

CURRENT LITERATURE

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General and Historical

✓ **Brubaker, Merlin L.** Leprosy: Fifty years of progress. Bol. Ofic. Sanit. Panamer. 6 (1972) 1-14.

Many outstanding developments in leprosy research and treatment have marked the past 50 years, most of them having come in the past decade. This paper reviews these events and discusses current animal studies and immunological research that offer an exciting glimpse of future possibilities.

In 1922 leprosy control was based entirely on segregation of the victim of this disease; at that time new esters of chaulmoogra oil were being heralded with enthusiastic optimism. Since that time, thanks to the emergence of new treatment and control methods, the individual with leprosy can hope for effective treatment. If diagnosed early and properly treated, he can expect his disease to be cured or arrested and disability or disfigurement prevented.

From the public health standpoint, early diagnosis and treatment reduces the infectious reservoir and can thereby have a major impact on control of the disease. Unfortunately, adequate and effective use has not been made of these treatment methods as often as one might have hoped. As a result, leprosy continues to increase and to pose a major health hazard throughout the world.—Author's Summary

Leprologia 15 (1971).

From São Paulo, Joao de Aguiar Pupo discusses at length the control of leprosy by search within families for early cases with faint skin lesions. From the viewpoint that leprosy is communicated largely within the family and spread abroad by separation of

members to form new families, he advocates the use of this "paradigm as the true route of the endemic control system." Sporadic cases are of less moment, and both BCG vaccination and search for the disease in the initial phases are essential. Belda writes on the use of the Mitsuda reaction in identification of "indeterminate" cases which constitute about 30% of those seen in Cordoba over a thirty year period, emphasizing that, to control leprosy, it is necessary to control all types of the disease. Bragadini reviews the importance of plastic surgery in rehabilitation. Vazquez, Carranza, and Chappius describe an interesting experience in a small community (James Craik) where 60% of the population was examined for leprosy specifically, yet together with an antituberculosis campaign probably reached nearly 80% of 3,387, of whom 3,300 were urban and 770 were rural residents. Only a few new cases of leprosy were discovered, but it is possible that all the leprosy in this isolated area in Cordoba is of mid-twentieth century development. DeGreef describes the logistics of an approach to the leprosy problem in the north of Sante Fe. Three short articles follow, dealing with surgical technics for treatment of plantar ulcers, loss of nerve function, and facial deformity.—G. L. Fite

Leprosy Rev. 43 (1972).

This issue is dominated by the topic of the stigma in leprosy. The historical aspects are reviewed in an editorial which, in closing, emphasizes that devotion to the problems created by the stigma is essential to a state of civilization, because, while the burdens of leprosy are created by the disease, the stigmata are the product of society's attitudes.

Warren then shows how surgical treatments of deformities of face and hands may be most effective as remedies of stigmata, even more valuable in this regard than as direct attempts at occupational rehabilitation.

Gussow and Tracy follow with an analysis of responses of Baton Rouge, Louisiana, residents to a set of questions. They feel that the evidence is equivocal; leprosy may be stigmatized to some extent, but so are mental illness, cancer, tuberculosis, and syphilis. A categorically strong public stigmatization was not demonstrated.

Pedley presents anecdotes, in brief, from China, Nepal, India, and England, illustrating that not only the public but also the medical profession believe that bacilli are discharged from the skin of people suffering from leprosy.

Finally, Rotberg of São Paulo, a stout champion for the substitution of "Hanseniasis" for "leprosy" presents his thesis, which significantly begins with the presentation of evidence that educational campaigns have been unsuccessful in de-stigmatizing leprosy. In Brazil, he says, "leprosy" is an anti-educative and stigmatizing "label of primary force." The history of the etymology is

given forcefully, showing the Latin American problem to be misunderstood by most of the rest of the world, emphasizing regional differences in significances of nomenclature, "leprosy" having pejorative overtones in the Americas of the Gulf States and further south.—G. L. Fite (Point 8, p. 104 is fallacious.—OKS, Ed.)

Rithey, D. A. W. The story of a leprosy patient. *Cent. Afr. J. Med.* 18 (1972) 230.

This the account of a man whose disease began in about 1925, and who at age 63, enjoys a fair state of health, as related by the patient himself.—G. L. Fite

Scott, G. Leprosy over the last 25 years. *Med. J. Aust.* 2 (1972) 799-801.

This is an editorial article written with the intention of acquainting the reader with the development of leprosy treatment and research over the last 25 years. He describes two stages of the method of study in leprosy, namely: that of description and classification, and the stage of measurement and quantitation. It is an educational article aimed at the medical profession.—J. C. Hargrave

Clinical Sciences

Carayon, A., Giraudeau, P. and Languillon, J. Sélection des cas résultats de la chirurgie directe de 535 nerfs mixtes dans la lèpre. [Selection of cases and results of surgical operations on 535 mixed peripheral nerve trunks in leprosy.] *Med. Trop.* 32 (1972) 157-167. (In French, English summary)

From their considerable experience in West Africa, the authors summarize the results obtained by their policy of operating early on peripheral nerves that become painful and tender in the course of treatment for leprosy. The relief of pressure by exposure of the nerve and longitudinal incision of its sheath, by intrafascicular dissection or by transposition, is said to be followed by relief of pain and by sensori-

motor recovery in some 60% of cases. In the case of refractory neuropathic ulceration of the feet, the authors claim a 93% recovery rate.

Details are given of the results obtained by operation, according to the form of leprosy, the time elapsing between onset of nerve symptoms and surgical relief, and the condition of the nerve trunk. The authors plead for early operation in order to avoid the fibrosis and destruction of nerve fibers that follow recurrent or persistent neuritis.—S. G. Browne (*From Trop. Dis. Bull.*)

Carayon, A. and Huet, R. Chirurgie nerveuse périphérique de la névrite lépreuse. (Techniques, valeur et indications respectives des procédés.) [The surgery of

the peripheral nerves in leprous neuritis. Techniques, their value and their indications.] *Med. Trop.* 32 (1972) 23-54.

This detailed and well-illustrated paper summarizes the authors' recent experience in their attempts to mitigate the results of peripheral nerve damage in leprosy. Their operative techniques are based on the accumulated results of observations extending over many years, and which lead them to emphasize the overriding importance of structural constriction of the nerve at certain well-defined vulnerable situations.

Depending upon the moment of surgical intervention, the authors recommend incision of the constrictive roofs covering the nerves (for example, the main trunk of the ulnar in the lower arm, the deep branch of the ulnar in Guyon's canal, and the median), the excision of fibrous bands, the interior transposition of the ulnar nerve ("limited" or complete), and resection of the medial epicondyle of the humerus when this bony prominence accentuates the constriction of the nerve.

A further refinement of their operative technic, seldom failing when precisely indicated, is careful intraneural dissection of a fibrosed nerve with due respect for the preservation of its blood supply, in case of progressive damage.

The paper concludes with a critical review of the value of and indications for the various procedures recommended. The authors consider that knowledge of the pathology of constrictive nerve damage is sufficiently advanced, and the good results of their surgical work so evident that operations on the peripheral nerves in leprosy, when performed for the indications they give, have now entered into the accepted scheme of "preventive rehabilitation."—S. G. Browne (*From Trop. Dis. Bull.*)

Foster, R., Katumbi, P. and Smith, D. The solar bath. *Leprosy Rev.* 43 (1972) 148-150.

The "solar bath" consists of an enclosed box exposed through a glass roof to the sun, into which hands may be inserted to receive heat treatment. Temperatures aver-

aging 44.2°C increased to 50°C to 52°C within 25 minutes, after which treatments were terminated. No untoward effects arose.—G. L. Fite

Gye, R. S., Hargrave, J. C., Loewenthal J., McLeod, J. G., Pollard, J. D. and Booth, G. C. Use of immunosuppressive agents in human nerve grafting. *Lancet* (1972) 647-650.

Freeze-dried, irradiated human nerve allografts were inserted into large defects in peripheral nerves of four patients with traumatic lesions and four patients with leprosy, all of whom were treated postoperatively with azathioprine for periods of four to six months. There was evidence of return of sensation in seven of the eight cases, but there was no sign of small-muscle reinnervation in either group—Authors' Summary

Hargrave, J. C. Problems of leprosy reconstructive surgery in Australia. *Med. J. Aust.* 2 (1972) 843-845.

