

CURRENT LITERATURE

This department carries selected abstracts of articles published in current medical journals, dealing with leprosy and other mycobacterial diseases. Abstracts are supplied by members of the Editorial Board and Contributing Editors, or are reproduced, with permission, from other abstracting journals.

General and Historical

PAPUA NEW GUINEA MEDICAL JOURNAL, 16, No. 2 (1973).

This is a centenary commemorative issue to coincide with the 100th anniversary of the discovery of the leprosy bacillus by Hansen. A greater part of it has therefore been devoted to a series of articles on leprosy by Papua New Guinea leprologists and others from Southeast Asia, Australia, the United Kingdom and the United States. The emphasis is on a summary of current knowledge about leprosy in the various disciplines: medicine, surgery, immunology and a number of others, rather than on the research of any of the individual authors. The contributors and their articles are listed below.

Editorial—A Leprosy Centenary.

Leading Article—Clezy, J. K. A., Hansen and his Bacillus.

Original Papers and Reviews—Browne, S. G., Leprosy Today—A Reappraisal; Russell, D. A., Leprosy in Papua New Guinea; Waters, M. F. R., Modern Advances in the Immunology of Leprosy; Shepard, C. C., Experimental Chemotherapy of *Mycobacterium leprae* Infection; Ridley, D. S., A Skin Biopsy Study of Lepromatous Leprosy; Rees, R. J. W., Experimental Leprosy and its Clinical Implications; Clements, N. and Ramsay, W. A., Leprosy Control: Five Years in the Southern Highlands, A Progress Report; McKeown, R., The Leprosy Mission in Papua New Guinea; Kerr, J. M., Social Factors Operating Against Effective Leprosy Control in the Highlands of Papua New Guinea; Kennedy, Myra, Institutional Care of Special Communicable Disease in Papua New Guinea. "A View from Gemo."

Current Medical Practice—Russell, D. A., The Treatment of Leprosy in Papua New Guinea; Clezy, J. K. A., Footdrop in Leprosy; Hamilton, Julie, Physiotherapy in the Management of Leprosy; Clezy, J. K. A., The Management of Plantar Ulcers.

Case Reports—Ramsay, W. A., Reactivation of Leprosy.

Bibliography of References on Leprosy in Papua New Guinea.

This issue of the PAPUA NEW GUINEA MEDICAL JOURNAL should be a valuable addition to the library of any practicing leprologist. A group of distinguished authors has successfully produced a succinct and up-to-date précis at a most opportune time, coinciding not only with the discovery of the bacillus but also with the Tenth International Leprosy Congress, 1973. The quality of each contribution is of a high standard, and the bibliography on leprosy in Papua New Guinea a welcome innovation that could well be copied by other countries.—J. C. Hargrave

Rotberg, Abrahao. The exorbitant and prohibitive price of sulfones: social degradation and economic collapse. Hanseniasis: Abs. News 3 (1972) 299-302.

Sulfones and other drugs are the only present means to control endemic Hanseniasis, but their action is too slow to be personally encouraging to the patient, who does not see the quick results he expects and forces him to long years of treatment, while his condition remains apparently unchanged—if not aggravated by intolerance, allergy, reactions and new lesions. To cooperate under so adverse conditions, and to go on

treating regularly he should at least receive the drugs free of charge. Instead, the health agencies charge him with the most prohibitive possible price: they force him to be registered as "leprosy patient" (in practice "leper"), which condemns him to economic collapse and social rejection for life.

With rare exceptions, no patient will cooperate and consciously pay such an exorbitant price. No educational attempt will succeed against the millenary and overwhelming antieducation with "leprosy," and while the official synonyms for "leprosy" continue—as in all Brazilian and many foreign standard dictionaries—"vice," "filth," "hideousness," "loathsomeness," etc.

It is necessary to start lowering the price of treatment, to attract the patient, and to facilitate education and integration, with a noninfamous terminology. The possible indifference of more fortunate countries, non-endemic and/or not tainted by the Graccolatin pejorative, should not deter a solution by the Latin American countries, so overwhelmingly burdened by the complex "LPE" (leprosy-pejorative and endemic).—Author's Summary

✓ **Stringer, T. A.** Leprosy and "a disease called leprosy." *Lepr. Rev.* **44** (1973) 70-74.

Despite arguments put forward in this journal (**43** [1972] 69-105), there is a case for retaining the substance of current terminology related to leprosy, particularly because of its value to fund-raising. In any event, the public will not cooperate in the adoption of new terminology, but find a vital role for the linguistic associations of leprosy. Acknowledging the nature of general knowledge about the "disease called leprosy," we have opportunities of educating the public in both endemic and nonendemic countries about the true nature of the disease. Identifying the nature of semantic confusion involved in the Christian motivation towards

leprosy sufferers, we may be able to influence the public reaction to leprosy by correcting the old terminology in religious texts, and by referring to the defined disease as "actual leprosy."—Author's Summary

TROPICAL DOCTOR, 3 (1973).

Contains a symposium on leprosy consisting of six articles dealing with practical aspects of leprosy management. "Recognition of Leprosy," by S. G. Browne briefly reviews the classical, yet most variable, features of the clinical picture. Writing further on community management, Browne would exclude from specific treatment only the burnt-out case, emphasizing broadly the many standard approaches to leprosy control, including BCG vaccination of children and tuberculin-negative adults. "Education of the public, the medical profession, and of the community leaders, is all part of the doctor's task."

W. H. Jopling notes long-active sulfonamides, 0.5 gm twice a week, to be effective but unlikely to displace dapsone from its pre-eminent position because dapsone is so inexpensive. The repository intramuscular diacetyl sulfone, DADDS, seems to need the results of further observation before this compound can be recommended for general use. He discusses clofazimine as especially useful in reactive cases. D. J. Harman emphasizes the value of study of Bacterial Indices in smears and the Morphological Index as a measure of bacteriological viability. D. P. Choyce's "Blindness in Leprosy," is followed by E. P. Fritsch's presentation of surgical management of the complications of leprosy.

The 27 pages compress an astonishing amount of pertinent information into a useful text, which, not pretending to be detailed or all inclusive, may still be useful.—G. L. Fite

Clinical Sciences

✓ **Barton, R. P. E.** The management of leprous rhinitis. *Lepr. Rev.* **44** (1973) 186-191.

The management of leprous rhinitis is discussed. In patients with early changes in the nose it is thought that local treatment is

of psychological rather than of any great physical value. There is, however, a group of patients with early lepromatous leprosy whose nasal involvement is severe and out of all proportion to their general clinical state. It is possible that intensive local treatment of the nose in these patients may help to

prevent deformity. Patients with advanced nasal changes giving rise to atrophic rhinitis and external deformities gain much physical, as well as psychological relief from regular local care of the nose and this is described below.—Author's Abstract

Dorman, Jane E. K. Ocular manifestations of leprosy. *Lepr. Rev.* **44** (1973) 216-219.

In this survey of leprosy patients in Nepal, half the patients examined were found to have some ocular abnormality associated with leprosy. However, many did not have marked ocular signs, and might have been passed as normal in the absence of a more detailed examination. This paper is intended to demonstrate the importance of regular examination of the eyes of every leprosy patient.—Author's Abstract

Frontera Vaca, J. L., Carranza Goycochea, C. E., Temporini, A., Rosati, A. A. and Rugieri, F. Prevencion quirurgica de las ulceras plantares. [Surgical prevention of plantar ulcers.] *Leprolgia* **18** (1973) 32-33. (In Spanish)

Results in 21 leprosy cases subjected to debridement of the posterior tibial artery, vein and nerve are reported.

Emphasis is placed on the importance of early surgery as a means of preventing subsequent ulcerous and mutilating lesions.

Angiographs of the affected area, corresponding to the posterior tibial nerve, were performed in ten leprosy patients, confirming the authors' choice of treatment for this condition.—(Adapted from English summary)

Imkamp, F. M. J. H. The treatment of corticosteroid-dependent lepromatous patients in persistent *erythema nodosum leprosum* with clofazimine. *Lepr. Rev.* **44** (1973) 127-130.

The trial of Lamprene (clofazimine) begun in 1966 and which has been the subject of a preliminary communication (Imkamp, 1968) has now terminated. All the patients had been suffering from lepromatous leprosy (LL) and all had been dependent on corticosteroids, given for persistent *erythema nodosum leprosum*. On five years of follow-up the trial has been most successful in that all patients (18 cases) have been weaned from corticosteroids and all have returned

to normal life. All except one have resumed dapsone treatment. The length of time the individual patients had to take clofazimine varied within wide limits. One male patient continued for 5 to 6 months, and the dosage had to be varied according to his clinical state.—O.K.S.

