **28** (1974) 452-455.

A sensitive and nondestructive radiometric method has been applied to the detection of metabolism of *Mycobacterium lepraemurium*, as a model for the study of the metabolism and substrate requirements of *M. leprae*. The method is based on the measurement of the $^{14}CO_2$ produced through the bacterial conversion of [U-^{14}C] acetate or [U-^{14}C] glycerol by 7×10^9 bacteria suspended in 10 ml of either a simple buffer system (K-36) or a complex medium (NC-5). Metabolism of the bacilli was easily detected within three days after inoculation and was measured daily. NC-5 medium supported metabolism of *M. lepraemurium* for several weeks longer than the simple K-36 buffer. The radiometric technic shows promise as a rapid and efficient system for evaluating the metabolism of mycobacteria without introducing any changes in the physiologic state of the organisms, studying their metabolic pathways, determining conditions potentially favorable for multiplication of these organisms *in vitro*, and studying their susceptibility to inhibition by drugs.—Authors' Abstract

Delville, J. Microbiologie de la lèpre. Comportement et affinites tinctoriales du bacille de Hansen dans les lesions lépreuses. [Microbiology of leprosy. Aspects and staining characteristics of Hansen bacilli in leprosy lesions] Ann. Soc. Belg. Med. Trop. **54** (1974) 457-462. (In French)

The Ziehl-Neelsen technic does not always detect acid-fast bacilli in all types of leprosy. In most leprosy lesions other staining technics (Gram, Ziehl-periodic acid, Fite-Faraco) reveal, together with typical acid-fast bacilli, also non acid-fast bacilli, the latter appearing first.

The Ziehl-Neelsen technic is thus not sufficient for deciding to stop treatment and to consider a leprosy patient as noncontagious.—English Summary

Imaeda, Tamotsu. Growth inhibitory activity of deoxyribonucleic acid-containing factor(s) isolated from lepromatous lesions. Infect. Immun. **10** (1974) 957-959.

Deoxyribonucleic acid-containing factor(s) isolated from *Mycobacterium leprae* suspensions obtained from lepromas of nine patients showed growth inhibitory activity against *Micrococcus* and both orange-red pigmented and coccoid mutants of mycobacteria. No growth inhibition was observed for parent mycobacterial species, *Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis,* and *Staphylococcus epidermidis.*—Authors' Abstract

Ishaque, M. and Kato, L. The cytochrome system in *Mycobacterium lepraemurium*. Can. J. Microbiol. **20** (1974) 943-947.

The respiratory chain system of cell suspensions of *Mycobacterium lepraemurium* was investigated spectrophotometrically. The results obtained indicated that whole cell preparations contained flavins, cytochromes of the $a + a_3$ and b type, as well as two CO-binding pigments; cytochromes a_3-CO and a second pigment similar to cytochrome o. The cytochromes were found to be in the reduced form. The presence of cytochrome systems could only be shown after the cell suspensions in the reference cuvette were exposed to oxygen. The positions of the peaks in the difference spectra were similar when cell suspensions were reduced anaerobically without added substrate or treated with dithionite. The whole cell suspensions of *M. lepraemurium* were not found to contain detectable quantities of cytochrome c.—Authors' Abstract

Matsuo, Yoshiyasu. Studies of *Mycobacterium lepraemurium* in cell culture. I. Continuous multiplication in cultures of mouse foot pad cells. Jap. J. Microbiol. **18** (1974) 307-312.

A serial increase in the number of *Mycobacterium lepraemurium* with successful subcultures has been obtained in the mouse foot pad (MFP) cell culture. Special attention has been given to maintaining the infected cells for longer periods: 1) the infected cells were incubated at 30°C rather than at 37°C, and 2) the concentration of serum in the culture medium was reduced from 10% to 2% as soon as a monolayer growth of the transferred cells was obtained. There have been cumulative bacterial increases of 1.47×10^{17} and 1.84×10^{15} fold for the Kurume-42 strain during a period of 1,255 days, and 2.23×10^{9} and 3.89×10^{5} fold for the Hawaiian strain during periods of 831 and 572 days. The overall generation times were estimated at 22.0, 24.8, 26.8, and 30.8 days, respectively. All attempts to grow the acid-fast bacilli obtained in cell cultures on artificial culture media have failed. The ability of the organisms to produce typical lesions in mice has been well preserved.—Authors' Abstract

Mori, Tatsuo. Cultivation of *M. lepraemurium* on the 1% Ogawa yolk medium and animal inoculation with cultivated *M. lepraemurium.* Lepro **43** (1974) 226-233. (In Japanese)

A follow-up experiment of Ogawa's method was begun in April 1971 and identification of cultivated *M. lepraemurium* passaged 11 generations was carried out by injection of mouse, rat, hamster, rabbit, guinea pig and quail by a diffusion chamber method.

