BOOK REVIEWS

Balakrishnan, S. *Biochemical Aspects of Leprosy (Erwin Stindl Memorial Oration, 1986).* Calcutta: Greater Calcutta Leprosy Treatment and Health Education Scheme, 1986. Softbound, 40 pp., US$3.

In recent years there has been a resurgence of interest in the biochemistry of leprosy, especially that of the causative agent *Mycobacterium leprae.* In the booklet, "Biochemical Aspects of Leprosy," Dr. Balakrishnan [Assistant Director (Biochemistry), Central Leprosy Teaching and Research Institute, Changalpattu, India] discusses studies on "chemical-pathological changes" in leprosy patients, biochemistry of *M. leprae,* as well as the metabolism of dapsone and other drugs used in the treatment of the disease. Although the author's approach is eclectic rather than being exhaustive, he gives a balanced appraisal of available information in the field.

The first section of the review deals with liver function, renal involvement, muscle function, connective tissue metabolism and also serum proteins, lipids, enzymes, hormones and minerals in the patients. One is constrained to say that, despite being important, all these massive data have not contributed significantly to the management of the disease. The second section of the booklet is devoted to the biochemistry of *M. leprae.* Among other things, it includes chemical composition of the bacterial cell wall, phenolic glycolipid present in the organisms separated from infected tissues, and various enzyme activities detected in *M. leprae* preparations. The substitution of alanine by glycine in the cell wall was considered to be unique to the bacilli. However, David and Rastogi questioned this finding in a later report, and attributed it to contamination of the bacterial suspensions by host tissue. Dr. Balakrishnan notes that oxidation of DOPA is the only metabolic activity so far found to be specific for *M. leprae.* The late Professor L. Mester of Paris synthesized a presumed DOPA antagonist, deoxyfructoserotonin (DFS). Studies by Balakrishnan and others showed that the compound suppressed the growth of *M. leprae* in mouse foot pads, and prevented the uptake of DOPA by the bacteria. Clinical trials of DFS in West Africa are said to have produced promising results. The metabolism of dapsone is covered in the last section of the review. Dr. Balakrishnan has done extensive studies in this field. He has developed a simple spot test for monitoring the intake of dapsone by the patients, which is quite useful, under the field conditions prevailing in the endemic countries.

The booklet contains a few minor printing errors. Although one would have wished for more, Dr. Balakrishnan deserves credit for giving an overall view of an interesting field of leprosy research in this booklet.—K. Prabhakaran

Groenen, Guido. *La Lèpre. Manuel Pratique pour les Services de la Lèpre sur le Terrain.* Brussels: Les Amis du Père Damien, 1984. Softbound, 187 pp., in French.

Effective integration of leprosy control into the general health service in Zaire—as in other countries in Central Africa—has been hampered by the paucity of good teaching material in the working language of the area, French. Dr. Groenen's manual, *La Lèpre,* has done much to remedy this problem.

La Lèpre is, as its subtitle implies, a practical manual for field workers in leprosy. It is written simply and clearly in French that a high school student—the reading level attained by most health center nurses in Zaire—can understand, yet it is comprehensive enough to be of value to a nonspecialist physician. The book is well organized, well illustrated, and well cross-referenced. Each chapter ends with a brief summary of the topic covered.

The nine chapters deal with all aspects of leprosy, from diagnosis through treatment, rehabilitation and organization of a leprosy service. Dr. Groenen's manual is written for field workers who may not have ready access to higher authority when faced with a case management problem. The book is therefore comprehensive, describing clearly and simply the problems commonly en-

countered in leprosy and describing how they should be handled. "Refer to hospital" never appears as the sole solution to a problem. In Zaire it is almost never a practicable solution.

The annexes provide useful information in more concise form, dealing with such problems as the classification of deformity, the eye in leprosy, microscopy, record keeping, and filling out reports.

