

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.

Epidemiology and Prevention

Rodrigues, I.: Leprosy control scheme among school children in Mangalore-St. Joseph's Leprosy Hospital. *J. Christian Med. Assn.* **45** (1970) 717-719.

This article records briefly the results of a school survey for leprosy, in which the survey included common skin diseases. A team of leprosy workers examined 19,689 children, among whom 329 cases were detected. Of these 6 were known contact cases receiving chemoprophylactic treatment. No contact survey in family members was carried out. Paramedical workers assisted in the follow-up work, and the teachers assisted in drug dispensing and control. The program seems to have been carried along with a minimum of social or psychological disturbance.—G.L. Fite

Santos, V. C.: A Problematica Social Do Egresso. (the social problem of the discharged patient.) *Publ. Cent. Est. Leprol.* **10** (1970) 93-103.

The social service of Parana, begun in 1951, was reorganized in 1961, to obtain adequate assistance for former patients grouped near the sanitarium "Sao Roque" in Piraquara township. The expatients prefer to live near the sanitarium, thereby forming a society peculiar to themselves. In 1966 a survey showed 285 patients living in 178 homes, 171 men and 114 women. All patients received financial and social assistance from the government.

This survey concludes that the integration of the former patient into society is very difficult, and that the financial assistance was unsatisfactory. To solve these problems the Social Service and the Division of Leprosy propose:

- a. sanitary education of the patients before leaving the sanitarium,
- b. amelioration of the financial assistance, and
- c. education of people in general about leprosy

From English summary by A. Ditchfield.

Yoshie, Y.: Results of the leprosy programme in Japan in the past 60 years. *Leprosy Rev.* **41** (1970) 9-13.

In all, 11 leprosaria have been established in the 60 years since 1907, and when private facilities are included, the total number of beds available has reached 13,300 or more. Patients with active leprosy who represent a danger by spreading bacilli are segregated in these leprosaria, and as a result of treatment the number of sufferers capable of infecting others is gradually decreasing in society at large. This is considered to have rapidly reduced the chances of leprosy spreading among close contacts, particularly among children of the patients' households.

The tendency towards a rapid decrease in new cases of leprosy in Japan cannot be considered to arise solely from the segregation policy followed; the improvement in national living conditions after World War II and the spread of up-to-date knowledge of sanitation and public health must also be considered as being important contributory causes.

It is hoped that the question of a possible relationship between BCG vaccination, which since 1948 is now given to all persons with a negative tuberculin reaction from the time they are babies, and the effect of the reduced number of new leprosy cases will be investigated in detail.—Author's Summary

Wheatley, B.: Pilot survey of a group of remote villages in Masasi District, Tanzania. *Leprosy Rev.* 41 (1970) 21-24.

This survey revealed that about 40% of the patients with leprosy in the area were not coming forward for treatment.

The survey confirmed the need to carry out a diagnostic search in the villages and schools, despite an apparently effective leprosy treatment scheme already in operation, and it has also demonstrated the size of the problem in this area. Even allowing for the fact that it has proved possible to discharge from the dispensaries about 15% of patients as clinically cured after 5 years' treatment, if all the potential patients are found and brought for treatment this will produce a considerably increased work load for the already hard-worked clinics. This is, however, a problem which now that its potential size is known, must be accepted and overcome if the Masasi Leprosy Scheme is to be successful for the necessary survey work. As a direct result of the present survey a new visiting point has been established between Napacho and Mburuza.—Author's Summary

Schulz, E. J., and Pentz, H. H. L.: Leprosy control in South Africa. *Leprosy Rev.* 41 (1970) 15-19.

In view of the declining prevalence of the disease even before the introduction of sulphones, one may conclude that the isolation of patients as practised in South Africa has played an important part in controlling the disease, although improvements in standards of living must also play a role. In South Africa it has been possible, because of favourable economic circumstances and the small number of cases, to carry out a humane policy of compulsory isolation. The institutionalization of all patients with active leprosy, apart from controlling the spread of the disease, also insures that patients receive adequate treatment.—Author's Summary

Bogaert Diaz, H.: Lucha Antileprosa En Republica Dominicana. (A n t i - leprosy

campaign in the Dominican Republic.) *Rev Dominicana de Dermat.* 4 (1970) 102-109.

There were 776 cases of leprosy registered with the department of public health at the close of 1965. During 1966 and 1967, 451 cases were added, an additional 494 were listed during 1968 and 1969, and a further 142 during the first five months of 1970, a total of 1863 cases.

A new antileprosy activity was launched in February 1966, accounting for the discovery of the new cases. Of the earlier registered 776, 414 were lepromatous, but the ratio was reversed in the added 1087 found during the 4½ year effort stemming from the Instituto Dermatológico. Here only 368 cases were lepromatous, as opposed to 719 indeterminate and tuberculoid. This almost 2 to 1 ratio probably presents the situation more accurately, suggesting that as in other campaigns milder cases are not registered unless actively sought.