Isolation of culture inoculum was better in cases of a subcutaneous leproma treated with alkali and using an air-loose stopper than in cases of no treatment using an air-tight stopper. When cultivation was carried out under 33°C for a long time, several microcolonies of *M. lepraemurium* appeared after one year. As *M. lepraemurium* grows very slowly, primary isolation should be kept at a low temperature to avoid degradation of medium composition. Isolation of *M. lepraemurium* succeeded in 83% of all test tube media in the case of aerobic conditions, while succeeding in only 50% in the case of air-tight conditions. Moreover, piled up, large colonies were seen in the aerobic condition. Some of these colonies could be passaged on new 1% Ogawa yolk media but not on 1% Ogawa whole egg media.

A three month old culture of *M. lepraemurium* passaged 11 generations was received from Dr. Ogawa and its bacterial suspension was inoculated subcutaneously into the backs of ddO white mice. After five months a small leproma was palpable in the local site which had been injected with more than 1.8×10^{4} bacilli. At the same time, bacterial suspension was mixed with mouse peritoneal cells and enclosed in a millipore diffusion chamber, which was placed in the abdominal cavity of a mouse. After five months many globi were seen in peritoneal cells mixed with 0.9×10^{3} bacilli. When the bacterial suspension grown in the diffusion chamber was inoculated into abdominal subcutaneous tissue of ddO white mice, five bacilli were able to form a palpable subcutaneous leproma after five months. The second passage of the leproma, which was grown on the back of a ddO mouse by an injection with cultivated *M. lepraemurium,* was carried out in C3H mice. After 8 to 13 months, large lepromas were formed in the injected sites of all mice.

At the present, for definition as *M. lepraemurium,* the organism must form a leproma containing globi of acid-fast bacilli in mice, rats, and hamsters and must not form a leproma in guinea pigs, rabbits, and birds. The organism should not grow on culture media for *M. tuberculosis.* Therefore, cultivated *M. lepraemurium* was injected into rats, hamsters, guinea pigs, rabbits and quails. After six to ten months, thinly developed lepromas were seen in the injected sites of rats and hamsters, but not in guinea pigs, rabbits and quails.

From these results, the acid-fast bacillus isolated on 1% Ogawa yolk medium by Dr. Ogawa can be identified as *M. lepraemurium.*—(*Adapted from* English summary)

Nakamura, Masahiro. Cultivation of *Mycobacterium lepraemurium* in a cell-free liquid medium. Jap. J. Bacteriol. **29** (1974) 517-525. (In Japanese)

A cell-free liquid medium, which was referred to as NC-5, was established for cultivation of *Mycobacterium lepraemurium.* It

was composed of the basal medium and some additives. The former was the Kirchner medium enriched with glucose, sodium pyruvate, and calcium pantothenate, and the latter were goat serum, α-ketoglutaric acid, cytochrome C, hemin, and l-cystein hydrochloride. All the additives had to be added aseptically to the basal medium.

When bacilli were cultivated in the NC-5 medium at 30°C, bacterial cells began to be elongated gradually at four to seven days of cultivation and started to multiply at two weeks. Finally, the growth of bacilli could be recognized macroscopically as a turbid mass. A possibility that the growth obtained in NC-5 might be due to multiplication of other acid-fast bacilli which might have contaminated the starting material was excluded, as no growth of bacilli was observed in the Kirchner medium, which is the most suitable for growth of most acid-fast bacilli.

The growth of *Mycobacterium lepraemurium* reached a maximum in NC-5 medium at eight weeks of cultivation. The increase rate was about 100 or 1,000 times. It is of great interest to note that the smaller the inoculum size, the higher the growth rate. The possible generation time calculated from the bacillary count might be approximately 8 to 14 days. The growth was inhibited by addition of isoniazid, streptomycin, and mitomycin C, but not by penicillin.

In a preliminary trial, no bacilli multiplied in the second generation when the bacilli grown in NC-5 medium had been inoculated into a freshly prepared NC-5 medium. An abundant multiplication of bacilli was observed however, when bacilli were transferred from a smear on the slide to the NC-5 medium at definite intervals. Finally, it was indicated in animal experiments that the bacilli cultivated in NC-5 medium for 223 days kept their pathogenic activity. On the contrary, no pathogenicity was observed in the bacilli cultivated in the Kirchner medium under the same conditions.—Authors' English Summary

Nakamura, Masahiro. Multiplication of *Mycobacterium lepraemurium* in cell-free liquid medium. 6. Elimination of components from NC-5 medium. Lepro **43** (1974) 250-253. (In Japanese)

The growth of *M. lepraemurium* was observed in various modified media which were composed of components eliminated from the NC-5 medium. The results obtained by morphologic observation and bacillary counting indicated that the same growth as that obtained on NC-5 medium cannot be observed when any component of NC-5 medium is eliminated. It was noted that α-ketoglutaric acid could be replaced by oxaloacetate.

