CURRENT LITERATURE

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Clinical Course


Case report of 37 year old Chinese male, who emigrated from Hong Kong to London in 1960. He had had left sided facial palsy since 1959, and numerous other nerve manifestations of disease. Skin lesions were first noticed in 1963, 4 years after the first sign of nerve damage. Examination disclosed numerous thickened nerves, facial palsy, bilateral claw hand and right drop foot, and a number of large annular erythematous lesions. Skin smears were negative for AFB, but the histology was typical for borderline tuberculoid leprosy. The lepromin test was positive. Treatment with thiambutosine was commenced in October 1967, with a regimen of slow dosage increase designed to avoid exacerbation reaction. Dapsone was considered contraindicated in the initial period because of the underlying nerve involvement, but will be initiated later and continued for 2 years after disappearance of skin lesions. Tarsorrhaphy have been carried out and a future program of surgery and rehabilitation is outlined.—E. H. Long


At the Schieffelin Leprosy Research Sanatorium, Karigiri, during the past 4 years there were 395 admissions for management of erythema nodosum lepromatous. Of these patients 78 had enlarged lymph nodes. Thirty patients developed rapid painful enlargement of lymph nodes with fluctuation and septicemic temperature. The majority of these patients were very ill and toxic, and responded rather dramatically to prednisolone or corticotrophin, without the use of any antibiotics. A few responded to the intravenous administration of potassium antimony tartrate alone. Histologic examination of lymph node biopsy specimens of 12 patients with erythema nodosum lepromatous showed almost complete replacement of the node by lepromatous granuloma, together with considerable infiltration of polymorphonuclear leucocytes. Ziehl-Neelsen staining demonstrated numerous M. lepra in the nodes. It is suggested that the histologic appearance may represent an intensive inflammatory response in lymph nodes followed by avascular aseptic necrosis.—N. D. Fraser


The authors report an investigation of endocrine changes associated with the development of gynecomastia and testicular atrophy in patients with known chronic leprosy, resident at the Gemo Island Leprosy Hospital, Port Moresby, New Guinea. Total urinary gonadotrophins, urinary estrogens, and plasma-testosterone were studied in leprotic patients with and without gynecomastia and testicular atrophy. Patients with gynecomastia and testicular atrophy had significantly raised levels of gonadotrophins and lowered plasma-testosterone. It is suggested that leprous orchitis represents a form of acquired Klinefelter’s syndrome.—N. D. Fraser


“The interesting article by Dr. Martin (Dec. 21, p. 1320) and his colleagues contains the misleading statement: ‘Gynecomastia and testicular atrophy occur in 10-20% of patients with leprosy.’ The sour-
ces cited refer to highly selected series of patients with long-standing lepromatous leprosy in Carville, Louisiana, and Karigiri, South India. The condition occurs not at all in tuberculoid and indeterminate leprosy, and very infrequently in borderline leprosy. Since these latter types of leprosy account for a large proportion (up to nineths or more) of the total number of leprosy patients in any country, it is evident that the gynecomastia of severe and long-standing lepromatous leprosy will affect a far lower proportion than 10-20% of patients with leprosy. (See preceding abstract)

Case report. A 37 year old Indian male, without significant family history of disease, who had lived in England 12 years, noted a swelling of rubbery consistency, measuring 2.5 x 1.5 cm., on the postero-lateral aspect of the left leg. Four months later there was numbness on the lateral aspect of the leg. There was an 8 x 5 cm. area of anesthesia on the lateral side of the left calf. The swelling proved to be the thickened hyperemic and edematous lateral popliteal nerve. Biopsy showed granulomatous reaction with epithelioid and giant cells. M. leprae were not found. Further study led to diagnosis of tuberculoid leprosy. The patient later developed drop-fort.

Rosenberg, B. N. and Lovelace, B. E. Mononeuritis multiplex in lepromatous leprosy. Neurology (Minneapolis) 18 (1968) 309.
This report describes a case of classic lepromatous leprosy with clinical symptoms and signs of a symmetric sensory polyneuropathy in which conduction studies demonstrated pronounced asymmetry of the peripheral nerve lesions (mononeuritis multiplex). The case was of interest because clinical testing revealed an essentially symmetric distribution of sensory loss, while EMG and conduction studies demonstrated the marked asymmetric nerve involvement. The affected nerves had an elevated threshold to stimulation, and slow motor nerve conduction velocities were recorded in several peripheral nerves with partial block of conduction in two. Motor nerve units were reduced in number, and complex polyphasic potentials were noted. Fibrillations and positive waves indicated denervation. The elevated threshold to nerve stimulation was consistent with thickening of nerve fibers. Segmental demyelination has not been demonstrated in lepromatous leprosy, but may occur, as indicated in the case described by the presence of peripheral neuritis with significantly slow conduction velocities.—(From authors' summary)

A previously reported prevalence of spastic paralysis among New Caledonian leprosy patients was confirmed. Various degrees of hyperreflexia were found among Melanesian and European patients, and not among a number of New Caledonian tuberculosis patients examined. The syndrome is probably related to diseases of nutritional and toxic origin reported elsewhere. The syndrome has not been reported in patients receiving sulfones in other areas, but it remains important to look carefully before ruling out sulfone treatment as a cause.—(From authors' summary)

Pathologic changes in electroencephalograms due to disorder of metabolic processes and pathologic influences on affected peripheral nerves are most pronounced in lepromatous patients with lesions of peripheral nerves, and least evident in tuberculoid leprosy without peripheral nerve disease. Low-amplitude small oscillations are found, which are sharp and peak-like. Various other changes occur. Their character is to a considerable degree connected with the course of disease. In more than a
third of 100 examined patients the "rhythm of tension" (P. K. Asochin) occurred, which the author believes to be a physiologic mechanism of brain adaptation to unfavorable biologic conditions.—N. Torsner


The active process in borderline leprosy development of nerve stem thickening, most often in elbow, is a sign either of leprosy neuritis exacerbation, or of a beginning transformation, i.e., a prelepromatous state.—N. Torsner


Full details are given of the technic used for involuntary muscle tests for weakness of the muscles of the hands and feet; it is suggested that the test has considerable value in assessment of leprosy neuritis and results of treatment. Four case histories illustrate the value of the tests and records of progress under treatment. The voluntary muscle test (V.M.T.) furnishes a rapid, reliable and reproducible assessment of the extent of nerve damage in leprosy neuritis. It requires no equipment. Definite muscle weakness is revealed in hands that appear normal to a casual observer; in such patients active treatment for neuritis is immediately indicated. The results of treatment can be judged objectively by serial V.M.T.'s, when V.M.T.'s are recorded in parallel columns they can be compared rapidly. For speed, interpretation and comparability V.M.T.'s are superior to sensory tests. As a guide to the treatment of patients in developing countries, electric studies probably do not add much vital information to that obtained by a V.M.T. Restoration of nerve function and muscle strength as shown by serial V.M.T.'s may frequently be accompanied by a preservation of protective sensation in the hand. The technic of a V.M.T. can be readily taught to nurses and physiotherapy auxiliaries; it has been found to be invaluable and entirely satisfactory in Chinese, English and Ethiopian leprosy patients.—N. D. Fraser