McDougall, A. C. and Rees, R. J. W. Ulcerating lepromatous leprosy in a patient with dapsone-resistant *Mycobacterium leprae*. *Lepr. Rev.* **44** (1973) 59-64.

While under treatment with dapsone for lepromatous leprosy, a 50 year old male Greek Cypriot presented with multiple widespread lesions of a bizarre type, many of them freely ulcerating.

Clinically and histologically, peripheral nerves were little affected but biopsy samples of skin and ulcers contained enormous numbers of leprosy bacilli. Mouse foot pad inoculation of the bacilli from skin homogenates showed resistance to all three levels of dapsone tested, namely 0.01, 0.001 and 0.0001% in the diet of mice.

From two of the larger ulcers bacilliferous discharges were collected in occlusive dressings over a 24 hour period. Attention is drawn to the very large number of bacilli counted in this discharge. Excluding the nose, the shedding of dapsone-resistant bacilli into the environment from body ulcers in this case could have been in excess of 20 million daily.—Authors' Summary

Merklen, F. P. and Cottenot, F. Le traitement de la lèpre. [Treatment of leprosy.] *Sem. Hop. Paris* **49** (1973) 267-268.

Since the introduction of sulfones and other drugs, the evolution of the disease and the future of the patient have been wholly transformed. Although the number of cases of leprosy known in the world continues to increase, partly from the tracking down of obscure cases, and partly because of population increases in underdeveloped countries in which hygienic conditions favor the spread of the disease; nevertheless, leprosy has progressively disappeared from Europe, where it persists only in Mediterranean foci, and along the Iberian Peninsula.—Authors' Summary

Nebout, M. L'Autotraitement de la lèpre Afrique. [Self-treatment of leprosy in Africa.] *Afrique Med.* **12** (1973) 13-16.

The author emphasizes that success of such self-treatment programs depends more than anything else upon the personnel in charge, their qualifications, their interests and sensitivities to the needs of the campaign, and selection according to professional merits. Additionally, other factors are important, such as interest of administrative authorities, collaboration with established health offices, and education of the patient himself. Temporary free hospitalization is suggested for the bacillus positive cases, and search for fresh cases among contacts. Cost of this type of program is approximately 35% lower than that of traditional circuits. Countries included in this review were Camerouns, Congo, Gabon, and Chad.—(From author's summary)

Pearson, J. M. H. and Helmy, H. S. The effect of stopping dapsone treatment for two months and then restarting it in full dosage in patients with moderately severe *erythema nodosum leprosum*. *Lepr. Rev.* **44** (1973) 75-82.

The authors, working at Sungei Buloh, Malaysia, set out to question the strongly held general opinion that ENL reaction in lepromatous leprosy becomes more severe when treatment with dapsone in high dosage is employed, and less severe when this treatment is discontinued, and for their study they made observations on nine patients suffering from persistent and moderately severe reaction. Although there was a fall in the severity of ENL reaction during the 8-10 weeks when treatment with dapsone was replaced by a placebo, this was not dramatic, nor was there an acute exacerbation of reaction when dapsone was restarted in a dosage of 100 mg daily.—W. H. Jopling (From *Trop. Dis. Bull.*)

Pedley, J. C. The study of smears of the noseblow in all types of leprosy. *J. Nepal Med. Assoc.* **11** (1973) 1-5.

In approximately 80% of untreated active lepromatous cases, nasal smears are positive for *M. leprae*. Organisms can be present in enormous numbers in advanced cases.

The Morphological Index is usually higher than that of bacilli from skin smears, especially when bacilli are plentiful. Bacilli commonly disappear from nasal smears after six months of standard DDS treatment, and

are never found in borderline cases, even with facial lesions in a state of exacerbation.—G. L. Fite

Ranney, D. A. and Furness, M. A. Results of temporalis transfer on fifty-four cases of lagophthalmos. *Lepr. India* **45** (1973) 62-67.

Fifty-six patients had 74 temporalis transfers over a five year period at the Schieffelin Leprosy Research Sanatorium, Karigiri. Forty-two patients (54 operations) were examined at follow-up. Exhaustive clinical examinations and electrical stimulation studies were performed in all cases and in half of them this was supplemented by electromyographic studies. Each eye was graded technically and assessed for symptomatic improvement and signs of eye disease. While the overall results were not as good as have been reported for nonleprosy cases there was an interesting correlation between extensive lid anesthesia and operative failure. The upper lid fibers of the orbicularis oculi were found to be affected at least as often as the lower lid in those cases severe enough to require temporalis transfer. The possibility of reinnervation of the lower lid has been implied. Preoperative tarsorrhaphy was found to be associated with adhesions and with much poorer results on subsequent temporalis transfers.—Authors' Summary

Said, Galal Z., Zohdy, A. and El-Akkad, I. N. External and internal neurolysis of ulnar and median nerves in leprosy neuritis. *Lepr. Rev.* **44** (1973) 36-43.

Out of 36 cases of leprosy neuritis treated by external and internal neurolysis of the ulnar and/or median nerve (17 bilateral), 91.2% of the followed-up cases were free from pain, 58.3% showed complete or partial clinical improvement of motor function, and 46.2% showed sensory improvement after the operation.

Electromyography of eight cases of ulnar neuritis (six bilateral) before and at varying intervals after the operation was performed. It showed marked or limited improvement of muscle action potentials in 64.3% of decompressed nerves.

Best results were obtained when the nerve trunk at operation showed hyperemia of its sheath, edema, and swelling. The worst results were noted in cases in which the

nerve was thin, ischaemic, and fibrosed. Nerve abscess was encountered five times; three times in the ulnar and twice in the median nerve.—Authors' Summary

Sehgal, V. N., Ghosh, S. K., Manerker, A. N. and Dukle, P. D. Angiogram—a means to assess trophic changes in leprosy. *Lepr. India* **45** (1973) 17-19.

A case of polyneuritic leprosy with nerve abscess and trophic changes is described. Brachial angiogram before and after therapy with dapsone and Duvadilan was done in order to assess clinical and radiological improvement. The results of this study are greatly convincing and warrant the use of angiographic studies in cases of leprosy with trophic changes.—Authors' Summary

Shah, A. P., Shah, S. S. and Doshi, H. V. Accentuation of ichthyosis vulgaris due to associated leprosy. *Postgrad. Med. J.* **49** (1973) 282-283.

A case of ichthyosis vulgaris associated with tuberculoid leprosy is reported. Ichthyotic scales were markedly accentuated within the anesthetic patches of leprosy.

The probable mechanism of the accentuation of ichthyosis by leprosy is discussed.—(From *Trop. Dis. Bull.*)

Srinivasan, H. The extensor diversion graft operation for correction of intrinsic minus fingers in leprosy. *J. Bone Joint Surg. (Am.)* **55B** (1973) 58-65.

1. A new procedure, called "the extensor diversion graft operation," has been devised for correcting the deformity and reducing the disability of the intrinsic minus fingers so commonly seen in leprosy.

2. The procedure consists of the insertion of a free tendon graft which spans the metacarpophalangeal joint along its volar aspect and is attached at both ends to the extensor mechanism, to the extensor tendon proximally and to the lateral band distally.

3. The procedure reduces extensor dominance at the metacarpophalangeal joint and improves the balance of forces, allowing the assumption of a straight posture by use of the extrinsic muscles.

4. The assessment of function of 97 fingers on an average of eight months after operation has shown that in addition to correction of deformity, this procedure in the

majority of cases also restores partial independence of movement at the metacarpophalangeal and proximal interphalangeal joints, to such an extent that the finger can reach and hold a functionally useful position.