Leprosy is common in aborigines in the tropical parts of Australia, and although there is a significant amount of deformity among patients, much of it can be corrected or relieved by reconstructive surgery. In the sparsely populated areas of the north, problems may arise in establishing a surgical service to cope with deformity in leprosy, and these are discussed with reference to those already experienced in the Northern Territory.—Author's Summary

Kothare, K. B. The results of physiotherapy in leprosy patients with early paralysis. *Leprosy Rev.* 42 (1972) 263-265.

A retrospective review of patients at the Acworth Leprosy Hospital in Bombay, indicated that physiotherapy was valuable in all cases, yet most effective when regularly administered, especially from the standpoint of continued benefit even after discontinuance.—G. L. Fite

Madramany, Chover. Aportaciones al estudio histopatológico del proceso evolutivo de los infiltrados laríngeos en los enfer-

mos lepromatosos. Rev. Leprol. 8 (1972) 547-553. (In Spanish, English conclusions)

1. The rhino-pharyngo-laryngeal lesions decrease in geometrical proportion from the nasal fossas to the larynx.
2. The percentage of laryngeal specific infiltrates, specially those which are of vocal cords, are very small.
3. The infiltration of the vocal cords is practically prevented by the use of sulfones.
4. Specific glottic infiltrates may reach the dangerous point of provoking asphyxia.
5. Sulfone treatment has put an end to tracheotomy.

—(Adapted from English conclusions)

Nebout, M. Autotraitement Des Lepreux A Moundou (secteur n°3) Tchad. [Self-treatment of leprosy in the Republic of Chad.] Afrique Med. (1972).

Because of the difficulty of delivery of direct treatment to the large number of patients with leprosy in the Republic of Chad, a program of self-treatment was started nearly ten years ago. This involves advertised semi-annual visits of a medical team to many individual communities in this tropical central African country. Assistance of local chieftains and social units is accompanied by making acceptance of treatment compulsory.

On the occasion of these visits, patients are examined and this article summarizes as well as possible the results through 1969. Although self-treatment appears, perhaps, to be something of a "last resort," in effect, the author insists that it is a truly valuable method of treatment, provided that it is correctly carried out. The patient receives a supply of 180 sulfone tablets, at the same time being group-instructed in all aspects of correct usage and limitation of safety. Thus far, according to the author, it is in his opinion the only method successfully applicable with the means at the disposition of the teams, far more effective than previous efforts at more frequent but more casual visits. In a country in which 1.8% to 2.7% of the people of different sectors have leprosy, this approach gets drug treatment

to 70% to 75% of the patient population, in some sectors of which the lepromatous cases comprise 20% of the total. Progress is being favored by the development of antileprosy campaigns in surrounding central African states. The program succeeds significantly by virtue of extended education of patients by trained personnel.—G. L. Fite

Pattyn, S. R., Rollier, R., Rollier, M. R., Muynck, A., Janssens, P. G. and Verdoolaege-Van Loo, G. Correlation of laboratory and clinical data during treatment of leprosy. Ann. Soc. Belge. Med. Trop. 52 (1972) 537-548.

Dapsone sensitivity has been determined for ten strains of *Mycobacterium leprae*. Three strains isolated from clinically dapsone resistant cases were highly resistant to this drug when tested in mice. Two strains were found to be moderately resistant in the mouse model: one was from a patient previously treated with sulforthomidine, the second from a patient treated with dapsone. Five strains were fully sensitive to dapsone: two were from previously untreated and two from possibly untreated cases; the fifth strain was isolated from a lepromatous relapse, occurring eight years after treatment had been stopped and bacteriologic negatization had been obtained with dapsone and thiambutosine treatment.

Of three strains of *M. leprae* tested in the mouse against a dietary concentration of 0.00001% DDS, one strain was completely inhibited, the two others partially.

Treatment of two cases of lepromatous leprosy—a primary and a relapsing case—with long acting sulfonamides was unsatisfactory, and resulted in one case in relapse with increased dapsone resistance.

Clofazimine treatment of white patients even in doses of 300 mg per week was unacceptable due to the pigmentation. The bactericidal action of rifampicin on *M. leprae* was extremely rapid. During this study there was a very satisfactory correlation between the MI and the clinical evolution.—Authors' Summary

Ranney, D. A., Furness, M. A. and Santhakrishnan, C. K. Mis-reinnervation in leprosy neuritis affecting the facial nerve. *Leprosy Rev.* 43 (1972) 151-158.

Evidence of misdirection of fibers in severe and well-established leprosy neuritis of branches of the facial nerve is presented. In the present study blinkbursts, twitches, and voluntary contractions were abundantly seen. Fibrillation and giant polyphasic potentials were rare. Leprosy neuritis is contrasted with Bell's palsy in terms of site of involvement, and the significance of this is discussed. Misdirection as a source of reinnervation is one of several factors in influencing recovery.—Authors' Summary

Texier, L. Etude clinique et épidémiologique de 56 cas de lèpre suivis à la Clinique Dermatologique de Bordeaux depuis 1947. [A clinical and epidemiological study of 56 cases of leprosy seen in the Bordeaux Skin Clinic since 1947.] *Med. Afr. Noire.* 19 (1972) 193-196. In French.

In the 23 years from 1947 to 1969 inclusive, the author made the diagnosis of leprosy on 56 occasions in patients attending his skin clinic. All except seven had contracted the disease outside Europe; four were from Spain and three had caught leprosy in France. Among the 31 patients born in metropolitan France, 10 had been in government service, 7 in commerce, 5 in the armed services and 5 were missionaries. The 25 immigrant patients were mainly students (8), or workmen (8), or wives and children (6).

The presenting signs that brought patients for diagnosis were confined to the skin in 44, in both skin and peripheral nerves in 8, and in peripheral nerves only in 4. Thirty-three were classified as having tuberculoid leprosy, 20 as lepromatous, and 3 as indeterminate. It is noteworthy that of the 20 patients with lepromatous leprosy, 15 were from metropolitan France. The average minimum "silent" period before signs of leprosy appeared would be under two years.

All patients were admitted initially to the hospital and those with lepromatous

leprosy were kept in the hospital until the nasal mucus no longer harbored *Mycobacterium leprae* (the morphology not being indicated). Patients with tuberculoid leprosy were discharged from the hospital after stabilization of treatment was achieved and continued taking dapsone at home under medical supervision, reporting to the clinic each month. The standard treatment is dapsone, with a starting dose of 25 mg daily, increasing to a maximum maintenance dose of 200 mg daily. No untoward complications attributable to this dose of dapsone are noted.

Most patients are correctly diagnosed within two years of appearance of the first signs, but one patient had to wait twelve years before diagnosis of leprosy was entertained.

Details are given of the three patients who contracted leprosy in France. One was a boy in boarding school, two of whose classmates (both immigrants) had leprosy. Another was a woman who had looked after a civil servant known to have had lepromatous leprosy. The third instance was a hotel maid and there was no suggestion of any contact with anyone suffering from leprosy and the source of her infection remains quite unknown.—S. G. Browne (*Adapted from Trop. Dis. Bull.*)

Warren, A. G. The management of tarsal bone disintegration. *Leprosy Rev.* 43 (1972) 137-147.

Tarsal bone lesions may occur in as high a proportion as 25% of leprosy patients. Some of these lesions develop into a progressive disintegration that results in marked deformity and increasing disability. For years this was considered to be part of the specific leprosy process and to be unresponsive to routine treatment methods. Recent investigations show that these lesions will heal in response to simple treatment methods, but require a considerable length of time. This paper describes these lesions, their diagnosis and treatment, with special reference to the clinical signs and symptoms for those who do not have facilities for radiographic examination.—G. L. Fite

Wyatt, E. H. and Stevens, J. C. Dapsone induced peripheral neuropathy. *Brit. J. Derm.* 86 (1972) 521-523.

This is a report from Newcastle-upon-Tyne of peripheral neuropathy occurring during the course of dapsone therapy for what was believed, at the time, to be dermatitis herpetiformis. The patient was a woman aged 24 years who had developed a rash two days after the birth of her second child, and was treated with 200 mg of

dapsone daily. The first neurological signs developed after six weeks of treatment, and electromyographic and nerve conduction studies showed the neuropathy to be axonal in type. She recovered completely after dapsone withdrawal.