Levels of serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) were estimated in 100 normal persons, 30 patients with nonlepromatous leprosy, 50 patients with lepromatous leprosy, 25 with nonlepromatous leprosy with reaction, 25 with lepromatous leprosy with reaction, 20 lepromin-positive cases, and 20 lepromin-negative cases. The mean SGPT level was raised in patients with nonlepromatous lepromatous leprosy and also in lepromin-positive and lepromin-negative cases. In cases of lepra reaction the treatment, however, could not lower the increased SGOT level. GPT and GOT levels were estimated in the skin extracts from 10 normal persons, 10 patients with nonlepromatous leprosy with reaction, and 10 with lepra reaction. The enzyme levels were found to be lower in diseased skin extracts. The level in lepra reaction was less than the level in nonlep-
romatous cases with reaction, CPT and GOT were determined in liver tissue extracts from 5 normal persons, 5 patients with infective hepatitis, and 5 with lepra reaction. The values in normal persons and leprosy patients were almost identical, whereas the values in infective hepatitis were considerably decreased. The decreased value of enzyme levels in skin tissue extracts and normal levels in liver tissue extracts indicates that increase of serum enzyme levels in certain conditions of leprosy is not due to any hepatocellular damage. (From author's summary)


Reports of 2 cases are presented. Each represented a long delay before recognition and institution of treatment. The first was characterized by redness and swelling of the eye lids, with lacerination, thickening of supraorbital and supratrochlear nerves, and a cord-like swelling in the neck. Pyogenic infection was first suspected. Later examination identified the cord-like swelling as a thickened nerve, not a thrombosed vein, as first diagnosed. Biopsy of the nerve disclosed M. leprae. The second case also was characterized by cord-like subcutaneous swelling in the neck, which likewise was first diagnosed as a thrombosed vein. Further tests led to the diagnosis of leprous neuritis. The second case illustrated the possible existence of pure neural type lepromatous leprosy. — E. R. Long


The author describes 3 cases of combined leprosy and mycosis, whose clinical aspects could induce errors in diagnosis on superficial dermatologic examination. Two observations are reported of patients with sporotrichosis and leprosy, one of them with acute nodular reaction, reminiscent of the clinical picture of sporotrichosis. The third observation was of a patient with chromomycosis who acquired leprosy, with result-ant modification of clinical aspects and histologic picture. Comment is made on dermatitis verrucosa, which has been the subject of many researches when observed in leprosy patients. It is considered by many workers as caused directly by leprotic infection. Several cases of dermatitis verrucosa are presented. In the author's opinion such cases may occur only when M. leprae are present. Leprosy does not have a preponderant action in the initial periods of the structural picture of dermatitis verrucosa in leprosy patients. — L. de Souza

Chemotherapy


Review of results in the treatment of leprosy 20 years after the introduction of sulfones. No other drug of many tested during those years, although possibly useful for complementary or subsequent treatment, has proved as efficacious as sulfones. Nevertheless sulfone drugs have not completely lived up to hopes and expectations and search for better drugs must continue. (From author's summary)

Desikan, K. V. Assessment of DDS therapy. Leprosy in India 40 (1968) 99-104.

DDS is the standard drug in treatment of leprosy. Its value has been assessed in field work in an experimental project of the Gandhi Memorial Leprosy Foundation. In lepromatous cases the drug is effective in lowering the bacteriologic index. In nonlepromatous cases results are less spectacular and assessment is correspondingly difficult. Deformities can be prevented to some extent by DDS. In nonlepromatous cases these seem due to irreversible nerve damage, but in lepromatous cases deformities can be rectified. — E. R. Long

This seminar paper (see India, News and Notes, this issue, p. 199) reviews salient features in the evolution of DDS therapy in leprosy, and such elements in its use as routes of administration, dose, toxicity, and drug resistance. Up to the time of writing the latter has not posed a problem in India. Relapse and leprosy reactions, of which a number of types are noted, are problems demanding serious attention.—E. R. Long.

Vellut, C. Ten years follow-up of lepromatous leprosy patients and DDS treatment. Leprosy in India 40 (1968) 111-114.

A follow-up study is presented of 142 lepromatous cases reported at the VIIth International Congress of Leprology (Tokyo, 1958). After 10 years, among patients originally in the course of severe reactions, 86% were bacteriologically negative and 77% completely inactive. In only 5% of cases was treatment a failure. Dosages were adapted individually. The present trend is to use smaller doses than formerly. Some 12% of cases showed renewed bacteriologic positivity after regular treatment and long negativity. In general, females showed a more favorable trend than males.—E. R. Long.

Balakrishnan, S. Blood and urinary levels of DDS in relation to dosage. Leprosy in India 40 (1968) 125-128.

Measurement of 24 hour post-administration DDS blood levels of lepromatous patients after 50-300 mgm. dosages showed no significant difference following once a week or twice a week administrations, particularly in the dose range 100-150 mgm. once a week. DDS was detectable in blood even on the 7th day after this weekly dosage. A minimum of 0.2 mgm./100 ml. appeared associated with clinical improvement. The drug could be detected even on the 14th day after 100-150 mgm. once a week. A DDS urine spot test is described. E. R. Long.


A woman aged 20 years swallowed 375 mgm. dapsone (provided for her husband, who had leprosy), at 9 p.m. Next morning she was found to be sweating and vomiting profusely and was taken to hospital. She was conscious and complained of severe nausea and giddiness. Respiratory rate was 20/minute; pulse rate 150/minute. The tongue and tips of the fingers were bluish. A sample of blood was greyish black and contained much methemoglobin on spectrophotometric examination. The urine was normal. She was given 1 pint of 5% glucose by intravenous drip, ascorbic acid 500 mgm./6 hourly, and ethylbutamide and propylbutamide 2 cc. intravenously/6 hourly. Cyanosis increased and she became restless. 100 cc. of 12.5% mannitol was given by intravenous drip. Methylene blue (30 mgm. capsule) was given every 6 hours, but she vomited. She gradually improved in 48 hours and began to pass urine. On the 4th day, the blood appeared free from methemoglobin, but tachycardia persisted for 2 weeks. The ascorbic acid and methylene blue were given in order to reduce methemoglobin to hemoglobin.—(Abstract by F. Hawking, Trop. Dis. Bull. 65 (1968) 1250.


A study of DDS chemoprophylaxis conducted by the Central Leprosy Teaching and Research Institute in Chingleput has established the value of the procedure in preventing leprosy among child contacts of lepromatous disease under certain conditions, but further analysis of the value under other circumstances is essential. Mass chemoprophylaxis, taking adverse circumstances into consideration, must be approached with caution. Its efficacy rate is about 55%. On an individual basis, where risk is high and motivation adequate, chemoprophylaxis can be used.—E. R. Long.