5. One advantage of the procedure is that it obviates the need for reeducation of muscles.—Author's Summary

Steklovsky, V. K. On sexual function disorders in patients with leprosy. *Vest. Derm. Venerol.* **3** (1973) 33-35. (In Russian)

Among 92 patients with lepromatous type of leprosy under observation impotence was established in 63 patients. Sexual weakness develops at four to five years of the disease and subsequently progresses. Reduction of sexual desire was observed in 56 patients, reduction of sexual desire and blunting of the sensation of orgasm in 7 patients, and in 18 patients this was combined with insufficient erection and premature ejaculation. On the basis of the data of examination of androgenous, excretory and incretory functions and histological examination of biopsied tissue of the testes, the organic nature of sexual disorders and symptoms of neuroendocrine insufficiency in patients with leprosy may be stated. The pathogenesis of sexual disorders in such patients presents a complex combination of a number of factors, primarily inhibition of the hormonal function of the testes, affection of diencephalo-hypophyseal area and personal reaction to the situation associated with the specific conditions of leprosy.—Author's Abstract

Vibrans, U. and Hesse-Novak, I. *Lepra lepromatosa: ein Fall mit ungewöhnliche morphologische Veränderungen.* [Lepromatous leprosy: a case with unusual morphological changes.] *Hautarzt* **24** (1973) 386-392.

The patient presented was a 27-year-old woman from Yugoslavia, who had apparently had leprosy for 12 years, the source of the infection being obscure. The skin lesions consisted of innumerable lepromatous, infiltrative lesions individually small, affecting almost all skin surfaces and the mucosa of the hard palate. Most were old, long-standing vacuolated-cell lesions, within which clumps or clusters of bacillus-rich cells appeared, although the vacuolated cells con-

tained much smaller numbers. The infiltrates were fairly deep in the dermis, but, in addition, superficial vesicular changes were common, related to the lepromatous foci, suggesting dermatitis herpetiformis. Still further, dermatofibromatous lesions or areas also appeared, reminding one of the changes in histoid lesions, with numerous bacilli. Many histologic evidences of vasculitis were observed, including lesions of *erythema nodosum*, and the reactive state of the process was obvious. Eighteen excellent illustrations accompany.—G. L. Fite

✓ **Warren, A. G. and Taylor, P. M.** The effects of cocktail anesthesia on blood pressure. *Lepr. Rev.* **44** (1973) 83-89.

In leprosy centers the absence of a second trained doctor to give anesthetics often limits the surgeon wishing to operate. "Cocktail anesthesia," as described here has proved to be useful in this and other situations, and is often preferred to general anesthesia by those accustomed to administering it. Many different drugs have been used for this purpose. In this paper a method that has been found effective in Chinese patients is described, with details of observations that indicate its safety and adaptability. After a described appropriate schedule of premedication, the "cocktail" used consisted of pethidine (100 mg), chlorpromazine (50 mg) and saline (or distilled water or glucose) to 20 ml. The "cocktail" is mixed 20 to 30 minutes before use and, in patients weighing about 50 kg, 8 to 10 ml is administered intravenously.—(Amended authors' summary)

✓ **Warren, A. Grace.** Radiographic examina-

tion of the feet. *Lepr. Rev.* **44** (1973) 131-138.

The standardization of radiographic techniques assists in the demonstration of bony abnormalities. This paper describes simple devices which provide easy methods of obtaining comparable radiographs of the feet that will aid in the early diagnosis of lesions and in the planning of effective treatment.—Author's Summary

✓ **Warren, A. Grace.** The bacterial load in the nasal mucosa of Chinese patients. *Lepr. Rev.* **44** (1973) 183-185.

In Chinese patients it is not possible to rely on the presence or absence of *M. leprae* in the nasal mucosa to confirm or deny a diagnosis of leprosy. Although the load of bacteria in the nose may be high in some untreated patients, during treatment it falls more rapidly there than elsewhere in the body.—Author's Abstract

✓ **Warren, A. Grace and Ledger, Joyce. A** study of the incidence and outcome of foot weakness in leprosy. *Lepr. Rev.* **44** (1973) 203-212.

The permanency of paralysis in the foot of a patient with borderline leprosy should not be considered inevitable. Spontaneous functional recovery does occur in a proportion of patients, and the percentage of those recovering can be increased by correct medication and other therapeutic means. Careful observation of 300 patients under treatment has shown that thiambutosine as the initial drug does reduce the incidence of acute paralysis and also appears to encourage recovery of function.—Authors' Abstract

Chemotherapy

✓ **Matajack, M. L., Bissett, M. L., Schifferle, D. and Wood, R. M.** Evaluation of a selective medium for mycobacteria. *Am. J. Clin. Pathol.* **59**. (1973) 391-397.

The Lowenstein-Jensen medium for cultivation of mycobacteria has served as a reference standard for many years, in spite of the problems of variation and difficulties in preparation and preservation. The authors studied two commercial bases for media,

which utilize nalidixic acid, lincomycin and cyclohexamide, decreasing contamination and increasing recovery of many mycobacterial species from clinical specimens. Results favored usage of a nonselective and a selective medium in a complementary manner.—G. L. Fite

✓ **Roos, G. A. W.** Is the macrophage the site of the immunosuppressive action of rifampicin. *Tubercle* **54** (1973) 291-295.

As a preliminary investigation of the site of action of rifampicin as an immunosuppressant, its effect on lymphocyte transformation, leukocyte migration, contact sensitization, and antibody production has been studied. The results confirm the existence of an immunosuppressive effect but indicate that it does not act directly on B or T lymphocytes but more probably on antigen handling by macrophages.—Author's Summary

Russell, S. L. and Russell, D. W. Isoniazid acetylase phenotyping of Amharas in Ethiopia. *Afr. J. Med. Sci.* **4** (1973) No. 1-5.

Eighty-seven male Amharas in Gondar, Ethiopia, 19 Tigreans, and 14 Gallas were given 100 mg isoniazid at 07.00, 12.00 and 17.00 hours. On the next day at 07.00 hours urine was collected and "acetylisoniazid: isoniazid ratios" (A:I) were determined. The "antimode" was at A:I 40 in the Gallas, A:I 10 in the Tigreans, and A:I 20 in the Amharas. Rapid acetylation was found in 5 Gallas, 9 Tigreans, but in only 15% to 17% of the Amharas. "The relevance of these findings to intermittent dapsone therapy of leprosy merits further study."—C. S. Goodwin (*From Trop. Dis. Bull.*)

Scott, G. L. and Rasbridge, M. R. The *in vitro* action of dapsone and its derivatives on normal and G6PD-deficient red cells. *Br. J. Haematol.* **24** (1973) 307-317.

In an attempt to define the mechanism of dapsone-induced hemolysis the *in vitro* action of dapsone (4,4', diaminodiphenylsul-

phone) and some of its derivatives on normal and G6PD-deficient red cells has been investigated. Dapsone, its N' acetyl- and hydroxy-derivatives have no measurable effect on metabolism, hemoglobin or the membrane in either normal or G6PD-deficient red cells. And 4-hydroxylamino-4' aminodiphenylsulphone (HADS) and 4-hydroxylamino-4' acetaminodiphenylsulphone (HMDS) have oxidant effects on red cells. Both of these compounds readily form methemoglobin but in normal red cells higher levels of methemoglobin are achieved with HMDS than with HADS. With both compounds less methemoglobin is formed in glucose-deprived or in G6PD-deficient red cells. In normal red cells hexose monophosphate pathway (HMP) activity is increased, HADS being a more potent stimulus than HMDS. It is suggested that methemoglobin formation is dependent upon the recycling of these compounds via the HMP.

Normal red cells incubated with the two hydroxylamine compounds did not show any change in reduced glutathione (GSH), globin or the membrane, apart from increased sensitivity to peroxide lysis. G6PD-deficient red cells, on the other hand, did lose GSH rapidly and underwent increased autohemolysis. The mechanism of these effects is discussed.

Some, but not all, of the *in vivo* effects of dapsone can be reproduced by the hydroxylamine derivatives *in vitro*. It is concluded that either some other derivatives are involved or that the effect of long exposure to these oxidant compounds *in vivo* is different.—Authors' Summary

Immuno-Pathology

Bernard, J. C. and Vazquez, C. A. Adenitis gigantocelular lepromatosa. [Lepromatous giant cell adenitis.] *Leprolgia* **18** (1973) 45-53. (In Spanish)

Different groups of visceral lymph nodes in 50 autopsies of leprosy patients of the Sommer Sanatorium of Argentina, were studied.

Macroscopic and microscopic changes were studied, and special reference was made to the lepromatous giant cells adenitis.

The authors observed these lesions in the patients which showed the most frequent

leprosy reactions and skin allergic failures, and considered these forms of adenitis as a new and different pathological entity in the lepromatous adenitis form.—(*Adapted from English summary*)

Manja, K. S., Bedi, B. M. S., Kasturi, G., Kirchheimer, W. F. and Balasubrahmanyan, M. Demonstration of *Mycobacterium leprae* and its viability in the peripheral blood of leprosy patients. *Lepr. Rev.* **43** (1972) 181-187.

