CURRENT LITERATURE

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Clinical Course

Miranda, R. N. Aspectos clínicos da reação na lepra tuberculoiide. [Clinical aspects of reaction in tuberculoid leprosy.] Publ. Centro Estudos Lepro. (Parana) 8 (1968) 75-78. (Same article in English, 79-82)

Tuberculoid leprosy is classified by the author as (1) torpid and (2) torpid made acute or in reaction. In torpid tuberculoid leprosy lesions have slight inflammatory character, characterized by the now well recognized physical signs, positive Mitsuda reaction, without visceral manifestations, and with a tendency toward spontaneous healing. Three types of tuberculoid leprosy in reaction are described: (1) infiltrative (most frequent, 96.5% in author’s experience), (2) nercative in reaction, and (3) characterized by caseous reaction (very rare). A patient may exhibit both types of lesion when tuberculoid leprosy in reaction originates from a torpid case. Tuberculoid leprosy in reaction accounted for 63.5% of the cases studied by the author. — (From authors’ summary).


A case of progressive lepromatous leprosy in a 21 year old female is reported, first clinical evidence of which was symmetric arthritis involving the large joints of the limbs and hands closely resembling an acute attack of rheumatoid arthritis. The synovial fluid was of inflammatory character and leprosy bacilli were found in the fluid and synovial membrane. Polyarthritis was the main feature in a reaction marked by fever, lepromatous nodules, anaemia, raised erythrocyte sedimentation rate, hypoglobulinemia and the presence of C-reactive protein. The arthritis regressed spontaneously, while other elements of lepromatous reaction persisted. The onset and course suggested an immunologic disturbance. — (From authors’ summary).


Granular deposits of immunoglobulin and complement were found by fluorescence microscopy in the dermis of lesions from patients with erythema nodosum leprosum. In some cases the deposits apparently also contained soluble mycobacterial antigen. The distribution of these deposits corresponded with the areas of polymorph infiltration. It is suggested that erythema nodosum leprosum is a manifestation of the Arthus phenomenon. In a few of the patients studied the level of the third component of complement in the serum was raised. — Authors’ summary.


The work of Møller-Christensen and other authors on osteo-dental alterations in adults with lepromatous leprosy has been confirmed. A case of 12 years’ duration in a 41 year old man is described, with absence
of upper incisors, bone rarefaction, destruction in the anterior region of the maxilla increasing the nasal opening, and absence of the nasal spine. In lepromatous children these characteristic alterations were not seen, although slight changes in the region of the roots of the upper incisors suggested their commencement. It is believed that typical changes require a longer time for their development.—E. R. Long


A case of nodular infantile tuberculoid leprosy in a 2 year old girl is reported. The lesions began to decrease after treatment (DDN, 30 mgm daily) was started.—Authors' Summary


In a study of leprosy cases, 21 lepromatous, 3 tuberculoid and 1 indeterminate, morphologic lesions were found in 12 lepromatous cases of which 9 were in reaction. Functional alterations in the group were limited to increase in alkaline phosphatase and 2 of them an increase in glutaminooxidase. Of the 11 patients showed an alteration in bromsulfalein clearance. The findings support the view that anatomic lesions of the liver involve the interstitial tissue and not the hepatocyte.—(From authors' summary, through E. D. L. Jonas) Jornalizes

Bogaert, H. Diagnostico de la lepra. [Diagnosis of leprosy.] Rev. Dominicana Dermat. 3 (1969) 5-16.

The main clinical and diagnostic findings in leprosy are reviewed, pointing out various dermatologic and neurologic entities that may be confused with leprosy. Reference is made to some misdiagnosed cases treated over long periods of time by general physicians.—Authors' Summary


Biopsy of the earlobe in leprosy patients has revealed histopathologic findings and acid-fast bacilli of a diagnostic nature, substantiating, on a histologic basis, the use of the earlobe as a site for useful clinical information. The best correlation of clinical appearance and histopathologic findings in the earlobes is found in patients with lepromatous leprosy. In most instances skin snare biopsies of earlobes of leprosy patients appear to provide similar information. The systemic form of leprosy reaction was reflected in the earlobe histopathologic findings. Positive histopathologic findings in dimorphous leprosy patients could not be predicted.—(From authors' summary)


Serum copper and PPD-oxidase activity have been observed to increase in lepromatous leprosy patients with and without gynecomasia; patients with gynecomasia show more elevated levels than those without. Comparisons are in course with the disease kwashiorkor to see if there is a similar correlation. The significantly raised levels of serum copper and PPD-activity in lepromatous leprosy with gynecomasia indicate that, in addition to chronic infection, hormonal imbalance might be an additional factor for further elevation of serum copper and PPD-oxidase activity.—E. R. Long


Case report of ainhum in 5th toe of neural leprosy patient with foot claw.—E. D. L. Jonas.
Chemotherapy


Dr. Barry has again placed us in his debt. In this Boyle Medal Lecture he re-traces with unadorned skill the fascinating Odyssey he pursued in company with his Dublin colleagues in the search for an ant茵ocellular drug. He allows us to peep into the captain's chartroom and to share with him, in retrospective imagination, some of the hazards of the voyage, the false courses taken in ignorance, and the crucial calls at the Isle of Serendip, where he made valuable and unsought discoveries. From synthetic antimetabolites to the conscious and progressive modification of diphacin (the first organic chlorine compound found in nature), we can follow the story of the synthesis of scores of ruminophenazine compounds, until the development of some that were far more active than streptomycin or the thiosermicarbazones in experimental murine tuberculosis. B.663 proved to be the most active, both as subsequent phages. This fact suggested to Barry and his fellow chemists, and subsequently to R. G. Cochrane and S. G. Brown, that B.663 should be tried in human leprosy. The subsequent results of the clinical investigations conducted at Uzuakoli have received wide publicity. B.663 has been found of value in treating ulceration due to M. ulcerans and also to an atypical avian strain of bacillus. The anti-inflammatory properties in erythema nodosum leprosum may be associated with some impairment of macrophage action in processing antigen, and hence to some immunosuppressive activity. Barry briefly touches upon the mode of action of these ruminophenazine compounds. Since B.663 is strongly taken up by living mycobacteria, it is possible that it interferes with terminal hydrogen transfer, but much is still obscure. B.663, or Lamprano (Geigy) has now passed the Dunlop Committee, and has received the approved name of clofazimine. -- S. G. Brown