A 1970 census shows the Dominican Republic's 4,011,589 people 40% urban and 60% rural in distribution, the leprosy index being 0.46 per 1,000. The actual and real number of cases is estimated as being 3 to 4 thousand, and the need for rehabilitation and treatment centers is shown by the significant degree of incapacitation found.

In the northern region along the Atlantic coast and the northern cordilleras the prevalence is the least, and the highest rate was observed in the national district, which includes the capital city, Santo Domingo. A significant number of newly recognized cases (16 to 21 per 100 during the final four years) were in individuals under 15 years of age.

Although much has been accomplished during the past 5 years, it is recognized that much still remains to be done, but it is hoped that during the decade of the 1970s leprosy work will be developed satisfactorily, thanks to the conjoint efforts of independent, private and governmental institutions.—G.L. Fite

Clinical Sciences

Noordeen, S. K.: Relapse in lepromatous leprosy. *Rev.* **42** (1971) 43-48.

The investigation based on a follow-up study of 125 lepromatous cases living in their natural environment and followed up for about 6 years, showed a relapse rate of 3.22% per year. It was also found that all the relapses occurred among those who, after becoming negative, either were very irregular in taking treatment or sought no treatment. The risk of relapse was found to decrease progressively with the number of years that passed after the patients attained a bacteriologically negative state.—Author's Summary

Gupta, M. C., and Parasad, M.: Associated infection of pulmonary tuberculosis and leprosy. *Indian J. Med. Sci.* **25** (1971) 183-185.

The present article is a report of two cases with simultaneous infection of tuberculosis and tuberculoid leprosy, showing remarkable improvement following therapy.—Author's Summary

Balakrishnan, S.: Some aspects of collagen metabolism in leprosy. *Indian J. Med. Res.* **58** (1970) 1044-1049.

The hydroxyproline and hexosamine levels in affected tissues from cases with different types of leprosy were compared with normal skin. The urinary excretion levels of hydroxyproline were studied in cases with lepromatous leprosy during reactive and subsided phases. The skin levels of hydroxyproline are significantly higher in patients with lepromatous leprosy compared to all other types of the disease and normal skin. The skin hydroxyproline levels in borderline leprosy are slightly higher than the controls while no deviation from the normal is observed in tuberculoid leprosy. Hexosamine levels of the skin are slightly higher in patients with lepromatous leprosy than in the controls, while no alteration is seen in cases with borderline and tuberculoid leprosy. In lepra reaction, there is a further increase in the skin levels of

hydroxyproline and hexosamine. The urinary excretion levels of hydroxyproline are significantly increased in lepromatous leprosy, particularly during the reactive phase. Increased levels of hydroxyproline in urine could be explained as due to a possible breakdown of collagen in the reactive phase. Further work is needed to explain the marked increases in skin levels of hydroxyproline and hexosamine in lepra reaction.—Author's Summary

Blumberg, B. S., and Melartin, L.: Australia antigen and hepatitis. *Arch. of Int. Med.* **125** (1970) 287-292.

Australia antigen is intimately associated with a hepatitis virus. It is found in the blood of many individuals who have acute viral hepatitis and in some patients with chronic diseases (ie, some forms of leukemia, Down's syndrome, etc) who have a form of chronic anicteric hepatitis. It is also found in relatively high frequency in apparently normal people living in the tropics, and in even higher frequency in patients with lepromatous leprosy who reside in these areas. Patients with lepromatous leprosy who have the antigen in their blood do not have acute hepatitis, but do have slightly elevated serum glutamic pyruvic transaminase levels. We could not detect any clinical or biochemical evidence of liver abnormality in the apparently normal individuals with Australia antigen.—Author's Summary

Carteron, B., Fauran, P. and Courmes, E.: Analyse immuno-électrophorétique de sérums de lépreux de la Guadeloupe. (Note préliminaire.) (Immuno-electrophoretic examination of sera from patients with leprosy in Guadeloupe) *Méd. Trop.*, **30** (1970) 347-352.

Immuno-electrophoretic investigations on 136 serums of hansenians from Guadeloupe, including 59 lepromatous forms, 51 'tuberculoïde' forms, 18 'indetermined' forms and 8 'borderline' forms showing:—an increase of total proteins, over 80

gm/litre in 65 of 100 sick people and over 100 gm/litre in 8 of 100 of them.

—a decrease of albumin, with hyperglobulinemia bringing the inversion of A/G relation among 60 of 100 sick people.

—This hyperglobulinemia deals with immuno-globulins and I globulins: The IgG are increased more regularly and considerably, the IgA and IgM are increased less constantly and importantly without relation with the clinical form of the disease. The increase of IgE globulin and siderophilin seems to show perturbations in the carriage of hemoproteins and serum iron.—Adapted from Author's Summary.

Céspedes, R. and Meoño, B.: Hallazgo de bacilos ácidos resistentes en la pulpa dental da pacientes leprosos. (Acid-fast bacilli in the dental pulp of patients with leprosy) Acta Méd. Costarric., 1970, 13 (1970) 105-110.