The manual does have its shortcomings, most of them typographical. A four-page insert entitled "Errata" covers most of these. There are a few other errors, probably of author origin. The only really dangerous error in the book is the drawing (page 121) depicting the application of the molded double-rocker plaster shoe. If applied as shown the shoe would cause an ulcer rather than cure one (Joseph, *et al.* Leprosy Review **54**:39–44). Perhaps an error of omission occurs in that the currently recommended multidrug therapy (MDT) regimens for Zaire do not appear in the treatment section, which does describe several MDT regimens, including a modified WHO-recommended regimen. Although not specifically written for Zaire, the book will find its greatest readership there, and any new edition should describe regimens currently in use in that country.

In summary, this is a book that should be widely distributed among field workers in French-speaking Africa. Hopefully, a second revised and corrected edition will appear within the next 2 or 3 years.—L. O. Lanoie

Hastings, R. C., ed. *Leprosy.* (Medicine in the Tropics Series.) New York: Churchill Livingstone, Inc., 1986, 319 pp. + index, hard cover, US$62.

This textbook is intended as a comprehensive summary of the vast amount of information on leprosy published since the 1964 edition of *Leprosy in Theory and Practice,* edited by Cochrane and Davies. It is a courageous and successful undertaking.

The contributors are well experienced in their respective fields and possess a fluency of thought and expression that is apparent throughout the 14 chapters.

In the lead chapter, the late Stanley G. Browne outlines the history of leprosy, starting with a description of the earliest objective evidence of the disease in the skull bones of four Egyptians buried in the oasis of Dakhleh in the 2nd century B.C. to its introduction into the New World by the Spanish and Portuguese conquistadores and African slaves. Browne's extensive experience in leprosy is evident as he describes the evolution of the treatment of the disease with the personal insight of a clinician who experienced the transition from an era when no effective treatment was available to one in which the clinician could select from among several drugs to effectively control the disease in patients under his care.

Nordeen provides an excellent overview of the epidemiology of leprosy, describing its distribution according to geography, age, sex, ethnic factors, time, and socioeconomic factors. Recent information on reservoirs of the infection, portal of entry and exit of *Mycobacterium leprae,* methods of transmission, and possible routes of infection are discussed.

Rees' chapter on microbiology includes recent advances in biochemical studies of *M. leprae,* and details the procedures needed to assess the bacteriological status of patients.

Harboe's mastery of the field is evident in his chapter on the immunology of leprosy. He starts by constructing an immunologic profile of *M. leprae* that includes a description of monoclonal antibodies against *M. leprae*-specific antigens. This is followed by a shift to an immunologic portrait of the infection itself that details the immunologic aspects of subclinical infection, indeterminate leprosy and, finally, persisting determinate disease. A summary is presented of the most significant studies on the possible role of T4 helper cells and T8 suppressor cells, with emphasis on the differences in distribution of T4 and T8 cells in the granulomas of tuberculoid versus lepromatous leprosy. Harboe describes the immunodeficiency of lepromatous leprosy and discusses the importance of interleukin-2 in restoring the immune response in patients with lepromatous disease. He also presents a well-organized description of the significance of antibodies in leprosy (an area which receives little attention in many discussions of the immunology of leprosy), and concludes with a commentary on the potential

value of vaccines used either prophylactically or therapeutically. Harboe's contribution to the text is invaluable.

Dharmendra's chapter on classification should help clinicians to resolve such differences of opinion that are due to terminology and not conflicting clinical findings.

The chapter on clinical leprosy by Pfaltzgraff and Bryceson, and the chapter describing the pathology of leprosy by Ridley and Job, are comprehensive and well illustrated. Seventy-three photographs depicting clinical aspects and 34 photographs illustrating histopathologic features provide the reader with an excellent opportunity to correlate the clinical and histopathologic findings in patients suffering from the different types of the disease and its complications.