Extensive review (96 references) of the action of the principal drugs used in recent years in clinical and experimental (chiefly mice) studies on the treatment of leprosy, including the bases for trials, toxicity of drugs, tests for determination of activity, the phenomenon of drug resistance, the metabolism of drugs tested, and their general pharmacology. -- E. R. Long


Lysosome is muramidase, an enzyme breaking up the polysaccharide wall of mycobacteria and probably preventing the rupture of the lysosomes and the action of their hydrolytic enzymes. Twenty reactional lepromatous patients were treated with lysosome in a dosage of 8 100 mgm. tablets daily or 1 or 2 injections of 73 mgm. daily. In 16 patients good improvement was noted. -- E. D. L. Jongewaard


This drug (isonicotinylhydrazine of 2-carboxyethoxybenzaldehyde, compound 377), Chang, Y. T., Internat. J. Leprosy 25 (1957) 130-136, synthesized at the Cal-
cutta School for this study, proved effective up to one year in the treatment of 79 cases of active, previously untreated lepromatous leprosy. Twenty active patients receiving DDS orally were observed simultaneously for comparison. Marked clinical improvement was noted in all the patients treated with compound 377 after 7-10 months of treatment. After 18-21 months of treatment, however, improvement ceased to progress and after 28-32 months was practically at a standstill. In the DDS group evident improvement was still continuing after 40-44 months. The authors conclude that drug resistance had developed in the experimental (compound 377) group, and suggested that in treatment with this drug DDS should be combined with from the start—E. R. Long.


The effect of streptomycin on the growth of *M. leprae* grown in cultures of mouse peritoneal macrophages was studied. Since these organisms do not grow in bacteriologic media, the influence of extracellular bacterial growth can be ruled out. The suppressive activity of streptomycin was observed in a total of 5 experiments. At the end of 4 weeks, the average number of organisms per macrophage for the controls was 85.7; for cultures with streptomycin at concentrations of 0.5, 1.3, 10, 50, and 100 μg/ml of medium, it was 45.4, 38.3, 28.7, 13.4, and 8.2 respectively. A good dose-response relationship was evident. *M. leprae* that had been treated in macrophage cultures with various concentrations of the antibiotic for 4 to 5 weeks was used to infect fresh macrophages. These cultures were in turn treated with streptomycin. Resistance of the organisms to streptomycin did not occur. (From author's summary)


In 12 Ethiopian men probenecid given with dapson caused a significant reduction in urinary excretion of acid-labile dapson metabolites, and to a lesser extent of free dapson, and also raised the blood levels of dapson. The method of estimating serum levels of dapson by Schiff base formation was modified for use with urine.—Authors' Summary


The clinical pictures of 2 young men who developed peripheral motor neuropathy in the course of dapson therapy are described. The clinical findings were supported by motor nerve conduction studies. In both cases, complete clinical recoveries were observed following discontinuation of dapson.—Authors' Summary


Eight cases of lepromatous leprosy were treated with B.663 for periods of 11 to 36 months. Three had B.663 combined with INH; 4 had B.663 alone; and 1 had B.663 combined with DDS. Antibacterial effect was demonstrated clinically, bacteriologically and histopathologically. The rate of improvement clinically and on serial biopsies was slower than that previously observed with standard sulfone treatment of uncomplicated lepromatous cases. (From author's summary)


A case of erythoderma due to DDS is reported in a patient (55 year old woman) with lepromatous leprosy. The erythrodermia relented on stopping medication.—Authors' Summary

Six lepromatous patients in cortisone-dependent reaction were treated with short courses of thalidomide, in a dosage of 400 mgm. daily for 1 week and 300 mgm. daily thereafter. Four patients were treated for 1 month, 1 for 40 days and 1 for 60 days. All patients improved. Edema of the legs was seen in 2 of the patients.—E. D. L. Jones-aines


In a Portuguese lepromatous patient a first attack of ENL was easily overcome by a daily dose of 100 mgm. of thalidomide, without need of modifying the specific treatment in course. A second attack, more severe, required not only 300 mgm. of thalidomide but also discontinuation of the specific treatment and association, with the latter, of Glucantime and streptomycin.—P. Hartner


A case of major tuberculoid leprosy with reactionary exacerbation in an African patient yielded on the first occasion to a daily dose of 400 mgm. of thalidomide, but a second attack, with ulceration, was not modified after 6 weeks of the same treatment. A second African case, of lepromatous type, in neuritic and febrile reaction did not yield after 10 days of the same treatment, but was improved by 3 blood transfusions.—P. Hartner

Surgery and Surgical Specialties


Salient neurologic and dermatologic features in differential diagnosis of the following diseases, in which plantar ulceration may occur, are discussed: leprosy, diabetes, tuberculous syringomyelia, traumatic sciatic nerve lesions, various hereditary neurologic disorders, including radicular neuropathy, and Charcot-Marie-Tooth disease and the hypertrophic interstitial neuropathy of Dejerine and Sottas.—E. H. Long


Seven cases of avulsion fracture of the calcaneus at the insertion of the Achilles tendon in leprosy during the last 6 years are reported. There was no subcutaneous rupture of the tendon. These fractures occurred on walking without any appreciable trauma. The mechanism of development of the fracture is believed to be pathologic fracture; it is logical to think that the avulsion fracture demonstrated in leprosy is related to the powerful force with which the gastrocnemius muscle acts on the calcaneus already the seat of slight atrophy because of disturbance of both sensory and motor nerves.—(From authors' summary)


Two hundred noninstitutional cases of leprosy were examined to determine the incidence of eye lesions caused by leprosy and to compare the incidence against that found in institutional cases of leprosy. Only 7.2% of the noninstitutional cases had eye lesions with defective vision, comparing favorably against 37.3% of the institutional cases. Trachoma incidence was found in
34.5% of the survey group, while the control group had an incidence of 51.5%. The ocular lesions are mainly corneal. Eradication of leprosy and trachoma will certainly reduce the incidence of ocular lesions.