Acid-fast bacilli (AFB) were found in the

blood of 38 untreated patients with lepromatous leprosy, and in 5 of 20 patients with borderline leprosy (whether the latter included treated patients is not mentioned), in 45% of 31 lepromatous patients treated for six months, and in 25% of 82 treated for more than six months. The AFB from 15 patients were inoculated into the foot pads of mice and "so far multiplication of AFB in the foot pads has been obtained in 7" (presumably with growth curves similar to that of *M. leprae*). The AFB were seen in macrophages and polymorphs, and most bacilli were evenly stained. The authors estimate there were up to 5×10^5 AFB per ml in the blood of some patients, and they conclude that blood-sucking arthropods could aspirate viable *M. leprae* during a blood meal.—C. S. Goodwin (*From Trop. Dis. Bull.*)

Miranda, Ruy N. Fagocitose e destruição de *Mycobacterium leprae* por leucocitos polimorfonucleares. [Phagocytosis and destruction of *Mycobacterium leprae* by polymorphonuclear leukocytes.] *Rev. Leprol.* 9 (1973) 33-45. (In Portuguese and English) 1969

1. The clinical observation and experimenting done in the present work illustrates that in the course of acute manifestations of lepromatous leprosy, *M. leprae* abandons the Virchow cell and is phagocytized by the polymorphonuclears.

2. After being phagocytized by the polymorphonuclears, the Hansen bacteria may be destroyed in these cells.

3. There is, therefore, a stable cycle of the Hansen bacteria in the human organism which develops in the histiocytic elements while the disease develops chronically; and another cycle, this one unstable, of the same bacteria outside the histiocytic elements which the bacteria abandon during the state of becoming acute lepromatous leprosy, which results in their destruction by the polymorphonuclear leukocytes.

4. The result of the development of this second cycle may cause great destruction of bacteria, followed by a marked improvement in the disease.

5. The acute state of lepromatous leprosy and the above-mentioned phenomenon may be obtained by giving iodate of potassium in an average dose of 1.5 gm per day.—(*Adapted from author's conclusions*)

Mohanty, H. C. and Murti, R. S. Serum transaminase in leprosy. *Lepr. India* 45 (1973) 163-166.

1. The serum transaminases, SGOT and SGPT have been investigated in 64 leprosy patients and in 15 normal controls.

2. A rise of these enzymes was noticed in 14 (58.3%) lepromatous, 3 (25%) tuberculoid, 2 (25%) primary polyneuritic, 1 (8.3%) maculoanesthetic, and 5 (62.5%) lepra reaction cases.

3. The rise in the levels of these serum enzymes is indicative of both hepatic and muscular damage produced by the leprosy bacilli.—Authors' Summary

Mukherjee, A. and Ghosh, S. A concomitant study of the liver function and coagulation factors in leprosy. *Lepr. India* 45 (1973) 19-27.

Liver function, using a battery of tests, was assessed and hemostatic status ascertained simultaneously in 52 leprosy patients, of which 20 were in the active stage of lepra reaction, and 7 were stable tuberculoid cases. Six healthy individuals were used as controls and the cases of acute lepra reaction were followed till the subsidence of reaction when all the tests were repeated.

The cases with lepra reaction showed moderate degree of hepatic dysfunction as revealed by marked changes in the protein profile, turbidity tests, serum alkaline phosphatase and urinary urobilinogen excretion. These changes were only less marked after subsidence of reaction.

A few of the lepromatous cases also showed some interference with liver function while the nonlepromatous cases showed but minimum changes only in regard to protein profile, turbidity values and serum alkaline phosphatase.

Deficit in coagulation factors (serum and/or plasma) was mostly found in cases of active lepra reaction and the hemostatic defects were found to be completely reversed after the subsidence of reaction.

It was inferred that manifest hepatic dysfunction possibly gave rise to the observed deficiencies in coagulation factors in leprosy.

—(*Adapted from authors' summary*)

Nebout, M. A propos d'un cas de lèpre tuberculoïde nodulaire chez un adulte africain porteur de scarifications rituelles.

[Report of a case of nodular tuberculoid leprosy localized, in an adult African male, on ritual scarifications.] *Med. Trop.* 33 (1973) 523-528. (In French, English summary)

The author reports the appearance of lesions of tuberculoid leprosy three years after ritual scarification of the forehead in an adolescent African male. The nodular lesions were initially confined to the lines of scarification, but subsequently extended to several areas of skin, particularly over the thorax. Histological examination of the nodules showed typical tuberculoid changes, and the response to standard treatment was good.

No conclusions can be drawn regarding the introduction of leprosy bacilli, but the occurrence of the visible lesion was obviously connected with trauma to the skin.—S. G. Browne (*From Trop. Dis. Bull.*)

Pinto, M. R. M., Arseculeratne, S. N. and Weliana, L. V. The differential tuberculin test in leprosy. *Lepr. Rev.* 44 (1973) 13-21.

The differential tuberculin test has been carried out on a group of leprosy patients using 5 different PPD antigens (S, Y, G, B and F) obtained from *Mycobacterium tuberculosis* and other mycobacterial species. The patterns of sensitization seen in the leprosy patients were found to be different from those of the general population and of tuberculous patients, but no marked differences in the patterns were seen between the patients with lepromatous and those with tuberculoid leprosy.

In both groups of patients, there was with all the antigens except PPD-F, a clear-cut group of nonreactors and a group of reactors. Both tuberculoid and lepromatous leprosy patients had, in contrast to tuberculous patients, a significant proportion of nonreactors. It was also found that the patterns of sensitization to antigens obtained from mycobacteria other than *M. leprae* were not different in the two immunological extremes of leprosy disease.—Authors' Summary

Ridley, D. S. A skin biopsy study of lepromatous leprosy in relapse. *Papua N. Guinea Med. J.* 16 (1973) 100-104.

Out of 51 biopsies of skin lesions from patients in relapse 16 showed very early

lesions. The distribution of solid-staining bacilli gave evidence that in most cases the relapse had originated in a dermal nerve of an old lesion; and that in patients in whom new lesions had developed the dissemination had taken place via the blood stream from another skin site. Thirty-five other biopsies showed relapse lesions in an advanced stage. Half of them showed certain histoid features which were attributed to the fact that the lesions were unusually acute, with a high cell turnover in the granuloma.

Skin biopsy is a sensitive method of detecting relapse provided the site is well chosen.—Author's Summary

Ridley, D. S. The pathogenesis of the early skin lesion in leprosy. *J. Pathol.* 111 (1973) 191-206.

A study of early skin lesions of leprosy patients, many of them with a history known to be of less than one year's duration, showed that by the use of serial sections the great majority could be classified on an immunological basis in much the same way as the lesions of established leprosy. It was also shown that they could be classified according to their predominant distribution as neural, vascular or subepidermal.

Lesions of the vascular type are multiple and blood disseminated, though they appear to originate in nerves. The subepidermal type are solitary lesions and there is evidence that in many cases transmission is through the epidermis. Intraepidermal lesions are described. The neural type constitute a mixed group.

Interpretation of the evidence concerning the route of transmission is complicated by two factors: 1) In the epidermis and subepidermal zone there is a "split ratio" of tissue reactivity to numbers of bacilli, which is either very high or very low. And 2) there is evidence of a two-way spread of leprosy bacilli, from epidermis to deep nerves and vice versa.

Bacilli were found at six sites in the skin. The optimum site for multiplication depended on the level of immunity, and to a less extent for a given level of immunity it depended on how well the infection was established. Bacilli were protected against elimination in patients with relatively high immunity not only in nerve but also in the subepidermal zone and to some extent in

muscle. But bacilli in the two latter situations may in fact be present in neural elements.—Author's Summary

Saha, K., Mittal, M. M. and Ray, S. N. Consequences of smallpox vaccination in leprosy patients. *Infect. Immun.* 8 (1973) 301-308.