The suppressive effect of thalidomide (N-thalimido-glutarimide) on lepra reactions has been proven by comparison with a placebo in direct and double-blind studies. The purpose of the present study was to establish if 1-morpholinomethyl-4-phthalimidopiperidin-2-6 (CG603) and 1-morpholinomethyl-3-phthalimidopiperidin-2-6 (CG601), both derivatives of thalidomide, are also active. Five patients with lepromatous leprosy and lepra reactions of long standing were treated. Four of them received up to 2 gm. of CG603 for 6 days; there was no effect on the lepra reaction and the use of the drug was stopped. Thirteen trials with a daily dose of 900 mgm. of CG601 were carried out; 5 trials lasted 6 days, and 8 up to 10 months. There was beneficial effect on lepra reactions, lowering the dose below 100 mgm. daily often resulted in a relapse. Definite subjective and objective improvement with the latter drug started in 24 to 72 hours, the improvement seemed to be slower then that induced by thalidomide; no side effects were observed during the trial period. A larger scale trial of CG601 appears justified.—N. D. Fraser


Twenty-four patients with various forms of leprosy were treated with thalidomide for periods of 3 to 19 months. In 11 the disease process ultimately became worse. In 5 there was no change. In 5 patients the cutaneous lesions improved. Histologically, the lepromatous component of the lesions was unchanged, but there was a lessening of associated nonspecific inflammatory infiltrate. The treatment had no antibacterial effect. The main side effects were constipation, drowsiness, dryness of the oral or nasal mucosa or both, and peripheral edema.—Authors’ Summary

Isa Caramde, E. Lepra y talidomida (Cg-217, Talidomida) [Leprosy and thalidomide (Cg-217 Thalidomide.)] Actas Dermo-sifillog. 59 (1968) 139-200.

Cg-217 (thalidomide-Softeman) surpasses all nonspecific drugs thus far used in lepromatous reactions. The author reports a series of cases, and a new method of administration of the drug, testifying to its value in leprosy reactions. Its value is best illustrated in cases not previously treated with nonspecific drugs, such as corticoids. In the cases here reported thalidomide was substituted for such drugs. Success was great in neuritis; pain and infiltration were notably lessened. The need for analgesics was relieved. The drug is valuable in iritis and all dermal forms of the disease. In two years of experience, no post thalidomide disturbance, visceral or other, has been observed; more time will be needed, however, for firm conclusions in this respect. The question was raised if thalidomide is effective in acute lepromatous disease as distinct from lepra reaction. A well studied case appeared to indicate that in association with the usual specific drugs the drug does have such an effect. In women of reproductive age it appears safe, provided essential studies indicate pregnancy does not complicate the disease. Considerations with respect to hospitalization and regulation of dosage are discussed.—E. R. Lyon


Seven patients with reactional lepromatous leprosy previously dependent on cortisone, were treated with thalidomide in a dosage of 500 mgm. daily. Rapid regression of erythema nodosum, fall in temperature, and relief from pain were observed, and after a period of improvement drug dosage was halved. After a period of freedom from symptoms of inflammation most patients were restarted on sulfone therapy. Suspension of the thalidomide treatment did not lead to rebound in symptoms, but occasionally moderate ENL occurred. As a collateral effect in thalidomide treatment painful
edema of the limbs occurred, but this was transient. It is concluded that thalidomide is highly efficient in control of lepromatous leprosy reaction. (From authors’ summary) Trinchieri, G. La talidomide nella "reazione" lebrosa. [Thalidomide in leprosy reactions.] Gior. Ital. Dermat. 107 (1966) 1333-1365.

The use of thalidomide in leprosy reactions of lepromatous type permitted registration, in five cases treated, of 12 satisfactory, 1 doubtful, and 2 negative results. Its action was generally evident in a few hours after administration, and complete resolution of the more acute lesions occurred within 48 hours. Its use often terminated a long series of reactions, permitting discontinuation of long-used corticoids. The drug was generally well tolerated. (From author’s summary.)


Ethionamide, in combination with Avlosulphone or Ciba-1906 has a pronounced therapeutic effect in patients not previously treated, as well as in those treated over a long period with other antileprosy remedies without visible effect. In most patients such complex treatment prevents leprosy exacerbations. Regression of skin eruptions was observed in the first months of treatment. Degenerative changes in M. leprae were usually detected in 1-2 months. In some patients under treatment with Ethionamide and Avlosulphone mild hypocromic anemia and dermatitis occurred. (N. Torev)


Ethionamide (Trecoter, preparation 13-14), i.e., thiamide of ethylisonicotinic acid, used for treatment of tuberculosis, when tested on 18 lepromatous patients, proved therapeutically effective, especially in patients not previously treated or treated over a long period with sulfone and other antileprosy preparations. Clinical and hystologic improvement, evident after a few months of treatment, was confirmed by histologic investigations of diseased skin. After 6 months of treatment the bacteriologic effect slowed, apparently because of developing resistance to the preparation. Ethionamide does not have a toxic effect on blood-forming organs or liver and kidneys. It can be prescribed in combination with other antileprosy remedies. (N. Torev)


Grisoculfurine exerts a beneficial effect on erythema nodosum leprosum with regard to improvement in general health, spacing of episodes and progressive diminution in number and size of skin lesions. There was no or only slight effect on nerve pain. This provisional report justifies further trial of grisoculfurine in leprosy. (Author’s summary)


Thirty-one leprosy patients (19 lepromatous, 5 intermediate, and 7 tuberculoid) suffering from ENL or reaction with polyneuritic involvement and marked pain, were selected for study. The duration of treatment varied from 3-30 days. Best results were obtained in patients with severe neuritis. Ten patients with skin lesions in reaction showed improvement, but in 12 the lesions were aggravated. In 2 patients no response was evident. The drug was well tolerated and there were very few side effects. (N. D. Fraser)


After 5-5 days of treatment of erythema nodosum-like exacerbations, with methylestron-diol and methandrostenolone (30-
50 mgm. t.i.d. sublingually, general status improved, but in 4 out of 7 patients there was no full regression. In 4 out of 5 patients with neuritis of the elbow a considerable improvement was observed in 4-5 days. In 9 patients with perforating plantar ulcers full healing occurred in 6-8 weeks (after sequestrotomy).—N. Tomov

Surgical Specialties and Treatment


Current knowledge indicates that neuropathic plantar ulcers are usually due to the normal stresses of walking. Paralysis of the intrinsic muscles seems to increase the chance of ulceration greatly. Maximum risk occurs among leprosy patients who have already had foot ulceration. Patients with plantar anesthesia and intrinsic paralysis have a high risk. Risk is low in patients with anesthesia alone, and negligible in patients with feet normal in sensory and motor status. The aim in treatment should be to cut the high risk populations to a minimum. A great advance has occurred in appreciating the importance of foot-wear in preventing ulceration.—E. R. Long


About 280 patients, averaging 2 ulcers per patient, have been treated in the clinic of the Central Leprosy Teaching and Research Institute at Chingleput. Healing occurred in 80% of cases with daily dressings of 4 types, viz., sterile dry, sterile dry with topical antibiotic ointment, sterile vaseline, and Eusol wet. The rest of the cases required plaster casts or ulcer debridement or both.—E. R. Long

Gude, S. L. Problem of ulcers of anaesthetic limbs of leprosy patients. Leprosy in India 40 (1968) 146-155.