Authors' Summary

Pathology


Although M. leprae was identified earlier than M. tuberculosis, it has still not been cultured in vitro. Only in 1960 was an infection obtained in laboratory animals. However, important advances have been made in experimental leprosy in the last decade, with development of new techniques and models for studying M. leprae in vitro, thus overcoming limitations imposed by a noncultivatable mycobacterium. Quantitative techniques using M. leprae murium provided the first model for an indirect method for distinguishing dead (noninfectious) from living (infectious) bacilli, based on morphologic differences in organisms stained by the Ziehl-Neelsen method. However, the most important advances resulted from the limited and localized growth of M. leprae inoculated into the foot pads of mice and, later, the more substantial and generalized multiplication of M. leprae in immunologically deficient mice (thymectomized and irradiated with a dose of 900 r). Moreover, in the immunologically deficient animals, the infection eventually resulted in a disease replicating that of lepromatous type leprosy in man, including the involvement of peripheral nerves.—(From authors' summary)


Multiplication in the foot pads of guinea-pigs was not recognized in the experimental inoculation of M. leprae, not only with an emulsion of leproma but also with an emulsion of mouse foot pad tissue containing M. leprae. In the skin reaction provoked by Dharmendra antigen, however, it was found that guinea-pigs may be sensitized with M. leprae at 5 months after the inoculation. These results are discussed with relation to the activity of phagocytes in foot pad tissue. Phagocytes in guinea-pigs was stronger than in the mouse. It may be concluded from the results of this investigation that successful transmission of M. leprae into the hind foot pad of guinea-pigs could not be obtained.—(From authors' summary)

Primary and mouse-passaged strains were inoculated into the hind foot pads of fowls. It may be concluded from the results obtained that successful transmission of M. leprae was attained. No cultivable acid-fast strain was isolated from a fowl as a contaminant.—AUTHORS' SUMMARY


The observation by Shepard of limited multiplication of M. leprae in the mouse foot pad, its confirmation by Rees and others, and the report by Waters and Niven of limited multiplication of M. leprae in the hamster ear and foot pad, stimulated the author to study the fate of M. leprae in the foot pads and ears of guinea-pigs. Bacterial suspensions recovered, at varying intervals, from tissues at the inoculation site where used for counting bacilli and for reverse transfer of mice to examine their multiplication and viability in the guinea-pigs. There was no evidence of multiplication of organisms in the ears and foot pads and viability of organisms therein was remarkably diminished with time.—(From author's summary)


In the previous experiments (Part 1) no finding concerned the macrophage-parasite relationship, although multiplication and viability of the bacilli were estimated by counting the bacilli and reverse transfer. Therefore a study was made of the macrophage-parasite relationship. Guinea-pigs were inoculated subcutaneously in the back with a suspension of murine leprosy bacilli. At intervals of 5 days subcutaneous connective tissues at the inoculation site were removed and spread on a glass slide, and the behavior of the bacilli within mononuclears was examined. After 5 days elongation of the bacilli was observed in mononuclears, and 15 days later many enlarged mononuclears filled with the elongated bacilli appeared at the site of inoculation. From the findings of this observation and of reverse transfer, it seemed that the growth patterns of murine leprosy bacilli subcutaneously inoculated in guinea-pigs were identical with those in mice up to 15 days after inoculation. From then on, however, infectivity of the bacilli in the guinea-pigs became remarkably reduced. After 30 days, non-leprous granulovasata appeared at the inoculation site and the number of bacteria was significantly decreased. In a similar experiment inoculation from Kirchner's medium back to the mouse, was performed to examine the viability of the in vitro cultured organisms. Elongation of the bacilli occurred in Kirchner's medium, but viability of the in vitro cultured bacilli was greatly reduced with time. On the basis of these observations it was considered that macrophages of guinea-pigs play only a short role in multiplication of murine leprosy bacilli (about 15 days). It is desirable to prolong that short duration for development of a study on transmission of murine leprosy to guinea-pigs.—(From author's summary)


In simple culture, within 72-95 hours, phytoagglutinin, a product extracted from the seeds of Phaseolus vulgaris, transforms 70% of the lymphocytes of normal peripheral blood into large cells with one or more nuclei and open nuclear network with vacuolated cytoplasm (blast-like cells). The rest of the nuclei are not transformed. Neutrophils are destroyed, but basophils and eosinophils are not. In malignant lymphoma and chronic lymphatic leu-

Forty-six untreated cases of "reaction in tubercu­loid leprosy" were selected for biopsy. Tissues were stained by hematoxylin and eosin, Fite-Faraco hematoxylin, and toluidine blue. Hyperkeratosis, granulomatous change, acanthosis and parakeratosis were observed, each in a high percentage of cases, with typical tubercle formation in 41%. Langhans giant cells were not common. When they were seen they were atypical and poorly formed. Mast cells were numerous, but more than 75% of these cells were degranulated. Most of the cases in the series showed conspicuous changes in the nerves, varying from complete loss of structure to persistence with cellular infiltration and edema.—E. B. Long


Report of a continuation of studies recorded in the previous abstract. Fifteen cases of "reaction in tubercu­loid leprosy" were selected for biopsy. Sections were stained with Lison's toluidine blue. In addition to changes in the size and shape of the mast cells, swelling and the phenomenon of degranulation, leaving degenerated "ghost cells," distributed at cell peripheries, were frequent. In contrast the granules of mast cells in tubercu­loid cases not in reaction were deeply stained and distributed throughout the cells. The mean of mast cells found per microscopic field in reaction cases was 0.9, as compared with about 40% in tubercu­loid cases not in reaction.—E. B. Long.

