CURRENT LITERATURE

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General and Historical

MEDICAL JOURNAL AUSTRALIA. Exorcizing the leper. Vol. **2** (1977) 345-347. (Editorial)

A good review of leprosy is presented for the nonspecialist, including stigma related to the book of Leviticus, history, present therapeutics and modern management. In spite of the title, a point is made for positive rejection of the word "leper." The Northern Territory of Australia is reported as having the highest prevalence in the world, with 724 patients registered in 1972. No stigma was attached to the disease among the Australian Aboriginals until segregation became law and patients were taken from their families. Recommendation is made that when a patient has to be isolated for his own interest or the interest of the community, reasons for this be explained sympathetically. This makes one wonder whether segregation is still enforced.—M. F. Lechat

Rea, Thomas H. and Levan, Norman E. Current concepts in the immunology of leprosy. Arch. Dermatol. **113** (1977) 345-352.

This competent summary is useful, as intended, to acquaint the nonleprologist with current immunologic concepts of leprosy.—Olaf K. Skinsnes

Tullis, James L. Annual discourse—Don't eat the quails. N. Engl. J. Med. **297** (1977) 472-475.

Physicians were the first individuals recorded by name in history. Their attempts to define disease influenced fundamentally the cultures and religions of the world. Surgical skills, although highly developed in ancient times, appear to have been less well documented historically than medical disorders. Because of the greater threat to survival that diseases posed, they became incorporated into religious customs. Contagious diseases also influenced greatly the laws, traditions and historical events of the Bible. Leprosy provided a physical example that presumably represented an image of sin, but it probably was not more prevalent as a disease during Biblical times than at present. Many of the Biblical stories assumed to be allegorical may have been founded on medical fact. For example, it appears likely that the quails that poisoned the wandering Jews were contaminated with cyanide.—Author's Abstract

Chemotherapy

Balakrishnan, S. and Desikan, K. V. Blood and tissue levels of diaminodiphenyl sulfone (DDS) in experimental mice. Indian J. Med. Res. **65** (1977) 201-205.

Blood and tissue levels of diaminodiphenyl sulfone (DDS) in 24 experimental mice receiving diets containing 0.01% DDS were estimated. An average concentration of 1.2 μg/ml of DDS was found in the blood. The concentration of DDS in the liver was about twice that in blood. In the spleen the level of DDS was slightly higher than in blood but the muscles contained much less. The drug was detectable in the nerves at a concentration almost equal to that in the blood. The clinical implications of these findings in the treatment of leprosy are discussed.—Authors' Summary (*From* Trop. Dis. Bull.)

Firkin, Frank C. and Mariani, Anthony F. Agranulocytosis due to dapsone. Med. J. Aust. **2** (1977) 247-251.

A case of agranulocytosis due to dapsone administered for the treatment of acne vulgaris is described. Agranulocytosis has previously been reported after administration of dapsone for other dermatological disorders, leprosy, and prophylaxis against falciparum malaria. The frequency of agranulocytoses when dapsone was used for malaria prophylaxis in United States servicemen in Vietnam was sufficient to result in its withdrawal from use for this purpose. Caution should therefore be exercised in the administration of dapsone for conditions for which less toxic agents are available.—Authors' Abstract

Gelber, R. H., Waters, M. F. R., Pearson, J. M. H., Rees, R. J. W. and McDougall, A. C. Dapsone alone compared with dapsone plus rifampicin in short-term therapy of lepromatous leprosy. Lepr. Rev. **48** (1977) 223-229.

Previously untreated lepromatous leprosy patients were randomly allocated to treatment with either 100 mg dapsone daily or 100 mg dapsone and 600 mg rifampicin daily for six months. Patients receiving rifampicin improved more rapidly, but by six months the regimens were equivalent. There was no difference in the incidence, severity, and time of onset of *erythema nodosum leprosum* (ENL) in the two groups. Skin smears and histological sections and mouse foot pad inoculation of biopsy specimens from skin, peripheral nerve, skeletal muscle and dartos muscle demonstrated more rapid killing of *Mycobacterium leprae* in those on combination chemotherapy. In the patients treated only with dapsone, viable *M. leprae* were generally found after three months of therapy, and frequently even at six months. Even on the combined regimens, viable *M. leprae* were commonly detected at three months, but only occasionally at six months.—Authors' Abstract

Jacobson, Robert R. and Hastings, Robert C. Rifampin resistant leprosy. Lancet **2** (1976) 1304-1305. (Letter to Editor)

The rifamycin antibiotics have been used in the treatment of leprosy since 1963. The orally active rifamycin, rifampicin, or rifampin has been utilized more recently. Rifampin exerts a rapid bactericidal effect on *M. leprae* in man, but concern has been expressed regarding the possible development of rifampin resistant *M. leprae*.

We have seen a patient with sulfone-resistant lepromatous leprosy who experienced clinical and bacteriologic relapse while on rifampin monotherapy. The patient is a 49 year old male of Scandinavian extraction who has had lepromatous leprosy since the age of 18. He was treated with sulfones, glucosulfones (Promine) and later sulfoxone (Diasone) both of which he took irregularly from 1946 until 1968. In 1968 he developed clinical relapse despite sulfoxone therapy, and mouse foot pad studies by Dr. Shepard in Atlanta, Georgia showed intermediate levels of sulfone resistance (multiplication in mice fed 0.0001% and 0.001% w/w dapsone in the diets but no growth in animals fed 0.01% dietary dapsone). The patient was put on high doses of dapsone (up to 200 mg daily) from 1968 to 1970, and because his disease continued to progress he was then treated with streptomycin from 1970 to 1972. His disease responded to streptomycin, but in July 1972 it became progressive once again despite continued therapy, and treatment was changed to rifampin 600 mg daily. The patient took 93.5% of his prescribed doses of rifampin from July 14, 1972 to July 10, 1976. In February 1976 after 43 months of rifampin therapy, a new nodular skin lesion developed on his left lower chest. Biopsy was done and mouse foot pad drug-sensitivity studies were started. The patient had slow progression of his lepromatous leprosy despite rifampin until July 1976 at which time he was placed on clofazimine (Lamprene) 100 mg daily. The results of drug sensitivity tests are given in our table [not included].

To our knowledge this is the first case of rifampin resistant leprosy confirmed by mouse foot pad studies. The pattern of rifampin resistance in *M. leprae* appears to be of a streptomycin type or single-step mutant. This contrasts to our experience with 75 dapsone resistant strains in which the pattern of growth in mice fed dapsone indicates a penicillin or multiple-step type mutation. The spectre of multiple drug-resistant leprosy bacilli suggests that consideration be given to routine multiple drug therapy of lepromatous leprosy, particularly in regimens including rifampin.—(*Excerpted from* authors' letter)

Naik, S. S., Tanksale, K. G. and Ganapati, R. Study of urinary nitrogenous constitu-

ents in reactions of leprosy. Indian J. Med. Res. **65** (1977) 193-200.

Nitrogen intake through vegetarian diet was studied in uncomplicated hospitalized leprosy patients and patients in different stages of reaction. The protein intake in hospitalized leprosy patients was more than in an average Indian diet. It was reduced in reactional cases of leprosy in accordance with the severity of the episode. Total nitrogen excreted through 24-hour urine was studied in leprosy patients along with urinary nitrogenous constituents; such as urea, uric acid, creatinine, creatine, α-amino acid nitrogen, hydroxyproline. These urinary constituents were found to increase in accordance with the severity of reaction. The excretion of α-amino acid nitrogen and hydroxyproline in urine was significantly increased in reactional leprosy. It is suggested that these parameters along with the hydroxyproline:creatinine ratio can be used to assess the severity, subsidence and onset of reaction in leprosy. Impairment in functions of kidney and adrenal cortex was observed during the reactions of leprosy. The causes for the increased excretion of the nitrogenous constituents in leprosy reaction are discussed.—Authors' Summary (*From* Trop. Dis. Bull.)

Clinical Sciences

Balina, L. M., Charosky, C. B., Kaufmann de Swiec, A. and Balina de Valdez, M. Garra cubital iatrogenica por impetuosidad diagnostica. [Iatrogenic claw hand from diagnostic biopsy.] Rev. Leprol. **11** (1977) 145-150. (In Spanish)

An ulnar nerve biopsy was performed on a patient to confirm the diagnosis of leprosy. This resulted in an iatrogenic claw hand. As this biopsy procedure has always been dangerous, the authors believe that in the present era of preventive medicine and prevention of incapacities, ulnar nerve biopsies should no longer be practiced. Prophylactic treatment can be practiced, as is usually done in syphilis, without having confirmed the diagnosis.—(*Adapted from* authors' English summary)

Bonneau, G., Seguinard, M. and Michel, M. A propos de trois diagnostics rares en O.R.L. Lèpre et Rhinosclérome [Three unusual diagnoses in E.N.T. practice: leprosy and rhinoscleroma.] J. Fr. Otorhinolaryngol. **23** (1976) 691-693. (In French)

These case studies relate to one observation of leprosy with nasal and laryngeal involvement in a 30 year old Portuguese living in France for 20 years, and two other cases suspected of rhinoscleroma with tracheal involvement treated by rifampicin. The confirmed leprosy case is of exceptional interest, since it relates the strategy which led to the diagnosis: anamnesis, clinical history, anterior rhinoscopy, posterior rhinoscopy, laryngoscopy, biopsy with histological examination of the tissue, and radiography. The biopsy revealed *M. leprae* in great numbers in the nasal mucosa. The authors insist on the value of epidemiology in the diagnosis, the patient having lived as an infant in an endemic country. This case study stresses the importance of being aware of leprosy for the diagnosis of unusual E.N.T. lesions in patients from endemic areas.—(*Translation by* M. F. Lechat)

Bravo, L. L. and Ratard, R. C. Leprosy disabilities in the New Hebrides. Lepr. Rev. **48** (1977) 247-260.