This study illustrates the consequences of smallpox revaccination in 45 lepromatous, 28 tuberculoid, and 47 normal individuals. Results obtained with intradermal inoculations indicated that the patients with leprosy were associated with a relative anergy against the vaccinia virus, the anergy being minimal in the tuberculoid leprosy but marked in the cases with lepromatous leprosy. Major vaccinal reactions were observed more often in patients with lepromatous leprosy than in the controls or patients with tuberculoid leprosy. Furthermore in a patient with lepromatous leprosy, vaccinia necrosum also developed. The smallpox vaccination with live virus also appeared as a provocative factor for the precipitation of lepra reaction in the lepromatous leprosy cases. After three weeks of vaccination, the frequency of the specific humoral antibody response was the same in the tuberculoid patients and controls while it was higher in the cases with lepromatous leprosy. The pre-vaccination titer of total hemagglutination inhibition antibody was significantly higher in the lepromatous leprosy cases. However, the postvaccinal, humoral antibody response of the lepromatous patients was of the same magnitude as that observed in the normal individuals, and it was mainly due to a 2-mercaptoethanol-resistant antibody.—Authors' Abstract

Samuel, D. R., Godal, T., Myrvang, B. and Song, Y. K. Behavior of *Mycobacterium leprae* in human macrophages *in vitro*. *Infect. Immun.* 8 (1973) 446-449.

Attempts have been made to cultivate *M. leprae* in human macrophages *in vitro*. In 27 out of 55 experiments a two- to nine-fold increase (mean 2.31 ± 1.46) in acid-fast organisms were observed over a period of 1.5 to 3 months of cultivation. No such increase was observed with heat-killed bacilli (mean fold increase 0.88 ± 0.19). Macrophages were necessary for obtaining increases. No multiplication was observed on artificial

media. A close correlation between increases of acid-fast organisms and changes in viability as determined by the morphology of the bacilli (Morphologic Index) was found. It is concluded that multiplication of *M. leprae* may take place inside human macrophages *in vitro*. Multiplication appears not to be dependent on whether the macrophages are derived from lepromatous or tuberculoid patients or healthy individuals. Moreover, multiplication took place both at 33° and 37°C. The applicability of this method is at present limited by the restricted survival of human macrophages *in vitro*.—Authors' Summary

Silva, C., Lima, A. O., Andrade, L. M. C. and Mattos, O. Attempts to convert lepromatous into tuberculoid-type leprosy with blood lymphocyte extracts from sensitized donors. *Clin. Exp. Immunol.* 15 (1973) 87-92.

Two groups of lepromatous patients (L type of leprosy) were injected intramuscularly and respectively with the Lawrence's transfer factor (LTF) or a ribonucleic acid (RNA) extracted from viable blood lymphocytes of healthy donors hypersensitive to lepromin (48-72 hr and 20-30 days), tuberculin (PPD), toxoplasmin and histoplasmin. Each patient received a single dose of LTF or RNA obtained from 10^9 lymphocytes and was carefully observed for a period of four months. Histopathology of skin lesions and of lymph nodes were repeatedly performed. The results of intradermal tests with antigens were read at different times up to 120 days after the injection of LTF and RNA. Delayed cutaneous reaction to some antigens was induced in three patients injected with LTF and in two others injected with RNA. The lepromin reaction read at the end of 48-72 hr and after 20-30 days remained negative in all patients during 120 days of observation. Clinical and histopathologic signs of transformation into tuberculoid leprosy could not be observed in the eight patients tested.—Authors' Summary

Thorsby, E., Godal, T. and Myrvang, B. HL-A antigens and susceptibility to diseases. II. Leprosy. *Tissue Antigens* 3 (1973) 373-377.

Thirty-nine leprosy patients (20 tuberculoid and 19 lepromatous) have been HL-A

typed and compared to 36 nonleprosy individuals of the same ethnic group (Amharas). The most significant deviation was related to the W21 antigen, which was found only among leprosy patients (both tuberculoid and lepromatous), not in the control group. No deviation in antigen frequency was found to be specific to the lepromatous group.—Authors' Summary

World Health Organization Memoranda.

Immunological problems in leprosy research: 1 and 2. Bull. WHO 48 (1973) 345-354 and 483-494.

Part 1 reviews the present status of knowledge of the immunology of leprosy, with particular attention to developments since the publication of a similar review in 1970. The different types of lepromin reaction and

their significance in healthy contacts and in patients with tuberculoid and lepromatous leprosy are discussed. The immunological responsiveness of patients with tuberculoid and lepromatous leprosy are discussed. The immunological responsiveness of patients with leprosy is also considered, with special attention to *in vitro* methods for evaluating this response.

Part 2 of this Memoranda covers possible mechanisms of altered immune response in leprosy (including a tentative scheme to explain the possible genesis of the lepromatous lesion); genetic, nutritional, and hormonal factors; the possibility of vaccination; attempts at immunotherapy; and areas in which further research is needed. A detailed protocol for evaluating the effect of transfer factor in leprosy is included as an annex.—(From summaries)

Microbiology

Kim, J. D. and Lew, J. Antigenic studies of *Mycobacterium leprae* and *Mycobacterium lepraemurium* by immunodiffusion. Kor. Lepr. Bull. 8 (1972) 23-37.

The human leprosy nodule extract contained at least two kinds of antigens, one of which was rather specific, heat labile, and precipitated only against rabbit antileprosy nodule-extract serum and antileprosy-bacilli serum, but not contained in normal human skin extract and human serum. The other antigen reacted with the rabbit antileprosy-bacilli serum and was shared commonly with *M. lepraemurium* and other mycobacteria.

M. leprae contained one or two common antigens with other mycobacteria, and two common antigens with other mycobacteria, and two common antigens most closely related to those of *M. lepraemurium*.

The murine leprosy infected rat testicle extract contained at least three kinds of antigens, two of which were rather specific, heat labile, but not contained in either normal rat testicles or normal rat serum. The other one was a common antigen shared with other mycobacteria.

M. lepraemurium contained one or two common antigens shared with other mycobacteria, and two antigens most closely related to those of *M. leprae* and *M. avium*.

Two kinds of antibodies were detected in the sera of leprosy patients against various mycobacterial antigens, and among the various antigens tested *M. lepraemurium* was found to be particularly suitable for the serological investigations of leprosy patients.—(From Kor. Med. Abstr.)

Mohysen, A. M. and Alemayehu, W. Application of Nyka's method for the staining of mycobacteria in leprosy skin sections. Acta Pathol. Microbiol. Scand. [A] 81 (1973) 71-74.

Biopsy specimens from 20 leprosy patients have been studied. Adjacent sections were in each case both stained by the ordinary Ziehl-Nielsen method and after oxidation with periodic acid (Nyka's method). Sections from tuberculoid, indeterminate and lepromatous lesions all revealed an increased number of acid-fast bacilli after oxidation. In ten examinations of tuberculoid and indeterminate cases the increase observed was in average fourfold. It is concluded that there is a considerable higher number of bacilli present in leprosy tissue than revealed by the ordinary Ziehl-Nielsen method.—Authors' Summary

Murohashi, Toyoho and Yoshida, Konosuke. Stimulating effect of pyruvate on the

growth of *Mycobacterium leprae* in cell-free, semisynthetic, soft agar medium. Bull. WHO 48 (1973) 571-579.

A bacterial suspension prepared from a nodule from a patient with lepromatous leprosy was inoculated into the cell-free, semisynthetic, semiliquid agar medium M-Y 11d—modified from the authors' medium M-Y 1c by omitting glycerol and adding pyruvate—and incubated at 37°C. The growth of the organism was stimulated so markedly that after about 50 weeks' incubation of the primary culture, microcolonies could be seen floating in the agar layer as tiny white particles while the medium fluid assumed a yellow tinge. These macroscopic colonies were sucked up by pipette and subjected to microscopic examination. A bacterial suspension prepared from the first subculture of this strain by centrifugation elicited the same skin reactions in leprosy patients as did the standard Mitsuda's antigen. The organism in the culture was therefore identified as *M. leprae*.—Authors' Summary

Nakamura, Masahiro. Elongation of *Mycobacterium lepraemurium* in vitro by α -ketoglutaric acid. II. Factors affecting elongation of *M. lepraemurium* in the NK medium. Lepro 42 (1973) 1-4. (In Japanese, English summary)

In a previous paper it was demonstrated that *M. lepraemurium* extraordinarily elongated in the NK medium which was composed of the Kirchner medium containing bovine serum and α -ketoglutaric acid. This paper is to report the factors affecting this elongation phenomenon of *M. lepraemurium* in the NK medium under several considerable conditions. The results obtained are as follows.