Riva, J. P. and Serial, A. Presencia de los mastocitos en los infiltrados tuberculoides y lepromatosos. [Presence of mast cells in tuberculoid and lepromatous infiltrates.] Lepidologie 13 (1968) 3-5.

Quantitative variations in mast cells were studied in 15 lepromatous and 12 tuberculoid cases. Averages of 16 mast cells per 10 microscopic fields for lepromatous cases and 3.8 for tuberculoid cases were found. The granules observed were intracellular in 36% of tuberculoid cases and extracellular in 44%. The corresponding figures for lepromatous leprosy were 75% and 25%. No conclusions are given.—E. D. L. Josquinets

Vishnevskaya, L. G. and Bogush, T. G. [Some conditions of the endometrium in patients with leprosy.] Akusherstvo i Gynecologia 8 (1968) 64-68.

The state of the endometrium was studied in 20 females of childbearing age suffering from lepromatous leprosy and treated with sulfone preparations. Menstruation was regular in all. Curettage was performed 3–4 days before menstruation. In 5 only out of the 20 the mucous membrane of the uterus corresponded to a stage of adequate secretion. In 7 there was inadequate secretion by the endometrium. In 5 there were no signs of endometrial secretion. A disturbance of growth was noted with marked atrophic changes in the endometrium. The most marked manifestations of endometrial hypotrophy were observed in an unfavorable course of the disease with frequent exacerbations, as well as in females in whom, for a protracted time, the disease was treated with nonsulfone agents.—Authors' Summary
Bacteriology and Immunology


Microscopic recognition of M. lepraes is still the only reliable method of bacteriologic diagnosis, and of assessing results of treatment. In 100 patients with leprosy, specimens were examined for acid-fast bacilli from nasal smears, ear lobe and leperous lesions. For nasal specimens, the mucosa of both nostrils was scraped with a platinum loop and the specimen smeared on a slide, which was then fixed by heat. The ear lobe and skin lesions were punctured with a needle, and a thick drop of fluid 3 mm. in diameter was allowed to exude on a slide. This was dried for 24 hours at room temperature, hemolyzed with ethanol diluted 1 in 3 for 15 minutes, and then washed with absolute alcohol and flame. All preparations were stained with Ziehl-Neelsen. Acid-fast bacilli were found in 44 patients. Positive findings were: nasal smear only: 5 weakly positive; ear lobe only: 5 weakly positive; leperous lesion only: 5 weakly positive; ear lobe and leperous lesions positive, nasal smear negative: 8 patients; ear lobe lesions and nasal smear positive, leperous lesions negative: 1 patient; ear lobe, leperous lesions and nasal smear all positive: 17 patients. As controls, specimens from the ear lobe of 100 students were examined. All were negative. The authors consider it necessary to examine all 3 specimens from each patient.—(From abstract by R. L. Vollum. Trop. Dis. Bull. 66 (1969) 922-927)


The morphologic appearance of M. lepraes in acid-fast stained sections of skin biopsy specimens from patients with lepromatous leprosy has been found to correlate well with the infectivity of the specimen for the mouse. Viable M. lepraes were demonstrated in 15 of the 36 patients with previously untreated lepromatous leprosy. Ten of 38 specimens obtained early in the course of dapsone therapy of previously untreated patients were found to contain viable M. lepraes; viability of the organisms was found to be much reduced in 3 of these 10 specimens. By contrast, of 15 specimens obtained during dapsone therapy of 5 patients proven to harbor dapsone-resistant M. lepraes, 14 were demonstrated unequivocally to contain viable organisms.—Authors' Summary


Uranine (Na₂C₂O₄·H₂O₂), the sodium salt of fluorescein, has been added as a stain for mycobacteria for rapid identification by fluorescence microscopy. The preparation of the stain, staining technic, and results are described. Acid-fast and nonacid-fast atypical mycobacteria, including acid-fast M. tuberculosis, are detected by this method. Positive slide specimens should be confirmed by the usual cultural methods.—(Abstract by E. Danner, American Rev. Resp. Dis. 100 (1969) 250)


A rapid method is presented for screening tuberculosis slide specimens by fluorescence and confirmation by Kinyoun stains on the same slide. An average of 40 specimens per day may be screened and confirmed on the same slide in about 2 hours, whereas 6 to 8 hours were required when two separate technics were used.—(Abstract by E. Danner, American Rev. Resp. Dis. 100 (1969) 250)

In 148 examinations of malum perforans, ulcer cruris, urine, nasal exudates, abscesses, sputum and proderma Pseudomonas aeruginosa was found in 36.4% E. coli in 36.6%, Streptococcus fecalis in 30.9%, Staphylococcus epidermidis in 14.6%, Staphylococcus aureus in 6.5%, Candida albicans in 5.9%, Aerobacter aerogenes in 1.6%, Proteus vulgaris in 1.09%, Bacillus propertium in 1.09% and Streptococcus sp. in 1.09%. The need of antibiograms to avoid bacterial resistance is emphasized.—E. D. L. Juvénolés