From the results mentioned above, it can be concluded that a component essential for the multiplication of *M. lepraemurium* might be α-ketoglutaric acid, and other components in NC-5 medium might be growth stimulators. However, it might be thought that α-ketoglutaric acid should not complete the growth, but act as the starting point of growth of the bacilli.—(*Adapted from* English summary)

Pattyn, Stefaan R. Survival of *Mycobacterium leprae* in newborn rat heart cell culture. Ann. Soc. Belg. Med. Trop. **54** (1974) 515-518.

Suspensions of *Mycobacterium leprae* obtained from mouse foot pads were inoculated into primary cultures of newborn rat heart cells at 33°C. At regular intervals after inoculation, homogenates of these cells were inoculated into mouse foot pads. Viable *M. leprae* were recovered up to the 63rd day, the longest period essayed.—Author's Summary

Talwar, G. P., Krishnan, A. D., Jha, P. and Mehra, V. Intracellular growth of an obligatory parasite *Mycobacterium leprae*. Host bacterial interactions. Biochimie **56** (1974) 231-237.

Patients suffering from leprosy present a wide spectrum of the disease with a variable degree of resistance to the infection. There is no depression of humoral immune responses. Serum immunoglobulins are invariably raised in lepromatous leprosy patients. The proportion of B lymphocytes as compared to T cells is elevated in lymph nodes and in circulation. Lepromatous leprosy (LL) patients can elicit normal response (antibody titers) on secondary immunization with vaccines such as TAB. Cell-mediated immune responses are however impaired in LL cases. The blast transformation of peripheral leukocytes with PHA and with *M. leprae* antigens is depressed. There is a diminished

formation of biologically active polypeptides influencing the migration and aggregation of macrophages. Bacterial growth has been measured *in vitro* in macrophages derived from peripheral blood of tuberculoid and lepromatous leprosy patients. *M. leprae* proliferate better in cultures devoid of lymphocytes. In tuberculoid leprosy cases, the presence of lymphocytes reduces significantly the intracellular growth of the bacteria.—Authors' Concluding Comments

Varughese, P., Helbecque, D. M., McRae, K. B. and Eidus, L. Comparison of strip and Ziehl-Neelsen methods for staining acid-fast bacteria. Bull. WHO **51** (1974) 83-91.

The efficiency of the Ziehl-Neelsen method for staining acid-fast bacteria was compared with that of the strip-staining procedure in which one kind of impregnated strip is used to stain the bacteria and another kind for simultaneous decolorization and counterstaining of the smear. The methods were evaluated in 1,136 duplicate smears prepared from digested sputum and 307 pairs of direct smears. The efficiency of the strip method was comparable to that of the Ziehl-Neelsen method with digested sputum; with direct smears, however, it generally depended on the quality of the smear. With thick, uneven smears, lower bacterial counts were obtained by strip staining. On the basis of this trial, the authors suggest improvement of the strip method.—Authors' Abstract

Yoshii, Z. and Nakamura, M. Scanning electron microscopic studies on the growth features of *Mycobacterium lepraemurium* in cell-free medium. J. Gen. Microbiol. **83** (1974) 145-152.

The morphology of *Mycobacterium lepraemurium*, Hawaiian strain, cultivated on a glass slide in a cell-free liquid medium (NC_5) at 30°C for 12 weeks, was observed every two weeks with a scanning electron microscope. Flourishing growth and microcolonial growth occurred in the peripheral and central areas, respectively, of a smear. Elongation, septum formation, division, budding and branching in the bacteria were seen between the second and fourth weeks of incubation, which may correspond to the beginning of the exponential phase. After this period, the number of bacilli suddenly increased, and intertwined, elongated cells with large granules appeared. These features gradually increased until the stationary phase was reached after 12 weeks of incubation. These observations are the first scanning electron microscopical descriptions of the growth patterns of *Mycobacterium lepraemurium in vitro*.—Authors' Summary

Experimental Infections

Balentine, J. D., Binford, C. H. and Storrs, E. E. Central nervous system pathology of armadillos infected with *Mycobacterium leprae*. Am. J. Pathol. **78** (1975) 19a-20a.