Cases at the Kothara Leprosy Hospital in the period 1964-1967 (1,849 cases), and in the outpatient department of the hospital, are analyzed. Percentage details are given for types and location of ulcer problems, their treatment and the success attained. In hospitalized patients the "potential for ulcers" was great, 77% of the hands and 79% of the feet showing some kind of deformity. Yet the problem was considered relatively small, since the degree of ulcer liability or proneness was not excessively high. Forty per cent of admissions to the hospital for ulcer treatment came from the outpatient department. Yet among the outpatients only 4.2% of 12,206 patients had foot ulcers. A significant number of outpatients were careless in following instructions, refused treatment, or would not use chappals.—E. R. Long


Plantar ulcers are classified in 3 groups: (1) very small ulcers, prone to heal rapidly with rest and suitable footwear, (2) an intermediate group of large, frequently recurrent ulcers, without deep extension to bone, and (3) cases with damage to deep structures, ranging from sinuses to bones or joints on the one hand to extreme cases with gross mutilation and bizarre walking patterns. Surgical procedures for the latter 2 groups are outlined. The average leprosarium does not have the facilities for all types of operation required, and liaison with general hospitals with special departments is desirable. The propaganda value of the general hospital with leprosy patients can be very great.—E. R. Long

Selvapandian, A. J. and Satwekar, R. B. Bone and joint changes in leprosy. Leprosy in India 40 (1968) 137-146.

Among 114 outpatients whose charts were studied, only 26 were noted in which ulceration had not occurred. Trophic ulcers are responsible for bone changes in the foot; distortion of the arch, with abnormal pressure in a particular area, is an important factor in their causation. Specific bone
changes occur only in a small percentage of cases. Most deformities are due to nonspecific bone changes. Ankle joints are involved occasionally where there is other joint damage. Metatarsophalangeal joint involvement is usually associated with trophic ulceration, while more proximal parts are less frequently associated with active or healed trophic ulcer. Bone changes with deformities are preventable, since they are not due to the disease itself. — (From authors’ summary)


Many workers have tried to relieve the pain of ulnar neuritis with drugs, and others have attempted different surgical procedures with the same intention. The surgical procedure of choice at the Leprosy Centre, Polambakkam, Madras, S. India, is external neurolysis. Details of the operative technic are given. Relief of pressure on the ulnar nerve by operative section of the constricting fibrous arch just above the heads of origin of the flexor carpi ulnaris is held to account for the good clinical results in 85 patients. Motor paralysis of short duration showed complete recovery, and sensation returned in a smaller proportion of patients. — N. D. Fraser


Case report. Clinical findings in a 38 year old Chinese female with finger deformities and intractable pain in the hands suggested rheumatologic disease as seen in New York. Neurologic examination, however, revealed areas of anesthesia along the course of the ulnar nerves. Ill defined maculopapular lesions were present on the skin. Smears from ear lobe scrapings and nasal secretions were positive for AFB, and the disease was diagnosed as leprosy. Treatment was started with Diamone. Corticoids, previously used when rheumatic disease was suspected, were gradually withdrawn. General improvement occurred. The case was considered an example of delayed diagnosis in a region where similar clinical findings suggest locally prevalent disease. — E. R. Lose


A high incidence of facial deformities in leprosy patients, detected in 2 surveys, one of 200 and one of 437, is documented. Eleven per cent of all the patients seen needed nasal reconstruction. Two out of 3 nasal constituents are missing in leprosy, viz., lining mucous membrane and support. The membrane is primarily involved; the support is destroyed by exposure necrosis, which starts in the epithelial-lined tissues, in which, with progression of the disease, squamous has replaced ciliated epithelium presumably a protective mechanism. Operative detail is described for 12 cases, first, the provision of skin lining by post-nasal inlay, and second, provision of support by bone graft (preferable) or nasal prosthesis. — (From author’s summary)


Nasal deformity in leprosy is described. Operation for reconstruction of the nose is performed only when the disease is “burned out.” Procedures include: (1) bone or cartilage graft in mild nose depressions, (2) postnasal epithelial inlay skin graft, combined at same sitting or later in great majority of depressions of nose, and (3) total reconstruction of nose for total loss in extremely rare cases. The operative details for these several types of rhinoplasty are given. Contrary to common belief wounds of leprosy patients healed as well as wounds subjected to similar treatment in nonleprotic patients. There has been no evidence of development of leprosy in operating surgeon, in spite of occasional finger pricks in suturing. — E. R. Lose


Simultaneously with general antileprosy therapy for neuritis a complex of physical-therapy procedures was used. Ultra-sound
Increases peripheral blood circulation, reduces pain, has anti-inflammatory and resolving action, intensifies oxidizing-reducing processes, and actively influences tissue biocolloids. Objectively a decrease was found in nerve stem thickness, with a reduction of pain and palpation. In zones of innervation by affected nerve trunks hyperesthesia gave way to hypesthesia.—N. Torsuev

**Pathology**


Chicken embryos inoculated with various strains of human leprosy develop nodular lesions macroscopically visible after 24 hours. Histologically the nodules are formed by granulocytes with acid-fast material. Electron microscopy shows the presence of bacilli. The lesions have been transmitted through 6 passages thus far.—**Authors’ Summary**

Bergel, M. Estudio histobacteriologico del injerto de tejido lepromatoso en ratas alimentadas con dietas prooxidantes [Histobacteriologic study of graft of lepromatous tissues in rats nourished with pro-oxidant diets.] Dermat. Internat. 7 (1968) 23-32.

Tissue from lepromatous patients was inserted into rats on control and pro-oxidant diets. In the control rats this tissue was resorbed after a year with essentially complete disappearance of bacilli. In contrast, the pro-oxidant rats showed signs of progressive lepromatization, with enormous globs with abundant bacilli.—**Author's Summary**


The choice of experimental models among wild and laboratory species of rodents will be easier if, simultaneously with their infection, the different physiologic properties of animals are studied. At present the most promising animal for infection with human leprosy is *Meriones tanaetacicus Pall.*, if the experiments are carried out in winter. This animal differs from the related *Meriones meridianus Pall* by its much greater weight, lower body temperature in winter and the beginning of spring, higher white blood cell count, and lower content of ascorbic acid. The level of oxygen consumption at 10°C in *Meriones tanacetacicus*, receiving vitamin E with food, drops to 87% in comparison with rodents deprived of this vitamin. In summer the body temperature is higher than in *Meriones meridianus*. The assumption that natural factors of sensitivity and susceptibility of animals and man to infectious diseases play a decisive part in their pathogenesis, should be the basis for the choice of experimental animals for the investigation of leprosy pathogenesis and further elaboration of the problems of prophylaxis and treatment.—N. Torsuev