The proportion of disabled among leprosy patients is 39% in the New Hebrides. This proportion is higher among lepromatous cases (67%) than among tuberculoid and borderline cases (38%). The disability index is higher among disabled lepromatous (1.2) than among disabled tuberculoid and borderline (0.8). Males are more often disabled than females (47% for males, 33% for females), but females seem to be more seriously disabled than males. There is an increase in the proportion of disabled and in the disability index with age. Disabilities are more frequent among positive cases, among patients taking irregular treatment or no treatment at all, and among patients with lepra reaction. The proportion of disabled among tuberculoid cases increases four to six years after diagnosis and then decreases. For lepromatous patients there is a high and stable

proportion of disabled from the beginning of the disease; there is also a steady increase in the severity of the disabilities. The nature of the initial symptoms influences the future occurrence of disabilities among tuberculoid and borderline cases. Only 13% to 16% will develop disabilities if there is no nerve involvement, 35% to 38% will do so if nerves are already involved. Bilateral lesions are more common among lepromatous than among tuberculoid or borderline cases. The prevalence of disabled for the whole population was estimated to be 2.7 per thousand.—Authors' Abstract

Choudhury, S., Kundu, S., Ghosh, S. and Hazra, S. Anabolic steroid as an adjuvant in the treatment of chronic lepra reaction and ENL under corticosteroid therapy. Lepr. Rev. **48** (1977) 181-184.

Fourteen lepromatous patients in the various stages of reaction with ENL episodes were put on Methandienone in addition to steroid therapy. Methandienone, an anabolic steroid, was found to be useful as an adjuvant and helped both in reducing the dosage of steroid needed, and in making possible the institution of DDS in about 60% of cases.—Authors' Abstract

Fusaro, Ramon M. Immunotherapy of leprosy. Arch. Dermatol. **113** (1977) 1129. (Letter to Editor)

In reading the minutes of the SOCIETY TRANSACTIONS in the August 1976 issue of the ARCHIVES, the reader is left suspended in one of the discussions on the immunotherapy of leprosy. The minutes alluded to some leprosy research by a "Korean physician" in an obscure manner that invites inquiry.

In 1972, Lim *et al* reported that repeated whole WBC transfusions given over approximately a three-month period substantially cleared patients with either lepromatous or tuberculoid leprosy. The clinical, bacteriologic, and histologic data all became normal soon after the end of the immunotherapy and remained normal. These results were recently confirmed in a communication (Saha, K. *et al,* 1975) that also reiterates the previous failure of the use of transfer factor (Bullock, W. E. *et al*).—Author's Letter

Hall, Gillian. A review of drop-foot corrective surgery. Lepr. Rev. **48** (1977) 185-192.

The late results of 65 tendon transfer operations for drop-foot are reviewed, especially in relation to the various surgical technics employed. It is concluded that, from the patient's point of view, range of movement was more important than gait. For young patients with good pre-operative mobility, single-tendon transfers were preferable, but for patients with inverted, deformed or stiff feet, where range of movement was less important than stability, the two-tendon Carayon technics could be preferable.—Author's Abstract

Karat, A. B. A. and Rao, P. S. S. Hematological profile in leprosy. Part 1. General findings. Lepr. India **49** (1977) 187-196.

Hematologic studies in 904 adult leprosy patients with different types of leprosy in various stages of the disease and treatment are described. Hemoglobin, packed cell volume, serum albumin and serum iron are significantly lower among lepromatous leprosy patients as compared with nonlepromatous patients. The serum B12 levels were significantly higher among the lepromatous group. Acid-fast bacilli have been demonstrated in skin smear negative leprosy patients with indeterminate and tuberculoid leprosy, suggesting occurrence of bacillemia in these groups of patients.—Authors' Summary

Mason, G. H., Ellis-Pegler, R. B. and Arthur, J. F. Clofazimine and eosinophilic enteritis. Lepr. Rev. **48** (1977) 175-180.

A case of eosinophilic enteritis associated with clofazimine (Lamprene) therapy is reported. A 29-year-old Samoan woman with leprosy developed abdominal pain after three years of clofazimine therapy at 600 mg daily. At laparotomy there was nodular thickening of the upper ileum with black-brown pigmentation of the ileal wall, mesentery and mesenteric lymph nodes. Ileal biopsy showed eosinophilic enteritis, and red crystals of clofazimine were present in unstained sections of the small bowel mucosa and submucosa, as well as in mesenteric lymph nodes. It seems that these histologic changes and her peripheral eosinophilia represent a reaction to the drug. The potential hazards of long-term high dose clofazimine therapy are stated again.—Authors' Abstract

McDougall, A. Colin. Onchocerciasis and streptocerciasis in patients with leprosy. Trans. R. Soc. Trop. Med. Hyg. **71** (1977) 360-361. (Letter to Editor)

In the course of analyzing over 13,000 biopsies submitted to the Leprosy Study Centre in London between 1952 and 1976, a remarkably large number of those from Africa have been found to contain microfilariae (*Onchocerca volvulus* or *Dipetalonema streptocerca*) either alone, or with evidence of leprosy. The findings show that in geographic areas where both diseases are endemic, errors in the diagnosis and management of leprosy are by no means infrequent (Lepr. Rev. **48** [1977] 161-168).

In writing up these results consideration was given to possible inter-relationships between leprosy and microfilariasis, and the letter appearing in this Journal by Meyers and Connor (1975) is of particular interest. These authors noted a low frequency and reduced severity of Mazzotti reactions in 32 patients with leprosy and microfilariasis, all but two of whom were under dapsone treatment at the time. They considered the possibilities that the Mazzotti reaction might have been altered by leprosy (particularly the lepromatous form) or dapsone.

I cannot submit original observations on this subject but thought it might be relevant to record a few thoughts, albeit unscientific, concerning leprosy, microfilariasis, dapsone and diethylcarbamazine. Since the introduction of dapsone in 1943, many leprologists have considered that it either causes or accentuates various types of adverse reaction in leprosy due to either cell-mediated or humoral responses. Others more interested in the mode of action of this drug in dermatitis herpetiformis have thought that it might be immunosuppressive. Thus, Thomson and Souhami (1975) reported that it could suppress the Arthus reaction in guinea pigs, and Millikan and Conway (1974) that it could change complement C_3 proactivator and C_3 levels in patients with dermatitis herpetiformis, and that it did this by acting directly on the alternate (Pillemer) pathway. Although the former results have not been confirmed (Thomson, 1977, personal communication) and the latter have recently been challenged (Katz *et al,* 1976), these publications nevertheless call to mind the rather indirect way in which diethylcarbamazine is currently believed to work on microfilariae. This drug is thought to first induce the release of an antigen from microfilariae which then combines with an immune globulin, causing microfilarial disintegration (Connor *et al,* 1970).

It seems possible, from the letter (in Trans. R. Soc. Trop. Med. Hyg.) quoted above, that lepromatous leprosy may influence the Mazzotti reaction in onchocerciasis. Rougemont *et al* (1977) have recently drawn attention to the effect of onchocerciasis on tuberculin skin tests and BCG vaccination and conclude their communication with the reminder that onchocerciasis may induce "severe and very frequent immunological perturbations of both the cell-mediated and humoral type."

Finally, while discussing the diagnostic confusion between leprosy and microfilariasis recently with Dr. E. Ode (personal communication, 1976) she drew attention to the fact that a number of patients with lepromatous or borderline—lepromatous leprosy in Cameroon have first presented with florid lesions of leprosy, closely following an injection of diethylcarbamazine for the treatment of onchocerciasis.—(*Adapted from* author's letter)

McDougall, A. C. and Archibald, G. C. Lepromatous leprosy presenting with swelling of the legs. Br. Med. J. Jan. 1 (1977) 23-24.

This is a report from Oxford of an adult Pakistani male who sought medical advice because of edema of both legs and was found, on examination, to have skin lesions of *erythema nodosum leprosum* (ENL). There was a past history of nasal blockage and epistaxis. Large numbers of leprosy bacilli were found in skin and nasal mucosa, and biopsies were diagnostic of lepromatous leprosy in reaction. The etiology of edema in leprosy is discussed.

[The important lesson to be learned from this paper is that skin lesions of lepromatous leprosy can be preceded, often for years, by nasal symptoms and by edema of the legs.] —W. H. Jopling (*From* Trop. Dis. Bull.)

McDougall, A. C. and Waudby, H. Dermal microfilariasis and leprosy. Lepr. Rev. **48** (1977) 161-168.

In the course of studying over 13,000 biopsies referred to the Leprosy Study Centre in

London between 1952 and 1976, it was found that approximately 26% showed no evidence of leprosy on histopathologic examination. Some of these were normal and others showed minimal nonspecific changes, but many revealed a wide range of dermatologic and tropical conditions, among which the most important and frequently recurring was microfilariasis, due predominantly to *Onchocerca volvulus,* but also including infections with *Dipetalonema streptocerca.* Biopsies were submitted from Zaire, Nigeria, Sierra Leone and Cameroon, mostly on account of a suspicion of leprosy, or in order to confirm a diagnosis of leprosy, in some cases after treatment had been started with dapsone.

A 12 year period (1964-1976) has been selected for detailed study and the histopathologic findings are considered in close relation to the doctor's letter or clinical information supplied. It is apparent that in geographical areas where both leprosy and onchocerciasis or streptocerciasis are endemic, there is continuing confusion, even among experienced observers, which may lead to errors in the diagnosis, classification, assessment and follow-up of patients with leprosy.

Skin biopsies, with appropriate attention to 1) the body site selected, 2) laboratory technic, and 3) the careful examination of serial sections, may be invaluable in minimizing or eliminating these errors.—Authors' Abstract

Naik, S. S. and Ganapati, R. Regularity of dapsone intake by leprosy patients attending an urban treatment center. Lepr. India **49** (1977) 207-215.