The authors quote two previously published cases, and after their patient's recovery, revised their original diagnosis and made a retrospective diagnosis of herpes gestationis.—W. H. Jopling (*From Trop. Dis. Bull.*)

Chemotherapy

Chanalet, G., Guyon, J., Beaute, J., Parc, F. and Boutier, F. Premiers résultats du traitement de la lèpre in Nouvelle-Calédonie par la rifampicine. [First results of the treatment of leprosy by rifampicin in New Caledonia.] *Med. Trop.* 32 (1972) 203-215. (English summary)

The authors gave 2-4 capsules of rifampicin (Rifadin) to 31 patients: 26 with lepromatous leprosy, 4 with tuberculoid, and 1 with borderline leprosy. For the most part, these patients had responded slowly to standard therapy, or had shown some deterioration in their clinical condition, despite treatment. No positive evidence of drug resistance was sought or obtained.

The results of the treatment with rifampicin are considered to be excellent with clinical improvement visible in weeks rather than months, reduction of the Morphological Index to zero in 23 of 26 patients within nine months, and a rapid fall in the Bacterial Index.

Clofazimine (Lamprene) was given, together with rifampicin, to six patients who had a "tendency to reaction," and thiambutosine (Ciba 1906) was given (with no recorded result) in an attempt to enhance the action of rifampicin.—S. G. Browne (*From Trop. Dis. Bull.*)

Holmes, I. R. and Hilson, G. R. F. The effect of rifampicin and dapsone on experimental *Mycobacterium leprae* infections: minimum inhibitory concentrations and bactericidal action. *J. Med. Microbiol.* 5 (1972) 251-261.

Using the mouse foot pad technic, the sensitivities of three strains of *M. leprae* to dapsone and rifampicin were determined. The minimum inhibitory serum concentrations of rifampicin appeared to be about ten times as great as those of dapsone. On the other hand, assessment of the bactericidal action showed that of rifampicin to be quite high, with complete killing of the lepra bacilli after 30 days administration of the drug in the diet at 0.01%, the equivalent of a serum concentration of 5 mg/ml. Dapsone exhibited no bactericidal action according to the method used.—G. L. Fite

Khaire, D. S. and Magar, N. G. Haemolytic effects of DDS in leprosy patients. *Indian J. Med. Res.* 60 (1972).

The data presented in this report demonstrate that anemia in leprosy cases having less G-6-PD activity was related to the increased dose of DDS up to nine months. After that when the dose was increased to 100 mg daily for six days a week and maintained at that level, the hemolysis or anemia continued to recover on its own and this tendency was maintained in subsequent months. At the end of two years, the Hb and RBC levels were almost the same as found initially without treatment.—G. L. Fite

Levy, L., Biggs, J. T., Jr., Gordon, G. R. and Peters, J. H. Disposition of the anti-leprosy drug, dapsone in the mouse. *Proc. Soc. Exp. Biol. Med.* 140 (1972) 937-943.

Dapsone (DDS) or monoacetyldapsone (MADDS) was given intraperitoneally to groups of mice and the plasma concentrations of DDS and MADDS were assayed at one hour and then at two-hourly intervals. DDS 1 mg/kg and 1.2 mg/kg had a half-life of 2.1 to 4.3 hours. MADDS was rapidly deacetylated to DDS, but DDS was acetylated to MADDS "only to a very small extent." Seven percent of DDS was bound to plasma proteins, which is similar to the situation in man. *In vitro* tests were required to reveal that 61% of MADDS was protein bound. The authors conclude that the antileprosy activity of MADDS cannot be studied in the mouse. They emphasize that the half-life of DDS in the mouse is much shorter than in man. They conclude that "the disposition of DDS in the mouse is much different from that in man." [But their studies were confined to plasma.]—C. S. Goodwin (*Adapted from Trop. Dis-Bull.*)

- ✓ Levy, L., and Moon, N. Inhibition of the multiplication of *Mycobacterium leprae* by methimazole. *Amer. Rev. Resp. Dis.* 106 (1972) 917-920.

The authors studied the effects of methimazole in mice with foot pad infections. Moderate degrees of inhibition of growth of *M. leprae* were observed when the drug was given in the diet, and the same degrees were observed if the administration was started eight weeks before or after inoculation. Because the drug also produces depression of thyroid function, a comparison was made in animals treated with radioiodine, which also depressed thyroid activity. This latter failed to inhibit bacterial growth, indicating a direct effect of the drug on the organisms.—G. L. Fite

- ✓ Levy, L., Shephard, C. C. and Fasal, P. Clofazimine therapy of lepromatous leprosy caused by dapsone-resistant *Mycobacterium leprae*. *Amer. J. Trop. Med. Hyg.* 21 (1972) 315-321.

Mycobacterium leprae recovered from skin biopsy specimens of 11 patients with lepromatous leprosy who had not responded to ordinarily adequate sulfone therapy

were tested for susceptibility to dapsone in the mouse foot pad. The organisms from five patients were found fully susceptible; two of these patients had discontinued sulfone therapy prematurely, and three had taken dapsone only irregularly or not at all. The organisms from the other six patients were resistant to dapsone—that is, they multiplied in the foot pads of mice to which dapsone had been administered in the diet. Five of the patients with dapsone-resistant organisms were treated with clofazimine (B.663) in a dose of 100 to 200 mg daily, and the infectivity of their *M. leprae* for the mouse foot pad was tested at intervals during treatment; loss of infectivity was interpreted as death of the organisms. As comparison, eight patients with dapsone-susceptible bacilli were treated with dapsone in a dosage of 50 mg daily and the death of their *M. leprae* was measured by the same procedure. Once started, the rate of bacterial killing was the same in both groups of patients. Killing of dapsone-susceptible *M. leprae* began immediately after dapsone treatment was started. Killing of dapsone-resistant organisms during B.663 therapy did not begin until 50 days after treatment was started.—Authors' Summary

- ✓ Pattyn, S. R. Comments on the chemotherapy of leprosy as influenced by present knowledge of *Mycobacterium leprae*. *Leprosy Rev.* 43 (1972) 126-136.

The chemotherapy of leprosy can now be based on firm laboratory knowledge about the responsible agent *M. leprae*, and the general principles applied in the management of tuberculosis. First-line and second-line drugs may be distinguished. At present there is no need to change the existing dosage of 600 mg of dapsone (DDS) per week for mass campaigns.

Efforts should be made to find new treatment schedules leading to increased supervision by the application of intermittent therapy. In lepromatous cases, this intermittent schedule will probably have to be preceded by a preliminary course of continued therapy. It is possible that the use of rifampicin will appreciably shorten the period of treatment.—G. L. Fite

Peters, J. H., Gordon, G. R., Ghoul, D. C., Tolentino, J. G., Walsh, G. P. and Levy, L. The disposition of the antileprotic drug dapsone (DDS) in Philippine subjects. *Amer. J. Trop. Med. Hyg.* **21** (1972) 450-457.

A genetic polymorphism for acetylation of dapsone was demonstrated in 50 Philippine subjects native to the island of Cebu; a direct correlation was found between percentage acetylation of dapsone in plasma and of sulfamethazine in urine. Repeat studies with sulfamethazine in 32 of these subjects showed that the results from plasma and urinary assays were directly related, and that plasma assays gave a better differentiation of individuals into rapid and slow phenotypes. The high percentage (72%) of rapid acetylators is consistent with the Mongoloid origin of these Philippine subjects. Percentage acetylation of sulfamethazine was inversely related to plasma levels of this drug, and directly related to levels of N⁴-acetylsulfamethazine. Percentage acetylation of dapsone was directly related to plasma monoacetyldapsone levels, but was not related in any way to dapsone levels. No evidence for the presence of dapsone conjugates in plasma was found. Half-times of disappearance of either dapsone or monoacetyldapsone were not different in the two phenotypes and ranged from 14 to 53 hours in the entire group. Repeat studies in the six subjects showing the most divergent values confirmed the initial observations. The mean half-times were substantially higher than had been observed previously in American subjects.—Authors' Summary

Shepard, C. C., Levy, L. and Fasal, P. The death rate of *Mycobacterium leprae* during treatment of lepromatous leprosy with acedapsone. (DADDS). *Amer. J. Trop. Med. Hyg.* **21** (1972) 440-445.