Three placentas of women with tuberculous and one with lepromatous leprosy and three placentas of healthy women have been investigated. In no case were *M. leprae* found. The morphology of ultrastructures of placenta tissue cells in healthy and diseased women was the same.—N. Torsuev

The foam structures of the leprosy cell represent highly vacuolated phagolysosomes. Morphologically it appears that defective phagolysosomes are concerned, which, in lepromatous leprosy, in contrast to tuberculosis and tuberculosis leprosy, are not fully competent in breaking down the invader. The leprosy cell is a phagoctytic histiocyte whose phagolysosomes contain invaders and are vacuolated in a characteristic way. It is uncertain whether the damage to the enzyme sac of the cell is conditioned by special properties of the invader or has to do with genetically determined cell properties of the affected macroorganism. Since the invader is not broken down, tissue reaction fails in lepromatous in contrast to tuberculous leprosy. Coincidentally hitherto undescribed changes occur in the mitochondria of the leprosy cell, the nature of which is not clear. — E. R. Long


Patterns of experimental lesions in mice are described with special reference to host-parasite relationship, and reticuloendothelial origin of the lepra cell. Three kinds of pretreatment, viz., typhoid vaccine as stimulant, Evans blue as disturant, and cardiolipin as depressant, were given to dd-mice before inoculation of Hawaiian strain leprosy bacilli. Fifteen weeks after infection, histologic, hematoxylogic, electronmicroscopic and enzymo.histochemical methods showed that the manifestation of types of leprosy lesion was significantly influenced by the functional activities of the reticuloendothelial system of the host, (2) that lepra cells developed from the histiocyte and its precursor, the "phagiohistio
cyte" in the loose connective tissue, and (3) that the functional activity on the bacilli determined whether the involved cells were transformed into lepra cells or not. — (From authors' summary)


Rat leprosy (morbus Stefansky) is a disease and generic. In a certain sense it is related to human leprosy, but is nearer to paratuberculosis than leprosy. — N. TORSUEV


On the basis of published data and his own observations the author believes the character of local and general reaction in experimental leprosy depends on the method of infection, the virulence, the etiologic agent, and the general condition of the animal's organism. The skin is the most resistant, and therefore local disorders and generalized infection after subcutaneous inoculation develops relatively slowly, results appearing usually in one year after inoculation. After massive dissemination of mycobacteria following intraperitoneal inoculation the incubation period shortens, and the probability of visceral disorder increases sharply. In denervated rats after inoculation in the testis parenchyma the development of the leprosy process lasts 4-6 months and results as a rule in the loss of animals. The passage of a rat leprosy strain through denervated animals increases its virulence, and this results in shortening of the incubation period and decrease of life expectancy in inoculated albino rats and mice. Inoculation with a suspension polluted by cocci results in sharp reduction of the incubation period and massive loss of experimental animals. — N. TORSUEV


Extensive review of literature. The author prefers to carry out experimental inoculation with the tissue of the diseased testis, where the concentration of mycobacteria is the greatest. Detailed instructions for experimental inoculation are given. — N. TORSUEV

Leprosy is rare in Germany. Many persons travel to Germany, however, and differential diagnosis is therefore important. Since leprosy does not begin in the nose, examination of the latter is not the primary test. Moreover acid-fast saprophytes in the nose are not uncommon. Skin biopsy is more important. If the latter test does not permit definitive diagnosis, nasal smears are not called for. In contrast, when M. leprae are found in skin or nerves in apparent lepromatous leprosy, investigation of the nose is obligatory. Proper technic is described. Positive results indicate that the patient is infectious. In tuberculoid leprosy nasal change is less frequently encountered.—E. R. Lowe


In diseased rats dying in the author’s laboratory a dilated right heart was often found, with dense, diffuse, white stratification-infiltrates. The hemoglobin blood level and the red cell blood count were decreased, particularly in rats with a skin-muscle form of disease. In glandular forms leukocytosis was absent; in the skin-muscle form it was moderate and transient, with a shift to the left. In blood there are 4-5% of polymorphonuclear neutrophils, and the number of these with segment nuclei is decreased to 18-20%, particularly in the skin-muscle form. Usually there was eosinophilia in the range of 3-5%. In the skin-muscle form lymphocytes increased to 70-75%; in this form the number of monocytes was decreased.—N. TORSUEV

Bacteriology and Immunology


In peripheral nerves neuritic changes are detected mainly of parenchymatous character, and, in contrast to human leprosy, are not accompanied by pronounced interstitial tissue reaction. Injection of M. lepraemurium into the brain in albino rats caused general disease with characteristic affections of skin and viscera. Typical granulomata appeared in the brain with many mycobacteria. In natural conditions and on experimental inoculation the agents do not penetrate into brain substance. In nerve fibers myelin membranes suffer especially. Small round-cell infiltrates are detected in the leptomeninges of the spinal cord. Decrease of excitability, lability and efficiency of cortex cells is observed in elecroencephalograms.—N. TORSUEV


Among 724 clinical specimens 259 were found positive for mycobacteria in culture. The fluorochrome method, using a combination of auramine and rhodamine dyes, can be employed to facilitate and enhance rapid examination of smears for mycobacteria. In view of its possible oversensitivity, originally positive fluorochrome smears should be restained by the Ziehl-Neelsen method and reexamined.—E. R. Lowe


In examination of biopsy material M. leprae were not found in striated muscle fiber, but were found not only between smooth muscle cells but also within the
cells themselves. Detailed reports are given of results of biopsies from two patients. It is well known that *M. leprae* multiply in Schwann cells, where they may be temporarily immune from attack by lymphocytes and plasma cells. The observations here reported suggest that protection is afforded also to organisms in smooth muscle cells, an important finding since organisms in nerves and smooth muscle are not so likely to be sampled in smears as in lepromatous skin infiltrates. False low findings for BI and MI may be obtained, which may account for relapses in patients taking dapsone irregularly, or stopping dapsone before they should. Leprosy workers should be on the lookout for solid-staining bacilli in smooth muscle in all patients suffering from leprosy toward the lepromatous end of the spectrum. Smooth muscle is abundant in the scrotum, facial skin and other hairy sites. Care should be taken to include hair follicles in skin biopsies.—N. D. Fraser


The author reports on the histopathology of a biopsy specimen from the glandular portion of the right breast of a woman following 10 weeks’ treatment, during which 450 mgm. of DDS had been administered. At first examination a majority of solid, rod-form bacilli were observed in the breast secretion. The biopsy specimen showed a scattering of numerous acid-fast bacilli, most of them in nonsolid-staining form, in the lumen of a lactiferous duct cut in longitudinal section. The result confirms the conclusion that 450 mgm. of DDS given over a period of 10 weeks to 3 months is effective in reducing the number of bacilli in the milk to insignificance.—N. D. Fraser