Dapsone/creatinine ratios in urine were determined in statistically randomized samples of 965 leprosy patients attending the outpatient department of Acworth Leprosy Hospital and in 44 inmates of the hospital. The percentage of irregularity in DDS treatment found was 43% and 22.6% respectively in outpatients and hospital inmates. The need to assess the possible response for irregularity in treatment is stressed and the hazard of infectious cases remaining without treatment or with incomplete treatment is pointed out.—(*Adapted from* authors' abstract)

Saint-Andre, P. B., Louvet, M., Penchenier, L., Giraudeau, P. and Discamps, G. Lèpre tuberculoïde inflammatoire avec importantes complications nerveuses. [Inflammatory tuberculoid leprosy with severe neurologic complications.] Med. Armees **5** (1977) 31-34. (In French)

This observation again raises attention to the possibility of tuberculoid leprosy undergoing an inflammatory evolution. It appears as though this evolution corresponds to a "downgrading reaction" with proliferation of bacilli. The tissues react differently to this increase in antigens according to their allergic status: hyperergic (strongly positive Mitsuda and neurological damages of sudden onset), or hypoergic (Mitsuda slightly positive, dubious, or becoming negative, with similar inflammation and edema in the dermis and moderate damage to the peripheral nerves). Cooperation of the physician and surgeon is strongly urged in such cases. —(*Translated by* M. F. Lechat)

Schmitt, J., Schmidt, C., Adam-Goldberg, E. and Floquet, J. La lèpre nerveuse en France Métropolitaine. [Neural leprosy in metropolitan France. Remarks on problems posed by it.] Ann. Med. Interne (Paris) **127** (1976) 247-251. (In French)

Two cases of pure neural leprosy in French patients are described. Both cases, one in a woman aged 46 years, the other in a man aged 53 years, were imported from Africa or Southeast Asia. The diagnosis is discussed, including functional and immunologic tests, as well as nerve biopsies. It is stressed that leprosy should be suspected as a possible diagnosis in nonendemic countries.—(*English translation by* M. F. Lechat)

Sehgal, V. N., Rege, V. L. and Kharangate, V. N. Limitations of clofazimine in reactions in leprosy. Indian J. Dermatol. Venereol. Leprol. **43** (1977) 152-154.

Exacerbation or precipitation of reaction in leprosy due to clofazimine treatment is described in 7 of 24 patients, highlighting its limitations in such cases and hence warranting its judicious use.—Authors' Summary

Sehgal, V. N., Rege, V. L. and Mascarenhas, M. F. Pattern of reactions in leprosy. A clinical appraisal. Lepr. India **49** (1977) 221-228.

The term "reactions" is applied in the present text to describe the acute episodes

recognized with different types of leprosy. The incidence of reactions was found to be 9.7% of 1,053 cases examined. Reactions were seen in all types of leprosy, but their frequency and severity was marked in lepromatous and borderline cases with the majority of ages ranging from 20-40 years.

The precipitating factor(s) could not be established in many; in some dapsone was incriminated followed by bacterial infection and malnutrition. Exacerbations of the existing lesions, either alone or in combination with new lesions (ENL) and ENL lesions alone, were the presenting clinical features. The constitutional symptoms were observed largely in types other than tuberculoid. Foot drop and contractures of the fingers were the common sequels of the reactions. An attempt has been made to explain their mechanism in the light of recent literature.—(*Adapted from* authors' abstract)

Immuno-Pathology

Boddingius, Janny. Ultrastructural changes in blood vessels of peripheral nerves in leprosy neuropathy. II. Borderline, borderline-lepromatous and lepromatous leprosy patients. Acta Neuropathol. **40** (1977) 21-39.

The ultrastructure of blood vessels in endo-, peri- and epineurium was studied in peripheral cutaneous nerve biopsies of 16 borderline (BB), borderline-lepromatous (BL) or lepromatous (LL) leprosy patients some of whom were in reversal reaction. Comparable vessels in nerve biopsies of control cases and vessels in skin lesion biopsies of the leprosy patients were also studied. Vascular changes were found in nerves of all the leprosy patients. The changes were pronounced in endoneurial vessels and affected 1) endothelial continuity and surface structure, 2) basement membranes of endothelium and pericytes, and 3) the vessel lumen. In addition, intra-endothelial *Mycobacterium leprae* were a feature in some of the patients.

Gaps occurring between endothelial cells and plasma exudation both noticed in vessels of fascicles with early to very early neuropathy suggested extensive leakage which, in all probability, causes early nerve fiber damage. Luminal and abluminal endothelial protrusions, which were frequently observed, may enhance transendothelial transport. Fenestrations and endothelial attenuation, possibly, lead to an increase in vascular permeability. Endothelial phagocytic activity, particularly in small (epineurial) arteries, appeared to be stimulated, possibly, by circulating *M. leprae*.

Basement membrane multilayering (a "hyaline zone") was found peripherally to pericytes, as is the case in tuberculoid leprosy (Boddingius, 1976). In a number of patients multilayering occurred also periendothelially. Perivascular zones, which are thought to initiate or aggravate neuropathologic changes by impairment of diffusion of oxygen and nutrients or metabolites, were very wide in endoneurial vessels of patients in reversal reaction and this suggested an immunologic etiology. Partial or total vessel lumen occlusion, seen in advanced lepromatous neuropathy, most likely contributes to final nerve fiber degeneration and endoneurial fibrosis. *M. leprae* were found intraendothelially in endoneurial vessels, though only in fascicles with advanced neuropathy whereas bacilli were not seen in vessel lumina. By contrast, in fascicles with relatively early neuropathy, solid (viable) bacilli were frequently encountered *intra-axonally* in myelinated fibers. This suggests that, in many instances, primary infiltration of *M. leprae* into nerve fascicles may arise from intra-axonal bacilli which ascend from dermal nerves and are released within main nerve trunks after demyelination of the host fiber.—(*Adapted from* author's summary)

Carayon, A., Languillon, J. and Giraudeau, P. Névrites réactionnelles micro-angiopathiques dans la lèpre borderline. [Microvascular lesions in peripheral nerves appearing in the course of acute reaction in borderline leprosy.] Med. Afr. Noire **23** (1976) 681-690.

The authors review the pathology of dam-

age to peripheral nerves that appears during reactional episodes in patients suffering from borderline leprosy and suggest that much of the damage is due to lesions in the blood vessels (vasa nervorum) surrounding the nerve trunks and penetrating intraneurally. They thus consider that the lesions are on a par with auto-immune phenomena, as in Guillain Barré's neuropathy, periarteritis nodosa and rheumatoid arthritis.

The most common history of these cases is for an initial downgrading reaction to be followed, usually after a period of antileprosy treatment, by a reversal reaction. The localization of the lesions in the nerve trunks is usually distant from the classical sites of predilection and may affect nerves that are less frequently damaged in leprosy, i.e., the radial, median (in its lower path), and internal popliteal. The enlarged nerve is usually soft on palpation, the consistency being due to the presence of localized edema.

Clinical suspicion of the occurrence of this type of neuropathy is based on unusual localization, late appearance of lesions, an association with pre-existing nerve lesions of the classical type, insidious and painless progression of nerve damage, and presence of submaximal electrophysiologic changes, notwithstanding the degree of motor and sensory deficit. Because no branches leave the nerve trunk at the sites affected, the extent of the functional destruction may long remain unsuspected. The result of the lepromin test and histopathologic picture are consistent with the hypothesis of a microvasculitis affecting the media of small vessels. Complement and immunoglobulin are deposited in these situations together with immune complexes.

The authors favor limited surgical intervention for precise indications, with operative endoneurolysis in selected cases to relieve pressure on nerve fibers and to accelerate nerve conduction velocity. They even suggest removal of a segment of irreversibly damaged nerve in order to remove a local source of antigenic material. They recommend long-acting sulfonamides with adequate doses of corticosteroids to control the acute manifestations. In their view, high doses of antileprotics (dapsone or sulfonamides) may safely be given to patients who have no sign of nerve damage, but where there are indications of pre-existing damage then drugs may precipitate a serious exacerbation.—S. G. Browne (*Adapted from* Trop. Dis. Bull.)

Gergatz, S. J., Drook, J. E., Kaiser, J. S. and Crutcher, W. A. Hodgkin's disease in Hansen disease. Arch. Dermatol. **113** (1977) 112. (Letter to Editor)

The association of Hansen's disease and lymphoma has been a recurrent, vexing problem. We are currently seeing two patients with inactive lepromatous leprosy who were found to have Hodgkin's disease within a three month interval while residing in the Carville leprosarium.

The association between lymphoma and Hansen's disease is interesting because of the immunologic deficiencies of the latter. Two large mortality studies failed to reveal an increased incidence of cancer in patients with Hansen's disease. Our patients have responded well to chemotherapy and are still alive two years later.—(*Excerpted from* authors' letter)

Gharpuray, S. M., Gharpuray, M. B. and Kelkar, S. S. Liver function in leprosy. Lepr. India **49** (1977) 216-220.

Thirty-eight leprosy patients were classified on the basis of clinical and biopsy findings in 10 lepromatous (all reactional), 20 tuberculoid (7 in reaction), and 8 dimorphous (5 in reaction). The liver function tests: serum proteins, albumin/globulin ratio, fractions in paper electrophoresis, serum glutamic pyruvic transaminase (SGPT), and thymol turbidity tests; and the serum cholesterol were estimated in each patient. The abnormalities were a reversal of the albumin/globulin ratio in all three groups and an increase in beta/globulin fraction in the lepromatous group, but total proteins were within normal limits. The thymol turbidity test showed moderately elevated levels in all three groups. SGPT was slightly raised in a few cases. Only a single patient with tuberculoid leprosy showed serum cholesterol to be over 250 mg per 100 ml.—(*Adapted from* authors' abstract)

Gladykowska-Rzeczycka, Judyta. A case of leprosy from a medieval burial ground. Folia Morphol. (Warsz.) **35** (1976) 253-264.

The pathologic changes found in skeleton number 20 from a medieval burial ground in Suraz, Lapy county in Poland are characteristic of leprosy, presenting a typical syndrome consisting of: 1) destructive lesions of the piriform aperture, similar to those in syphilis, yaws and chronic facial lupus, but more specific. The anterior nasal spine was entirely destroyed. The inferior margin of the piriform aperture was also atrophic, including the alveolar processes and resulting in loss of the incisor teeth; 2) extensive defects of the hard palate; 3) inflammatory lesions of the nasal septum; 4) changes in the long bones, particularly legs, considered typical of leprosy; 5) trophic changes of the bones of the feet, usually beginning in the metatarsophalangeal joints. The character of these changes was trophic-destructive, leading to various articular deformities. A brief history of leprosy is also presented in addition to characteristic pathologic changes exhibited by skeleton number 20.—(*Excerpted and adapted from* article)

McAdam, K. P. W. J., Fudenberg, H. H. and Michaeli, D. Antibodies to collagen in patients with leprosy. Clin. Immunol. Immunopathol. **9** (1978) 16-21.