Studies on morphologic changes of M. leprae murium grown in cultures of mouse peritoneal macrophages revealed 2 types of nonsolid or irregularly stained M. leprae murium. One type occurred in the growth phase of the organisms during the stage of preparation for bacillary multiplication. The nonsolid bacilli appeared as elongated organisms having pointed ends, isolated acid-fast dots, or faintly stained areas at the ends of the bacilli. It is possible that this irregularity in staining is due to a very gradual, versus an instantaneous, acquisition of acid-fast material during bacillary multiplication and maturation. Solid forms were again observed upon maturation. Nonsolid bacilli were also observed in macrophage cultures infected with autoclave-killed M. leprae murium. Under these conditions organisms emerged showing irregularly stained areas and various forms of deformity unaccompanied by elongation or multiplication. These irregularities were most probably due to the destructive process of digestion of bacillary protoplasm. The present study does not support the current hypothesis that all nonsolid acid-fast organisms are nonviable.—(From authors' summary)


Crystalline inclusions have been found in an occasional cell of the bacterial strain 22M, isolated from a case of leprosy by C. V. Reich (Internat. J. Leprosy 33 (1965) 527-531). They have not been found in fresh cultures, in the first 18 hours of incubation, but can be seen in cells from centers of colonies after prolonged incubation. Arrays consist of parallel rows of polyhydral subunits, 7.5 mm. in diameter, 2.0 mm. apart, with a distance of 3.0 mm. between rows. A relation between the inclusions and defective bacteriophage does not appear likely. Strain 22M is lyogenic and when induced with ultraviolet light does not produce bacteriophage. In induced cells the authors have not observed crystalline inclusions.—E. R. Low


Fifty per cent of patients with lepromatous leprosy could not be sensitized to 2,4-dinitrochlorobenzene (DNCB). However, 10 DNCB reactors could be induced to show delayed hypersensitivity to keyhole limpet hemocyanin (KLH). Failure of cell-mediated immunity is, therefore, not absolute. This is confirmed by the finding of small numbers of small lymphocytes in the depleted paracortical areas of lymph nodes from these patients. No difference could be found in the lymph nodes of DNCB reactors and nonreactors, a fact consistent with the nonspecific failure of cell-mediated immunity being relative. It is concluded that induction of DNCB sensitivity is a relatively weak indication of cell-mediated immunity as compared with KLH. In leprosy, nonspecific loss of cell-mediated immunity, as evidenced by loss of ability to be sensitized with DNCB, is probably secondary to the infiltration of the paracortical areas of lymph nodes with histiocytes, rather than a primary event leading to the development of the lepromatous state.—Authors' Summary
[Cellular immunity in infectious diseases]


The role of cell-mediated immunity (CMI) in leprosy has lately attracted great interest, much of which has been stimulated by the work of Rees and his coworkers, who found that a disease similar to lepromatous leprosy could be produced in experimental animals only after a general depression of CMI by thymectomy and deep X-irradiation. Under these conditions M. leprae could be induced to disseminate widely throughout the tissues as in the human disease. The possibility therefore arose that lepromatous leprosy could develop in man as a result of a general deficiency in CMI, similar to that seen in babies with congenital aplasia of the thymus. Job and Karat recorded a delay in heterologous skin-graft rejection for as long as 70 days in patients with lepromatous leprosy. An additional phenomenon which has been associated with a deficiency in CMI is an impairment in lymphocyte function, which can be demonstrated by a decreased ability of these cells to be transformed into blast cells in culture by phytohemagglutinin (PHA). Impairment of transformation of lymphocytes by PHA has been shown to parallel the inability of patients to be sensitized with contact sensitizers, such as DNCB in Hodgkin’s disease, sarcoidosis, and primary biliary cirrhosis as well as leprosy and congenital thymic aplasia. It seems that inability to be sensitized to DNCB, or a deficiency in the response of lymphocytes to PHA may reflect only a relative depression of CMI insufficient to make the patient more susceptible to infection. That impairment of contact sensitivity does not demonstrate a complete inability of the patient to develop CMI is clear from a paper by Turk and Waters (see preceding abstract). Patients with lepromatous leprosy who could not be sensitized with DNCB could be induced to develop hypersensitivity reactions to a more powerful antigen—hemocyanin. Failure of CMI in leprosy is probably directed at first specifically against M. leprae. The failure of immunologic response does not, however, affect humoral antibody production, since these patients can have a high concentration of anticytobacterial antibodies in their sera and they may have a chronic “serum-sickness”-like disease (erythema nodosum leprosum) due to deposition of immune complexes, formed between antigen and antibody, in their tissues. Nonspecific impairment of CMI would then be a secondary rather than a primary event, and it would be the result of the replacement of those parts of the lymphoid tissue where lymphocytes proliferate during the development of a cell-mediated immune response by histiocytes containing mycobacteria. These cells probably drain down to the central lymphoid organs from the peripheral tissues where they are present in large numbers. The evidence suggests that lepromatous leprosy develops in patients with an intrinsic constitutional defect. Conceivably a primary inability of the cellular immune mechanisms allows the infective agent to gain a foothold in the tissues. The organism then proliferates to such an extent that a state of specific immunologic tolerance develops. This state, however, affects cellular immune processes only, leaving humoral antibody-producing mechanisms intact. Evidence so far indicates that the tests used, such as the development of DNCB sensitivity, reflect a secondary rather than a primary defect in CMI, and more sensitive tests will have to be found to discover the cause of the initial defect which allows the organism to proliferate in the first place.


Immunization against mycobacterial infections has been directed mainly against tuberculosis, as representing the most serious of these infections. Although BCG vaccination has been available since 1921, it has taken 40 years to establish beyond doubt its efficacy against tuberculosis. Evidence is now accumulating which indicates that BCG may also be of value in protecting against other mycobacterial infections, including leprosy (Uganda, New Guinea and Burma trials), and M. ulcerans infections (Uganda trials). This would be consistent with the wide range of common anti-
...gns shared by many species of mycobacteria. It is the appreciation of these immunologic features of mycobacteria that during the last decade has helped to unravel the complexities surrounding vaccination against mycobacterial infections.—Author’s Summary.