Nearly 100 different fish, among them some gold fish, have been infected intraperitoneally or intramuscularly with agents of human and rat leprosy. Mycobacteria have often been detected in their tissues and organs, sometimes in considerable number, but neither pronounced growth nor clinical changes were found. Passage experiments also gave no results. Some fish had, in their viscera, greyish-white nodules the size of a poppy grain or less, in which on microscopic investigation round formations the size of a red cell were detected, filled with fuchsinophil granulations, rarely containing single acid-fast bacilli. But the same picture was observed in some control fish. In the intestines of healthy fish and in the mucus collected from the bottom of the aquarium where the healthy fish lived, some single, small groups of thick, short, acid-fast bacilli with rounded borders were found, which were morphologically distinctive. One hundred and thirty-five hybrid mice, received from K. R. Chatterjee, have been infected with *M. leprae*, from 1961 to 1964, but not a single animal had generalized or local disorders.—N. Tomoev


Previously reported work done elsewhere and in the author’s laboratory is reviewed. The author’s own experiments, carried out in Loeffler medium, thus far have not resulted in sufficient survival in tissue culture after foot pad inoculation to observe development of the bacilli. Foot pad inoculation itself was successful, positive results being evident in 5-6 months. The leprotic granulomas were complicated by pyogenic infection.—E. R. Long


Study of the immunology of leprosy, particularly in relation to what is known with regard to immunology in other mycobacterial diseases, is one of highest priority, but until *M. leprae* are grown on artificial media, or an experimental animal can be discovered, discussions of the immunologic concepts of leprosy will remain technical and largely academic.—Authors’ summary
A polysaccharide, PolyINb, which is a polymer of D-arabinose and D-galactose, was isolated from Nocardia brasiliensis and N. asteroides. It was shown to behave as a group-specific precipitinogen with antisera for both organisms, but also for other acid-fast bacilli, including mycobacteria, and to form precipitates with sera from patients with leprosy and mycetoma. The present paper presents results obtained with sera of rabbits immunized with M. smegmatis, M. phlei, M. runyonii, M. acapulceae and M. peregrinum. Each serum reacted positively by the Ouchterlony diffusion method, and immunoelectrophoresis and treatment with 2-mercaptoethanol of sera from tuberculous patients showed that the antibodies in these sera were IgG globulins. The B polysaccharide, along with at least one other immunologically active polysaccharide, was detected in tissue extracts of lepromatous tissue from patients with leprosy.—(Abstract by S. R. M. Bushby, Trop. Dis. Bull. 65 (1968) 1211)

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Lepromin and dermis suspension emulsified in incomplete Freund adjuvant, and adjuvant alone and a buffered diluent, were injected in guinea-pig foot pads. Sequential comparative study of gross and histologic changes in the foot pads and draining lymph nodes showed that lepromin caused the most marked and persistent response. The effect was conspicuous in the lymph nodes, which showed persistent increase in pyroninophilic cells. It was concluded that the effect was due to the bacillary component of lepromin. The lepromin-stimulated lymph nodes did not show massive epithelioid response or fibrosis, and had an evident pyroninophilic cell increase as late as 112 days after inoculation. This may justify the use of cells from such nodes in transfer experiments many weeks after initial sensitization.—(From authors' summary)


Two hundred and seven normal children of lepromatous parents and 474 children with no family history of leprosy all failed to respond to tuberculin and were given a single injection of lyophilized vole-bacillus vaccine. Six months later 17.7% of the children of lepromatous parents responded to tuberculin and 80.3% of the children with no family history of leprosy. The overall lepromin-positive rate among the 207 children with family histories of leprosy was 57.6% and 53.3% in those with no family history of the disease. These rates of lepromin-positive responses are compatible with the incidence of leprosy (between 1.5% and 2%) in the population of Katsina Province. The lepromatous rate among the leprosy patients under treatment was in the region of 30%. Many authorities believe that tuberculosis in a community gradually replaces leprosy. The implication is that cell-mediated immunity to tuberculosis carries with it some degree of immunity to leprosy. It is upon this hypothesis that widespread vaccination campaigns using BCG have been carried out. The low incidence of tuberculin-positive responses among the children of parents with leprosy could mean that they had not the same opportunity of coming into contact with M. tuberculosis as children whose parents have no leprosy, or that, given an equal opportunity of contact with M. tuberculosis, they have not the same ability to respond. The results of vaccination with vole-bacillus vaccine suggest that inability to respond to M. tuberculosis is characteristic of children of parents with leprosy. The failure of a high proportion of children of parents with leprosy to convert from tuberculin-negative to tuberculin-positive after vaccination may be an indication of increased susceptibility to mycobacterial infection. This could be genetically determined.—E. R. Liss
Epidemiology and Genetics


The geographic distribution of the diseases named from extreme north to extreme south, in varying ranges of climate, was studied on the basis of statistics published by university dermatologic clinics. A remarkably high frequency of verrucous skin tuberculosis was noted, with a low prevalence of lupus vulgaris, in Kyushu, the most southern province of the country, in contrast to a relatively low frequency of verrucous skin disease and high distribution of lupus vulgaris in Hokkaido, the northernmost province. A significantly high frequency of leprosy was found in Kyushu, in contrast to the prevalence in any of the other 7 provinces. A gradually decreasing prevalence of sarcoidosis was noted in the population from the northern to the southern provinces.—(From author’s summary)


In spite of the low degree of contagion, persons who come into metropolitan France from areas where leprosy is endemic bring with them a risk to other persons, as is shown by the development of leprosy by those in intimate contact with the immigrants.—Author’s Summary


Five cases of leprosy diagnosed in Toronto are described: (1) Male born in Malta and resident of Australia 2-3 years. Skin and nasal biopsies showed abundant acid-fast bacilli, considered to be M. leprae. (2) Enlisted soldier born in Malta of mother who had died of "mutilating disease." Operation was performed for deviated nasal septum; subsequent examination led to diagnosis of leprosy. (3) Housewife who emigrated from India to Canada. Erythematous swelling of finger proved to be lepromatous acid-fast bacilli were found in nerve trunks. (4) Husband of No. 3, psoriasis was diagnosed, but punch biopsies of ear lobes and skin of back disclosed M. leprae. (5) Elderly woman of Russian nationality who had lived in Russia, Germany and Paraguay, with diagnosed "neurodermatitis." Biopsy revealed M. leprae. ENL reaction occurred later. The 5 cases illustrate the need of a high level of suspicion in regions free from endemic leprosy.—E. R. Long:


A leprosy morbidity survey was made in Limas, a village in Minas Gerais, satellite to the largest leprosarium in Brazil, with a population of 1,381 living in 433 dwellings. Sanitation was bad, the educational level was low, and malnutrition was common. Examination of 1,259 persons disclosed 431 cases of leprosy, most of them lepromatous; only 456 were under regular treatment. The contact-patient ratio was close to 2:1. 56% of the contacts were in the age group 0-14 years. There is little evidence to justify the opinion that there is an actual increase in leprosy in Texas; there is abundant evidence that exhaustive case-finding
methods detected cases that would otherwise not be recognized for years. Currently new cases reported are in the earlier years of life, being detected 10-15 years sooner than would otherwise be the case. Likewise, the disease detected is in early stages. Moreover, the disease detected is in early stages.