Eighty two biopsies from active Hansen's disease removed from dental pulp were studied.

Ten patients had invasion of the pulp tissue by acid resistant bacilli with important histopathologic changes.

We emphasize the fact that finding the bacilli in the dental pulp also implies the possibility of finding the bacilli in the dentine with the corresponding histopathologic alterations.—Author's Summary

Gruhl, V. R., and Reese, M. H.: Disseminated atypical mycobacterial disease presenting as "leukemia." Amer. J. Clin. Path. 55 (1971) 206-211.

A case of disseminated infection with *Mycobacterium kansasii* is described. The diagnosis was made by demonstrating acid-fast bacilli in a biopsy specimen of the liver and by cultures of the sputum and bone marrow. Although the initial hematologic findings suggested subacute myelogenous leukemia, the clinical course was that of leukemoid reaction secondary to the mycobacterial infection.—Author's Summary

Chaudhury, D. S.: Spina bifida occulta causing plantar ulceration. Leprosy Rev. 41 (1970) 236-237.

The differential diagnosis of the underlying cause of plantar ulceration will include such well-recognized conditions as diabetes and yaws, and the relatively rare diseases of tabes dorsalis and syringomyelia. Plantar ulcer is the commonest serious foot lesion associated with leprosy, but anesthesia and intrinsic muscle paralysis due to other diseases causing nerve damage must always be remembered. The following history of chronic plantar ulcer in a boy aged 16 years serves as a salutary reminder of this fact.—Author's Summary

Martins, S. R. C., and Seabra Santos, H.: Reação leprotoia. (Reactive leprosy.) Revisco País II (1970) 241-249.

An interesting case of reactive leprosy (which this reviewer would consider to be dimorphous in type), showed heavy involvement of the vascular plexus at the roots of hair bulbs, accompanied by peribulbar infiltrates, granulomas in the dermal papillae, and perifollicular abscesses leading to destruction of the follicles. Clinically, a peculiar clinical picture consisted of follicular papulopustular lesions of the face, neck, and upper chest suggesting acne rosacea. The article is illustrated by a nice color plate.—G.L. Fite

Maruna, R. F. L., Gründig, E., Simanyi, M., and Weithaler, K.: Klinisch-chemische Untersuchungen mit Seren von Lepra-patienten, (Clinicochemical studies on sera from leprosy patients) Tropenmedizin und Parasitologie. 21 (1970) 425-432.

The concentration of amino acids in 11 out of 15 sera of leprosy patients (*Lepra lepromatosa*) was found to be significantly higher than in sera of healthy persons, and the quantitative interrelation of the amino acids was altered. The content of serum total protein was at the lower limit of the normal range. These results indicate a higher catabolic rate of the proteins. The high activity of the ϕ -fraction of alkaline and acid phosphatases is in agreement with this assumption. The high activity of the lysosomal enzymes lysoszyme and acid phosphatase suggest participation of the lysosomes in leprosy reactions. The α^1 -glob-

ulins were considerably elevated, and in some cases were even higher than the α_2 -globulin values. Normal levels of β -globulins and alkaline phosphatase activities indicate absence of liver damage in the patients examined. The immunoglobulin values of leprosy patients were only occasionally higher than the normal values for Ethiopians.—Author's Summary

Nayar, A., and Job, C. K.: A study of epidermal melanocytes in the hypopig-

mented patches of leprosy. Indian Jour. Med. Res. 58 (1970) 187-193.

Epidermal sheets were prepared from skin biopsies taken from the hypopigmented lesions of leprosy. They were stained with dopa to observe the melanocyte density and morphology. In the majority of cases studied a reduction in melanocyte population was noted. A significant number of cases also showed changes in melanocyte morphology indicating depressed melanocyte function.—Author's Summary

Bacteriology Immunology

Turk, J. L., and Waters, M. F. R.: Immunological significance of changes in lymph nodes across the leprosy spectrum. Clin. exp. Immunol. 8 (1971) 363-376.

Seventy-seven lymph nodes were examined histologically from sixty-two leprosy patients representing the whole range of the disease spectrum from the high resistance form (tuberculoid) to the specific immunity deficiency form (lepromatous). At the lepromatous end of the spectrum paracortical areas were infiltrated with undifferentiated cells of the histiocyte-macrophage series which failed to eliminate mycobacteria. As resistance to infection increased across the leprosy spectrum, histiocytes became more differentiated eventually appearing epithelioid. This was paralleled by increasing numbers of small lymphocytes in the paracortical areas. In the borderline tuberculid form of the disease an appearance was seen similar to that found in sarcoidosis. In polar tuberculoid leprosy where there is a high degree of cellular immunity, paracortical areas were well developed and populated with lymphocytes and immunoblasts. The immunological significance of the findings are discussed, especially the relation of the changes in morphological appearance of cells of the histiocyte series to the ability of the patient to develop cell-mediated immune reactions.—Author's Summary

Pedley, J. C.: Composite skin contact smears: a method of demonstrating the

non-emergence of *Mycobacterium leprae* from intact lepromatous skin. Leprosy Rev. 41 (1970) 31-43.