Antigen obtained by physiologic saline and alkali extraction from healthy human skin was tested in serial dilutions against sera from 21 tuberculoid and 15 lepromatous cases of leprosy and 7 normal persons, also in serial dilutions. Large bobbles were seen with 1:40 and 1:50 dilutions of antigen only in lepromatous leprosy. Changing the pH of the antigen slightly toward the acid side prevented the later demonstration of flakes. The authors note that the antigen was from homologous but not autogenous skin, and that therefore the absence of precipitable antibody may not be of help in discounting the possibility of an auto-immune mechanism in leprosy.—E. R. Lowe


A long review of previous work on this subject is given. In the present investigation 500 patients were studied in a tuberculosis hospital in Mexico City; 0.1 ml. of the various antigens was injected intradermally and the size of the resultant induration was measured 48 hours later. Of the patients, 90% were male; they were of all ages, but 36% were aged 21-30 years. With the Mantoux test, 94.6% were positive and 5.2% negative. With histoplasmal, 96 cases (11.25%) were positive. With coccidioidin antigen, 10 patients (2%) were positive. With the polysaccharide of S. schenckii, 33 patients (9.1% of 359 tested) were positive; with the levaduriform antigen of S. schenckii 134 cases out of 359 (38%) were positive. Among 100 patients tested with lepromin, 3 were positive. Many patients reacted to more than one antigen, indicating a cross-sensitivity which may be due to similar chemical groupings occurring in the different organisms. It is considered that skin reactions are valuable to investigate the geographic distribution of mycotic infections and also to some extent for individual diagnosis. It is necessary, however, to standardize the technique and to use purified antigens.—(From abstract by F. Hawking. Trop. Dis. Bull. 66 (1969) 923)

Genetics


Dermatoglyphics of 105 hands were analyzed (50 normal controls, 77 contacts, 22 tuberculoid and 46 lepromatous patients). A statistically significant increase was found of the furrows of lepromatous women, as compared with those of normal women. An increase in the proximal triaduli in the T’ and T” positions was demonstrated, indicating a more distal position in contacts and lepromatous patients than in normal persons.—E. D. L. Jones

Epidemiology and Prevention


In leprosy control, WHO continued assistance to countries and provided technical advice for UNICEF-assisted projects. Case-finding proceeded satisfactorily in many projects. Over 90% of infectious cases
had been registered and treated in some projects but diphenylsufone (DDS) has to be taken for many years, and poor attendance of outpatients continued to be a problem. In a "double-blind" trial with thalidomide in Venezuela beneficial results have been reported in the treatment of the acute lepra reaction that may occur in lepromatous patients. Cases of acute polyneuritis incidental to the lepra reaction were also reported to be controlled rapidly and completely with thalidomide. A preliminary appraisal of WHO double-blind coordinated trials in India, Mali, Somalia, and Spain seems to confirm this result. In the long-term chemoprophylaxis trial with DDS in India, it was found, after 5 and one-half years' observation, that 33% protection had been conferred. Certain subgroups among the contacts appeared to have received greater protection than others. In the WHO-controlled field trial in progress in Burma since August 1964 to ascertain the value of BCG vaccination in the prevention of leprosy, preliminary results indicate that BCG vaccine has not conferred significant protection either on household contacts or on children not exposed to M. leprae at home but possibly exposed elsewhere. At this stage, it is premature to recommend worldwide BCG vaccination for prevention of leprosy.


Leprosy exists in all the countries of the Americas with the exception of mainland Chile, but the true magnitude of the problem is unknown for want of complete information. According to data supplied to the Pan American Sanitary Bureau of the World Health Organization by 30 countries and territories in the Americas, there were 178,572 cases of leprosy in the active register at the end of 1968, of which 136,298 (76.3%) were under surveillance. Available figures on the number of cases in the active register in 17 countries and other political units show that out of 121,175 cases, 64,706 (53.4%) were lepromatous, 26,627 (22.0%) tuberculoid, 26,075 (21.4%) indeterminate, and 1,767 (1.4%) of other clinical forms. Data submitted by 18 countries and other political units indicate 330,705 registered contacts, of which 159,645 (48.7%) were under surveillance. A series of tables and several paragraphs of text summarize statistical data and the character of programs in individual countries. Countries with more than 0,000 registered cases, included, in descending order, Brazil (1.7,510), Colombia (1.6,391), Mexico (14,387), Argentina (9,783), and Venezuela (9,066).

In recent years there have been significant developments in the control of leprosy. Leprosaria have tended more and more to be converted into leprosy hospitals where special cases are treated over a limited period, instead of being subjected to lifetime isolation. Periodic supervision of patients and contacts is considered essential in the early diagnosis of new cases, and a means of breaking the infection chain and preventing deformities. Leprosy has been added to the category of communicable diseases, from which it had formerly been excluded by prejudice. Control of this disease as a regular activity of the general health services has been accepted, and renewed emphasis has been placed on physical and social rehabilitation and the prevention of deformities.

The Pan American Sanitary Bureau worked in close cooperation with the governments of Argentina, Ecuador, and Venezuela in various aspects of organization, conduct, and evaluation of programs in conformity with the administrative methodology recommended by the Guanajuato Seminar (1963). The 3 countries subsequently presented the results of the experience to the Seminar on Administrative Methods for Leprosy Control Programs held in Guadalajara, Jalisco, Mexico. In order to ensure the submission of comparable reports to the Seminar, the PASB prepared a guide for their presentation, which was discussed in detail with the authorities responsible for leprosy control in the 3 countries.—E. R. Lowe

From 1894-1921, 330 new patients were admitted to the U.S. Public Health Service Hospital at Carville (then the Louisiana Leprosy Home). Additional new cases admitted to Carville plus those reported to the registry and not admitted have totaled 4,513 as of 1 January 1969. Of 3,461 leprosy patients reported from 1894 to 1965 inclusive 345 have had military service. There is no record of leprosy among service men or veterans prior to the Spanish-American War (1898). Figures for veterans of the several wars are as follows: Spanish-American War, 26; World War I, 97; World War II, 137; Korean War, 25; Vietnam War, 11; peace time veterans or undetermined, 39. The majority (236 out of 345) had Army service; 56 served in the Navy, 24 in the Air Force and 17 in the Marine Corps. The numbers were much smaller in the other service branches. Service-acquired leprosy due to foreign assignment is considered of minor significance in relation to other sources of the disease in the United States.—E. R. Long.