In previous communications, infection of peripheral nerves of armadillos inoculated with human *Mycobacterium leprae* was noted to be similar to that occurring in human lepromatous leprosy by light (Issar and Binford: Int. J. Lepr. **41** [1973] 499) and electron (Balentine *et al:* Int. J. Lepr. **41** [1973] 502) microscopy. Numerous bacilli were found in Schwann, perineural and endothelial cells. Macrophages containing many bacilli were found within nerves. Small cutaneous as well as large nerves (brachial and sciatic) were effected. Cranial and intraspinal nerves and satellite cells of peripheral ganglia were also involved.

In a small number of armadillos, continued autopsy studies of animals sacrificed or dying with disseminated leprosy have revealed infection of the central nervous system as well. Intracellular *M. leprae* have been found in cells of the meninges, cerebral cortex, olfactory bulb and choroid plexus. The inflammatory response has been limited in these areas, however, some macrophages containing bacilli have been identified. The location of bacilli in the olfactory bulb is important in considering the route of spread to the central nervous system in view of the prevalence of *M. leprae* for the nasal passages of infected armadillos. The presence of ba-

cilli in choroid plexus is also of significance, especially in view of the meningeal involvement.—Authors' Abstract

Binford, C. H., Storrs, E. E. and Walsh, G. P. Leprosy in the armadillo: A new model in leprosy research. Am. J. Pathol. **78** (1975) 66a.

Although mild infections with *Mycobacterium leprae* have been produced experimentally in the foot pads and ears of several rodents since 1960, the introduction of the nine-banded armadillo (*Dasypus novemcinctus*) in 1971 by Storrs, and Kirchheimer and Storrs (Int. J. Lepr. **39** [1971] 703-714, 693-713) has opened an entirely new era in research in lepromatous leprosy. At necropsy, 9 (45%) of the first 20 armadillos inoculated intradermally or intravenously with suspensions of the human leprosy bacillus, *Mycobacterium leprae,* showed severe, widely disseminated infection histopathologically similar to that of lepromatous leprosy in man. Presumably because of the low body temperature (32° to 35° C) of the armadillo, lesions were observed in sites not affected in man. Invasion of peripheral nerves by mycobacteria, a feature considered pathognomonic of *M. leprae* was regularly observed.

The massive amounts of lepromatous nodules, averaging more than 100 gm per animal, obtained from subcutaneous tissues and beneath the carapace, now make possible the harvesting of quantities of *M. leprae* for definitive biochemical and physiologic studies. Because *M. leprae* has not been acceptably cultivated *in vitro,* such studies have not been possible on the small quantities of bacilli obtained from human lepromatous leprosy.

The report will include salient observations made histopathologically on 15 armadillos with disseminated leprosy.—Authors' Abstract

Closs, Otto and Haugen, Olav A. Experimental murine leprosy. 2. Further evidence for varying susceptibility of outbred mice and evaluation of the response of five inbred mouse strains to infection with *Mycobacterium lepraemurium.* Acta Pathol. Microbiol. Scand. **82** (1974) 459-474.

Female mice of the outbred strain NMRI, and the five inbred strains AKR, BALB/c, C3H, C57/BL, and White Label were infected with *Mycobacterium lepraemurium.* Infectious lesions in the liver were evaluated histologically with regard to the type of inflammatory reaction and content of bacilli. In the outbred strain the host response of individual mice varied considerably. This variation diminished if a large inoculum was used and the infection allowed to proceed for a long time. Within the inbred strains individual animals showed a more uniform type of reaction. However, clear differences in the host response to murine leprosy could be demonstrated in these strains, most markedly between the strains C3H and C57/BL. In C3H, the infection seemed to make uninhibited progress and the granulomas contained large numbers of bacilli with few or no surrounding lymphocytes. The granulomas of C57/BL mice contained fewer bacilli and regularly showed infiltration by lymphocytes. However, after a large inoculum of bacilli this difference in host response seemed less evident. The present study confirms our previous observation that outbred mice differ in their host response to murine leprosy. Evidence is presented that this variation is due to differences in the ability of individual mice to mount a cell-mediated immune response against the mycobacterium. The capability to respond is shown to depend on genetic factors of the host.—Authors' Abstract

Convit, J. and Pinardi, M. E. Leprosy: confirmation in the armadillo. Science **184** (1974) 1191-1192.

Bacteria isolated from lesions of lepromatoid leprosy in the armadillo were studied in comparison with *Mycobacterium leprae* isolated directly from human lepromatous leprosy lesions. Three methods were used to show that the bacteria from the lesions of the armadillo were identical to those of the human lesions: 1) extraction of the bacteria with pyridine and subsequent staining with various technics; 2) the competence in clearing bacilli (CCB) test; and 3) the Mitsuda test.—Authors' Abstract

Frye, F. L., Carney, J. D. and Loughman, W. D. Feline lepromatous leprosy. Vet. Med. Small Anim. Clin. **69** (1974) 1272-1273.