Leiker's chapter on differential diagnosis provides numerous illustrations of great value to the clinician who must be able to recognize those diseases that may be confused with leprosy. The chapter on treatment by Jacobson will also be helpful to the clinician in designing appropriate treatment regimens.

Margaret Brand's and T. ffytche's review of eye complications of leprosy, and Barton's chapter describing the ear, nose, and throat involvement in leprosy patients, demonstrate that leprosy can involve more than skin and peripheral nerves, and emphasize the need for careful evaluation and treatment when these vital tissues are involved.

The chapter on experimental leprosy by the late C. C. Shepard contains a comprehensive and detailed description of the animal models used in leprosy. The advantages and disadvantages of each model are described. This chapter provides an excellent review of all the studies done using the mouse foot pad model, and because Shepard pioneered the use of the mouse foot pad in leprosy, the interpretation of the results in mice is keen and insightful. It should be noted that in this chapter the possibility is mentioned that *M. leprae* may be reclassified from a Biosafety Level 2 category, in which it is considered less of a biohazard than *M. tuberculosis* and other pathogenic mycobacteria, to a Biosafety Level 3 category, which requires special and unusual precautions when handling the agent. Since then, however, in the revised 1984 edition of the CDC/NIH publication entitled *Biosafety in Microbiological and Biomedical Laboratories, M. leprae* retains its Level 2 classification and is considered of only moderate potential hazard to personnel handling the organism.

The chapter on control programs by Lechat, and the final chapter on rehabilitation by Paul Brand and Ernest Fritschi, are informative and provide the practical information so important in dealing with these aspects of leprosy.

Dr. Browne concludes his chapter on the history of leprosy with the statement: "The last page of the 'strange, eventful history' of leprosy has not yet been written. The redoubtable *Mycobacterium leprae* is still capable of surprising and challenging the peoples of the world." This textbook will provide clinicians and researchers in leprosy with a greater ability to meet these surprises and challenges.—Gerald P. Walsh

Ramalingaswami, V. *Annual Report of the Director-General 1984–85, Indian Council of Medical Research.* Satyavati, G. V., ed. New Delhi: ICMR Offset Press, 1986. Softbound, 113 pp.

[The following is that portion of the report dealing with leprosy.]

Research on various aspects of leprosy was continued at the Council's Central JALMA Institute for Leprosy (CJIL) at Agra and also at other institutes/centers at Chingleput, Madras, etc.

Chemotherapy

Chemotherapeutic trials using the newer anti-leprosy drugs in different combinations with DDS were continued at the CJIL, Agra. A combination of rifampin, prothionamide, isoniazid and DDS has been found to be highly effective in lepromatous leprosy. To study the effect of prothionamide in reducing infectivity, a study was undertaken at the CJIL, in two groups of patients on two different doses *viz.* 250 mg daily and 500 mg daily. Monotherapy with the drug was given for two months. At the end of eight weeks, no viable organisms were found in either of the groups indicating that prothionamide is a very effective drug. It was

also observed that lower doses produced lesser side effects.

Immunological Studies

While studying the antigens of mycobacteria, a special silver staining technique to identify the antigens of *Mycobacterium leprae,* Dharmendra lepromin, *M. vaccae* and *M. tuberculosis* (H37Ra) was attempted. This comparative study showed common as well as distinct antigenic bands in these mycobacterial species. Dharmendra lepromin was evaluated in four different centres and all the centres have provided comparable results. In an effort to determine the role of antibody in activation of the alternative pathway of complement, it was found that anti-*M. vaccae* serum was able to significantly increase the activation of complement. A similar study is in progress with *M. leprae.*

Efforts have been made to detect immunoglobulins and *M. leprae* antigen in urine of patients of leprosy. IgG, IgA and IgM were detected in the urine of patients of leprosy, whereas all the healthy volunteers were negative except one in whom the urine sample was positive for IgG. *M. leprae* antigen has also been detected in some of the samples.