Patients with previously untreated lepromatous leprosy were treated by injections of acedapsone (DADDS), a repository sulfone given at 77-day intervals. The response to therapy was evaluated primarily by the results of inoculation of mice with *Mycobacterium leprae* from serially ob-

tained skin punch biopsy specimens. In three of ten patients, infectivity for mice was lost in less than 100 days; in the others the infectivity was lost more slowly, and in the slowest more than 300 days were required. The results were compared with those in 14 patients treated with dapsone (DDS) in dosages of 50 mg daily; in 12 of these, infectivity of the bacilli was not demonstrable after 100 days. Tests of the *M. leprae* isolates for DDS-sensitivity in mice showed that drug-resistance, in the usual sense, was not involved in the slower loss of infectivity. The implications of this slower response for the long-term therapeutic response to acedapsone are not yet clear.—(Adapted from authors' summary)

Shepard, C. C., Levy, L. and Fasal, P. Rapid bactericidal effect of rifampin on *Mycobacterium leprae*. *Amer. J. Trop. Med. Hyg.* **21** (1972) 446-449.

Rifampin was rapidly bactericidal for *Mycobacterium leprae*. Leprosy responds very slowly to current therapy, so there is a special need for more rapidly effective drugs. In mice rifampin exerted a bactericidal-type effect with single administration by gavage; the effect increased with dosage in the range 10 to 40 mg/kg of body weight. Five patients with lepromatous disease were treated with 600 mg rifampin daily, and the viability of the bacilli in their skin lesions was tested by inoculation of mice. Infectivity for mice had completely disappeared in the first specimen collected after the start of therapy—at seven days in four patients and fourteen days in one. In four control patients treated with dapsone, infectivity for mice was lost much more slowly and in one was still present, though decreased, 112 days after the start of treatment. The slower loss of infectivity with dapsone is in accord with our previous experience in which the same methods were used.—(Adapted from authors' summary)

Terencio de las Aguas, J. Seis años de experiencia con talidomida. *Rev. Leprol.* **8** (1972) 587-598. (In Spanish, English summary)

After six years of experience in using thalidomide for the treatment of leprosy reactions, the author discusses the results.

One hundred and sixty-five patients, 100 of which had typical reactional episodes and 65 having discreet or monosymptomatic reactions, were studied.

In the former group, 62 men and 38 women had a total of 390 reactions, 236 being in men and 154 in women.

In all cases treatment was completely successful. The effective initial dose was 300 to 400 mg per day. In patients previously treated with steroids it was necessary to begin with 500 to 600 mg a day. The time needed to reach the asymptomatic state was two or three times longer than

that needed for the untreated leprosy reaction and the subsequent period of necessary maintenance therapy was also longer.

The cutaneous lesions of the two reactional tuberculoid cases improved very slowly.

Of the 100 patients with typical reactional episodes, two who had polyneuritis did not respond to this treatment.

Tolerance to treatment was good.

Other cyclic-imides were used but results were not encouraging.

A discussion and hypothesis regarding the manner of drug action as an immunosuppressant are present.—(Adapted from English summary)

Immuno-Pathology

Bullock, W. E., Fields, J. P. and Brandriss, M. W. An evaluation of transfer factor as immunotherapy for patients with lepromatous leprosy. *New Eng. J. Med.* **287** 1053-1059.

Transfer factor or whole lymphocytes from donors with delayed hypersensitivity to antigens of *Mycobacterium leprae* were employed to reconstitute delayed hypersensitivity in nine patients with anergic leprosy. Five received a mean of 4.1×10^8 lymphocytes, and four received transfer factor from equivalent cell numbers. One to six days after transfer, six of nine patients experienced erythematous indurative changes within leprosy skin infiltrates that regressed by the twelfth day. Simultaneously, *erythema nodosum* occurred in four patients, and fever and arthralgia in three. Six of seven converted from anergy to a delayed hypersensitivity response to *M. leprae* antigens. The seventh became skin-test positive at the "local" site of injection only, and the test reverted to negative seven days later. Two of three patients showed an increase in perivascular lymphocytic infiltration in the post-transfer skin-test biopsy site. Delayed hypersensitivity reactions to *M. leprae* antigens can be produced, with lymphocytes or their extracts, in patients with anergic leprosy.—Authors' Summary

Convit, J., Avila, J. L., Goihman, M. and Pinardi, M. E. A test for the determination of competency in clearing bacilli in leprosy patients. *Bull. WHO.* **46** (1972) 821-826.

A skin test has been developed to determine the degree of competency in clearing bacilli from the tissues of patients suffering from various forms of leprosy. The test involves the intradermal infection of a suspension of killed *Mycobacterium leprae*. The response of leprosy patients to the injection of other mycobacterium antigens, one prepared from *M. lepraemurium* and another from an atypical mycobacterium from a hamster, was also investigated in order to study the isopathic phenomenon. Since lepromatous patients react negatively in tests with standard Mitsuda antigen, a concentration of 640×10^6 *M. leprae* per ml was used to produce macroscopic responses. The results of the test can be applied to determine the duration of consolidation treatment for lepromatous and indeterminate bacteriologically negative patients after regular treatment has ended. The test can also be used to indicate which Mitsuda-negative contacts should be given preventive treatment and might be used to identify a given mycobacterium as *M. leprae*.—Authors' Summary

- ✓ Chaudhury, D. S., Chaudhury, M. and Armah, K. Histoid variety of lepromatous leprosy. *Leprosy Rev.* **42** (1971) 203-207.

The authors, working in Ghana, describe 15 patients with the histoid variety of lepromatous leprosy encountered over a period of seven years. Nine were relapsed cases and the remaining six had not previously been treated. They described the clinical, bacteriological and histological characteristics of histoid lesions, and confirm the generally held view that they indicate a highly active lepromatous process.—W. H. Jopling (*From Trop. Dis. Bull.*)

- ✓ Drutz, D. J. and Cline, M. J. Incorporation of tritiated thymidine by leprosy bacilli in cultures of human lepromatous macrophages. *J. Infect. Dis.* **125** (1972) 416-419.

Mycobacterium leprae, which circulates in mononuclear phagocytes in the blood of patients with untreated lepromatous leprosy, has never been successfully cultivated in an artificial medium and can presently be studied only in animal models. A method for the evaluation of the *in vitro*, DNA-synthetic activity of *M. leprae* was devised. Monocytes from the blood of bacteremic patients with lepromatous leprosy were cultivated *in vitro* and exposed to tritiated thymidine of high specific activity. Leprosy bacilli within the developing macrophages were shown by radio-autography to incorporate tritiated thymidine. Consistent with the known 14-day generation time of *M. leprae* in animal models, relatively few leprosy bacilli were engaged in DNA synthesis at any given time. This technic provides an *in vitro* approach to the evaluation of *M. leprae* within its natural host cell, the human macrophage.—(*Adapted from authors' summary*)

- Ebert, L. Ya., Teplova, S. N. and Malafeeva, E. V. A study of the 24-hour rhythm of certain factors of nonspecific body resistance. *J. Microbiol. Epidemiol. Immunobiol.* **N-2** (1972) 88-92. (In Russian, English summary)

A study of the level of various nonspecific factors of natural body resistance (comple-

ment activity, lysozyme of blood serum and saliva, total bactericidal activity of serum, properidin and β -lysin titre, bactericidal function of the skin), at various periods of the 24 hours in experiment and in man has demonstrated that the activity of nonspecific immunity factors becomes intensified at the period of physiological activity of the organism (during daytime) and diminishes in the evening.—Authors' Summary

- ✓ Faye, I., Ruscher, H., Tsala, M. P. and Bloc, G. Lèpre et groupe sanguin à Dakar. [Leprosy and blood groups in Dakar.] *Bull. Soc. Med. Afrique Noire Lang. Franc.* **16** (1971) 551-553. (In French, English summary)

The authors present a study they undertook on a group of 107 patients with leprosy. They found no difference between the patients' blood groups they typed (O, A, B, AB, Rh factor) and those of the healthy Senegalese population.

These results tally with those of most authors and it is a generally accepted fact that there is no relation between the phenotype and the morbidity of leprosy.—(*From Trop. Dis. Bull.*)

- ✓ Finlay-Jones, R. A. and McComish, M. J. Prevalence of diabetes mellitus in Aboriginal lepers. The Derby survey. *Med. J. Aust.* **2** (1972) 135-137.

The total aboriginal population of 168 patients aged 15 years and over in the Derby Leprosarium was investigated to determine the prevalence of diabetes mellitus.

Sixteen percent of the men and 19% of the women had a glucose tolerance test result diagnostic of diabetes. The diabetic subjects were significantly older and more obese than the normal subjects.

During a three year period prior to diagnosis, diabetics were becoming more obese at a rate three times that of normal subjects.—Authors' Summary

- ✓ Furness, M. A. and Ranney, D. A. Nerve enlargement in relation to classification of leprosy. *Leprosy Rev.* **42** (1972) 208-218.