Granulomatous skin lesions in cats are not rare; however, the finding of acid-fast organisms resembling *M. lepraemurium* in multiple subcutaneous granulomata and region-

al lymph nodes in a domestic cat merits attention.

We can only speculate where and how the cat became infected. The possibility of nonspecific acid-fast bacilli being responsible for these lesions was considered; however, the massive numbers of organisms seen in this cat's tissues would be more consistent with infection with *M. lepraemurium* than with soil bacteria (in which numerical replication is far smaller in scale.) Had fresh material been saved for animal inoculation, a definitive diagnosis of the organisms involved could have been made.—(*Excerpted from* article)

Krahenbuhl, J. L., Levy, L. and Remington, J. S. Resistance to *Mycobacterium leprae* in mice infected with *Toxoplasma gondii* and *Besnoitia jellisoni.* Infect. Immun. **10** (1974) 1068-1071.

Mice chronically infected with the intracellular protozoan *Toxoplasma gondii* or *Besnoitia jellisoni* were resistant to foot pad challenge with *Mycobacterium leprae.* Resistance was manifested by lower numbers of recoverable *M. leprae* in the foot pads of protozoal-infected mice and was enhanced in *Toxoplasma*-infected mice by a booster injection of *Toxoplasma* antigen in the infected foot pad. The results suggest a major role for the activated macrophage in the control of *M. leprae* infection.—Authors' Abstract

Navalkar, R. G., Patel, P. J., Dalvi, R. R. and Levy, L. Immune response to *Mycobacterium leprae:* plaque-forming cells in mice. Infect. Immun. **10** (1974) 1302-1306.

Intravenous immunization with a cell extract of *Mycobacterium leprae* produced a primary immune response of considerable magnitude, followed by an equally large response after secondary stimulation, as measured by assay of plaque-forming cells (PFC). Infection with *M. leprae* or immunization with cell extract by the foot pad route produced a lower level of response than that seen in the intravenous group. Identical patterns of response, although not of the same magnitude, were observed after both primary and secondary challenges in the two foot pad groups, one infected with viable *M. leprae* and the other immunized with *M. leprae* cell extract. The secondary response after a booster dose to all these groups appeared to be an enhanced immunoglobulin M response. Control studies confirmed that the immune response was a direct result of the host-parasite interaction and that the PFC observed resulted from stimulation of antibody-forming cells by antigens of *M. leprae.* The similarity in time of appearance of peak PFC levels in the two foot pad groups may be attributed to the live challenge passing through a latent phase. Alternatively, the challenge is known to contain a large proportion of nonviable cells, and it may also contain soluble *M. leprae* antigens. Studies of the cross-reactivity of the antigens have extended previous observations on antigens shared between *M. leprae* and other mycobacterial species. Use of the two antigen-containing fractions of the *M. leprae* cell extract has suggested that one of the fractions contains some shared antigens, whereas the other has an antigen specific to *M. leprae.*—Authors' Abstract

Santos Damasco, M. H. dos, Thomas, E. M., Andrade, L. M. C. de, Viana, S. M. and Silva, C. de O. Transmissão experimental da lepra a camundongos submetidos a imunossupressão química. [Experimental transmission of leprosy to mouse foot pads by chemical immunosuppression.] Bol. Div. Nac. Lepra **33** (1973) 94-106. (In Portuguese)

The authors studied the possible effect of cyclophosphamide (Enduxan) in the experimental transmission of *Mycobacterium leprae* to mice on the basis of Shepard's technic. The bacilli with very good Morphologic Index (viables) were collected from patients and inoculated in the foot pad of the animals and intravenously. The mice were given 200 mg/kg body weight of cyclophosphamide intraperitoneally each fortnight and had been carefully observed for more than 17 months. At proper times necropsies and histopathologic examinations were performed in both the cyclophosphamide group and the control group. No dissemination of the bacilli throughout the organism was found. As a rule, there was seen a certain slowness in the decline of the local infection and more richness in acid-fast bacilli among the mice of the cyclophosphamide group in comparison with those of the control group. The authors stress that with this technic the animals can be maintained under the

immunosuppressive effect of cyclophosphamide for a long period of time. Further research work must be done in this field.—(*Adapted from* English abstract)

Sushida, Kiyo. Experimental transmission of *M. leprae* in the testes of mice, born of ^{131}I-injected females. Lepro **43** (1974) 234-240. (In Japanese)

Six strains of *M. leprae* taken from lepromatous leprosy patients were inoculated into the testes of ^{131}I-F_1 mice, which were divided into two groups. The animals in the first group were born of females which had been subcutaneously injected with ^{131}I-100 μc during pregnancy; and those in the second group were born of females injected before pregnancy.