Diagnostic Studies

A radioimmunoassay based on quasi-specific anti-*M. leprae* monoclonal antibody MLO_4 has been developed by the CJIL, Agra. This is likely to provide a highly specific and sensitive diagnostic test for leprosy. Its efficacy in the identification of leprosy patients and their household contacts is being assessed.

Studies employing FLA-ABS and lepromin tests have been extended to cover nearly 200 household contacts of patients at Leprosy Clinic at CJIL, Agra, and Leprosy Control Unit at Deeg (Bharatpur District, Rajasthan). FLA-ABS positivity was higher in contacts of multibacillary patients, as compared to contacts of paucibacillary patients. There was no correlation in the reactivity of either lepromin or FLA-ABS tests with sex of the contacts. In the contacts of multibacillary forms, the lepromin positivity was low in 0–5 and 6–10 years age groups whereas FLA-ABS positivity was high. The FLA-ABS is a better parameter than the skin test for the detection of subclinical infection in younger age groups. It may also help to understand the temporal relationship between humoral and cell mediated immune responses.

Investigations aimed at detecting subclinical infection and pre-clinical state were carried out using several methods such as (i) Nasal mucosal biopsies; (ii) lepromin skin test; (iii) FLA-ABS test; (iv) bacillaemia by the haemolysis method; (v) serological assay for antibody activity by serum inhibition of binding of I^{125} labelled MLO_4 monoclonal antibody; and (vi) quantitation of circulating mycobacterial immune complexes by using a standardized ELISA technique. Of these methods FLA-ABS was found to be the single best test for detecting subclinial infection, being positive in 79.12 per cent patients.

The Regional Medical Research Centre, Bhubaneswar, has initiated studies on antigenic analysis of mycobacteria. The *M. leprae* specific phenolic glycolipid-I antigen has been isolated from tissues obtained from lepromatous leprosy patients and specific antisera are being made. These antisera will be used to develop a method for early detection of infection with *M. leprae.* Analysis of specific restriction fragments of mycobacterial DNA has been started with a view to developing a system for identification of *M. leprae* on the basis of a unique sequence of DNA.

Evaluation of Vaccines

A few candidate vaccines against leprosy were evaluated by using the mouse foot-pad technique. Animals were vaccinated intradermally with autoclaved intact *M. leprae, M.w.,* ICRC bacillus and *M. vaccae* individually as well as in combination with live BCG. Mice immunized with *M.w.* gave the highest induration, whereas induration was slightly less with *M. leprae* and ICRC bacillus. Addition of BCG to the antigens did not enhance the DTH reaction. At 48 hours, the reaction was greater with BCG+ICRC and BCG+*M. leprae* followed by BCG+*M. vaccae.* Reaction with BCG+*M.w.* was poor. In mice challenged with live *M. leprae* in foot-pads, *M.w.* gave the best protection by complete suppression of the infection, ICRC

and *M. leprae* being next in order. *M. vaccae* was found to be non-protective against *M. leprae* infection.

Under the Indo-US collaborative Programme, studies have been undertaken at Bombay and New Delhi on various aspects of leprosy like characterization and biological significance of specific phenolic glycolipids in infected human tissues, development of *M. leprae* specific human T cell clones, macrophage metabolism and functions, and on the role of dendritic cells in the antigen induced *in vitro* lymphoproliferative responses.

Drug Resistance

A random study conducted to screen resistant strains of *M. leprae* in lepromatous patients from eight Northern states of India revealed 69 clinically suspected patients of whom 33 harboured *M. leprae* with various degrees of dapsone resistance. Most of these patients were from Uttar Pradesh and Madhya Pradesh.

An epidemiological study conducted in Dharmapuri and Pallipatti areas of Tamil Nadu for a period of 5 years to assess the prevalence of drug resistance revealed 266 bacteriologically positive patients out of 6664 leprosy patients. Among these, 25 patients were suspected clinically to be dapsone-resistant. The prevalence rate of drug resistance was found to be 1.1 per cent in these two areas using the mouse foot-pad technique.