The pattern of skin diseases in 3,168 patients seen in several dermatologic clinics in the Kenyan highlands is presented. Results are compared with other surveys from sub-Saharan Africa. A resemblance with the pattern of dermatoses in 20th century Europe is found, whereas typical tropical conditions are notably rare. Disparities in frequency with other African surveys and western countries are discussed and some particular African conditions are described more extensively.


Natural endemicity of leprosy may be connected with district humidity and may be brought to light by comparing two population groups identical in socio-economic respects. The influence of natural factors may be neutralized by conditions created by man in the process of industrial and domestic activity, and by active antileprosy measures. Recognition of natural endemicity in leprosy calls into question existing views on its spread by means of direct contiguity only ("skin to skin" contact). Other mechanisms of leprosy spread must be investigated. Together with the influence of natural factors on leprosy transmission the possibility of climatic influence on population susceptibility to leprosy cannot be excluded.


Intensity of leprosy transmission is much greater than its clinical morbidity because of a high natural resistance in most people. Even in conditions of maximum infection risk clinically pronounced morbidity does not exceed 35%. Leprosy control must depend on (a) isolation and treatment, (b) prevention of spread of agent through general socio-hygienic and special medical measures, and (c) increase in population resistance (vaccination by BCG).

Chodankar, V. P. Statistics and leprosy. Indian J. Med. Sci. 22 (1968) 144-152.

General review, considering subject from points of view of presentation of data, descriptive statistics and testing of means and samples, tests of association and homogeneity, and pitfalls in their interpretation, occurrence of spurious correlation, and evaluation of end results of therapy.

Authors’ Summary


Improvement of economic, cultural, and medico-higienic conditions is capable of reducing the propagation of leprosy.


Computer analysis of combined data from several series of reported studies, showed a significant excess of A as compared with O ($\chi^2$ (d.f.1) = 11.98x; p =
The frequency of B, on the other hand, was still lower than that of O, but the difference was not significant. The heterogeneity $\chi^2$, however, was high and significant ($p=10^{-22}$). Comparisons between lepromatous and nonlepromatous cases yielded important results. A slight but significant excess of A as compared with O was found in lepromatous cases ($\chi^2 (d.f.1)=7.709; p=0.005$). The heterogeneity $\chi^2$ was relatively high ($p=0.02$) and due almost exclusively to inclusion of the 1965 results of Yankah. B seemed to behave like A, and $\chi(B-O)$ was significant. The highest $\chi^2$ was found on comparing A + B + AB:O ($\chi^2=10.085; p=0.001$). Hence a slightly higher incidence of A and B among lepromatous cases, corresponding to an increase of O in tuberculoid cases, seemed fairly well established.—E. R. Long

General and Historical


The author's introduction states that the term "leprophilia" has been proposed to designate the phenomenon of the wish to have or be thought to have leprosy, shown especially by some wives of leprosy patients who try to prove that they have this disease so that they can remain with the segregated husbands. The self-explanatory term "leprophobia" is commonly used to indicate fear of leprosy. In this paper the term "Lepra-Angst" is employed to cover the various emotions shown by persons who do not have leprosy, but believe themselves to be so afflicted, and are disturbed by the possibility. Pertinent data from 23 patients who attended clinics in Hong Kong for treatment of leprosy patients are summarized. Much of the fear attendant on leprosy is related to misconceptions such as those here identified as significant in the genesis of "Lepra-Angst." The greatest strides in overcoming society's leprophobia can be expected from extended publicity designed to dispel such misconceptions and to relate known facts concerning the disease to prevent possibilities of prevention, cure and rehabilitation. In the 23 patients interviewed the findings identified the source of their fear complex as a fear of retributive consequences of sexual pecancy. The genesis of "Lepra-Angst" in this ethnic group is correlated with prior studies of the folklore and concepts of leprosy prevalent in S. China.—N. D. Fraser


The modern view of leprosy is reflected in the Public Health (Leprosy) Regulations that came into operation on 1 March 1966. Despite widespread popular fear of the disease, and much ignorance, there is no valid medical reason for special legislation on leprosy. Some of the provisions of The Public Health Acts of 1936 and 1961 concerning contagious diseases are now applied to leprosy. Confidentiality is maintained. The author indicates how old beliefs and misconceptions have been changed in recent years. The duties of the Medical Officer of Health of a county or borough under the Public Health (Leprosy) Regulations of 1966 are outlined. They are based on modern knowledge of leprosy and standard practices in public health administration.—E. R. Long


The author describes the methods he has used with success in discovering new cases of leprosy in Mexico. The chief feature is to find the key person and through them "sensitize" the community. In the center of Mexico this key person is generally the village priest.—Author's Summary

The general practitioner has the most vital role in the control of leprosy today. In India the total number of leprosy patients is estimated as approximately 20 lakhs. About one-fifth are infectious. There is no substantial reason why leprosy patients, particularly in early stages, should not be admitted to private dispensaries for diagnosis and treatment. Cooperation by doctors in general could have large impact. If one doctor treats 10 patients, 4 lakhs can be brought under treatment.—E. R. Long

Kapoor, P. The role of social and voluntary workers in arousing public interest in leprosy. Leprosy in India 40 (1968) 94-98.

Leprosy is a public health problem with important social implications, which must be met in a combination of effort by public health workers and social organizations. Control rests on detection of cases in early stages and prompt treatment. Small industries and agro-industrial projects should aid in the rehabilitation of patients.—E. R. Long


A historic record of leprosy in mediaval times in Central Europe is presented in 12 plates, 2 of them with several illustrations. The detail is relatively sharp. The significance of each illustration is described. Ankylosing and nerve forms are pictured. The illustrations suggest that the pathomorphosis of leprosy has changed in the course of centuries.—E. R. Long


Three painters from the Renaissance were found to show tinea capitis or even psoriasis rather than leprosy as the artist intended. The artists may have been influenced by the severity of tinea capitis at that time and also by emphasis on details of scalp lesions in Leviticus 13. One canvas, by Ferdinand Bol, suggests favus.—Author’s Summary.


A representation of a facies leontina of lepromatous leprosy was discovered on an ancient Canaanite jar (Tel Amarna Period, 1400 B.C.) that originated from excavations carried out in Beth-Shan, Israel (See Yoeli, M. JIL (Current Literature) 24 (1956) 108.) The leonine face has been identified as symbolizing the Canaanite god Mot, lord of the underworld. Identification of Mot with the leonine face of a person suffering from leprosy has been based on archeologic study and correlated research on Ugarit-Canaanite texts and biblical sources.—(From author’s summary.)