The results were as follows:

The ^{131}I-F_1 mice, born of females injected during pregnancy with ^{131}I-100 μc, and then inoculated with leprous bacilli as described above, showed the presence of so-called globi in the testes. When samples of leprous bacilli (LL28, LL32, LL33) taken from patients who had not been receiving antileprous drug treatments were used in the above ^{131}I-F_1 mice, then globi were found in this investigation (Relationship, I). When the leprous-bacilli were secured from lepromas removed from patients being treated, and then injected into mice born of females which had been injected with ^{131}I-100 μc either during or before their pregnancy, no globi were found in the mice (Relationship, II-b). Even if the bacilli (LL32, LL33, LL34) taken from nontreated patients were injected into mice which were born of females injected with ^{131}I-100 μc before pregnancy no globi were found (Relationship, II-a).—(*Adapted from* English summary)

Epidemiology and Prevention

Arenas, G.R. Movilización de población. Otro problema social de los enfermos de lepra. [Migration of population. Another social problem of leprosy patients.] Medicina Rev. Mex. **54** (1974) 542-543. (In Spanish, English summary)

The author presents a brief social-medical study of 34 patients with different forms of leprosy in a rural community in Mexico. He found two very important problems: endemic malnutrition and migration of the population to the slum section of Mexico City.

The author proposes the name "foci transference" to the phenomenon conditioned by the migration of leprosy patients from one region to another. In this study 50% of lepromatous cases and 80% of indeterminate cases migrated.

This process makes it very difficult to control the patients and it is quite different from the phenomenon of slow diffusion of leprosy observed in Mexico with the arrival of the Spanish conquerers.—A. Saul

Chaudhury, M. The role of BCG against leprosy. Lepr. India **46** (1974) 1-5.

Theoretically, it may be stated that the action of BCG against leprosy, given other technical factors as comparable, can vary from one part of the world to another as much as the epidemiologic picture varies. BCG vaccination may protect some individuals against leprosy for a limited period of time, except for the lepromatous type, but such beneficial action of the vaccine may depend on a complex host of factors operating in the area where it is being tried. In view of the foregoing, we feel that the conclusion made by Bechelli *et al* (1970) that at this stage it would be unwise to recommend BCG vaccine for the prevention of leprosy is justified. Further research and trials are needed to comprehend the intricate nature of this problem.—(*Adapted from* author's discussion)

Davey, Thomas F. Realism in leprosy control. Lepr. Rev. **45** (1974) 197-200.

This editorial emphasizes, in forthright and percipient fashion, certain psycho-social factors often neglected in the planning and execution of leprosy treatment/control programs. Despite the availability of a cheap bacteriostatic drug and advice on methodology, the half-hearted applications of modern technics are, in general, making little impression on the incidence of leprosy. Early diagnosis is still a chimera, and case holding is lamentably inefficient. Examples are cited from several countries in support of this thesis.

Two germane factors, long suspected, have recently received confirmation in careful studies: a considerable proportion of patients given a supply of dapsone tablets fail to take them; and leprosy has been shown to be more contagious than has hitherto been thought possible.

The author advocates renewed attention to such essential aspects of the problem as: education of political and medical leaders in the importance of leprosy in planning and teaching; the integration, wherever possible, of leprosy into the general health services; research into methods of effective prophylaxis; and a flexible approach to methods of leprosy control (such as a modified "segregation") that may be at present unfashionable, but which in the context of poverty and stigma may be the best measure in a given situation.—S. G. Browne (*From* Trop. Dis. Bull.)

Gershon, W. An approach to urban leprosy control. The Greater Madras Leprosy Treatment and Health Education Scheme (Greamaltes) sponsored by the German Leprosy Relief Association. Lepr. Rev. **45** (1974) 211-217.

An account is given of an imaginative and enthusiastic approach to the daunting problems presented by a high leprosy prevalence in an overcrowded Indian city of three million inhabitants. By means of a happy combination of mass surveys of slum areas (which constitute 30% of the population), annual medical examinations of schoolchildren (representing 25% of the population), and health education, it has been possible to detect and register 4,360 leprosy patients. The prevalence rates in those examined lie between 17 and 19 per 1,000.

Emphasis is placed from the outset on good public relations and individual care. Laboratory cover is simple, but probably adequate in such a scheme, and 20 beds are available for inpatient care. About 7,400 contacts are regularly examined.

Health education relies on well-tried methods and on utilization of films and radio. Doctors are not neglected in the educational out-thrust, a pilot orientation course for 250 of them having been organized.—S. G. Browne (*From* Trop. Dis. Bull.)