This statistical (numerical) survey of 540 patients offers much in the way of data which examine types and degrees of nerve involvement according to the several recognized types of leprosy.—G. L. Fite

Job, C. K., Nayar, A. and Narayanan, J. S. Electron microscopic study of hypopigmented lesions in leprosy. A preliminary report. *Brit. J. Derm.* 87 (1972) 200-212.

The electron microscopic appearance of the epidermis in two cases of indeterminate leprosy was studied. There was a significant decrease in the number of melanocytes and several of those present showed signs of depressed activity and atrophy. Langerhans cells were increased in number and seemed to replace the melanocytes. Further study is indicated to elucidate the pathogenesis of melanocyte inactivity and reduction in number. [See *Trop. Dis. Bull.* 67 (1970) abstr. 2827.] (*From Trop. Dis. Bull.*)

Languillon, J., Linhard, J. and Diebolt, G. Groupes sanguins: hémoglobines anormales et lèpre. [Blood groups, abnormal hemoglobins, and leprosy.] *Bull. Soc. Med. Afrique Noire* 16 (1971) 581-584. (In French, English summary)

The authors present a study concerning 480 patients with leprosy (235 lepromatous and 245 tuberculoid) from "Institut Marchoux" (Mali), compared with 238 healthy subjects free from leprosy.

They noted a greater incidence of A group (28.9%) in the lepromatous form compared with tuberculoid one (19.6%) and to healthy subjects (19.3%), and an increase of AB and B groups in tuberculoid form.

There is no relation between the form of leprosy and Rh factor and between abnormal hemoglobin and leprosy.—(*Adapted from Trop. Dis. Bull.*)

Languillon, J., Linhard, J. and Diebolt, G. Antigène Australia et lèpre. [The Australia antigen and leprosy.] *Bull. Soc. Med. Afrique Noire* 16 (1971) 585-587.

The well-known association between

Australia antigen (Au) and lepromatous leprosy was confirmed by the authors in an African population in Mali. Since there was no difference in living conditions between those patients with lepromatous leprosy and those with the tuberculoid form, the criticisms advanced by Blumberg of his own investigations are not applicable to this enquiry.

Although the series consisted of only 117 patients with lepromatous leprosy, and 77 with tuberculoid, together with 42 healthy persons, the occurrence of Au shows significant differences between the three groups, being respectively 20.5%, 1.3% and 7.14%.

The authors discuss the importance of other findings in relation to susceptibility to leprosy infection. By the lymphoblastic transformation test conducted on a representative section of these three groups, they found that 10 out of 11 persons who were Au+ had a poor or absent immunity reaction. Another interesting finding was that a higher proportion of Au+ was found in young males. [See Blumberg *et al.*, *Trop. Dis. Bull.* 64 (1967) 1330; 68, abstr. 1445.] —S. G. Browne (*From Trop. Dis. Bull.*)

Languillon, J., Linhard, J. and Diebolt, G. Déficit en Glucose-6-Phospho-Deshydrogénase et lèpre. [Glucose-6-phosphate dehydrogenase deficiency and leprosy.] *Bull. Soc. Med. Afrique Noire* 17 (1972) 132-134. (English summary)

Several authors have looked for a possible relation between G6PD deficiency and leprosy. Kher and Grover in India [*Lancet* 1 (1969) 1318], found a higher rate of patients with a deficiency (22%) among persons with leprosy than among general population (9.4%).

The authors tried to locate this deficiency in a first series of 248 leprosy patients, then in a second series of 219 leprosy patients, comparing them with 50 healthy people. No significant difference could be proved.

Hansen's disease has no relation with G6PD deficiency which is a congenital defect, and when both affections are combined in a patient, enzymatic deficiency has no effect upon the severity of leprosy and its treatment.—(*From Trop. Dis. Bull.*)

Papaevangelou, G. J., Papastravropoulos, J. and Kourea, T. Hepatitis associated antigen (HAA) in leprosy. *Leprosy Rev.* 42 (1972) 273-276.

The authors measured hepatitis associated antigens by the immunodiffusion technique in 427 patients, approximately one third of all leprosy patients in Greece, under close observation. Incidences are reported according to sex, age, duration of disease, institutional residence, bacteriological status, and treatment. Incidence of antigen was equal in lepromatous and dimorphous(?) cases (5.9% and 5.7%) but much lower in the tuberculoid (0.7%). These results compare closely with those observed in similar populations from other geographic areas, and with a frequency of 1.9% observed by the authors in healthy Greek individuals.—G. L. Fite

Pinol, J., Teréncio de las Aguas, J., Rodellas, C. Montfort, J., Telese, A. and del Hierro Ruiz, J. Estudio sobre la inmunidad retardada en enfermos de lepra, sometidos a tratamiento. *Rev. Leprol.* 8 (1972) 555-573. (In Spanish, English summary)

A review was made of papers by several authors on delayed immunity in leprosy. With the object of confirming the results of those authors, we have made a study of the delayed immunity in 323 patients classified into four groups: the first group was composed of 193 lepromatous patients; the second group 41 tuberculoid leprosy patients; and the other two groups formed one of 41 tubercular patients and the other 48 healthy persons taken as a control group. All were submitted to the following tests: 1) intradermal reaction to eight different types of bacterial and fungal antigens; 2) scarification with castor-oil, BCG and DNCB; 3) homografts; and 4) lymphoblastic transformation test.

The results of these trials make clear the similar positive intradermal reactions and scarifications in all the groups, except the low positive to lepromin and BCG in the lepromatous group. The skin grafts manifest a late start of the rejection in the lepromatous group in comparison with the other groups. The average rejection time

expressed in days is of 14.7 days for the lepromatous group, 8.5 days for the tuberculoid, 9.3 for the tubercular patients and 8 days for healthy persons.

These results indicate that the leprosy patient, once under treatment has an immunologic reactive capacity similar to that of a normal person. It may be postulated that the more persistent immunologic alterations depend on the infiltration of the paracortical areas of the lymph nodes.—(Adapted from authors' summary)

Saul, A. and Calva, D. Alteraciones renales en la lepra. A propósito del estudio de tres pacientes. *Rev. Leprol.* 8 (1972) 575-585. (In Spanish, English summary)

Three patients with chronic lepromatous leprosy and frequent attacks of lepra reaction are presented and discussed. All of them had renal involvement which was the cause of death in two.

The autopsy of one of the patients demonstrated amyloidosis in both kidneys and suprarenal glands, and in the others a chronic glomerulonephritis was present. The necessity to investigate the attack of renal apparatus in lepromatous cases even without clinical symptoms is stressed.—(Adapted from authors' summary)

Sehgal, V. N., Tyagi, S. P., Kumar, S., Gupta, M. C. and Hameed, S. Microscopic pathology of the liver in leprosy patients. *Int. J. Derm.* 11 (1972) 168-172.

Leprosy is a chronic infective disease which produces lesions not only in skin and nerves, but other organs of the body are also afflicted. The present study was carried out in 28 cases of leprosy comprised of 9 lepromatous, 4 dimorphous and 15 tuberculoid. In all cases liver biopsy was taken with Vim Silverman's needle. Serial histological sections were studied after staining with hematoxylin and eosin. Special staining for the demonstration of acid-fast lepra bacilli and amyloid deposits was also undertaken.

The histological features seen in lepromatous and dimorphous types of leprosy were quite in agreement with the observations already reported. However, the

demonstration of tuberculoid granulomas in all cases of tuberculoid leprosy, except a lone case, was striking. The tuberculoid granulomas seen in the liver were characterized by their disposition around the portal region, though a few of them were also found in other parts of the liver lobule. The morphology of the granulomas varied from a mere collection of lymphocytes to a well-formed compact granuloma comprised of lymphocytes, histiocytes, eosinophils and a few plasma cells. Proliferation of Kupffer's cells was noted in a few cases. Occasionally, the sinusoids were found to contain neutrophils, and eosinophils in some cases. Amyloid deposits were not seen in any of the three types of leprosy. The granulomas seen in the liver were in no way different from what is seen in the histological section from skin lesions, except for the nerve changes which are seen in the latter. (Adapted from authors' summary)

✓ Shwe, T. Clinical significance of autoimmune antibodies in leprosy. Trans. Roy. Soc. Trop. Med. Hyg. **66** (1972) 749-753.