The author's method of preparing composite skin contact smears is fully described. From the microscopical examination of a large number of these smears, taken from various sites on patients with lepromatous leprosy but with intact skin, he concludes that the main source of infection in such cases is not the intact skin, on which very few leprosy bacilli were found, but the nasal mucus.—Author's Summary

Matsuo, Y.: Multiplication of *Mycobacterium lepraemurium* in mouse foot-pad cell culture. Jap. J. Microbiol. 14 (1970) 233-240.

A limited multiplication of *Mycobacterium lepraemurium* was observed in cultures of mouse foot-pad cells up to the third subculture. After 96 hr of incubation at 33°C for phagocytosis, infected cells were washed to remove unphagocytized bacteria and transferred to new culture vessels. There was a 4.9-fold increase in the number of bacteria during 70 days of successive cultures up to the third culture in flasks, giving an overall generation time of 30.4 days. Acid-fast stained cover-slips taken from the culture in Leighton tubes revealed intracellular multiplication of *M. lepraemurium*, frequently in bundles of hundreds of bacteria, and gave an average generation time of 16.4 days in the primary

15.7 days in the secondary, and 8.1 days in the tertiary culture. Elongation of *M. lepraemurium* was observed as early as 6 days after infection. All attempts to grow the acid-fast bacteria from the original bacillary suspension and the cell suspension at the end of the experiment on artificial culture media have failed. However, subcutaneous inoculations of these materials to mice produced the typical lesions caused by *M. lepraemurium*.—Author's Summary

Katz, S. I., DeBetz, B. H., and Zaia, N.: Production of macrophage inhibitory factor by patients with leprosy. *Arch. Dermat.* **103** (1971) 358-361.

Patients with lepromatous (low resistance) leprosy exhibit depressed cell-mediated immunologic reactivity. This is reflected by anergic responses to intradermal injection of various antigens, including lepromin, by relative inability to become sensitive to haptens (dinitrochlorobenzene), and by poor blastogenic response of lymphocytes to various mitogens in cell culture. Patients with tuberculoid (high resistance leprosy) usually respond normally to these stimuli. Ability of lymphocytes to produce macrophage migration inhibition factor (MIF) has been shown to correlate with patient's ability to exhibit cell-mediated delayed-type hypersensitivity reactions. Lymphocytes of patients with lepromatous leprosy who are anergic fail to produce or produce only small amounts of MIF in response to lepromin in vitro, but lymphocytes of patients with tuberculoid leprosy who exhibit normal cell-mediated reactions respond to lepromin in vitro by production of greater amounts of MIF.—Authors' Summary

Brown, C. A., and Draper, P.: An electron-microscope study of rat fibroblasts infected with *Mycobacterium lepraemurium*. *Jour. Path.* **102** (1970) 21-26.

The ultrastructure of 14pf rat fibroblasts infected with *Mycobacterium lepraemurium* for 6 or 7 days are described, and compared with that of uninfected cells. In Eagle's medium containing 10% of calf

serum the cells will not support bacterial growth and are ultrastructurally normal. Multiplication occurs inside cells grown on 1:1 human cord serum:Hanks' balanced salt solution. In these cells there is an abundance of lysosomes and the appearance of autophagy. The bacteria are often surrounded by lysosomal material, a situation that is rare in cells growing on the low-serum medium. The implications of these observations are discussed.—Author's Summary

Brown, C. A.: Association of lysosomal enzymes in cultured fibroblasts with the intracellular growth of *Mycobacterium lepraemurium*. *Br. J. exp. Path.* **51** (1970) 209.

An established line of rat fibroblasts (14pf), growing in either of two media, was infected with *Mycobacterium lepraemurium*. One of the media (equal parts of human cord serum and Hank's balanced salt solution) supports active intracellular bacterial multiplication, whereas the other (10% calf serum in Eagle's medium with added peptone) fails to do so. Within one week of infection, the cells were stained for acid phosphatase, aryl sulphatase and β -galactosidase activities and examined by light microscopy. Cells in equal parts of cord serum and Hank's balanced salt solution showed an accumulation of all three enzymes around the bacteria whereas cells in 10% calf serum in Eagle's medium showed only light, diffuse, general staining with little localization around the bacteria. Cells in the former medium also had greater lysosomal activity before infection with *Myco. lepraemurium* than cells in the latter medium showing that the increased activity was not the result of intracellular multiplication of the bacteria. It is concluded that the failure to support mycobacterial growth by the cells growing in the medium containing calf serum must be unconnected with direct lysosomal action. A possible beneficial effect of lysosomal enzymes on the growth of these obligate intracellular mycobacteria is suggested.—Author's Summary

Surgical

Riedel, G. G.: The timing of reconstructive surgery in relation to the course of leprosy. *Leprosy Rev.* **41** (1970) 45-51.