Pakdi, A. C., Sanayakorn, C. K. and Seal, K. S. Some results from sixteen years of leprosy control work in the Khon Kaen Province of N.E. Thailand. Lepr. Rev. **45** (1974) 205-210.

The changes in the epidemiological situation of leprosy in the province of Khon Kaen in northeast Thailand are assessed from the results of two comparable stratified leprosy surveys conducted at an interval of ten years. A marked decline in the overall prevalence of the disease is demonstrated despite the persistence of a large reservoir of unregistered cases. It is considered that intensification of certain operational and investigatory measures could reduce further the transmission of the disease.—Authors' Abstract

Pérez, Benigno Pérez. Profilaxia antileprosa en países de pequeña endemia. El BCG en la profilaxia de la lepra. [BCG in the prophylaxis of leprosy.] Rev. Leprol. **9** (1974) 559-629. (In Spanish)

This detailed 70 page review of the use of BCG in leprosy prophylaxis includes 96 references and 23 tables. In general, BCG was found able to cause positivation of the Mitsuda reaction and on this basis BCG vaccination is regarded as of indubitable value in the prophylaxis of leprosy. But there are cases where such conversion is not possible and for these prophylactic chemotherapy is needed. The paper should be read in the original to adequately assess its detailed contribution to the problem.—O. K. Skinsnes

Rotberg, Abrahao. Prevencão moderna da Hanseníase: caminhos e obstaculos. [Modern treatment of Hanseniasis: methods and obstacles.] Bol. Div. Nac. Lepra **33** (1973) 107-124. (In Portuguese)

The failure of indiscriminate compulsory segregation, the clinical aspects, bacteriology, experimental infection, "Factor N" of resistance reconnaissance of the "anergic margin" through BCG, teaching, research, integration with general public health services, social rehabilitation of disease and patients, cooperation of voluntary agencies, health education (basis of all preventive work), and a nonstigmatizing and nondefamatory educative and scientific terminology are briefly reviewed having in view control of Hanseniasis. Unfortunately, many obstacles continue blocking the practical application of new advances. The important

and urgent task of removing such obstacles shall be studied in the second article of this series.—Author's English Summary

Saint-André, P. and Clastre, J. L. Une enquête sondage d'évaluation de la campagne contre la lèpre dans une zone de grande forêt en Côte-d'Ivoire (Région de Danané). [A pilot evaluation enquiry into a leprosy campaign in an area of dense forest in the Ivory Coast (Danané district).] Med. Trop. **34** (1974) 361-365. (In French, English Summary)

This brief paper summarizes the findings of a pilot survey designed to evaluate the results of a leprosy control program in typical groups of small villages scattered in an area of dense tropical forest. The whole population numbered about 18,000; the prevalence of leprosy was low, and a very low proportion of patients suffered from the lepromatous form. Total coverage was believed to have been achieved.

The authors consider that the routine treatment—fortnightly injections of suspensions of dapsone—resulted in clinical arrest in 65% of patients in three to four years, despite an undisclosed proportion making 50% of clinic attendances or less. The prevalence of leprosy has fallen to 5 per 1,000. The authors recommend that doctors release patients from treatment with greater readiness and, in such an area, that the leprosy program be combined with a campaign against other prevailing diseases, such as onchocerciasis.—S. G. Browne (*From* Trop. Dis. Bull.)

Seal, S. C. and Ghose-Hazra, Amal. Clinico-epidemiological study of leprosy in Calcutta. J. Indian Med. Assoc. **61** (1973) 375-382.

This study has shown that social factors play a significant role in the epidemiology of leprosy and these factors should be taken into consideration when planning control measures. The disease is endemic in Calcutta and its epidemiologic features differ from those of rural areas in certain respects. In this city the higher age groups are relatively more affected than the children, and more or less all shades of social, economic, religious and cultural groups are affected. Children seem to suffer more from nonlepromatous leprosy than the lepromatous variety. Thus, they seem to be partially protected (? passive resistance from mothers). Although there is some migration of patients from outside the city for treatment, the source remained unknown in as high as 90% of patients and was not detected even after careful investigation due to several handicaps such as: absence of method of cultivation of the organism, difficulty in assessing the incubation period and often suppressed clinical manifestation. In addition, the city provides enormous opportunities for unknown exposure due to extreme overcrowding and movement of population.—(*Adapted from* authors' conclusions)

Rehabilitation

Hasselblad, Oliver W. Psycho-social aspects of leprosy. PAHO Bull. **8** (1974) 283-288.

A stifling smog of ignorance, fear, myth, and superstition surrounds the problem of leprosy, often diminishing the chances for early diagnosis and effective treatment. Furthermore, existing prejudices are apt to exert a strong influence on the patient's own view of himself and his role in society, and to sharply reduce his chances for recovery.