Surgical Rehabilitation

Collapse of nasal architecture persists in patients of multibacillary leprosy, particularly if they remain untreated for a long time. One stage nasal reconstruction using bone grafts (modified Brand's procedure) is being done for moderately deformed patients at the CJIL, Agra. Ten patients operated during the year under report were followed up for survival of graft, its absorption at the recipient site and donor site complications. There were no local complications in the donor foot from where the metatarsal bone had been removed and used as a graft. The grafts retained well without any local sepsis or extrusion. Clinically, there was no significant absorption of the grafts.

A long term follow up study of corrected claw hands is in progress at the CJIL, Agra. Eighty five claw hands (of 78 patients) were studied during the year under report from different occupational groups. Post-operative evaluation was done for stiffness of hand, closure pattern of fingers, fist closure, grip power, post-operative deformities, subsequent injuries and infections. Only seven operated hands out of 85 had evidence of injury or infection. Sublimis minus deformity was seen in 14 patients out of 39 but this was not disabling. Stiffness gradually disappeared with time and the grip improved.

Sociological and Psychiatric Morbidity Studies

A sociological study of two colonies of patients comprising (i) self-rehabilitated patients near CJIL, Agra and (ii) beggars in Bijnor district, Uttar Pradesh, showed that per capita income in the self-rehabilitated patients is higher, social acceptance is greater and treatment status was better than in the beggar group.

Psychiatric morbidity in 93 patients attending the clinic at JALMA revealed depression and anxiety, which was significantly enhanced in patients who had reactional episodes.

Transmission Studies

Investigations on the possible role of biting arthropods as vectors in transmission of *M. leprae* from man to man were carried out at the CJIL, Agra. The phlebotomine sandflies and leprosy co-exist in tropical and subtropical countries where the climate is dry and humid. Screening of sandflies caught from houses in the vicinity of the leprosy hospital as well as from houses far from the hospital revealed that 19 sandflies out of 50 caught near the hospital harboured acid fast bacilli. Those caught from houses away from the hospital did not show any AFB. Investigations are in progress to isolate and identify the AFB obtained from the gut contents of sandflies.

Morphological Studies

Leprosy is a polymorphic granulomatous disease with a spectrum of lesions ranging from the paucibacillary epithelioid cell granulomas surrounded by abundant lym-

phocytes in the tuberculoid form of leprosy to lymphopenic lesions with bacilli laden foamy macrophages in lepromatous leprosy. Studies were carried out to characterize the cells in the lesions which may lead to a better understanding of the mechanism of granuloma formation in leprosy.

Single cell suspensions from the granuloma of leprosy patients using collagenase were prepared to enable an *in vitro* study of the properties of infiltrating cells. The granulomas were found to contain lymphocytes and 'large cells' (epithelioid cells and macrophages). The number of lymphocytes was significantly higher in the suspension of tuberculoid granuloma in comparison to the suspension from lepromatous granuloma. A high percentage of lymphocytes from tuberculoid granuloma formed rosettes with sheep erythrocytes and also showed the presence of esterase as dots in the cytoplasm. However, the lymphocytes did not form any rosettes with sheep erythrocytes sensitized with antibodies and complement (EAC). Most of the large cells from both the granulomas were esterase positive, exhibited peroxidase activity and did not carry receptors for the C3 component of complement. A high percentage of large cells in the tuberculoid granuloma was non-adherent to plastic surface as compared to lepromatous granuloma which contained a high proportion of adherent large cells. These observations indicated that (i) the lymphocytes derived from a tuberculoid granuloma appear to be T-lymphocytes, and (ii) the large cells in both the granulomas appear to belong to cells of the mononuclear phagocyte series. Studies are in progress to characterize these cells using monoclonal antibodies and other cell biological techniques.