In this discussion of the effects of reconstructive surgery on the state of the disease in leprosy patients the author concludes from experience with his own cases, that the timing of surgery is important, in that surgical stress can have an activating effect on the leprosy, and conversely that activity of the leprosy may have a deleterious effect on the surgical results.—Author's Summary

Warren G.: Plaster casts. *Leprosy Rev.* **42** (1971) 55-59.

A step-by-step description is given of a method of applying a plaster of Paris walking cast that can be performed by one technician with minimal assistance.

Plaster of Paris walking casts are recommended for the treatment of foot ulcers in leprosy. They are also an essential part of the treatment of tarsal-bone disintegration

in leprosy. To be effective, a cast must be strong, light, and well fitted so that it does not rub and cause an abrasion which because of anesthesia, may remain unnoticed until a deep ulcer has developed. Since a plaster applied to an edematous leg or foot becomes loose as the swelling subsides, steps should be taken to reduce swelling before the walking plaster is applied.—Author's Summary

Garst, R. J.: Prosthetics in leprosy, *Leprosy Rev.* **42** (1971) 60-68.

This paper deals with the implications for amputation of the lower extremity of the patient with Hansen's disease, the preparation of the prosthesis, and the care of the stump. Particular attention is given to the making of a hard socket to prevent breakdown of the skin of the stump. Inexpensive methods of producing useful and acceptable prostheses are described.—Author's Summary

Other Mycobacterial Diseases

Pattyn, S. R., Vandepitte, J., Portaels, F., and De Muynck, A.: Cases of *Mycobacterium borstelense* and *M. abscessus* in infection observed in Belgium. *Jour. Med. Microbiology.* **4** (1970) 145-148.

Cases of multiple cutaneous abscesses due to *Mycobacterium borstelense* and *M. abscessus* are described. One occurred in Belgium after insulin injections and the other as a result of a wound infection sustained in Central Africa.

The differentiation of *M. borstelense* from *M. abscessus*, *M. fortuitum* and *M. peregrinum* is discussed.—Author's Summary

Hand, W. L., and Sanford, J. P.: *Mycobacterium fortuitum*—A Human Pathogen. *Ann. Internal Med.* **73** (1970) 971-977.

Mycobacterium fortuitum is often considered to be merely a saprophytic organism in spite of adequate evidence to the

contrary. To illustrate the clinical manifestations and relative frequency of *M. fortuitum* infections, six recently observed cases are presented. These include five patients with cutaneous infection or abscess disease after trauma (one of whom also had suppurative adenitis) and one patient with a cauda equina abscess and meningitis. The most frequently reported *M. fortuitum* illnesses are cutaneous and deeper infections after trauma, pulmonary disease, and corneal infection. Infections associated with contaminated trauma, including corneal infection, are related to the widespread distribution of *M. fortuitum* in nature. Pulmonary infection is usually superimposed on preexisting lung disease. Local measures, including debridement, drainage, and sometimes excision, are the treatment for cutaneous infections, abscesses, and corneal infections. Although drug therapy has been ineffective, patients with pulmonary disease frequently recover spontaneously.—Author's Summary

Pathology

Karat, A. B. A., Job, C. K., and Rao, P. S. S.:

Liver in leprosy: histological and biochemical findings. *British Med. Jour.* 6 (1971) 307-310.

The histological findings and their correlation with biochemical functions of the liver in 240 leprosy patients are presented. In 21% with tuberculoid leprosy and in 62% with lepromatous leprosy leprosy granulomata were found in the liver. A significant prevalence of granulomatous lesions in the liver among patients with tuberculoid and borderline-tuberculoid leprosy of less than one year's duration suggests that bacilemia occurs in all forms of leprosy.

There was a direct correlation between bacterial index and the presence of acid-fast bacilli in the liver. Of 50 patients with negative skin smears seven had acid-fast bacilli at liver biopsy. From none of these liver homogenates were acid-fast bacilli grown on culture in Löwenstein-Jensen medium.

The alterations in liver functions were more consistently seen when acid-fast bacilli were associated with the presence of leprosy granulomatous lesions. The acid-fast bacilli were found to persist even after one to five years of specific antileprosy therapy and after the bacilli in the skin had cleared up. This may explain the relatively

frequent recrudescence or relapse of the bacillated types of leprosy when specific antileprosy therapy is stopped soon after bacterial negativity is attained on skin smears.—Author's Summary

Gaugas, J. M., Payne, S., and Wharton, F. P.: Association of macrophage lipids with *Mycobacterium lepraemurium* in the mouse thymus and lymph node. *Br. J. exp. Path.* 51 (1970) 87-91.