Leprosy is contagious. The number of susceptible persons varies (averaging about 20%). In endemics of the kind found in Argentina, the interrelation between patients and susceptibles is such that the secondary attack rate decreases to 4%. Susceptible persons contract the disease as soon as they enter the leprosy environment, regardless of age. Patients detected among contacts are usually closed cases (74%); in cases originating from other sources closed cases drop 55%. Early sulfone therapy is most effective. Treatment must be regular and lasting. Suspension gives rise to relapse. In the first year effective dosage is taken by 80% of patients, 60% in the second year, 40% in the third, and after the fourth year 13%. Bacilloscopy remains positive in 40-50% of patients who have taken 75% of the useful dose up to the fourth year.—(From authors' summary, through E. D. L. Jonquères)


The number of leprosy patients in the world is estimated to exceed 10 millions, less than one-third of which have been registered. The majority live in Asia, but Africa has the highest relative prevalence of leprosy, with 10 in 1,000 people. In countries where leprosy is endemic, males are more frequently affected than females, the ratio being approximately 2 to 1. The fact that leprosy is nowadays more or less confined to tropical and subtropical regions is attributable mainly to environmental factors, among which the climatic conditions are of secondary importance. The prevalence of certain clinical manifestations of the disease varies in the different ethnic groups; whereas the tuberculoid type predominates in the negroid races, the lepromatous type is more frequently encountered in Caucasians. In many developing countries the impairments due to leprosy are a major public health problem which can be overcome only with international collaboration.—Author's Summary


Leprosy has again stirred exaggerated fears and led to charges of governmental secrecy in its reporting; largely because of discovery of cases in Leicester. Actually only 22 patients have been registered in the Leicester district since 1951, a number considered small in the light of the size of the population, and care that has been taken by general practitioners and dermatologists in the recognition of cases.—E. R. Long.


The early history of leprosy in the State of Jalisco, at present one of the most affect-
ed states in Mexico, is reviewed. At the
time of the Spanish conquest of Mexico,
leprosy was rife in Spain, and presumably
the disease was brought to Mexico by the
Conquistadores. Cortez founded a leprosy
hospital in Mexico between 1521 and 1524.
It is not known why the disease went so
long unrecorded in Jalisco, but presumably
little attention was devoted to it until it
reached epidemic proportions. The later
high prevalence is attributed to commerce
with the Orient, and the important role
played by Guadalajara, capital of the State
of Jalisco, in this commerce.—E. R. Lown

**General and Historical**

Said, A. Los nuevos caminos de la lepro-
logía. [New roads in leprology] Der-
matología (Mexico) 13 (1969) 1-3. (Edi-
torial.)

In the last international congress on lep-
rology, held in London in 1969, a new
tendency in the study of leprosy was evi-
dent, marked by departure from empiri-
cism, with stronger emphasis on scientific
and experimental research. This ancient
disease has stimulated bacteriologists, im-
nunologists, geneticists, biochemists, neu-
rlogists and others to apply their particu-
lar talents to its great and difficult prob-
lems. Experimental studies predominated
in the London reports. The themes of major
attention in previous years, viz., therapy,
classification and control, were treated less
extensively in London. Did it mean that
there was nothing more to know about the
clinical manifestations of this ailment?
Working on leprosy in the laboratory is not
the same as dealing with patients' problems
in the dispensary or the field. The answer is
that all is important. The two types of
endeavor are not in opposition but in real-
ity complementary. What is truly lamenta-
bale is that many of those who deal so
competently with the bacillus in the labora-
tory, and the sera of patients, never see the
patients themselves and therefore do not
know leprosy as a disease, with its myriad
problems. In contrast those who work
where leprosy is an overwhelming burden
commonly lack the background, training
and resources to carry out investigations
that are obviously needed. In other words
practice and experimental study are disar-
chitecture. It is inseparable that lepro-
sy will benefit steadily from work in the fields
of technical science, a wholly desirable
future. Not to be overlooked, however, is
the fact that our principal and immediate
objective is adequate attention for the
thousands of sick who live and hope in
countries where leprosy is always present.—
E. R. Lown

(Note: The abstractor, who holds firmly
to the view that an abstract should be just
that, viz., a condensation of an author's own
report, not supplemented by the views of
the abstractor himself, cannot refrain in this
case from departing from his own princi-
ple. Dr. Said's lament, if it can be called
that, is a familiar one today in many fields.
What he has said has been expressed many
times with respect to tuberculosis, cancer
and other major diseases of wide concern.
It will surely be agreed that his call for
closer partnership between the practicing
profession and the technical experts in pur-
suit of a common goal is sound logic.)

Emma, C. D. and Byrd, C. F. The history
and development of the National Lep-
rosarium in the United States. Internat.