1. Optimal temperature of cultivation for extraordinary elongation was a somewhat lower temperature, 30°C rather than 37°C.

2. Significant elongation could be observed when the bacilli were cultivated in the medium in which 8 ml of the NK medium was contained in a test tube, 10.5 cm in length and 1.3 cm in diameter.

3. No elongation took place under an obligate anaerobic condition.

4. The same phenomenon was also observed when partially purified *M. lepraemurium* was used.

5. Such a characteristic elongation phe-

nomenon as seen in the NK medium was also demonstrated when oxaloacetate was used instead of α -ketoglutaric acid.

6. It was presumed that isoniazide and malonate had a destructive effect on the bacilli after elongation in the NK medium, while penicillin and streptomycin had no such effect.

7. No morphological change in the bacterial cells was illustrated in the case of *M. leprae*, even though the bacilli were cultivated under the same condition as used for *M. lepraemurium*.—Author's Summary

Nakamura, Masahiro. Elongation of *Mycobacterium lepraemurium* in vitro by α -ketoglutaric acid. III. Relationship between elongation phenomenon and the increase of the bacilli and the morphological findings of elongated bacilli. Lepro 42 (1973) 5-11. (In Japanese, English summary)

In this paper it is noted that the number of bacilli of *M. lepraemurium* increased approximately four times compared with that of the initial inoculum when the bacilli were cultivated in the NK medium at 30°C for one month. There was no increase of the bacilli when the bacilli were cultivated in the EK medium which was used as a control. However, no significant relationship between the increase of the bacilli and that of protein contents of bacterial cells was recognized. It was illustrated by electron micrographs that the elongated *M. lepraemurium* in the NK medium had band structures which were found to be observed in acid-fast bacilli and in addition no destructive findings of the cells should be noticed. However, it was observed that there was a slight decrease in the number of phosphate granules in the cell of elongated bacilli in comparison with that cultivated in the EK medium.—Author's Summary

Nakamura, Masahiro. Multiplication of *Mycobacterium lepraemurium* in cell-free liquid medium. Proc. Jap. Acad. 49 (1973) 42-46.

Additional evidence was given to show that *Mycobacterium lepraemurium* which has been thought to be an obligate intracellular parasite so far, could multiply in the enriched Kirchner medium containing α -ketoglutaric acid, cytochrome C, hemin, and

l-cysteine HCl or l-cysteine (NC-5 medium). When the bacilli were cultivated in this cell-free culture medium at 30°C for 60 days, the number of bacilli quantitatively increased approximately 25 to 100 times compared with the inoculum.—Author's Summary

Nakamura, Masahiro. Multiplication of *Mycobacterium lepraemurium* in cell-free liquid medium. 1. Establishment of the NC medium. *Lepro* 42 (1973) 47-51. (In Japanese, English summary)

Evidence is presented indicating the growth of *M. lepraemurium* in cell-free liquid medium of enriched Kirchner (EK) containing α -ketoglutaric acid and cytochrome C (NC). When the bacilli (Hawaiian strain) were smeared on a silicone coated slide, and cultivated in NC medium, the bacilli gradually elongated and multiplied. After 60 days of cultivation at 30°C, the growth of the bacilli was recognized macroscopically as a turbid mass. On the other hand, no growth was recognized in the EK medium, which is the most suitable for the growth of usual acid-fast bacilli, and used the control for the NC medium.

Therefore, it could be concluded that the growth of acid-fast bacilli observed in the NC medium was unequivocally the growth of *M. lepraemurium*.—(Adapted from author's English summary)

Nakamura, Masahiro. Multiplication of *Mycobacterium lepraemurium* in cell-free liquid medium. 2. The growth curve of *M. lepraemurium* in the NC medium and the pathogenicity of the bacilli grown in the medium. *Lepro* 42 (1973) 52-55. (In Japanese, English summary)

In a previous paper, microscopic as well as macroscopic multiplication patterns of *M. lepraemurium* in cell-free liquid medium composed of enriched Kirchner medium enriched with α -ketoglutaric acid and cytochrome C (NC medium) were described. In order to determine whether the remarkable growth patterns observed in the NC medium are due to quantitative multiplication or not, bacillary counting was periodically performed.

The results obtained indicated that the number of bacilli in the NC medium lineally increased after ten days latency (lag phase),

and reached the maximum on the 50th day after cultivation. The increase rate and a possible generation time, calculated from the growth curve obtained were approximately eight times compared with the initial inoculum and 12.3 days, respectively.

In addition, it was noted the pathogenicity of the bacilli cultivated for 60 days in the NC medium to mice was retained, whereas no pathogenicity of the bacilli incubated in the EK medium was shown.—(Adapted from author's English summary)

Nakamura, Masahiro. Multiplication of *Mycobacterium lepraemurium* in cell-free liquid medium. 3. Factors affecting the growth of *M. lepraemurium* in the NC medium. *Lepro* 42 (1973) 155-160. (In Japanese, English summary)

Factors affecting the growth of *M. lepraemurium* in the NC medium were studied and the following results were obtained.

1. Possible essential substance involved in the NC medium for the growth of *M. lepraemurium* is α -ketoglutaric acid which is replaceable by oxaloacetate.

2. It is noted that the optimal temperature for cultivation is 30°C rather than 37°C, and the culture is carried out under a slight anaerobic condition.

3. It is noted that an optimal pH of the basal medium is somewhat alkaline and the serum to be used is goat serum. On the contrary, acidic basal medium, horse or rat serum are inadequate for the growth of the bacilli.

4. It is demonstrated that the degree of the growth of the bacilli also depended upon the inoculum size on the meshcement coated slide; heavy inoculum resulted in a bad growth pattern, and the growth of the bacilli was stimulated by transfer of the smear to newly prepared medium at an appropriate interval.—(Adapted from English summary)

Nakamura, Masahiro. Multiplication of *Mycobacterium lepraemurium* in cell-free liquid medium. 4. Establishment of the NC-3 medium. *Lepro* 42 (1973) 161-164. (In Japanese, English summary)

It is reported that a liquid medium which is referred to as NC-3 is more satisfactory for the growth of *M. lepraemurium* than that of NC medium which was reported previously. After inoculating the bacilli smeared

on a silicone glass slide in the NC-3 medium, the bacilli gradually elongated and multiplied. These findings are reproducible. The NC-3 medium is composed of enriched Kirchner medium added with α -ketoglutaric acid, cytochrome C and hemin.—(Adapted from English summary)

Olitzki, A. L. Growth inhibiting and promoting effects of amino acids and glucose of five strains of *M. leprae* and their growth on an inhibitor-free medium. Boll. Ist. Sieroter. Milan. **52** (1973) 281-286.

Five strains of *M. leprae* multiplied on a medium poor in nutrients, but supplemented either by a sonic extract (SE) or a 70% ethanol extract (E 70) prepared from *M. smegmatis*, or by both extracts. The growth of three strains (A, B, and C) was significantly inhibited by all amino acids applied in these experiments and by glucose. The growth of one out of five strains (D) was not inhibited, but rather stimulated by 0.03% L-glutamine, 0.0075% L-tyrosine, 1.0% glucose and an amino acid mixture, while 0.06% glutamine exerted a slight inhibition. A fifth strain (E) was inhibited by L-tyrosine, 1.0% glucose, 0.06% glutamine and the amino acid mixture, while 0.03% glutamine exerted a stimulating effect. All strains multiplied on a medium containing SE, E 70, the noninhibiting cysteine and glutamic acid and seven vitamins.

These results show that strains of *M. leprae* are different in their reactivity to certain nutrients and that different concentrations of the same nutrients, e.g., L-glutamine, L-tyrosine or glucose may exert a growth promoting or inhibiting effect.—Author's Summary

Olitzki, A. L., Levy, L. and Sheskin, J. Studies on *Mycobacterium leprae* in media enriched by mycobacterial substances. Boll. Ist. Sieroter. Milan. **51** (1972) 268-277.

M. leprae multiplied on media poor in nutrients, present in conventional bacteriological media, when mycobacterial substances were present. Patient strains grew *in vitro* after lag times of five to seven months; on subcultures the lag times became shortened to one to two months. Some of the added mycobacterial substances contained phospholipids and triglycerides,

others contained nitrogen-containing active substances which were not proteins; they remained active after boiling and even autoclaving. Mycobactin S contributed to the growth effect, though alone it did not provoke continued growth.