Mice infected systemically with *Mycobacterium lepraemurium* ("rat leprosy bacillus"), an obligate intracellular parasite, showed uneven spread of triglyceride, phospholipids, and certain unsaturated fatty-acids in infected macrophages throughout the lymphoid system (determined histochemically and by chromatographic analysis). Such materials were abundant in parasitised macrophages in the thymus, but little or none were demonstrable in parasitised macrophages in the lymph node medulla; only relatively small amounts were present in the few affected cells in the lymph node cortex. Lipids apparently influenced bacillary multiplication, for multiplication was greater in macrophages in the thymus than in the lymph node, despite much lysosomal activity.—Author's Summary

General and Historical

Sabin, T. D.: Neurologic features of lepromatous leprosy. *Family Physician.* 4 (1971) 84-94.

This article presents the neurological features of leprosy to the physician less familiar with the disease.—Author's Summary

Leprologia 14, No. 2, July-December 1969. (Pages 107-209)

In this issue, numerous brief articles illustrated various aspects of leprosy and its management. Following a note by Baliña to the effect that mutilations are prevented by early attention (107-108), Ribichini dis-

cussed the differences in reticular and connective tissue reactions according to types of leprosy (109-112). Wilkinson and Calori (113) suggest that diminished oxygenation of lepromatous skin is factorial to the cellular response. Serial, Arcuri and Cattáneo (114-116) presented a case of tuberculoid leprosy characterized by the presence of Schaumann bodies, discussing differences between skin changes of leprosy and sarcoidosis. Nudenberg stressed the significance of increased gamma-globulins in reactive phases (119-121), and Melamed (122-123) summarized treatment of reactions, especially with corticosteroids. Mogila (124-126) introduced the country practi-

tioner and his role in infectious disease control, especially with reference to leprosy.

A group of physicians and a psychologist from leprosy agencies in Rosario discussed the several current attitudes toward the word "leprosy" and its derivatives. Sympathetic to Rotberg's proposals, they stress education, scientific investigation, and rehabilitation of patients as the roads to effective success regarding change in name as helpful but palliative.

Wilkinson, Besuchio and Calori report variation in amino acid content of urine in leprosy, especially glutamic acid and alanine, relating changes to type, dietary, genetic, age, and other factors (131-138). Piva, de Tiscornia, Serial, and Chiara studied plasma cells in skin lesions, finding their presence related to the immunoglobulinemic status. (139-141). Giménez surveyed leprosy in Formosa (143-146), past and present, noting particularly agencies currently active in this country. Risso (147-148) reported briefly on leprosy control in the state of Chaco.

A brief note by Ríos reported on the antileprosy campaign in Formosa (149), and six authors from the dermatologic leprosy center (Resistencia, Chaco) presented the leprosy control program in Chaco of the 1959-1969 period. Mercau and others report an interesting 5-year experience with mobile leprosy units, an effort which meets with this reviewer's enthusiasm (153-156). A brief discussion of the meaning of social services in leprosy work was described by Arcuri and Grosskopf de Travi (157-159). Enríquez discussed necrotizing lesions in leprosy, reporting an interesting example (160-163). The "Baldomero

Sommer" sanitarium reported on their expansion in rehabilitation (164-169), Melamed (170) reported a case of necrotizing angiitis, and the effects of hyperbaric oxygen treatment of leprosy (Wilkinson, Rosasco, Calori, Eguía, and Rubio) (171-176) were disappointing. Wilkinson and others reported favorably on a tetracyclin derivative as a therapeutic agent in 20 cases of leprosy. From "Baldomero Sommer," the report of Manzi, Marzetti, Lefèvre and Pacín stressed avoidance of pressure and trauma in most cases as the first ingredient of any treatment of plantar lesions (183-185). The surgical treatment experience in plantar ulcers was reported from the same institution (186-188). Thalidomide in the treatment of reactions was favorably confirmed by Baliña, Gatti, Cardama and Avila (189-193). Mengoni, Horowitz, Pérez Maldonado, Bondancia, De Riso and Echeverría (194-206) offered a comprehensive review of the same topic. A clofazimine trial in Paraguay (207-209, Rodríguez) noted an "inconvenient" pigmentation, with less than a majority of the chronically ill responding to treatment.—G.L. Fite

Schadewaldt, H.: Geschichte der Lepra. (The History of Leprosy.) *Hautarzt*, 20 (1969) 124-130.

This excellent and nicely illustrated account of leprosy concerns itself dominantly with the development of knowledge of leprosy in Europe, yet seeks to present with some comprehensive effort the gradual understanding of the disease prior to the days of Hansen, and of Neisser, ending essentially with the beginning of the 20th century.—G. L. Fite

Chemotherapy

Shepard, C. C., Walker, L. D., Van Landingham, R. M., and Redus, M. A.: Comparison of B1912 and clofazimine (B663) in *Mycobacterium leprae* infections (35654), *Exper. Biol. and Med.* 137 (1971) 728-729.