Specimens of sera from 73 leprosy patients and from 20 controls were tested for rheumatoid factor, antinuclear factor, thyroglobulin antibody and for certain organ specific antibodies (gastric parietal cell, thyroid cytoplasmic, and mitochondrial antibodies). A significant proportion of the lepromatous leprosy patients showed positive reactions to rheumatoid factor, thyroglobulin, and antinuclear factor in low titre. The presence of non-organ specific autoantibodies bears no clinical significance to the disease. Organ specific autoantibodies were not common in leprosy sera.—Author's Summary

✓ Shwe, T. Serum complement (C3) in leprosy. Leprosy Rev. **42** (1972) 268-272.

Serum complement (C3) was estimated in fresh sera of 45 patients and 10 controls. The complement level was elevated in most lepromatous cases, but was depressed in four of six patients during the first two weeks of acute attacks of *erythema nodosum*, which latter was only temporary. The author suggests that complement was con-

sumed in these cases by an antigen antibody reaction often associated with proteinuria.—(Adapted from author's summary)

✓ Shwe, T. Immune complexes in glomeruli of patients with leprosy. Leprosy Rev. **42** (1972) 282-289.

Renal biopsy specimens were studied from seven leprosy patients by immunofluorescence methods. In three immunoglobulins and complement were by immunofluorescent appearances, granular in form, and localized along the walls of the glomerular vessels. Fluorescence was observed in all glomeruli examined, but not in other renal structures. The strongest reactions were seen in sections stained with IgG. Strong fluorescence was seen in two of the specimens, weak fluorescence in the third. None was seen in the other four.—G. L. Fite

✓ Shwe, T. and Petty, R. E. Activation of complement (C3) in patients with leprosy. Leprosy Rev. **42** (1972) 277-281.

Serum complement was measured in sera of 45 patients and 10 control individuals. The complement levels in lepromatous patients were usually elevated, but in four of six patients during periods of acute *erythema nodosum*, with or without proteinuria, the levels were depressed. To the author this suggests that complement was depleted during these episodes, partly by utilization in antigen-antibody reactions, and partly from loss in urinary protein excretion. (Adapted from authors' summary)

Shwe, T. and Zuckerman, A. J. Australia antigen and antibody in British patients with leprosy. J. Clin. Path. **25** (1972) 401-402.

The authors base their findings on the examination of 75 sera obtained from patients resident in England and suffering from leprosy. [No data are given concerning origins or countries of previous residence. All had contracted leprosy outside the British isles.]

Australia antigen was found in only two patients with lepromatous leprosy, and one with borderline leprosy. Antibody to Australia antigen was found in one patient with lepromatous leprosy.

The authors suggest that depression of cellular immunity is the likeliest explanation for the association of Australia antigen with lepromatous leprosy, and point out that the antigen is not found with increased frequency in lepromatous leprosy in those areas where it is uncommon in the general population.—S. G. Browne (*From Trop. Dis. Bull.*)

Sirisinha, S., Charupatana, C. and Ramasoota, T. Serum immunoglobulins in leprosy patients with different spectra of clinical manifestations. *Proc. Soc. Exp. Biol. Med.* 140 (1972) 1062-1068.

The sera from both lepromatous and tuberculoid leprosy patients contained significantly more IgG, IgA, IgM and IgD than sera of normal adults (Thailand). Although the IgG component was the greatest in net increase, the increase in IgA was more striking relatively, having been found to be almost double the value in normal controls. Complications such as *erythema nodosum* or amyloidosis appeared factorial to IgA levels in some cases. An agglutination test for leprosy similar to the rapid plasma reagin (card) test for syphilis did not appear to be sufficiently sensitive because of too high a percentage of negative reactions in lepromatous cases.—G. L. Fite.

Thomas, M. and Job, C. K. Serum atypical pseudocholinesterase and genetic factors in leprosy. *Brit. Med. J.* (Aug. 12, 1972) 390-391.

The search for objectively demonstrable and genetically determined criteria for susceptibility to lepromatous leprosy is carried one step further by this paper.

By using as a genetic marker the presence or absence of the atypical form of pseudocholinesterase in the serum of 390 leprosy patients and 343 healthy people, the authors were able to show that a significant number of patients with lepromatous leprosy had this abnormal form of the en-

zyme in comparison with healthy people or patients with tuberculoid leprosy.—S. G. Browne (*From Trop. Dis. Bull.*)

Turk, J. L. and Bryceson, A. D. M. Immunological phenomena in leprosy and related diseases. *Adv. Immunol.* 13 (1971) 209-266.

Failure of host resistance frequently results from a defect in cell-mediated immunity (CMI). However, hypersensitivity reactions resulting in tissue damage can occur as readily from CMI as from the deposition of immune complexes involving humoral antibody. Such an interaction between immune procedures and a given microorganism can display a wide spectrum of pathological processes, which in turn leads to markedly different clinical manifestations.

Such a spectrum is particularly well-demonstrated by the recent elaboration of the varied clinical patterns in leprosy. Postulations from time to time related these differences to variations in the host's resistance, yet experimental and clinical evidence has been available only during the last few years. With elucidation of the immunological basis for the disease spectrum in leprosy, a parallel has been sought and found in other infectious diseases. These include especially certain protozoal diseases such as leishmaniasis and others caused by yeasts and fungi such as candidiasis and the systemic mycoses. This review is, therefore, concerned with immunological concepts in leprosy leading to a discussion of analogous states now recognized in other infectious diseases.—Authors' Introduction (*From Trop. Dis. Bull.*)

Zuravleva, G. F. Histochemical investigation of the activity of oxidoreductases in the skin lesions of lepromatous leprosy patients. *Bull. WHO.* 46 (1972) 813-819.

This paper reports an investigation of the activity of three basic groups of oxidoreductases in lepromatous leprosy: specific dehydrogenases, flavoprotein enzymes, and cytochrome oxidase. The activity of the enzymes was studied before treatment, at

various stages of treatment during exacerbations, and in the stage of regression. The data obtained are of importance for evaluating metabolic process in the cells of the specific infiltrates and the dermal con-

nective tissue in leprosy, for determining the nature and intensity of the inflammatory process, and for control purposes in cases of regression.—Author's Summary

Microbiology

Kwapinski, J. B. G., de Almeida, J. O. and Kwapinski, E. H. Immunological determination of *Mycobacterium leprae* by means of cytoplasmic antigens. Bull. WHO 46 (1972) 509-513.

Cytoplasm preparations, as prepared by the authors' methods, of *M. leprae* from human sources cross-reacted well with pertinent antisera from several patients from whom they were obtained. Additionally, cross-reactions with *M. lepraemurium* sera and those of other mycobacteria showed significant immunological relationships. Avian bacilli, *M. gallinarum*, and a few other mycobacteria also showed cross-reactions. The authors postulate that *M. leprae* and its closest relative *M. lepraemurium* are derived genetically from an Actinomyces-like organism, and that this progenitor through associated relationships with birds acquired immunological properties of the avium-type mycobacteria.—G. L. Fite

Nakamura, M. Effect of procedures for making bacillary suspensions on elongation of *M. lepraemurium in vitro*. La Lepro 41 (1972) 33-38.

Factors involved in the procedures for making bacillary suspensions affecting the elongation of *M. lepraemurium in vitro*, were studied and the following results were obtained.

1. The most significant elongations of the bacilli were observed when the bacillary suspensions were made by a mild procedure in which a leproma was cut with scissors and suspended in 0.1% bovine albumin V (Armour) saline by pipetting, or was gently ground and homogenized in a mortar for one or five minutes.

2. Slight elongation took place in the cases of experiment in which were used

partially purified bacilli or bacilli obtained from a homogenate which was ground for 15 minutes in a mortar.

3. There was a remarkable difference between two kinds of medium used for observing elongation phenomena; in the original Kirchner medium elongation occurred at pH 6 and in the enriched Kirchner medium at pH 7.

The data mentioned above should contribute toward experiments for cultivation and use in animal experiments of *M. lepraemurium*.—(Adapted from author's summary)

Nakamura, M. Effects of the depth of medium and CO₂ gas on elongation of *M. lepraemurium in vitro*. La Lepro 41 (1972) 39-41.

Effects of the depth of medium and CO₂ gas on elongation of *M. lepraemurium in vitro* were studied and the results obtained were as follows: elongation of the bacilli was not stimulated under the culture conditions in CO₂ gas as well as air atmosphere; the most significant elongation was observed when the bacilli were cultivated in 9 ml of the enriched Kirchner medium pH 7, per tube, covered with a rubber stopper which had been used previously.—(Adapted from author's summary)

Olitzki, A. L., Levy, L. and Sheskin, J. Bacterial counts of *Mycobacterium leprae* on media enriched by substances of mycobacterial origin. Israel J. Med. Sci. 7 (1971) 1171-1177.