Antibodies to human collagen (ACA) were detected by hemagglutination assay in the serum of leprosy patients from two different geographic areas of Papua New Guinea. In the highland patients, the prevalence of elevated titers (1:4 or more) of ACA varied according to the clinical spectrum of leprosy. There was a significant gradient from high prevalence in the immunodeficient polar lepromatous patients (53%) to a low prevalence at the tuberculoid end of the clinical spectrum (9%). This gradient was not observed in coastal patients, who had a higher overall prevalence of ACA (53% compared with 37.5% in the highlanders), possibly caused by the many intercurrent infections endemic in the coastal region. It is not clear to what extent these antibodies are implicated either in the pathogenesis of the complications of leprosy, or in the prolongation and intensification of inflammatory reactions involving collagen at sites such as the skin, nerves, and glomerular basement membrane.—Authors' Abstract

Quismorio, F. P., Rea, T., Chandor, S., Levan, N. and Friou, G. Lucio's phenomenon: an immune complex deposition syndrome in lepromatous leprosy. Clin. Immunol. Immunopathol. **9** (1978) 184-193.

Lucio's phenomenon is an acute lepra reaction in diffuse lepromatous leprosy characterized by cutaneous infarctions secondary to a necrotizing vasculitis. Five cases of Lucio's phenomenon were studied to elucidate the pathogenesis of this complication of leprosy. Direct immunofluorescent studies of the lesions revealed the presence of deposits of complement and immunoglobulin in the walls of dermal blood vessels and in perivascular areas. The deposits were eluted when the cryostat sections of skin were incubated with an acidic buffer. Cryoglobulins of the "mixed type" containing IgG, IgM, IgA, C3, and Clq were found in the serum of four patients. Analysis of the cryoglobulins revealed an enrichment of rheumatoid factor activity in the cryoprecipitate over that of the serum. Immune complexes were found in the serum of all patients. Hypocomplementemia was observed in one patient. These data suggest that Lucio's phenomenon is mediated by the deposition of immune complexes in dermal blood vessels.—Authors' Abstract

Racanelli, A. Osteosclerose dans la lèpre. [Osteosclerosis in leprosy.] J. Radiol. Electrol. Med. Nucl. **56,** Suppl. 1 (1975) 120-121. (In French)

The authors reviewed the radiological aspects of hand and foot deformities in 233 patients hospitalized in Bari, Italy. Bone biopsies were also studied by fluorescent microscopy and tissue autoradiography. Osteosclerosis is frequently observed in spongious epiphysis and compact diaphysis in metacarpal and metatarsal bones, phalangue and sesamoids. Three aspects can be identified, that is reactional osteosclerosis, sclerosing periostosis, and massive osteosclerosis.—(*English translation by* M. F. Lechat)

Sher, R., Mackay, M. E., Macnab, G. M., Kok, S. H. and Koornhof, H. J. Hepatitis B antigen, hepatitis B antibody, and subtypes in leprosy. Infect. Immun. **17** (1977) 1-3.

The prevalence of hepatitis B antigen

(HBsAg), hepatitis B antibody (HBsAb), and subtypes in 242 cases of leprosy is reported. Patients were divided into three subgroups, lepromatous (174), tuberculoid (55), and borderline (13). A total of 131 patients were tested on admission; the remaining 111 had been institutionalized for a period of three months or more when tested. Of the 131 cases tested on admission, 88 were retested 6 to 12 months after admission. There was no statistical difference in the incidence of HBsAg and HBsAb among the three groups or between normal controls and the leprosy patients. The predominant subtype was ADW (84.1%). After institutionalization, one lepromatous case converted to HBsAg positive and four converted to HBsAb positive.—Authors' Abstract

Walter, J., Tamondong, C. T., Garbajosa, P. G., Bechelli, L. M., Sansarricq, H., Lwin, K. and Gyi, M. M. Note on some observations about the post-lepromin scar. Lepr. Rev. **48** (1977) 169-174.

The post-lepromin scar was studied in 764 leprosy patients of the former (1964-1975) WHO Leprosy BCG Trial in Burma, Mandalay area. A 160 million bac./ml lepromin was used. Scar formation was analyzed in its relation to the different forms of leprosy, its frequency to the size of the Mitsuda reaction, to BCG vaccination, to the tuberculin reaction, and, in some instances, in different age groups. Of the BCG vaccinated cases, 90.2% (336) showed post-lepromin scars while in the controls (410 cases) 80% had a scar. Of 746 cases, 553 (74%) had post-lepromin scars on first testing; and of the remaining 193 cases, 78 (40%) developed lepromin scars on subsequent lepromin testing. A total of 115 patients (15%) remained scar negative throughout the period even after repeated lepromin testing (up to six tests). Ten of these constant scar-negative cases subsequently developed lepromatous and borderline forms; 38 were diagnosed as having indeterminate, 63 tuberculoid and 4 "Tr" leprosy.

It is tentatively suggested that the post-lepromin scar may be considered as an indicator for a stabilized immune situation, taking into account that 17% to 32% of the 2-5 mm late Mitsuda readings also leave post-lepromin scars. Further studies with weaker lepromins (20 or 40 million bac./ml) in leprosy patients and in apparently non-leprosy affected groups of populations are suggested.—(*Adapted from* authors' abstract)

Microbiology

Desikan, K. V. Viability of *Mycobacterium leprae* outside the human body. Lepr. Rev. **48** (1977) 231-235.

It is important to recognize whether *Mycobacterium leprae* discharged from the body will remain alive after they settle down over articles of daily use, and if so the duration of their viability. The common belief is that the organisms die soon after they are discharged from the body, particularly in tropical countries. In order to verify this concept, an experimental procedure has been designed using the mouse foot pad model. It has been found that the organisms remain alive for more than nine days. This finding has an important bearing on the epidemiology of leprosy.—Author's Abstract

Harada, Kiyoshi. Staining mycobacteria with periodic acid-carbol-pararosanilin: principle and practice of the method. Microsc. Acta **79** (1977) 224-236.

Mycobacteria may be acid-fast, nonacid-fast or even chromophobic in staining under different conditions. Pretreatment with oxidants, including periodic acid, increase effectually the acid-fastness of acid-fast bacilli. This is caused by additional free carboxyl groups resulting from nonacid-fast wax in the cell walls by demethylation with oxidants.

Only after prolonged periodic oxidation can the aldehyde groups formed as oxidation products of 1-amino-2-hydroxy groups in the cells be demonstrated with carbol-fuchsin stain. This reaction is most probably attributable to the formation of Schiff's bases between fuchsin and aldehydes. Since pararo-

sanilin is the active molecule in the diphenamine reaction, periodic acid (10%, 24 hours) followed by carbol-pararosanilin strain is a most sensitive and selective method to demonstrate mycobacteria including chromophobic forms.—Author's Summary

Hastings, Robert C. Growth of sulfone-resistant *M. leprae* in the foot pads of mice fed dapsone. Proc. Soc. Exp. Biol. Med. **156** (1977) 544-545.

One hundred twenty-three viable isolates of *M. leprae* from skin biopsies of leprosy patients have been tested for sulfone resistance in the mouse foot pad since 1970. In 33 strains, growth occurred in animals fed 0.0001% (w/w) dapsone, but not at higher concentrations; in 22, growth occurred at 0.001% and 0.0001% (w/w) dapsone, but not at the higher concentration; and in 20 isolates, growth occurred at all three concentrations, 0.01, 0.001, and 0.0001% (w/w) dapsone. In each group, in animals fed the highest concentration of dapsone at which growth occurred, the number of bacilli harvested was significantly less that that in controls. Thus 75 strains of *M. leprae* had some degree of sulfone resistance, and with each degree of sulfone resistance, there was a threshold above which dapsone could still inhibit multiplication of the resistant strain in the mouse foot pad. This finding, in light of the probable mechanism of action of sulfones and mechanism of bacterial resistance to sulfones, strongly implies that maximal subtoxic dosages of dapsone are indicated in all leprosy patients with multibacillary disease treated with this drug.—Author's Summary

Kronvall, G., Closs, O. and Bjune, G. Common antigen of *Mycobacterium leprae, M. lepraemurium, M. avium,* and *M. fortuitum* in comparative studies using two different types of antisera. Infect. Immun. **16** (1977) 542-546.

No. 21 mycobacterial antigens of *Mycobacterium lepraemurium, M. avium, M. fortuitum,* and *M. leprae* were compared in crossed immunoelectrophoresis using two different antibody sources, a serum pool from lepromatous leprosy patients (LSII) and a rabbit anti-*M. smegmatis* antiserum. *M. lepraemurium,* like *M. avium,* was found to contain the 21 A and 21 C determinants. *M. fortuitum* contained in addition a new type of determinant, 21 D. *M. leprae* antigen no. 21 carried the A as well as the B determinants, the latter found so far only in the leprosy bacillus. The separate taxonomic position of *M. leprae,* suggested by earlier studies of the no. 21 antigen, is further supported by the present results, which also demonstrate the potential use of submolecular heterogeneity for such investigations.—Authors' Abstract

Matsuki, G., Kashiwabara, Y., Nakagawa, H., Kobayashi, K. and Fujimiya, T. Studies on the collection of leprosy bacilli from infected tissues for metabolic experiments. Jap. J. Lepr. **46** (1977) 14-23. (In Japanese)

A simple and rapid method for collecting leprosy bacilli from infected tissues was sought in order to obtain purified bacilli for metabolic investigations.

The results are summarized as follows. Murine leprosy bacilli were collected from leprous spleens of mice by repeated centrifugation, followed by the treatment of crude bacillary fraction with water adjusted to pH 10.5 and shaking at 37°C for 60 minutes. The bacilli obtained by this method were found to be almost free from host tissue components by the test for acid phosphatase and β-glucuronidase activities which are involved in lysosomes of host tissues, in addition to microscopic and electron microscopic analyses. The bacillary preparations thus obtained showed high activities of mycobacterial enzymes such as FAD-dependent NADPH-cyt.c reductase and NADH-cyt.c reductase. The human leprosy bacilli, collected from armadillo leproma by this method, were also pure microscopically and enzymatically and were shown to maintain the ability to incorporate label from L-methionine-$^{14}CH_3S$ into bacterial lipids.