A leprosy patient is often unable to build up a self-identity that will reestablish his feelings of self-respect and integrity. Leprosy institutions are full of persons of this kind. For this and other reasons, an institutionalized patient's ability to regain a useful, creative role in community life and his chances for doing so tend to diminish in direct proportion to the length of time he has been away from his home and community.

Even when the patient is not institutionalized and when his self-identity is not irremediably damaged, the psychological problems that he faces are immense. In any society where leprosy has opprobrious connotations he must still perform the following tasks: 1) manage tensions in his relations with others; 2) cope with both facts and uncertainties about the disease; and 3) reconcile differences between his former and present perceptions of himself and his role in society.

While there are no certain solutions for the psycho-social problems of leprosy, a

number of positive steps have proven productive. These include a variety of measures to assist the patient's development of a sound mental attitude during diagnosis; a public health approach to leprosy management that permits the person being treated to remain at home; treatment of leprosy cases at general medical facilities rather than special facilities; accurate and carefully thought-out programs of public health education; and health education of the patient and his family aimed at prevention and treatment of the adverse psychological effects of his condition.—Authors' Summary

Other Mycobacterial Diseases and Related Entities

Megirian, R., Stephenson, J., Lorenzen, J. and Saba, T. Temporal alterations of the phagocytic activity of the reticuloendothelial system following bacillus Calmette-Guerin (BCG) administration. J. Reticuloendothel. Soc. **16** (1974) Supplement 53a.

The role of the macrophage system and BCG in tumor defense is presently under intensive investigation. In the present study the temporal effects of BCG on the reticuloendothelial (RE) system were studied following the single intraperitoneal injection of viable BCG organisms ($2\text{-}6 \times 10^6$ or $6\text{-}25 \times 10^6$) in a range often employed to alter experimental tumor growth. Male Holtzman rats (200-250 gm) were utilized in all experiments. RE function was assessed by the use of the gelatinized (I^{131} labeled) RE test lipid emulsion and clearance kinetics as well as hepatic, splenic, and pulmonary colloid localization were determined between two hours and 28 days after BCG inoculation. Initially, there was a significant ($p < .02$) depression of the RES at two hours which was 45%-50% below controls with either dose of BCG. The control clearance halftime was $9.73 \pm .65$ minutes. Thereafter, there was a rapid elevation in RE activity which was significantly ($p < .05$) above controls (30%-35%) by day one before gradually returning to pre-injection levels. The enhanced vascular colloid clearance activity was primarily a reflection of hepatic hyperphagocytosis which was often associated with a concomitant decrease in splenic and pulmonary colloid localization. Alteration in RE function following BCG may in part be mediated through humoral (opsonic) changes especially at the early time intervals with increases in macrophage activity occurring at later time periods. Studies are currently in progress to analyze these two parameters.—Authors' Summary

Meyers, W. M., Connor, D. H., McCullough, B., Bourland, J., Moris, R. and Proos, L. Distribution of *Mycobacterium ulcerans* infections in Zaire, including the report of new foci. Ann. Soc. Belg. Med. Trop. **54** (1974) 147-157.

Approximately 430 patients with *M. ulcerans* infection have been reported from Zaire. The first of these patients was probably diagnosed in 1942, but evidence is presented suggesting that the disease was present prior to that date. *M. ulcerans* patients have been reported from all regions of Zaire except the Kasais. New foci of the infection are reported in Bandundu and equator regions. Epidemiologic factors are discussed.—Authors' Summary

Pattyn, Stefaan R. Bacteriology and pathology of mycobacterioses other than tuberculosis and leprosy. Pneumonologie **148** (1973) 211-214.

Basic knowledge in relation with classification, nomenclature and identification is briefly presented and applied to mycobacteria other than *M. tuberculosis* and *M. leprae*. The mycobacterial species are presented in three groups: saprophytic, pathogenic and opportunist species. The histopathologic aspect of the lesions is presented.—Author's Abstract

Sato, H., Arai, H., Yokosawa, A., Motomiya, M., Konno, K. and Yano, I. A study on mycolic acids from a scotochromogenic strain of *Mycobacterium scrofulaceum*, P-6. Sci. Rep. Res. Inst. Tohoku Univ. (Med) **2** (1975) 54-59.

An α-mycolic acid was isolated from P-6, a strain of scotochromogenic species of *Mycobacterium scrofulaceum* and its chemical structure was determined. The α-mycolic acid had a main chain of 58 carbons and two cyclopropane rings. Its structure as a whole was found to be similar to the α-mycolic acid from *M. kansasii* and that from *M. phlei*.—Authors' Summary.