"Mycobacterial strain no. 2" [Trop. Dis. Bull. 63 (1966) 765] was cultivated on Dubos medium, the growth washed off and suspended in ethanol and then extracted for one to three days at room temperature,

or 37°C or 60°C. After the extraction the bacteria were spun down by centrifugation and then disintegrated and the supernatants and sediments separated. "This process was repeated until no intact bacteria were visible. . . . The bacterial growth in other bottles [unspecified] was taken up in 5 ml saline per bottle, disintegrated by sonic vibration, centrifuged and the supernatant fluid heated at 100°C for 30 min. . . . Further cultures were directly taken up in acid ethanol." From two untreated patients with lepromatous leprosy "infectious material" was taken. The tissue was ground with glass powder and centrifuged at a low speed and "the supernatant bacterial suspension distributed into culture tubes," which contained a modified Eagle's medium or a synthetic medium. The mycobacterial extracts were added to the culture tubes, with some tubes uninoculated. The extracts alone, when incubated with the

Eagle's medium, "remained sterile." After periods of three or seven or ten months at 30°C and 37°C the cultures were sampled and bacterial counts performed. After three months, the tubes at 30°C without mycobacterial extract contained 6.2×10^6 bacteria/ml while in the tubes with extract added the count varied from 9 to 38×10^6 bacteria/ml. The numbers of bacteria found in tubes incubated at 37°C were less, ranging from 4 to 28×10^6 bacteria/ml. After ten months' incubation the numbers of bacteria had decreased to the same level as in the "control" tubes. Three tables give full details of the numbers of bacteria in the various tubes. The authors conclude that "a sediment prepared by sonic vibration from unheated, ethanol-treated and disintegrated mycobacteria was more effective than the sediments of heated mycobacteria and soluble extracts." —C. S. Goodwin (*Adapted from Trop. Dis. Bull.*)

Experimental Infection

Boddingius, J., Rees, R. J. W. and Weddell, A. G. M. Defects in the blood-nerve barrier in mice with leprosy neuropathy. *Nature New Biol.* **237** (1972) 190-191.

Earlier studies have shown that a blood-nerve barrier exists in the sciatic nerve of healthy mice to intravenously injected proteins like serum albumin and horseradish peroxidase, and in rabbit and monkey sciatic nerves to intravenously injected trypan blue. Our results show that a blood-nerve barrier to trypan blue is also present in the sciatic nerve of the healthy mouse. A comparable barrier to ferritin, also demonstrated here, has not been shown previously, but it is known that ferritin applied around the nerve will not pass the perineurium.

Defects in the blood-nerve barrier have been shown to occur experimentally following trauma or administration of isoniazid. Our studies have gone further for they demonstrate that distinct morphological and physiological defects in the blood-nerve barrier, permitting proteins to enter the endoneurium, can occur in mice which

develop leprosy neuropathy in a manner which closely resembles the development of the disease in man. It remains to be demonstrated that leakage through endoneurial capillaries occurs to a lesser extent in less severely affected nerves in leprosy. If this is the case, the diminution in conduction velocity in early stages of leprosy, and possibly in other neuropathies also, may be due as much to a change in endoneurial environment as to destruction or damage of the axons themselves.—(Partial reprint)

Evans, M. J. and Levy, L. Ultrastructural changes in cells of the mouse foot pad infected with *Mycobacterium leprae*. *Infection & Immunity* **5** (1972) 238-247.

Ultrastructural changes in cells of the mouse foot pad are described which occurred during the log phase of multiplication, the plateau, and the stationary phase of growth of *Mycobacterium leprae*. BALB/c mice were inoculated in the right hind foot pad with 5×10^3 organisms and

sacrificed in pairs at 86 to 173 days after inoculation. Tissue samples were prepared for electron microscopy by standard techniques. During the early growth phase of *M. leprae* in the mouse foot pad, few organisms can be detected. Those present are in macrophages and are bound by a single membrane. The cytoplasm of the macrophage is less dense around the organism. There are few lysosomes and the bacteria do not appear to be degenerating. At the peak of the growth phase, the organisms within a macrophage are bound by either a single or double membrane. There is an increased number of vacuoles, which are also bound by a double membrane, and lysosomes. During the stationary phase, most of the macrophages have taken on a vacuolar appearance and contain lysosomes. The vacuoles are bound by a double membrane, as are most of the organisms within the macrophage. Many of these organisms appear to be degenerating. Occasionally, organisms are encountered in the sarcoplasm of striated muscle. They are usually bound by a single membrane and do not appear to be degenerating.—Authors' Summary

Kirchheimer, W. F. Animal models for research in leprosy. J. Med. Ass. Thailand 55 (1972) 605-609.

This article deals largely with the rationale of the use of the armadillo as a research animal in the study of leprosy and records

briefly the approximate results observed thus far.—G. L. Fite

Matsuo, Y. The multiplication of *Mycobacterium leprae* in mouse foot pads and the ambient temperatures. Jap. J. Microbiol. 15 (1971) 527-530.

The influence of fluctuation of the environmental temperatures on the multiplication of *Mycobacterium leprae* in mouse foot pads was investigated. After infection with 10^4 *M. leprae* into the foot pads, mice were divided into the following four groups: Group 1, mice were housed in a room maintaining the air temperature at 20 C with thermo-regulatory devices throughout the experiment; Group 2, kept at 20 C for the first 16 weeks, and at a regular animal room where the air temperatures fluctuated seasonally and diurnally for the next 15 weeks and then returned to the 20 C room; Group 3, kept at 20 C for the first 16 weeks and thereafter at the regular animal quarters; Group 4, kept at the regular animal room throughout the experiment. In the mice in Group 1, *M. leprae* increased as expected. Acid-fast bacilli also multiplied in the mice kept under fluctuation of air temperatures at the regular animal quarters but distinctly more slowly than in those kept at 20 C. Acid-fast bacilli rose in the mice transferred to the 20 C room from the regular ones, suggesting that viability of *M. leprae* is not significantly affected by ordinary fluctuation of air temperatures.—(From Trop. Dis. Bull.)

Epidemiology and Prevention

Bechelli, L. M. and Martinez Dominguez, V. Nueva informacion sobre el problema mundial de la lepra. [Further information on the leprosy problem in the world.] Bol. Ofic. Sanit. Panamer. 73 (1972) 501-515. (In Spanish, English summary). Published in English in Bull. WHO 46 (1972) 523-536.

This paper presents various recent data relating to the world leprosy situation. According to available information, 2,887,481 leprosy cases are registered in 124 coun-

tries, representing about 500,000 more than the total reported in an evaluation of these same countries in 1965. This rise would have seemed even greater if patients discharged as being definitely cured had not been eliminated from many countries' total number of reported cases.

In some regions where long-term programs are being conducted, the rate of registration of new cases appears to be stationary or declining slightly. The proportion of lepromatous cases is low in the countries of tropical Africa (around 10%),

higher in Asia (27% in Burma; 35% in Thailand), and traditionally substantial in the Americas (over 40%). A high proportion of lepromatous cases is observed in those European countries where the endemia persists (30% in Greece, 60% in Spain, and 72% in Portugal). It is estimated that 10% to 40% of the cases in Oceania are lepromatous, and 26% to 74% tuberculoid.

Within each continent, the percentage variation of each form of leprosy would probably have been smaller if there had been uniform classification criteria and uniform efficiency in locating cases. It is noteworthy that the proportion of indeterminate cases is very similar in Paraguay (20%), Colombia (21%), Brazil (24%), and Venezuela (24%).

Statistics from various countries indicate that the number of inactive cases (544,719) and discharged patients (368,789) have increased considerably.

Only 41 countries supplied information on patients with whom contact has been lost. The proportion of such cases is high, even in countries where the campaign against leprosy is apparently well-organized.

Data relating to disabilities are relatively scanty and generally limited to second and third degree disability, first degree cases (anesthesia) being excluded. The percentages of different types of disability vary considerably from country to country, even on a particular continent, probably because most cases are diagnosed earlier in some places than in others. It may be assumed that in the countries with a high disability ratio most recorded cases are in advanced stages.