From these results, the influence of alkaline treatment employed for collecting bacilli from infected tissues on bacterial enzyme activities was discussed—(*Adapted from* English summary)

Mori, Tatsuo. Cultivation of *Mycobacterium leprae* on modified 1% Ogawa yolk media. Jap. J. Lepr. **46** (1977) 48-51. (In Japanese)

Follow-up experiments of Ogawa's method for cultivation of *Mycobacterium lepraemurium* were conducted by Kozeki and Mori. This steadfast method of isolation of *M. lepraemurium* may be regarded as having been established. Now it is urgently necessary that this method should be applied to cultivation of *M. leprae* encouraged by success in the case of *M. lepraemurium*. As was found in the past from a biochemical study of *M. lepraemurium* that it might be injured by excess of oxygen (Prabhakaran reported that *M. leprae* has diphenoloxidase and the diphenol might play an important role in *M. leprae* metabolism) some suitable reducing agents and diphenol compounds must be used in culturing *M. leprae*.

Inhibition tests for some reducing agents and diphenol compounds were carried out by using *M. lepraemurium* and 1% Ogawa yolk medium. The suitable concentrations of DOPA, cystein, thioglycolate and adrenalin were 31γ -62γ, 31γ, 15γ -31γ and 10γ per ml, respectively. The other reducing and modified reagents were unsuitable for the growth of *M. lepraemurium*. The leproma materials were cultivated for one year at 30°C to 35°C on 1% Ogawa yolk media modified with 33.3γ/ml DOPA, 33.3γ/ml l-cystein, 17γ/ml thioglycolate and 10γ/ml l-adrenalin. Materials from eight patients in the National Leprosarium Airakuen, three from one patient in the National Leprosarium Nanseien, one sent from Professor Nakamura, one from the National Leprosarium Seishoen, and three from three new patients in our clinic were cultured. The results of all experiments were negative even when cultivated under the 5% CO_2, 1% oxygen and nitrogen condition.—*(Adapted from* English summary)

Mori, Tatsuo. Cultivation of *Mycobacterium lepraemurium* under low oxygen tensions. Jap. J. Lepr. **46** (1977) 44-47. (In Japanese)

Cytochrome b_1 and cytochrome a_2 were detected in *in vivo* and *in vitro* grown *Mycobacterium lepraemurium;* however cytochrome c and cytochrome a were not found. Cytochrome a_2 is a complex of D and C type cytochrome which is mainly seen in *Pseudomonas aeruginosa* grown under anaerobic conditions and is not seen in bacteria grown under aerobic conditions. *Mycobacterium lepraemurium* was grown under aerobic conditions on 1% Ogawa yolk medium; however the growing place of the organisms could have a fairly anaerobic condition because cytochrome a_2 was found in this organism. When a few bacteria were inoculated on 1% Ogawa yolk medium, the organism was unable to make an optimal anaerobic condition on this medium. A trial of the cultivation of *M. lepraemurium* was then made by the author under low oxygen tension.

Media were put in a glass desiccator and exchanged with the gas mixture through a sponge gum cap. The gas mixture was added to the desiccator once a week. The gas mixture was composed of 5% CO_2, 1% O_2 and 96% N_2 which gave the best result for cultivating a few organisms, but no colony formation was obtained in the case of the inoculation with 10^5 bacilli. In the primary isolation of *M. lepraemurium* 100% success was not obtained, especially difficult was primary isolation from infectious tissue containing relatively few numbers of bacilli. The low oxygen condition was better than normal air conditions. Primary isolation from ten times diluted inoculum failed in normal air condition, but succeeded on some tubes in 1% condition. Primary isolation of *M. lepraemurium* from tissue culture of A31 cells which contained less bacilli than the murine leproma is also possible in 1% O_2 condition.—*(Adapted from* English summary)

Ogawa, Tatsuji. Studies on the murine leprosy bacillus. XIV. Some observations on primary and secondary cultures of *M. lepraemurium:* gross appearance and transplantability of primary isolates and occurrence of smooth variants during serial culture passage. Jap. J. Lepr. **46** (1977) 29-36. (In Japanese)

In preceding papers several reports were made on the *in vitro* cultivation of *M. lepraemurium*. This paper describes further observations on the primary and secondary cultures of this organism.

1. *Gross appearance and transplantability of primary isolates.* Macroscopically the primary cultures of *M. lepraemurium* isolated on the egg yolk slant may be divided into three groups: 1) discrete colonial growth; 2) growth on a debris of the tissue homogenate inoculated, either colonial or membranous; 3) membranous growth. Although each

growth was obtained from various kinds of materials, cultures from tissues with large amounts of bacilli had a tendency to develop into group 2 or 3, and the ones from tissues with a smaller amount into group 3. The positive rate of the first passage of primary isolates varied over a wide range depending on the type of growth; namely the rate of those cultures which appeared as 1) colonial growth, 2) colonial or membranous growth on the debris, and 3) membranous growth which was 84%, 50% and 28%, respectively.

2. *Occurrence of smooth variants during serial passages.* Cultures of *M. lepraemurium* on the egg yolk slant are originally rough but during serial passages they occasionally become smooth. Retrospective analysis on the occurrence of smooth variants was made on a total of 2,118 subcultures of Hawaiian strain and of 257 subcultures of Keishicho strain during the course of their respective 20 and 16 passages. Smooth variants occurred in the 7th to 14th passage and rate of occurrence was found to be 0.7% and 2.3%, respectively. Gross appearance of the primary isolate and the kind of tissue material used for primary isolation bore no relation to the occurrence of smooth variants. The *in vitro* characteristics of smooth variants were the same as those of the original rough ones, except that the former were more easily emulsified.—*(Adapted from* English summary)

Olitzki, Aryeh L. Cultivation of *Mycobacterium leprae.* Lancet **1** (1977) 196. (Letter to Editor)

Shukla *et al* (1976) report that *M. leprae* multiplied simultaneously with a *Blastomyces* and staphylococci on two Sabouraud media, the first containing penicillin and streptomycin as protection against contamination, the second containing desiccated human thyroid as well. On the second medium the growth was three times more abundant than on the first. Godinger and I (1967) cultivated *M. leprae* on Eagle's medium containing human foreskin extracts and mycobacterial extracts prepared after ultrasonic vibration of culturable mycobacteria by filtration through Seitz filters. We also paid attention to the appearance of culturable acid-fast microorganisms in lesions of leprosy patients and differentiated them from the causative agent. Later, bacterial extracts originating from nonacid-fast microorganisms (e.g., yeasts and *Escherichia coli)* were tested (1975). These extracts too promoted the growth of *M. leprae.* Thus mistakes in counting, caused by acid-fast bacterial particles, were excluded.

Is *M. leprae* the only causative agent of leprosy in certain body regions or do concomitant microorganisms, which provide it with necessary sources of energy and building substances, contribute to the clinical symptoms of the disease?

In oxidation-reduction tests with cultures of *M. leprae* (Olitzki, 1976) D-, L-, and D, L-3, 4-dihydroxyphenylalanine (DOPA) were oxidized as described by Prabhakaran and Kirchheimer (1966) and simultaneously malachite-green oxalate was reduced to a colorless compound. Matsuo *et al* (1975) observed growth enhancement of *M. leprae* in the abdominal wall of mice in the presence of hyaluronic acid and growth suppression by saccharic acid and vitamin C, both inhibitors of β-glucuronidase. I have observed enhanced *in vitro* multiplication of *M. leprae* in the presence of 0.2-1.0% glucuronic or galacturonic acid, and also in the presence of 0.5-2.0% citric and pyruvic acid, but a strong inhibition by gluconic acid, even at concentrations of 0.02-0.5%. These experiments were done on the medium NM3 (Olitzki, 1976).—*(Adapted from* author's letter)

Sato, Norio and Fieldsteel, A. Howard. New method for concentration and quantitation of *Mycobacterium leprae.* J. Clin. Microbiol. **5** (1977) 326-328.

A new method of enumerating *Mycobacterium leprae* has been developed. Suspensions containing the organisms were filtered through a polycarbonate membrane filter (25 mm diameter, 0.4 μm pore size, 10 μm thick; Nuclepore) to concentrate the organisms. The membrane was then mounted on a glass slide and stained with a standard acid-fast stain. Finally, the membrane was treated with a small amount of chloroform to fix it to the slide and make it transparent. This method enabled us to detect *M. leprae* in quantities as small as 4.98×10^2 regardless of the total volume of the original material. Comparison with a standard method for enumerating *M. leprae* showed

that both methods gave similar results when the organisms counted by the standard method were present in sufficient quantity for reproducibility. Because the least number of organisms that can be detected with the standard method is 10^4 ml and because the organisms detected with the new method could be concentrated on the polycarbonate filter from a large amount of infected fluid, a substantial number of suspensions were shown by the new method, but not by the standard method, to contain *M. leprae.*—Authors' Abstract.

Tsukamura, M. Numerical classification of slowly growing mycobacteria. Int. J. Systematic Bacteriol. **26** (1976) 409-420.

A total of 138 strains of slowly growing mycobacteria, which were received as members of 18 named species, were classified by scoring matching coefficients. Eighty-eight characters were tested for each strain; of these 48 were useful for differentiating between stains. *Mycobacterium tuberculosis* and *M. bovis* were clearly separated from the other species. *M. kansasii, M. marinum, M. gastri,* and *M. shimoidei* were regarded as species clearly distinct from each other and from other species in the genus. The other species studied formed a large cluster within which *M. szulgai* and *M. simiae* were distinct. The remaining species could be divided into two large subclusters, one consisting of *M. asiaticum, M. avium, M. intracellulare, M. scrofulaceum, M. gordonae,* and *M. xenopi,* and the other consisting of *M. nonchromogenicum, M. terrae, M. novum,* and *M. triviale.* Within the former cluster, *M. gordonae* was regarded as a distinct species, and *M. asiaticum* and *M. xenopi* as fairly distinct species. In contrast to these, *M. avium, M. intracellulare,* and *M. scrofulaceum* were not clearly differentiated from each other and appeared to belong to a single species, for which the name *M. avium* has priority. Within the latter cluster, *M. triviale* appeared to be fairly distinct from the others. *M. nonchromogenicum, M. terrae,* and *M. novum* could not be differentiated from each other, and they appear to belong to a single species, for which the name *M. nonchromogenicum* has priority.—Author's Abstract.