B1912 is a newly synthesized type of rimino compound; it has about the same

activity against tubercle bacilli in mice as clofazimine (B663). Clofazimine is now generally accepted as the drug of choice in treating infections of man with sulfone-resistant *M. leprae*. Like clofazimine, B1912 deposits in the tissues of mice and other experimental animals, but it gives higher serum levels and lower tissue levels (except in fat) than clofazimine under

similar conditions. We have compared B1912 and clofazimine in *M. leprae* infections in mice.

The effect of clofazimine was compared with another, more newly developed rimino-compound, B1912, in *M. leprae* infections in mice. The two drugs were found to have very similar activity.—Author's Summary

Shepard, C. C., Walker, L. L., Van Landingham, R. M., and Redus, M. A.: Discontinuous administration of clofazimine (B663) in *Mycobacterium leprae* infections (35653). *Exper. Biol. and Med.* **137** (1971) 725-727.

The prophylactic and spaced administration of clofazimine in mice was studied. The drug had an effect when given orally for two days immediately after infection, but had no effect when given five weeks before infection. When given once every four weeks from Day 70 to Day 140 after infection, the drug had a distinct effect. It was also active when injected intraperitoneally on the day of infection.—Author's Summary

Prabhakaran, K.: Cataract in leprosy: a biochemical approach. *Leprosy Rev.* **42** (1971) 11-13.

The possible role of phenoloxidase of *Mycobacterium leprae* in producing cataract in leprosy is discussed. It is suggested that diethyldithiocarbamate, a potent inhibitor of the enzyme, could be of value as a therapeutic agent.—Author's Summary

Shepard, C. C., Walker, L. L., Van Landingham, R. M., Redus, M. A.: Kinetic testing of drugs against *Mycobacterium leprae* in mice. *Amer. J. Trop. Med. and Hygiene* **20** (1971) 616-620.

A series of drugs that had been found active against *Mycobacterium leprae* in mice by the continuous method of drug administration was tested by the kinetic method. Vadrine and viomycin were found inactive. Cephaloridine, streptovaricin, and rifampin gave bactericidal-type results. In

a second experiment, rifampin was found to have distinct bactericidal effect when given for only two days. The plasma levels of rifampin that were associated with bactericidal effect in mice were in the range reported for man receiving acceptable dosages of rifampin. Cephaloridine and especially rifampin merit further investigation in clinical trials in leprosy patients, either as single drugs or in combination with other active drugs. The combination of rifampin and dapsone (DDS) or acedapsone (DADDS) appear to provide the advantages of both drugs.—Author's Summary

Boughton, C. R., Scott, G. C., and Russell, D. A.: A preliminary report on the use of the depot sulphone preparation acedapsone ("Hansolar") in the control of leprosy. *Med. Jour. Australia.* **1** (1971) 1258-1263.

A preliminary report is presented of the results of two years' treatment of a group of leprosy patients with a depot sulphone preparation. The drug is a diacetyl derivative of diaminodiphenyl sulphone (acedapsone, Hansolar), which is administered by intramuscular injection every 75 days.

The clinical and bacteriological response of 327 patients has been very satisfactory, and this form of treatment has been accepted by the population. Administration of the drug has resulted in reduction of infectivity of patients with dimorphous and lepromatous leprosy, as measured by the morphologic and bacterial indices. There has been no indication to date of the development of resistance by *Mycobacterium leprae* to acedapsone.

This drug offers considerable advantages over orally administered medication in the control of leprosy, particularly in underdeveloped areas where leprosy is endemic.

No "flares" have occurred in cases of indeterminate and tuberculoid leprosy during treatment, and in no case has the disease progressed towards the malignant (dimorphous-lepromatous) end of the spectrum. This form of treatment has been well accepted by the Karimui population.

Some lepra reactions have occurred in the dimorphous and lepromatous cases, but

these have been of only moderate severity, and no significant nerve damage has been detected during or after the reactions.

The importance of early diagnosis and regular treatment of leprosy in the prevention of deformity and in producing a rapid response to therapy is obvious from this study.—Author's Summary

Ellard, G. A., Gammon, P. T., and Rees, R. J.: The minimal inhibitory concentrations of sulphadimethoxine and sulphadoxine against *Mycobacterium leprae*, *Leprosy Rev.* **41** (1970) 223-228.

Sulphadimethoxine inhibited the multiplication of *M. leprae* in the mouse footpad system when given at a dietary concentration of 0.01%. Sulphadoxine inhibited the multiplication of *M. leprae* at a dietary concentration of 0.04%, but not at one of 0.004%. Determination of the plasma concentrations of the two drugs in mice fed with these dietary concentrations of sulphadimethoxine and sulphadoxine indicated that the MICs of these two compounds against *M. leprae* were between 20 and 35 μg per ml. The significance of these findings is discussed, both in relation to the previously determined MIC of dapsone against *M. leprae* and to the use of these two long-acting sulphonamides in the treatment of human leprosy.—Author's Summary

Leiker, D., and Kamp, H.: First results of treatment of leprosy with rifadin. *Leprosy Rev.* **41** (1970) 25-30.