Establishment of the leprosarium at Car-
vile, Louisiana, is credited to the discern-
ment and perception of a 17-year-old "cub"
reporter of the New Orleans Picayune. J.
K. Smith, who wrote a series of articles on
leprosy which were published in that pa-
paper. An overwhelming response from the
public, the medical profession, and the
state legislators led to the founding of the
"Louisiana Leper Home" at Carville in
1894. The home was purchased in 1921 by
the United States Government and desig-
nated as the National Leprosarium. It is the
present U.S. Public Health Service Hospi-
tal. Early care was primitive, but marked
devoted service from the nursing staff.
Most patients were lepromatous and
severely ill. Because of the frequent
presence of unsightly deformities patients
assumed aliases. Distinguished service was
rendered by many patients and staff mem-
bers, including Sister Hilary Ross, long
Chief of the Laboratory Branch, and Sid-
ney Leyson, founder of the Carville Star,
who became famous under the alias of
Stanley Stein, working incessantly to pro-
mote the interest of leprosy patients
throughout the world. Medical leaders
have included Drs. O. E. Denny, first med-
ical officer in charge, and Coy Fugit, the
first to recognize the efficacy of sulfone
drugs. The institution now has approxi-
ately 100 buildings on 336 acres of land,
providing a wide variety of medical, social
and recreational services.—E. R. Long

Bushnell, O. E. The United States Leprosy
Investigation Station at Kalawao. Hawai-
ian J. Hist. 2 (1968) 76-94.

This is a documented history of federal
care of leprosy on the Island of Molokai in
Hawaii. Its starts with the promise, set
forth by Hawaiian islanders, that the finan-
cial benefits to the American people
through the territorial annexation of
Hawaii were not met in the beginning by
suitable provision for certain of the Islands'
problems, among which was leprosy. In
time the defect was partially remedied, but
at first help through Congress was on a
limited scale. Land from the leprosy settle-
ment on the island of Molokai was granted
to the Federal Government for a site to be
devoted to the investigation of leprosy, in
return for which Congress appropriated
funds for buildings and staff. In June 1905,
by proclamation of the Hawaiian governor,
one-sixth of the area of the existing leprosy
settlement at Kalanapua was conveyed to
the Federal Government in perpetuity. For
a variety of reasons, however, relations be-
tween the patients and the newcomers
were strained. The patients were aware of
a great difference between the program of
the new scientific staff and that set up by
Father Damien and Brother Dutton years
before. Ultimately the investigative station
failed in its purpose and closed, but, in the
author’s words, "the tragedy of errors
dragged on for many more years." In 1923
Congress passed on act restoring the station
to the Territory of Hawaii, but administra-
tive difficulties in the rearrangement were
such that the appropriation lapsed. Ulti-
ately part of the once ambitious institu-
tion was torn down.—E. R. Long

Bogaert, H. Seminario sobre métodos de
administración en programas de control
de la lepra. [Seminar on administrative
methods in programs of leprosy control.]

A brief review of the main conclusions
reached at the Leprosy Control Adminis-
trative Program meeting in Guadalajara
last year (1968).—Author's SUMMARY


General review of leprosy from historical
and epidemiologic points of view, with
consideration of its bacteriology; manner of
spread, course and diagnosis, and the char-
acteristics of its principal forms.—E. R.
Long

Other Mycobacterial Diseases

Barter, C. E. and Carmens, I. M. H. Lung
infection with anonymous mycobacteria.

During the period Jan. 1963 to Sept.
1966, 146 cases of suspected tuberculosis
were investigated at the Repatriation Gen-
eral Hospital, South Australia. Six were
considered to have atypical disease. All
were men, with an average age of 40 years,
and anonymous mycobacteria were isolated
from each on at least one occasion. In only
2, however, was there convincing evidence
of pathogenicity. The findings were in
striking contrast to those of Queensland
and Western Australia, where anonymous
mycobacteria have proved a problem, but
no satisfactory explanation for this has, as
yet, been determined.—J. G. Hargrave
success of leprosy campaigns may appear
and some of his expressed views on the
problems of the developing countries.
Tend to over emphasize and these
interested in leprosy as it occurs in
cash and publicity.
commandeer more than their fair share of
pathogenicity for rabbits, the two isolates
were identified as M. intracellulare rather
than M. avium.—(Abstract by I. T. Ehi-
sawa, American Rev. Resp. Dis. 100 (1960)
201)

Imman, P. M., Beck, A., Brown, A. E., and
Stanford, J. L. An outbreak of injection
abscesses due to Mycobacterium absces-
Over a period of 14 months 12 patients
were seen with multiple abscesses of their
arms following histamine injections. From 3
of these cases a fast-growing nonpigmented
mycobacteria was isolated. This was
identified by detailed bacteriologic and
serologic investigations as M. abscessus, an
organism different in several respects from
M. fortuitum. The difficulties in distin-
guishing between these two species are
stressed. It is thought that the outbreak was
caused by injection of a batch of histamine
solution which had become infected with
this organism.—Authors’ Summary

Book Review

Aujolet, L. P. Santé et Développement en
Afrique. Librairie Armand Colin, 103
Boulevard Saint-Michel, Paris 5. France.

For far too long, and with some justifica-
tion, leprologists used to be accused of
isolationism. They kept themselves to
themselves, blissfully unmindful of the fer-
ment and turbulence going on around them
in the world of scientific medicine.
Nowadays, they may face the charges that
they are so concerned that leprosy should
not be forgotten or neglected that they
tend to overemphasize its importance and
commandeer more than their fair share of
cash and publicity.

Here is a book that should be read by all
those interested in leprosy as it occurs in
the setting of the medical and economic
problems of the developing countries.

Dr. Aujolet is not a specialist leprologist,
and some of his expressed views on the
success of leprosy campaigns may appear
unjustifiably optimistic, but he has an un-
rivalled and intense practical knowledge of
the larger problems of health and dis-
case, of rural and tribal Africa, of control of
tropical endemic disease and the diagno-
sing health hazards of the new industriali-
sation and urbanization. He paints on a wide
canvas, with sweeping strokes, but his
touch is so sure and so elegant that the
reader follows him with mounting interest.
He insists time and again that medical
policy has to take account of the human
factors and nonmedical considerations: it
must anticipate, and if necessary mitigate,
the results of its own spectacular successes.

The book is written in the eloquent
French characteristic of the author, and its
severely practical passages are illumined
by flashes of personal experience called
from distant days in the African bush or
more recent contacts with health admin-
istrators around the conference table. It is
unfortunate that the proofreading is below
standard.—S. G. Brown