Yamagami, Akira and Chang, Yao T. Growth of *Mycobacterium lepraemurium* in cultures of macrophages obtained from various sources. Infect. Immun. **17** (1977) 531-534.

Studies were made on the growth of *M. lepraemurium* in cultures of macrophages obtained from various sources, such as bone marrow, spleen and blood of mice. Macrophages were maintained in good condition for more than 12 weeks. Marked intracellular multiplication of *M. lepraemurium* was observed in cultures from all three sources. Whereas *M. lepraemurium* freshly prepared from the animals showed good growth in the cultures, those that were kept at 4°C for 10 or 14 days showed no growth.—Authors' Abstract

Experimental Infections

Binford, C. H., Meyers, W. M., Walsh, G. P., Storrs, E. E. and Brown, H. L. Naturally acquired leprosy-like disease in the nine-banded armadillo *(Dasypus novemcinctus)*: histopathologic and microbiologic studies of tissues. J. Reticuloendothel. Soc. **22** (1977) 377-388.

Histopathologic studies were conducted on tissues from necropsies on 41 nine-banded armadillos from Louisiana with a natural disease resembling lepromatous leprosy, hereafter often referred to as the "natural disease." The lesions were composed of macrophages (histiocytes) containing numerous acid-fast bacilli and were similar to those seen in armadillos experimentally inoculated with *Mycobacterium leprae.* Invasion of small and large nerves by phagocytes containing acid-fast bacilli was a characteristic feature of the natural disease. The *Mycobacterium* presumed to cause the disease was not cultivable on standard mycobacterial media; however, mycobacteria belonging to the *M. avium-intracellulare* group were cultivated from lymph nodes of 8 and the spleen of 1 of 32 of the diseased armadillos but not from other organs. Cultures of lymph node

specimens and other organs from each of the remaining 24 diseased armadillos were negative. Acid-fastness of the bacilli in all tissues was abolished on exposure to pyridine. The bacilli were DOPA oxidase positive, but interpretation of this finding is difficult because some tissues from normal armadillos also gave positive reactions in the spot test employed. Histopathologic studies of tissue from autopsies on the 41 armadillos and microbiologic studies on tissues from 32 of the animals provided evidence indicating that the cause of the natural disease in armadillos may be *M. leprae.*—Authors' Abstract

Bullock, Ward E. and Vergamini, M. Sue. Impairment of lymphocyte mobilization from lymphoid organs by granulomatous infection. Cell. Immunol. **29** (1977) 337-346.

The kinetics of the lymphocytosis induced by intravenous (iv) injection of the lymphocyte mobilizing agent polymethacrylic acid (PMAA) were studied in C3H mice chronically infected with *Mycobacterium lepraemurium* and in normal controls. After the tenth week of infection, lymphocyte mobilization to peripheral blood by PMAA diminished progressively and at 18 weeks it was significantly less than normal ($p < 0.05$). ^{51}Chromium-labeled lymph node cells from syngeneic donors were given i.v. to 18-week infected or control mice and allowed to home for 18 hours prior to PMAA injection. Radioactivity in the blood of infected mice was significantly less than the levels in controls 2, 4, and 6 hours after PMAA ($p = 0.02$). Similar studies of splenectomized mice from the normal and infected groups indicated that impairment of lymphocyte mobilization in infected mice was secondary to lymphocyte trapping by the spleen and lymph nodes.—Authors' Abstract

Collins, Frank M. and Auclair, Linda. Lymphatic drainage in BCG-infected guinea pigs. J. Reticuloendothel. Soc. **22** (1977) 35-44.

Normal strain 2 guinea pigs were injected subcutaneously via the foot pads, intradermally into midflank skin, or intramuscularly in the triceps or vastus muscles with Chicago Blue dye or with living *Mycobacterium bovis* (BCG Pasteur). Pigs were sacrificed 1, 4 and 24 hours later and the presence of dye in the various draining lymph nodes was determined macroscopically. Viable BCG counts were carried out on saline homogenates of each lymph node and the drainage patterns seen following the three different inoculation routes were compared. Viable BCG spread from the site of implantation to the primary draining lymph node within an hour, but recoveries of viable organisms at 24 hours represented only about 1% of the inoculum. There was a similar drop between the primary and secondary node counts and bacilli did not appear in the spleen until 14 to 21 days. Some bacterial growth may have occurred in the primary node over the first 14 days of the infection but, once BCG appeared in the spleen, the peripheral viable counts declined, both at the original site of implantation and in the draining nodes. The significance of these changes in terms of the use of BCG in the immunotherapy of cancer in the guinea pig model is discussed.—Authors' Abstract

Kawaguchi, Yoichiro and Matsuoka, Masanori. Observation of host reactions to murine leprosy bacilli in spread subcutaneous tissue preparations of various strains of mice. Jap. J. Exp. Med. **47** (1977) 71-79.

Matsuoka, Masanori and Kawaguchi, Yoichiro. Observation of *M. lepraemurium* in subcutaneous tissue of mice by spread tissue preparations. Jap. J. Lepr. **46** (1977) 37-43. (In Japanese)

Male mice of six inbred strains (C3H, CF#1, KK, BALB/C, DDD and C57BL/6) were inoculated subcutaneously in the back with 0.25 ml of a 1:1000 leproma suspension (Hawaiian strain). Growth patterns of murine leprosy bacilli in subcutaneous tissue at the inoculation site were examined on the spread tissue preparations.

No remarkable differences were observed among these mouse strains during the first three weeks after inoculation. An acute inflammatory reaction with accumulation of many polymorphonuclears disappeared in one week and elongation of the bacilli was evident in mononuclears without increase in number. The bacilli were about two to three times as long as the initial length. At two weeks the elongated bacilli were fairly abundant within the cells, but some were present extracellularly. At three weeks enlarged

mononuclears, being crowded with long bacilli, could easily be demonstrable by low magnification. Four weeks after inoculation, however, significant differences in the growth patterns were seen among these mouse strains. In C3H and CF#1 mice, an infiltrate consisting mainly of mononuclears was seen in the subcutaneous tissue at the inoculation site. Most of the mononuclears were heavily loaded with the long bacilli and were scattered or accumulated in the whole specimens. In contrast, lymphocytes and polymorphonuclears were predominant in the other four strains of mice, and they surrounded a smaller number of mononuclears containing the long bacilli. Such difference between mouse strains became more remarkable at five weeks because of more pronounced cellular reactions in these four strains. The difference between C3H and CF#1 mice was manifested in 8 to 10 weeks by infiltration of lymphocytes, surrounding accumulated mononuclears loaded with the bacilli, which was seen only in CF#1 mice.

The mouse strain differences as above in response to murine leprosy bacilli are discussed on the basis of cellular immunity in the hosts.—*(Adapted from* authors' summary) [*These appear respectively to be the English and Japanese presentations of the same work. The abstracts for each are very similar. The abstract here presented is from the English publication.*—Ed.]

Levy, Louis and Peters, John H. Some characteristics of the action of dapsone on multiplication of *Mycobacterium leprae* in the mouse. Lepr. Rev. **48** (1977) 237-245.

In a number of experiments, male BALB/c mice were inoculated with *Mycobacterium leprae* and administered dapsone (4,4′-diaminodiphenylsulfone, DDS) incorporated into the mouse chow in concentrations of 10^{-2} to $10^{-4.5}$ gm% for periods of about 90 days during logarithmic multiplication of the organisms. Both the duration of the delay between beginning treatment and the onset of inhibition of bacterial multiplication and the duration of the delay between cessation of treatment and resumption of bacterial multiplication were dependent on the dosage of DDS. The number of doublings of *M. leprae* after the start of DDS treatment appeared more sensitive to minor variations of DDS concentration than the duration of the delay of resumption of multiplication after treatment was stopped.—Authors' Abstract

Meyers, W. M., Walsh, G. P., Brown, H. L., Rees, R. J. W. and Convit, J. Naturally acquired leprosy-like disease in the nine-banded armadillo *(Dasypus novemcinctus)*: reactions in leprosy patients to lepromins prepared from naturally infected armadillos. J. Reticuloendothel. Soc. **22** (1977) 369-375.

Lepromins prepared from six armadillos with a naturally acquired leprosy-like disease in Louisiana were assayed in 146 leprosy patients with lepromatous and nonlepromatous leprosy. The patients resided in Ethiopia, Malaysia, Venezuela and Zaire. The classic pattern of Mitsuda reactions was observed. Whereas patients with lepromatous leprosy gave weak or negative reactions, those with nonlepromatous leprosy gave positive reactions. Because *Mycobacterium leprae* is the only microorganism known to give this pattern of response, these data indicate that the organism responsible for the naturally acquired leprosy-like disease of armadillos in Louisiana is closely related to, if not identical with, *M. leprae.*—Authors' Abstract

Narayanan, E., Sreevatsa, Kirchheimer, W. F. and Bedi, B. M. S. Transfer of leprosy bacilli from patients to mouse foot pads by *Aedes aegypti.* Lepr. India **49** (1977) 181-186.

Aedes aegypti mosquitoes which were first allowed to feed on untreated lepromatous leprosy patients, and then to refeed on mouse foot pads were found to transfer *Mycobacterium leprae* to the foot pads as seen by the subsequent multiplication of the bacilli in the foot pads. Results presently available are insufficient to come to any conclusion about the actual role of mosquitoes in the transmission of leprosy in the field.—Authors' Abstract

Rees, R. J. W. and McDougall, A. C. Airborne infection with *Mycobacterium leprae* in mice. J. Med. Microbiol. **10** (1977) 63-68.