A first report on the treatment of seven lepromatous patients with rifadin, a new antibiotic with antituberculosis properties, related to rifamycin S.V. Significant clinical improvement was seen in all patients after administration of 600 mg of rifadin daily for periods of between 12 and 20 months. In all cases some increase in the percentage of granular bacilli was seen already after one month. In all patients this percentage increased rapidly in the months that followed. In one patient, however, it took almost nine months before nearly 100% of the bacilli had become granular. Although a satisfactory decrease in the average B.I. was seen after six months of treatment, in

the second half-year no further average decrease was seen; this could be explained as being due to a greater concentration of bacilli in lesions which had rapidly subsided. In none of the patients has conclusive evidence of drug-resistance been found so far. In five patients reactions occurred; these were mild to moderately severe and rifadin treatment was continued during the reactions. There was no evidence that the reactions were aggravated by rifadin. No other side-effects were observed. It is concluded that rifadin is an effective anti-leprosy drug which merits further investigations, especially with regard to the incidence of reactions and the development of drug resistance.—Author's Summary

Morgan, J.: Management of steroid-dependency with clofazimine [Lamprene or B663 (Geigy)], *Leprosy Rev.* **41** (1970) 229-232.

All 23 patients in this series treated with clofazimine had severe complications of leprosy. Fourteen were steroid-dependent when they started to take clofazimine. None had had adequate treatment with any antileprosy drug.

Treatment with clofazimine had the following results: (a) patients could be weaned from dependence on steroids; (b) the acute exacerbation was brought under control; (c) normal bacillary forms disappeared rapidly from routine smears, and the bacillary index fell consistently; (d) peripheral neuritis was controlled; (e) return to dapsone treatment became possible.

It was demonstrated that: (1) reactions occurred less often during the period of clofazimine treatment; (2) the mean duration of each reaction was shorter during treatment with clofazimine; and (3) the total duration of reactions occurring in the clofazimine treatment period was less than during treatment with other anti-reactional drugs.—Author's Summary

Ozawa, Toshiharu, Shepard, C. C., and Karat, A. B. A.: Application of spectrophotofluorometric procedures to some

problems in *Mycobacterium leprae* infections in mice and man treated with dapsone (DDS), diacetyl-DDS (DADDS), and di-formyl-DDS (DFD). Amer. J. Trop. Med. and Hyg. **20** (1971) 274-281.

Recently described spectrophotofluorometric procedures for the determination of dapsone (DDS), which are sensitive to about 10 ng per ml blood or plasma, were applied to several problems in experimental and natural infections with *Mycobacterium leprae*. Measurements on blood of mice receiving minimal effective dosages showed that the minimal inhibitory concentration of DDS for *M. leprae* is in the range 2.5 to 10 ng per ml. In mice that had received DDS by mouth, DDS was rapidly eliminated from the blood with a half-life of three to five hours or less; thereafter a presumed metabolite of DDS was eliminated with a half-life of six to ten days. A procedure was developed for the determination of di-formyl DDS (DFD) in the presence of DDS: measurements on the blood of mice receiving DFD by mouth indicated that the DFD was nearly completely converted to DDS. In patients receiving repository injections of DADDS (diacetyl DDS), the blood levels averaged 50 ng per ml, or about what would be expected for the absorption of 2.4 mg DDS per day; no blood levels below the minimal inhibitory concentration were encountered. In patients receiving 5 or 10 mg DDS per day orally, some unexpectedly low serum levels of DDS were found.—Author's Summary

Sheskin, J., and Zauberman, H.: Iridocyclitis in lepra reaction treated with thalidomide, Leprosy Rev. **41** (1970) 233-235.

Signs of iridocyclitis accompanying other

lesions of lepra reaction were seen in three patients suffering from lepromatous leprosy—twice in one of the patient and once in each of the others. In a fourth patient with indeterminate leprosy signs of iridocyclitis were found in the absence of a systemic lepra reaction.

Thalidomide therapy in doses of 300 to 400 mg daily, added to the existing DDS treatment, rapidly improved both the ophthalmic condition and the systemic signs of the reaction in the three patients with lepromatous leprosy, and daily maintenance doses of 50 to 100 mg of thalidomide (again added to DDS) prevented recurrences of the iridocyclitis. In the patient suffering from indeterminate leprosy, the iridocyclitis was not improved by thalidomide, and it was necessary to administer steroids.—Author's Summary

Wagner, W. H.: Neue Methoden der experimentellen Lepra-Chemotherapie. (Recent experimental methods in the chemotherapy of leprosy.) Der Hautarzt, September 1969.

The results of the investigations presented in this review are an expression of the great advances that have been made in experimental leprosy research in the past 15 years. The propagation of the causative organism of leprosy in the animal body has opened new possibilities to pathologic-histologic, diagnostic and immunobiologic relationships, as well as endowing experimental chemotherapeutic findings with the greatest significance. For the study of new drugs a useful experimental model is available, which gives results comparable to the clinical, even to the degree of investigation of problems of drug resistance.—From Author's Summary