Pathological changes that occur in skin and nerves of leprosy patients during the course of infection were observed in ultrathin sections. Sections of tissues from borderline tuberculoid leprosy patients showed vascular changes of the mitochondria in the cytoplasm of the giant cells. Epithelioid cells showed clusters of *M. leprae* as well as myelinated droplets in their cytoplasm. Borderline lepromatous lesions showed myelinated nerve fibres and intact bacilli in mature foamy cells. Sections of lepromatous nerve showed a large number of bacilli inside Schwann cells and degeneration of the nucleus of the cell.

Microbiological Studies

Isolation and characterization of mycobacterial mycolates at CJIL, Agra, showed that mycobacterial species can be classified into five groups on the basis of unidimensional thin layer chromatography. Analysis of mycolates extracted from leprosy infected tissues showed presence of alpha and keto mycolates in *M. leprae.* This pattern is not shown by any other related taxon and therefore is of paramount taxonomical importance.

A preliminary investigation revealed that esterases are present as isoenzymes in various species of mycobacteria. Their role in classification and identification is being studied.

The difference in morphological structure of bacilli is an important factor to know the efficacy of antileprosy drugs. Structural changes were observed in *M. leprae* in leprosy tissues before and during adequate treatment.

Ridley, Dennis S. *Skin Biopsy in Leprosy.* 2nd ed. Basel: CIBA-GEIGY Limited, 1985. Softbound, 63 pp., includes index and color plates. Available free of charge from CIBA-GEIGY.

The second edition of the book, *Skin Biopsy in Leprosy,* authored by Dr. Dennis S. Ridley, has incorporated most of the advances in the pathological study of leprosy since the first edition was published nine years ago. The author's work on the classification of the disease is so well known that perhaps he is the most frequently quoted person in leprosy literature.

The book, as expected, is properly organized, beautifully illustrated and extremely well presented. Several new sections have been added which increases the usefulness of the book. The section on diagnosis and differential diagnosis will be very helpful, particularly to those pathologists who do not routinely see biopsies from leprosy patients. By and large the book sticks to the internationally recognized Ridley-Jopling six-group classification of the disease.

This book will no doubt continue to serve

a useful purpose and will be referred to by every pathologist involved in leprosy work.

May I congratulate the author and compliment CIBA-GEIGY for making this excellent reference book available free of charge to leprologists and to pathologists interested in leprosy.—C. K. Job

Thangaraj, R. H. and Yawalkar, S. J. *Leprosy for Medical Practitioners and Paramedical Workers.* Basel: CIBA-GEIGY Limited, 1986. Softbound, 92 pp.

With this booklet, the authors intend to inform nonspecialists, physicians, and paramedical workers about the major aspects of leprosy. As a publication of CIBA-GEIGY, the booklet represents another indication of the company's long-standing commitment in the fight against the disease.

The booklet is superbly produced and is obviously the product of authors with a comprehensive understanding of leprosy. As pointed out by Dr. S. K. Noordeen, Chief Medical Officer, Leprosy, of the World Health Organization in an introduction to the booklet, the challenge of leprosy can only be met by comprehensive control efforts with participation at all levels including general medical practitioners. The booklet is intended as a guide for all individuals engaged in leprosy work. It is remarkably complete in covering the essentials of the disease and its management. Fourteen chapters outline the major points in the history of the disease, its epidemiology, bacteriology, clinical features, differential diagnosis, essentials of diagnosis and treatment, reactions and their management, the management of deformities, the prevention and control of the disease, and finally a chapter emphasizing the importance of rehabilitation programs as an integral part of every leprosy control program. The number of references for the entire booklet is limited to 100, and the list is followed by recommendations for further reading and a listing of historical milestones in the field of leprosy since 1873.

The booklet is a masterful condensation of the essence of leprosy, and Dr. Thangaraj and Prof. Yawalkar are to be congratulated together with CIBA-GEIGY Limited in having produced an extremely attractive as well as useful guide for nonspecialists called upon to care for leprosy patients.—RCH