This study was designed to investigate the possibility of airborne infection with *Mycobacterium leprae.* The authors used thymec-

tomized irradiated mice exposed to aerosols containing *M. leprae* with an immediate lung retention of 1×10^5 bacteria. Fourteen to twenty-four months later, 10 of 30 mice had considerable numbers of acid-fast bacilli with the characteristics of *M. leprae* in one or more homogenates prepared from ears, foot pads, nose or lungs. Evidence is presented from the distribution of *M. leprae* that the infection had arisen from the systemic spread of bacilli initially entering the lungs, rather than from the multiplication of organisms locally retained there, or in the nose, at the time of airborne infection. The relevance of these results to the possible route of infection with leprosy in man is discussed. —T. F. Davey *(Adapted from* Trop. Dis. Bull.)

Walsh, G. P., Storrs, E. E., Meyers, W. and Binford, C. H. Naturally acquired leprosy-like disease in the nine-banded armadillo *(Dasypus novemcinctus)*: recent epizootiologic findings. J. Reticuloendothel. Soc. **22** (1977) 363-367.

Fifty armadillos from 12 locations have been found with a naturally acquired disease caused by an agent that is indistinguishable from *Mycobacterium leprae*. Forty-seven of the animals were from 459 examined from 11 locations in Louisiana. Two were from unknown locations in Louisiana and one animal was from eastern Texas. Most of the infected animals were initially diagnosed by the examination of ear specimens.—Authors' Abstract

Watson, S. R., Brown, I. N. and Sljivic, V. S. Enhancement of the antibody response *in vitro* by adherent cells from mice infected with *Mycobacterium lepraemurium*. Infect. Immun. **17** (1977) 263-267.

Spleen cells from mice systemically infected four to six weeks previously with *M. lepraemurium* gave an enhanced primary antibody response *in vitro* to sheep erythrocytes, but responded normally to dinitrophenylated polymerized flagellin. The ability to enhance the response was associated with the glass-adherent spleen cell population and with peritoneal cells. Similar cells obtained from infected mice depleted of T lymphocytes failed to enhance the antibody response. These studies suggest that macrophages that become activated during the development of cell-mediated immunity to infection can also stimulate antibody responses to thymus-dependent antigens.—Authors' Abstract

Epidemiology and Prevention

Forbes, John A. Management of leprosy in Victoria. Med. J. Aust. **2** (1977) 30-32. (Letter to Editor)

The comments in the article "Doctor Attacks Leprosy Care" published in THE AGE on Friday, May 6, 1977, are ill-informed and misleading and prompt me to describe the principles of management of leprosy in Victoria.

The procedures adopted with any infective disease necessarily vary with the resources available in the countries in which they occur, and in Victoria where the appropriate facilities are available, optimum care may be achieved. As with other infections, management of patients with leprosy is governed by the medical requirements of the individual patients (which differ widely, depending on the type and stage of the disease), and having regard for the need to protect the family and close contacts from unnecessary risk. Not all leprosy patients are an infective risk to their close associates, but some of them are in varying degrees. Fortunately, particularly in the light of recent advances, these patients may be assessed and readily treated. Treated early, the disease can be cured and an increasing array of suitable drugs has made this more certain in recent years.

When the disease is first recognized in a patient, it is desirable that the initial assessment and treatment be undertaken in a hospital where specialized facilities and personnel are available: 1) to assess their infectivity and need for isolation from household contacts for periods of weeks or a few months until treatment has obviated the risks of transmission. With early treatment, this is a brief period, and usually involves a sanator-

ium-like rather than a hospital existence. With simple precautions, visitors are encouraged; 2) to manage the frequent complications of drug treatment and institute a safe regimen of drug treatment for continuation when discharged; and 3) to treat aspects of the disease which necessitate hospital care. Patients need hospital care not only for these reasons, but also, at times, complications necessitate admission to a hospital, perhaps repeatedly, for appropriate treatment. This is not to be confused with admission for isolation. There are other instances which are avoidable and, it is to be hoped, rare in which the disease has been allowed to progress untreated for many years giving rise to complications secondary to nerve damage, such as paralysis, anesthesia and trophic ulcers, which necessitate sanatorium-type care. As in the case of tuberculosis, surveillance and early diagnosis of family contacts is an important and successful public health aspect the continuity of which can only be provided by institutional care.

Leprosy, as it is well known, is not confined to the skin but is capable of involving all organs and often produces incapacitating deformities when neglected. Failure to provide the service described here in this community would be unacceptable to those with responsibility in this field both on humanitarian and on public health grounds. In this context, it is reassuring that leprosy is not an indigenous disease in Victoria and need not become one. The National Health and Medical Research Council recommendation that "every attempt should be made by the States and Territories to avoid unnecessary isolation by providing proper facilities for regular outpatient treatment" in no way disagrees with Victorian policy. The traditional fear of leprosy has largely been subdued by readily available efficient treatment, and indeed the risks of infection of others, particularly members of the patient's family, are much reduced by early treatment. The apprehension engendered by a misrepresentative article serves to deter patients from early diagnosis and cure before irreversible changes occur.—(*Adapted from* author's letter)

Ramasoota, T., Samputtavanich, S., Ochasanendha, P. and Ito, T. Results of five years of integration of leprosy control into the provincial health service of Phuket Island, Southern Thailand. Lepr. Rev. **48** (1977) 261-268.

Five years experience of integration of leprosy control in Phuket Island, Southern Thailand, showed that known cases of leprosy had increased by 251% from 0.77 to 1.93 per thousand, through the efforts of local health workers; and by 318% from 0.75 to 2.45 per thousand on a second survey conducted in the fifth year of integration. Local health workers detected 43% of total registered cases, the remaining cases being found by a specialized leprosy survey team.

The accomplishment of three main targets in leprosy control, namely treatment, contact examination and bacteriologic smears had gradually declined by 35% from 66 to 31% indicating a great need for better supervision and motivation. Adequate survey before integration was also necessary, followed by regular supervision and field guidance to promote proper efficiency and effectiveness of leprosy control.—Authors' Abstract

Saikawa, Kazuo. Epidemiologic study of leprosy in Okinawa Island. Third report. On the islets. Jap. J. Lepr. **46** (1977) 1-7. (In Japanese)

The Okinawa Archipelago consists of 72 islands in which 48 have a small population; most of them are isolated and have had little social communication and interchange between each other for a long time. These islands are suitable fields for the study of the leprosy epidemiologic status and pattern.

Data on the leprosy annual incidence rate (IR), lepromatous annual incidence (LIR), lepromatous ratio (L ratio) and child ratio (C ratio) have been collected from ten of the islands since 1931. New leprosy cases were sometimes not considered as newly manifested patients for the respective year because leprosy is chronic and usually takes several years for the patient to be diagnosed as having leprosy after development of the disease. Therefore, the facts are counted by five year periods. This becomes clear after the epidemiologic assessment on the data of the islands is presented: 1) leprosy in the islands of Iheya, Ie, Aguni, Tonaki and Zamani is almost eradicated; 2) leprosy in the islands of Irabu, Tarama and Kume is still endemic and new cases are predicted for the future; 3) leprosy in the island of Yonaguni is still highly endemic.

According to final data analysis the leprosy epidemiologic patterns indicated by graphs are as follows: 1) in the high leprosy endemic stage the graph of IR, LIR, L ratio and C ratio show equal increases and are located in the higher level; 2) in the eradication stage all four graphs show a decline parallel to each other located in the lower level or reaching zero, in this case C ratio precedes the other three graphs in its decline or zero level.—(*Adapted from* English summary)

Saikawa, Kazuo. Epidemiologic study of leprosy in Ryukyu Island. Fourth report. Leprosy in urban areas. Jap. J. Lepr. **46** (1977) 8-13. (In Japanese)

Recently the epidemiologic improvement with respect to leprosy in the Ryukyu Island was observed. The leprosy prevalence rate (PR) and leprosy incidence rate (IR) were 1.97% and 0.088% in 1970; while in 1975 the PR and IR were 1.34% and 0.059%. Generally, the leprosy epidemiologic status in Ryukyu improved after the reversion of the island to Japan in 1972. The drift of population to the urban areas from rural areas has occurred since 1971, more so after the reversion. The rural areas (Miyako Islands, Yaeyama Islands and other islands in Okinawa) are sparsely populated, while the urban areas (Naha City, Urazoe City and their outskirts) have rapidly grown in population.

According to the population drift, the geographic status of leprosy endemicity in Ryukyu has changed since 1971. The following changes were observed regarding the place of leprosy onset: in Naha City (urban area) the total number of newly-detected patients was only 5 (IR 0.017%) in 1969, but increased to 20 in 1974 (IR 0.065%); in the Miyako Islands (rural area) the number was 38 (IR 0.552%) in 1969, but decreased to 17 in 1974 (IR 0.293%).

Other statistics are as follows. The ratio of the annual newly-detected patients in Naha City to the total number on Ryukyu Island was 5.2% in 1969 and 28.2% in 1974; but the ratio in the Yaeyama Islands was 21.6% in 1969 and only 7% in 1974. Therefore, before the reversion the endemic pattern of leprosy was as follows: leprosy infection and onset occurred in the same place in rural areas. After the reversion the pattern changed to leprosy infection occurring in rural areas and developing in urban areas. The phenomenon of the change of place of leprosy onset in Ryukyu after the reversion seems to be caused by the movement of population, social development in rural areas, and also by the improvement of the leprosy endemic status in the islands.

From the facts presented it may be concluded that leprosy control programs in urban areas in Ryukyu should be emphasized more in the future.—(*Adapted from* English summary)

Vinet, J. La lèpre dans l'Empire Centrafricain. [Leprosy in the Central African empire.] Afr. Med. **16** (1977) 365-367. (In French)

Epidemiologic trends of leprosy in the Central African empire are reviewed together with control measures. Annual incidence (most likely detection rates) have shown marked variations, from 0.86 [presumably percent] in 1953 to 0.07 in 1975. Prevalence was 2.6% in 1953 and 0.99% in 1975. Distribution shows geographical differences with a hyperendemic focus in the central and eastern parts of the country. New cases include 16% children. It is concluded that control measures undertaken for the last 20 years have not succeeded in interrupting transmission.—(*Translation by* M. F. Lechat)

World Health Organization. Leprosy control. Review of technical cooperation and the available funds. WHO Chronicle **31** (1977) 506-511.