Growth substances, present in conventional media, mainly several amino acids, acted as growth inhibitors. Glutamic acid promoted growth in all growth periods and cysteine in the beginning. Growth was also inhibited by glucose, while a mixture of vitamins did not inhibit the growth of *M. leprae*.

The question, why *M. leprae* does not grow on the hitherto known bacteriological media should therefore be investigated in two directions: 1) elimination of growth inhibitors, and 2) isolation and identification of growth factors present in other microorganisms.—Authors' Summary

Prabhakaran, K. Dopa metabolism by *Mycobacterium leprae*: its implications in culture of the bacillus and chemotherapy of leprosy. Lepr. Rev. **44** (1973) 112-119.

An integrated review is made of the investigations on a new type of tyrosinase (*o*-diphenoloxidase) detected in *M. leprae*. The enzyme was different in several respects from tyrosinase obtained from plant or mammalian sources. Inhibitors of *o*-diphenoloxidase suppressed multiplication of leprosy bacteria in mouse foot pads, indicating that the enzyme might have a key metabolic role in the growth of *M. leprae*. Suspensions of the organisms exposed *in vitro* to one of these inhibitors (diethyldithiocarbamate) completely lost their viability. The host tissues preferentially invaded by the bacilli (i.e., the skin and the peripheral nerves) are of ectodermal origin where metabolism of DOPA or its derivatives is important. Our results show that DOPA and other phenolic substrates are rapidly utilized *in vitro* by *M. leprae*. These observations suggest that, besides other factors, small amounts of DOPA continually generated by living cells may be essential for the survival and proliferation of the leprosy bacteria.—Author's Summary

Stanford, J. L. An immunodiffusion analysis of *Mycobacterium lepraemurium* Marchoux and Sorel. J. Med. Microbiol. **6** (1973) 435-439.

Six strains of *Mycobacterium lepraemu-*

rium Marchoux and Sorel have been subjected to immunodiffusion analysis. They were found to be identical with each other and to possess 12 demonstrable antigenic constituents. Five of these were antigens common to all mycobacteria, two were shared only with slow-growing mycobacterial species, three were amongst those antigens hitherto considered specific to *M. avium* and two were specific to *M. lepraemurium* alone. Thus it was concluded that *M. lepraemurium* is a member of the slow-growing group of mycobacteria with an exceptionally close serological relationship to *M. avium*.—Author's Summary

Yoshii, Z. and Nakamura, M. Scanning electron microscopy of *Mycobacterium lepraemurium* cultivated on the glass slide. *Proc. Jap. Acad.* **49** (1973) 47-50.

Mycobacterium lepraemurium (Hawaiian strain) cultivated on a glass slide in the NC-5 medium devised by Nakamura was observed with the aid of scanning electron microscopy. After eight weeks' incubation, remarkable growth and multiplication of bacilli were observed. Therefore, the primary cultivation of *M. lepraemurium* was considered to be successful.—(Adapted from authors' summary)

Experimental Infections

Storrs, Eleanor E. Leprosy in the nine-banded armadillo. *Z. Tropenmed. Parasitol.* **24** (1973) 53-65.

It is concluded that leprosy is a much more severe disease in the armadillo than in man since leprotic pneumonitis and esophageal and meningeal involvement are found, which to our knowledge have not been reported in human leprosy. Also, a leproma taken from an armadillo contained 10^{10} bacilli per gram compared to 10^7 to 10^8 per gram usually found in skin biopsies taken from advanced human cases. The time required for the disease to develop is ten months or less compared to an estimated three to five years in man. Preliminary results suggest that the incidence of susceptibility in the armadillo may be as high as 40% compared to an estimated 5% in man. A total of 243 g of lepromas containing 10^{10} bacilli/gram was obtained from two armadillos with advanced lepromatoid leprosy. Armadillos have now developed leprosy after inoculation with bacilli obtained from man, the mouse foot pad, and another armadillo. The magnification of leprosy observed in the armadillo suggests that this animal model will be useful as a source of leprosy bacilli, for studies

on disease transmission and for the evaluation of experimental drugs.—Author's Summary

Waksman, Byron H. The early immune response to *Mycobacterium lepraemurium* in inbred rats. *Clin. Immunol. Immunopathol.* **2** (1973) 82-97.

Killed *Mycobacterium lepraemurium* suspended in mineral oil, when injected into mice and rats produced early delayed sensitization of similar intensity to that obtained with tubercle bacilli under the same conditions, as well as a strong antibody response. The cytoplasmic extract of *M. lepraemurium* used for testing cross-reacted both in skin tests and serologically with Old Tuberculin. Active or passive introduction of humoral antibody prior to challenge inhibited delayed sensitization, and passive antibody reduced the active antibody response. The two organisms were equally effective adjuvants in delayed sensitization to ovalbumin and bovine γ -globulin. Rat strains varied slightly in their responses to *M. lepraemurium*. However, C57BL/6 mice gave strong delayed sensitization and CBA mice virtually none.—Author's Summary

Epidemiology and Prevention

Browne, Stanley G. The epidemiology of leprosy. *Z. Tropenmed. Parasitol.* **24** (1973) 1-8.

Leprosy lags behind tuberculosis in many respects. It poses many unanswered epidemiological questions. The study of mycobac-

terioses in the West should shed light on problems of culture on artificial media, transmission and immunology.

The distribution of leprosy in the world has many interesting features: it is found in virtually every country, the great bulk of sufferers living within the medico-geographical tropics; the extremely wide range of leprosy prevalence is linked with the varied lepromatous/tuberculoid ratio; leprosy has disappeared within historic times from north-western Europe, but persists in the south. Leprosy is an uncontrolled problem in the world.

Certain factors of possible epidemiological importance are reviewed, including the spread of leprosy, and the social and environmental conditions that might favor that spread. Many epidemiological data await explanation.

Microbiological: The organism is delicate and fastidious, yet it shows remarkable powers of persistence: extracorporeal forms are unknown: *M. leprae* is passed (without intermediary of a vector) from person to person. Nonstainable forms may exist. *M. leprae* may after treatment relinquish the power to multiply but the effete mycobacterial debris remains in the tissues, especially in nerve tissue.

Clinical: The portals of exit are known (particularly the nasal mucosa), but the portal of entry has not yet been identified. Healthy carriers and inapparent infections may exist.

The clinical response to infection varies within the widest possible limits—from complete refractoriness to complete susceptibility. There is an ill-defined genetic predisposition that determines in some measure this response.

The only proved accessory environmental factor in determining the leprosy rate in a community is domestic overcrowding, which is associated with several other factors.

The importance of previous infection with *M. tuberculosis* on susceptibility to *M. leprae* is debatable. Cell-mediated immunity, and the potential to develop it are probably paramount. The nutritional state *per se* (as in tuberculosis) has no direct and demonstrable bearing on susceptibility to leprosy, but changes in the hormonal state certainly influence the onset of the disease and the incidence of clinical extension and acute

exacerbation.

The outlook for leprosy control is far from bright at the moment, since a sufficient proportion of leprosy sufferers disseminating viable bacilli is not yet receiving adequate treatment with the slow-acting bacteriostatic drugs available. A specific vaccine—better than BCG—would help, but it would not solve all the puzzling problems that this mycobacteriosis still presents.—Author's Summary

Fazelbhoy, Z. A. Leprosy control in Pakistan. *J. Pakistan Med. Assoc.* **23** (1973) 129-135.

This article mentions superficially many areas of Pakistan, with an indication of the prevalence of leprosy apparently based on either the numbers attending clinics or random surveys. In 5 out of 34 areas in Karachi the prevalence ranges from 0.98 to 3.3 per thousand, but in some small areas in other districts it is 40 per thousand. Because rooms were not available in government dispensaries, separate buildings have been built as leprosy clinics. Apparently most work among patients with leprosy is done by voluntary agencies.—C. S. Goodwin (*From Trop. Dis. Bull.*)

Hartman, A. The prevalence of leprosy at the coast of Kenya. *East Afr. Med. J.* **50** (1973) 181-188.