It is difficult to analyze the data relating to the number of inpatients and to the number of institutions or units caring for them; available information is very incomplete and concerns only a few countries. According to a rough estimate, the proportion of hospitalized patients is lower in Africa and Asia than in the Americas and Europe.

It is inferred from the data gathered that maximum prevalence does not exceed 50 per 1,000 in the countries exhibiting the highest endemicity when the level is meas-

ured for a municipality, county, or larger territorial unit. However, in lesser areas, such as small towns, the prevalence rate may be as high as 82 per 1,000.

Considering the number of cases estimated in 1965, the five-year forecast of new cases made at that time, and the number of deaths and discharged cases since then, it seems likely that most countries were maintaining approximately the same level of endemicity in 1970 as was found in 1965.—(*Adapted from English summary*)

✓ **Berkeley, J. S.** Leprosy in Bhutan: A pilot survey. *Leprosy Rev.* 42 (1972) 188-196.

Bhutan, south of Tibet, and well north of the Brahmaputra River, is a rather mountainous and thinly populated country, the geographical features of which make delivery of patient care difficult, especially with the scarcity of trained doctors and their helpers. In two districts, the rates of 13.4 per 1,000 and 24.8 per 1,000 respectively are enough to indicate the seriousness of the problem. Compared with leprosy in India, disability rates and lepromatous to tuberculoid ratios appeared higher, while ages of onset were at slightly later average age.—G. L. Fite

✓ **Boughton, C. R.** Leprosy and Australia. *Med. J. Aust.* 2 (1972) 837-842.

As leprosy is endemic in certain areas of Australia, and as some immigrants to Australia from leprosy-endemic areas are entering this country and subsequently developing the disease, medical practitioners need to be aware of relevant clinical and diagnostic aspects of the condition, and to consider it, when appropriate, in differential diagnosis.

The following brief account deals with these aspects.—*Author's Summary*

Bradley, D. J. Regulation of parasite populations. A general theory of the epidemiology and control of parasitic infections. *Trans. Roy. Soc. Trop. Med. Hyg.* 66 (1972) 697-708.

The mechanisms by which parasite populations are regulated may be grouped into three types: regulation by the transmission

process (type I), by the host population by such means as host mortality or sterile immunity (type II), and by the host individuals (type III), often by premunition and similar forms of incomplete acquired resistance. The last two types are density-dependent feedback processes. The concept of endemicity implies that these two types are operating. The spatial arrangement of hosts and transmission patterns particularly affects type II regulation as does the distribution of parasites among hosts. Highly endemic infections may sometimes have their focal variation in intensity of transmission obscured, and may show relatively separate yet contiguous transmission foci. The most suitable control measures will depend on the type of parasite population regulation, and epidemiological study should include an experimental measure of the stability of the infection. Types II and III of regulation here roughly correspond to the density-dependent regulation of animal ecologists, though type I may fall sometimes into this category.—Author's Summary

McDougall, C. Leprosy in Peru. *Leprosy Rev.* 42 (1972) 197-202.

Leprosy occurs largely in the northeast and central parts of Peru, while the coastal areas are almost free of the disease, and the tropical humid department of Loreto is the principal focus of infection. Two of three leprosaria remain. One, the San Pablo Leprosarium, near the Brazilian border, is officially closed, but the 400 patients still in residence are cared for by the Ministry of Health staff and mission sisters. Although the care of these people is not adequately resolved, a still vital part of the problem is the need for trained workers.—G. L. Fite

Merklen, F. P., Cottenot, F. and Pennec, J. Progression et variations d'origine des lèpres d'importation à Paris au pavillon de Malte. [The changing pattern of countries of origin of cases of leprosy seen in Paris in the Malta Ward (Hôpital Saint-Louis).] *Bull. Acad. Nat. Med.* 156 (1972) 63-68.

In 1952, the majority of 48 patients under treatment in Paris for leprosy were West Indians (21) or Europeans who had contracted the disease abroad (17). From 1952 to 1960, the respective figures of newly diagnosed patients were 38 and 36 out of a total of 99.

In 1961 the pattern began to change. The number of new cases diagnosed annually doubled (from 11 to 21), the increase being largely attributable to the influx of students and workers from the African continent. Since 1964, the number of new cases shows a progressive increase, the highest being 51 in 1971. Both the Caribbean and Africa still account for one-third of the new cases diagnosed, but Portugal now enters the picture, with six cases diagnosed (in 1971) among workers from that country.

Attention is drawn to the observation that, whereas most of the patients from French-speaking African countries have tuberculoid leprosy, a not inconsiderable proportion of those from the Caribbean have the lepromatous type.

These figures concern only patients diagnosed at the specially designated Malta annex in the Saint-Louis Hospital in Paris. There are no accurate figures for the rest of France: the authors associate this fact with the legislative insistence on notification by name, and subsequent public health enquiry and disinfection of premises. They quote with approval the procedure current in Britain and express the hope that France may follow the British pattern.—S. G. Browne (*From Trop. Dis. Bull.*)

Other Mycobacterial Diseases & Related Entities

Convit, J., Pinardi, M. E. and Rondon, A. J. Diffuse cutaneous leishmaniasis: A disease due to an immunological defect of the host. *Trans. Roy. Soc. Trop. Med. Hyg.* 66 (1972) 603-611.

Diffuse cutaneous leishmaniasis, with its characteristic diffusion of lesions, great abundance of parasites, anergy to skin test with the specific antigen and resistance to treatment, has been described as a disease

produced by a special strain of *Leishmania*, *L. pifanoi*.

Our concept is that this form of leishmaniasis is due, not to a different type of parasite, but to an immunological defect of the human host, which makes him respond with these special clinical and parasitological manifestations. The basis for our belief is: (1) epidemiologically, the disease appears as isolated cases in endemic areas; (2) accidental inoculation of a laboratory technician with a strain taken from an animal with diffuse cutaneous leishmaniasis lesions produced a nodule with the clinical, pathological and parasitological characteristic of an American cutaneous lesion, with a strongly positive leishmanin reaction; (3) the coexistence, in a leishmaniasis focus, of two patients living in the same house, one of whom had diffuse cutaneous leishmaniasis and the other American cutaneous leishmaniasis; (4) clinical and pathological characteristics of an experimental inoculation in human volunteers with material obtained from diffuse cutaneous leishmaniasis lesions. This produced, in all the hosts, a typical American cutaneous leishmaniasis-type of response.—Authors' Summary

Holland, M. D. Rifampicin—What dose for pulmonary tuberculosis? *S. Afr. Med. J.* **46** (1972) 604-608.

The results of a blood-level study with a single 450-mg dose of Rimactane administered to 100 patients are presented. Blood levels in excess of the minimum inhibitory concentration against *M. tuberculosis* persist, on the average, for approximately 12 hours.

Continuous medication leads paradoxically to lower levels in men and higher levels in women. Taken in conjunction with the clinical findings, 450 mg appears to represent the ideal routine daily dose in pulmonary tuberculosis.—Author's Summary

Kambara, T., Katsuya, H. and Maeda, S. Experimental study on the mechanisms of delayed hypersensitivity reaction, with special reference to emigration and function of mononuclear cells. *Acta. Path. Jap.* **22** (1972) 465-476.

Delayed hypersensitivity reaction is characterized by infiltration of mononuclear cells (macrophages and lymphocytes). The mechanisms of emigration and function of mononuclear cells in local skin lesions were studied in experimental tuberculosis. A chemotactic activity for mononuclear cells was found in the extract of tuberculin skin sites, and protease activity at pH 3, 6, and 9 was found in the extract and partially purified using ammonium sulfate and column chromatography. Relationship between chemotactic activity and protease activities was discussed. Similar protease activities were found in the extract of sensitized lymph node cells, and protease active at pH 6 and 9 were increased when homogenate of sensitized lymph node cells was incubated with PPD for three hours at 37°C. It appears that PPD may be of concern in the release of protease from sensitized lymphocytes and involved in delayed hypersensitivity reactions. The role of mononuclear cells in tuberculosis skin lesions was studied relative to their bactericidal activity for tubercle bacilli. Some macrophages in skin lesions were produced locally by cell division. Macrophages in granulation tissue around necrotic foci were specifically matured and strongly active for β -galactosidase, and the number of acid-fast bacilli in macrophages and the intensity of staining for β -galactosidase were reversely correlated. This was also confirmed in irradiated rabbits with 400 rads of whole body radiation. These findings suggest that high levels of lysosomal enzymes are involved in destruction of bacilli.—(Adapted from authors' summary)