The actual number of leprosy cases requiring treatment in the world is not known. In 1970, there were close to three million registered patients but a conservative estimate of the total number of cases was over ten million (6.5 million in Asia, 3.5 million in Africa, and 350,000 in the Americas). During 1976-1977, questionnaires were distributed to countries through WHO Regional Offices and the results, when available, will give an up-to-date appraisal of the leprosy situation. The article, which is based on the Director-General's report to the World Health Assembly this year, describes WHO's efforts in technical cooperation to control leprosy in various regions and the available resources for carrying out this work.—Author's Abstract

Rehabilitation

Hamilton, Jean M. The place of electrical stimulation in the physiotherapy of leprosy. Lepr. India **49** (1977) 197-206.

The production of nerve and muscle impulses by faradic and interrupted direct current, and the "strength-duration curves" plotted for normal, denervated, and partially denervated muscles are described. The advantages and disadvantages of such electrical stimulation in the testing of recent paralysis, the treatment of recent paralysis, and following tendon transfer surgery in leprosy patients are discussed. In the light of these, electrical stimulation is concluded to have only a minor role in the physiotherapy of leprosy.—(*Adapted from* author's abstract)

Other Mycobacterial Diseases and Related Entities

Behl, P. N. and Pradhan, B. K. Neuronal studies in vitiligo. Indian J. Dermatol. Venereol. Leprol. **43** (1977) 133-137.

Forty-eight cases of vitiligo including six cases of segmental zosteriformis variety were subjected to histologic examination to study the peripheral nerves. All three components of the peripheral nerve, viz., axis cylinders, myelin sheath and Schwann cell nuclei were examined with special strains. No structural damage to the nerve either in vitiliginous or adjacent normal skin or below the junctional area could be demonstrated even in lesions of long duration. Hence the implication of organic damage to the nerve fibers in the etiology of vitiligo, as has been suggested in the literature, requires reconsideration.—Authors' Summary

Boisvert, H. L'ulcère cutané a *Mycobacterium ulcerans* au Cameroun. II. Étude bactériologique. [*Mycobacterium ulcerans* infection in Cameroon. II. Bacteriologic study.] Bull. Soc. Pathol. Exot. **70** (1977) 125-130. (In French)

Nine strains of *M. ulcerans* isolated in Cameroon, in the Congo, and in France, were compared with six reference strains found in Zaire, Australia and Mexico, and *M. intracellulare, M. simiae, M. paratuberculosis.* These 15 strains constitute a species whose typical features were: difficult and slow growth at the optimum temperature of 30°C, biochemical tests showing sensitivity to rifampin, streptomycin, kanamycin, viomycin, cycloserin and probably capreomycin. In mice inoculated by the intravenous route, *M. ulcerans* provoked ulceration of external teguments and sometimes internal lesions.—(*Adapted from* English summary)

Engbaek, H. C., Vergmann, B. and Bunch-Christensen, K. Pulmonary tuberculosis due to BCG in a technician employed in a BCG laboratory. Bull. WHO **55** (1977) 517-520.

X-ray examination of the lungs of a laboratory technician in the BCG Department of the Statens Seruminstitut, Copenhagen revealed a lung tumor and possible signs of tuberculosis. The diagnosis was confirmed by macroscopic and histopathologic examination of lung tissue removed by surgery. Subsequent bacteriologic examination showed the infection to have been caused by BCG. The possibility is discussed of whether the condition had developed from a metastatic lesion following BCG vaccination, or was the result of an aerogenic infection during the production of BCG vaccine. The simultaneous development of the tuberculous condition and the tumor is remarkable but is not discussed further. The requirements of WHO when signs of tuberculosis are found in a worker in a BCG laboratory were complied with in this instance, but it was not considered necessary to change the routine procedure in the BCG Department.—Authors' Abstract

Ipp, M. M., Minta, J. O. and Gelfand, E. W. Disorders of the complement system in lipodystrophy. Clin. Immunol. Immunopathol. (1977) 281-287.

Studies of the complement system have been carried out in ten patients with lipodys-

trophy. Only the partial form (PLD) was associated with complement abnormalities in six out of seven patients. These patients were hypocomplementemic (low C3) and an anticomplementary factor was isolated and partially purified from the serum of five of the patients. One PLD patient and three patients with total lipodystrophy (TLD) had normal complement profiles. In parallel studies with the serum from a patient with membranoproliferate glomerulonephritis (MPGN), it was shown that the anticomplementary factor in PLD had similar functional activity and physicochemical properties to the C3 nephritic factor (C3NeF) of MPGN.—Authors' Abstract

Nyka, W. The chromophobic tubercle bacilli and the problem of endogenous reactivation of tuberculosis. Materia Medica Polona **3** (1977) 175-185.

The antituberculosis drugs have dramatically reduced the incidence of acute ulcerative tuberculosis, the main source of exogenous infection, but the rate of new cases of active disease has not only not declined proportionately but shows a tendency to increase. As a result the endogenous origin of the disease, long considered to be only of academic interest, is now widely accepted. The pathogenesis of endogenous reactivation can be understood on the basis of the new concept of the two-phase nature of *M. tuberculosis*. Acid-fast bacilli do not die and disappear in the caseous lesions as is generally supposed, but survive in their metabolically inactive chromophobic forms. Since these have been demonstrated to be extremely resistant to adverse environments, indifferent to drugs and reversible, the opinion is warranted that they may recover their original characteristics and reactivate the disease after years of clinical healing.—*(Adapted from* author's summary). [*It has long been known that arrested, encapsulated and caseous tuberculous lesions may contain viable bacilli virulent for animals; e.g., Am. J. Pathol.* **9** *(1933) Suppl. M; Am. J. Pathol.* **15** *(1939) 473.*—Ed.]

Ravisse, P. L'ulcère cutané a *Mycobacterium ulcerans* Au Cameroun. I. Ètude clinique, épidémiologique et histologique. [*Mycobacterium ulcerans* infection in Cameroon. I. Clinical, epidemiological and histopathological study.] Bull. Soc. Pathol. Exot. **70** (1977) 109-124. (In French)

The clinical, epidemiological and histopathological aspects of *M. ulcerans* infection in Cameroon are presented including a report of 47 cases with isolation of eight strains of *M. ulcerans.*—*(Adapted from* English summary)

Smith, P. G., Revill, W. D. L., Lukwago, E. and Rykushin, Y. P. The protective effect of BCG against *Mycobacterium ulcerans* disease: a controlled trial in an endemic area of Uganda. Trans. R. Soc. Trop. Med. Hyg. **70** (1976) 449-457.

In 1967 the Uganda Buruli Group initiated a BCG trial in the control of Buruli ulcer among 2,557 Rwandan refugees at a settlement at Kinyara. There appeared to be a considerable protective effect in the first six months (72%) which then disappeared producing an average protection of 50% over the two years of the trial. A further trial was then planned among a stable population (not refugees) and the subcounty of Ibuje in the Lango District was selected. This area lies on the southeast bank of the Nile in flat swampy country, and is distinguished by a high incidence of Buruli ulcer (1.5% during the years 1968-1970).

In the period of July to September 1970 virtually the entire population (9,327 of 9,396) was examined for signs of previous or present ulcers and tuberculin tested (2 TU). There were finally 8,856 available for the trial. A total of 602 (6.8%) had evidence of previous or current ulcers, and 357 had scars of previous BCG vaccination. Those with a tuberculin reaction of a diameter less than 20 mm in children and 10 mm in adults were divided randomly into two groups. One group of 2,775 received BCG; the control group of 2,764 did not. One year later the population was reexamined and 7,210 (81.4%) were seen. A repeat tuberculin test was done and new ulcer infections looked for. Finally all cases presenting with ulcers at health centers and hospitals in the next three years were investigated. The results are set out and analyzed in various tables. It was shown that the BCG vaccination was effective by a marked shift in the tuberculin reaction to greater size and positivity.

Development of the disease was found in 113 patients; 13 of these were eliminated for various reasons, leaving 66 cases who did not receive BCG, and 34 who had been vaccinated. Standardized for age and sex this represents a 47% protection, however this protection was largely in the first year (63%). In the last three years there was virtually no difference and this was associated with very few cases in either group. BCG seemed only to be of value to those whose initial tuberculin reaction was less than 4 mm. Nor was it of any value in those who had an initial BCG scar or evidence of previous ulcer infection. The lesions of Buruli ulcer in those who had had BCG but developed the infection were smaller than in those who had not been vaccinated.

The authors discuss but cannot explain the the curiously short-lived effect of BCG vaccination, so different from its value in other infections.—A. C. E. Cole *(Adapted from* Trop. Dis. Bull.)

Staples, P. J., Boujak, J., Douglas, R. G., Jr. and Leddy, J. P. Disseminated candidiasis in a previously healthy girl: implication of a leukocyte candidacidal defect. Clin. Immunol. Immunopathol. 7 (1977) 157-167.

A previously healthy 15-year-old white female presented with a nearly fatal *Candida albicans* fungemia, peritonitis, and several perforations of the stomach wall with evidence of *Candida* infiltration. Investigation of this patient's immunologic functions revealed no deficiency of anti-*Candida* antibody production, *in vitro* lymphocyte response to mitogens or *C. albicans* antigen, delayed cutaneous reactivity to *Candida* antigen, immunoglobulin levels, or serum complement activity. Candidacidal assays using the patient's peripheral blood leukocytes repeatedly gave values significantly below the normal range in both autologous and normal AB serum. This leukocytic defect was still demonstrable more than a year after full recovery from *Candida* sepsis. Phagocytosis of *C. albicans,* leukocyte bactericidal activity against gram-positive and gram-negative organisms, nitroblue tetrazolium dye reduction, myeloperoxidase levels, and oxidation of [1-^{14}C]glucose and [^{14}C]formate were normal. This patient apparently has a unique leukocytic defect for which final characterization must await newer methods of investigating leukocyte function.—Author's Abstract.