Twenty-one villages on or near the coast of Kenya, selected at random, were visited by teams of teachers and students from the University of Nairobi, and the villagers examined for leprosy and other diseases. The object of the survey was not mentioned and the author concludes that this method prevented the hiding of suspect cases. In four villages the team first carried out a census. Of 8,011 people examined, 62 were found to have leprosy, with ages ranging from 7 to 76 years. Twenty tribes or subtribes were identified and people with leprosy were found most frequently in the largest tribes; it occurred in some smaller tribes but not in others. In certain districts the prevalence was high (up to 1.5%) and more staff for leprosy clinics is recommended. The author estimates that, in a total coastal population of 800,126 there would be 6,700 people with leprosy.—C. S. Goodwin (*From Trop. Dis. Bull.*)

✓ **Malchow-Møller, Axel.** A three-year leprosy control program in Tamil Nadu (India). *Dan. Med. Bull.* **20** (1973) 198-203.

A leprosy control program has been established in Nannilam Taluk, Tanjore District, Tamil Nadu, India. No previous systematic treatment has been afforded in the control area. The population is about 300,000 with an estimated prevalence of leprosy at 2.5%.

As per 30 June 1972, almost 5,000 leprosy cases have been detected since the beginning of the program in September 1969. Four case finding methods are employed: health education and propaganda, mass survey of the total project area, contact survey, and school survey. Under treatment are 4,501 cases, of which 161 cases have been declared inactive (according to WHO criteria). No cases have been released from control yet.

About 65% of the patients are taking treatment regularly from the mobile clinics. Roughly 3.5% of the patients are admitted to the hospital per year for further treatment, mainly because of ulcers.

More than 90% of the patients were detected because of health education or through mass survey. School survey was introduced in the beginning of 1972. Preliminary results from this suggest an annual incidence rate of not less than 5 per 1,000 among schoolchildren.

All the case finding methods described will be used in future control work. With the completion of the second mass survey (expected ultimo 1974), data should be available for more reliable calculations of the prevalence rate in the control area and incidence rates among selected groups, especially schoolchildren.—(*Adapted from author's summary*)

✓ **Mehta, J. M.** Some suggestions for the leprosy program in the fifth five year plan. *Lepr. India* **45** (1973) 73-75.

In this recommendation, considerable stress has been given to control-treatment work, family planning and research. Control dissociated from all round treatment is not effective. Family planning will certainly de-

crease the total number of patients. Research is the ultimate answer. The other aspects of leprosy have not been neglected.—*Author's Conclusion*

Série, Ch., Sabourin, G., Dujou, G. and Mercier, J. Considérations sur l'endémie Hansenienne en Guyane Française. [Views on endemic Hansen's disease in French Guyana.] *Bull. Soc. Pathol. Exot.* **66** (1973) 371-380. (In French)

Discussion of the results and conclusion. The sum total of these results show that: 1) the frequency of the disease is identical in Guyanese children, whether or not they come from contagious families; 2) the degree of contagion of the milieu where the child is located does not influence the form of his disease; 3) there is no relationship between the form of the disease in the parents and the children.

These various findings added to the results of the statistical analyses previously given supports the idea that the "terrain" is of first importance and brings (implicates) into play basic and constitutional factors.

To follow up the factor N hypothesis of Rotberg, we thought that a project including the study of certain variables must be undertaken in the areas of immunology, genetics, enzymology and endocrinology.

At the present, an important study in genetics and enzymology is underway at the "Centre d'Hématologie" of the C.N.R.S. under the direction of Prof. Ruffie. This study is being carried out in family units in which there have been both healthy individuals and leprosy patients for two or three generations, for whom the genealogy has been established very precisely—outside of the civil status. This study concerns 150 individuals and 15 families. A second program in endocrinology is in the planning stage between the Research Unit of Prof. Durand and the Pasteur Institute of Guyana.

These projects will be reported subsequently. Such are the accomplishments and suggestions that we would like to present in this article.—(*Adapted and translated from authors' conclusion*)

Rehabilitation

✓ **Gardiner, Jean.** Querying the absolute need for either faradic or galvanic stimulation

in the physical treatment of leprosy. *Lepr. Rev.* **44** (1973) 213-214.

Without negating all possible good from electrical stimulation in leprosy—from the lack of essential need, and also taking into account the time spent in giving one treatment of electrical stimulation against the hundreds of patients waiting for help—it may be justifiable to say that it is not altogether warranted or necessary to include this special equipment in the leprosy clinic.—Author's Conclusion

✓ **Mecklenburg, Monika.** Chiropody and lep-

rosy. *Lepr. Rev.* **44** (1973) 65-69.

The idea of employing a chiropodist in leprosy schemes is presented. After a detailed description of a chiropodist's knowledge and of his or her possible role in leprosy, the reasons for employing chiropodists in leprosy primarily relate to their specialized knowledge of foot care and the probability of their greater attention and care of ulcers that is permitted by the limited time of the physician who has also other multiple problems to contend with.—O. K. S.

Other Mycobacterial Diseases & Related Entities

✕ **Barker, D. J. P.** The distribution of Buruli disease in Uganda. *Trans. R. Soc. Trop. Med. Hyg.* **66** (1972) 867-874.

Cases of *Mycobacterium ulcerans* infection which presented in Uganda in 1970 were recorded by inspection of hospital records, biopsy reports, dispensary records in Serere and Pallisa Counties and elsewhere, and the tsetse control division records; also by surveys in Madi, Busoga, Lango and Teso Districts and special regular clinics in Lango and Bunyoro. A total of 601 patients were detected, with adequate demographic and locational data on 572 patients and histological confirmation of diagnosis in 424. The patients came from six districts contiguous to the Nile, including 327 from Lango and 143 from Bunyoro. Standardized annual incidence rates by subcounty reached 1.81% in Ibuje (Lango) and exceeded 0.1% in 11 subcounties, sited just downstream from Lake Kyoga, and in West Madi where the Nile leaves Uganda. In areas of high incidence there is a higher relative preponderance of cases in young males than older ones. Maximal female incidence is always between 5 and 14 years. Adult infections affect females more often than males and the converse is true of young children. When standardized for age and sex, the location of lesions on the body is unrelated to the incidence in different subcounties.

The disease occurred chiefly near the Nile and tended to spread from the river. Strong anecdotal evidence supports the view that incidence rose following Nile floods of 1962-1964 and yet tended to spare uplands near

the Nile which escape flood effects. The grass *Echinochloa pyramidalis*, found in permanent swamps, has a similar distribution to the disease. The sex differences in incidence among adults may be related to frequency of visiting swamps.—D. J. Bradley (*From Trop. Dis. Bull.*)

✕ **Radford, Anthony J.** Nomenclature for infections due to *Mycobacterium ulcerans*. *Trans. R. Soc. Trop. Med. Hyg.* **67** (1973) 197. (Letter to the Editor)

Sir: I would make a plea for the cessation of the term "Buruli ulcer" or "Buruli disease" to describe infections with *M. ulcerans*.

Whilst the disease is undoubtedly a place-clustered disease in most cases, I submit it is inappropriate to refer to "Buruli disease in New Guinea" or anywhere else outside of the Buruli area of Uganda.

The term "Buruli ulcer" is used because it is most frequently described from Uganda. If an eponym is called for, it should surely be either, "Bairnsdale ulcer" after the area of Victoria, Australia, from where it was first described or "Searls' ulcer" after the general practitioner who first recognized it as an unusual disease entity.

Mycobacterium ulcerans is the organism of causation and "ulcerans" is descriptive of its most common mode of presentation. Let us, therefore, refer to the disease as such, and describe its epidemiology and other features in relation to the areas where it is found.—Author's Letter

Stanford, J. L. An immunodiffusion analysis of strains of *Mycobacterium ulcerans* isolated in Australia, Malaya, Mexico, Uganda and Zaire. *J. Med. Microbiol.* **6** (1973) 405-408.

Analysis of 35 strains of mycobacteria variously labeled *M. ulcerans* or *M. buruli*, originating in Australia, Malaya, Mexico, and in Africa showed all to be members of a single distinct species, for which *M. ulcerans* (MacCallum) is the correct name. Immunodiffusion studies showed antigens typical of other slowly growing mycobacteria, and five antigens specific to the organism itself alone.—(From author's summary)

Terencio de las Aguas, J., Hierro, J. del, Richeri, D. and Alemany, A. Lepra y filariasis por *Acanthocheilonema perstans*. [Leprosy and filariasis by *Acanthocheilonema perstans*.] *Rev. Leprol.* **9** (1973) 143-149. (In Spanish, English summary)

Presented is a case of lepromatous leprosy simultaneously occurring with filariasis by *Acanthocheilonema perstans* with cutaneous lesions of pruritus. A discussion follows on the increase of tropical diseases in Europe in this day and age.—(Adapted from English summary)