Other Mycobacterial Diseases


A study was made of mycobacterial species isolated from zoo animals in Antwerp between 1960-1966. Six strains of M. tuberculosis (4 in monkeys and 1 each in a leopard and a tapir), 13 strains of M. bovis (10 in ruminants, 2 in carnivores and 1 in a procyonid); 34 strains of M. avium (32 in birds and 2 in cercopitheques and 1 strain of M. kansasi (in a ruminant) were isolated. These strains were studied in comparison with the following strains isolated from domestic animals: 1 M. tuberculosis (from a cow), 14 strains of M. bovis (11 from bovines, 1 from swine, 2 from dogs), 8 strains of M. avium (6 from swine, 2 from...
poultry) and 2 strains of M. kansasii (from swine) one of which was of the album variety.--Authors' Summary


Infection with M. ulcerans leads to chronic crippling skin ulcers and is a major cause of morbidity in some tropical areas. This study of a closed community with a high prevalence of the infection was undertaken to determine how tuberculin sensitivity was related to susceptibility to this condition, and if BCG vaccination protected against it. Both a positive tuberculin skin test and BCG vaccination were associated with a substantially lower prevalence of M. ulcerans infection. The protection rate varied with the geographic prevalence of infection—from only 18% protection from BCG in high-prevalence areas to 74% in the low-prevalence areas. Patients who either were tuberculin-positive or had received BCG vaccine had the onset of symptoms delayed by 2-3 months, compared with those who were tuberculin-negative. For most populations living in areas endemic for M. ulcerans, BCG should provide a valuable degree of protection.--Authors' Summary


Of 458 samples of pasteurized homogenized milk sold in cartons, 13 (2.8%) contained cultivable mycobacteria. Cultural characteristics identified M. fortuitum and 9 Runyon Group III strains among them. None resembled M. kansasii. Possible sources of the mycobacteria were the piping and pasteurization plant, the cartons, and, finally, the milk itself as a result of survival from the pasteurization process.--E. R. Long.


Of 1,610 patients on the chest service of a New England (U.S.A.) hospital 15, or 0.9%, had pulmonary disease caused by mycobacteria other than tubercle bacilli. Mycobacteria without evidence that they caused disease (so-called "random mycobacteria") were found in the sputum specimens of 5% of 1,610 hospitalized patients and 6% of 669 clinic patients. They were isolated in 1% of specimens from inpatients and 2% from outpatients. It is conceivable that most random mycobacteria in the sputum emerge as contaminants from the nose and mouth.--(From author's summary)


Isolation of M. kansasii from an experimental mouse leproma is described. Isolation of this mycobacterium from human cases is rare in Japan (only 4 cases reported), and this is the first report of isolation in Japan from experimental M. leprae infection. The isolate was an outgrowth of cultural studies by standard methods of the mycobacteria in a softening leproma found among 35 mice autopsied 4 months after infection with the Kurume strain. Colonies were photochromogenic, round, flat and smooth. The biologic, biochemical and serologic characteristics and pathogenicity of the isolate corresponded closely with those of a known control strain of M. kansasii.--E. R. Long.

Symposium. Biology of Mycobacteriosis


The papers in this series were presented in a conference, held by the New York Academy of Sciences, 18-20 October 1967. The conference was supported by the National Institutes of Health, Public Health...
Service, U.S.A. under special contract (No. PH-43-68-65). The papers included presentations on tuberculosis and leprosy, and on biologic factors of concern in these and other mycobacterial diseases. The originals must be consulted for details. Short summaries of the content of papers dealing particularly with leprosy and metabolic and immunologic considerations in the mycobacteria in general are given below.—(Abstracts by E. R. Loose.)

Hart, P. D'A. Statement of the questions. 

It is noteworthy that both leprosy and tuberculosis could be discussed in a single conference, in the light of their numerous similarities and dissimilarities. A vast body of information has accumulated recently on the chemical and biologic properties of the agents concerned, and on those of other mycobacterial diseases, including their in vitro and in vivo characteristics. Intriguing aspects of host-mycobacterial interactions occur at the cellular level. Phenomena of hypersensitivity and macrophage activity are of great importance. Ingenious models for experimental infection have been devised. The application of BCG vaccination has raised many questions of theoretic as well as practical importance. One of these is: does the protection apparently afforded in leprosy apply to the lepromatous as well as the tuberculoid type?


The tubercle bacillus and tuberculosis have long been the prototypes of mycobacteria and the diseases they cause. In the 1880's and 1890's numerous mycobacteria were found and classified, varying in their susceptibility to artificial culture, and ranging in virulence from simple saprophytes to organisms more or less pathogenic for different forms of animal life. Within the last 30 years mycobacteria were discovered in lesions of human disease that did not belong to any of the previously described groups, and hence were designated as "atypical" or "anonymous." These are now well categorized and grouped. The many mycobacteria now known have in common acid-fastness when stained, and antigenic substances in common, an attribute reflected in cross sensitizations complicating the practical procedure of tuberculin testing. The "anonymous" bacteria are concerted with this phenomenon, and possibly so is the leprosy bacillus. Various overlaps in the understanding of tuberculosis and leprosy occur in their immunology, epidemiology, and treatment.


Much current knowledge of the pathogenesis of leprosy is based on study of other disease entities, particularly tuberculosis. Subjects covered in this paper include: the immunopathologic spectrum of leprosy, with detailed consideration of immunologic and histologic characteristics of the tuberculoid and lepromatous types; relationship to tuberculous manifestations in various animals; and relationships to other infectious granulomata.


Tuberculosis is in recession in most parts of the world and leprosy is still prevalent; yet the two diseases present a major problem in most of the developing nations. Analysis of their epidemiology is complicated by the fact that each has a long period of incubation. Recognition of index cases is important in all studies of contagion. Indications are that leprosy is less contagious than tuberculosis. Belapse in each case is an important source of new infections. In the large recessions in history in each case geography, race, and poverty have been significant. Age and sex involve important relations. At present intensive studies are underway on the highly complex problem of immunologic relationships and on the value of antigenic (e.g., BCG) stimulation. Facts at hand point clearly to an immunologic relation among leprosy and tubercle bacilli and other mycobacteria.
For understanding in this field, suitable test systems for immunity, and isolation of specific immunity-inducing mycobacterial cell compounds are essential. Assessment of response to vaccination is made by (1) count of grossly visible lung lesions after challenge, and (2) enumeration of bacilli in target organ, or organ distant from site of challenge. Attention has been focused on the cell wall (BCG) as an immunizing agent, in comparison with its extracts and with unvaccinated controls. Oil treatment of cell walls seems to facilitate transport of immunogen to the lungs. The effect of extractives is as yet not wholly clear, but studies thus far have indicated the need for specific follow-up along a number of lines.


The intensity of acid-fastness varies widely among mycobacteria; it is weakest in saprophytic strains and strongest in *M. leprae* and *M. lepraemurium*. Ultraviolet irradiation in combination with a low concentration of acid-alcohol over a long time is effective in detecting differences within the group. The cell-wall property concerned in acid-fastness among mammalian strains may be a primary factor in parasitism of the host. Results suggest different metabolic pathways, especially for difficultly grown or still uncultivable mycobacteria. A general conclusion is that acid-fastness conforms to the principle that no morphologic property of an organism exists without a distinct biologic significance.


"Leaky" bacterial cells lie in a metabolic pool of microbial and host factors. The cells of noncultivated species are adequately endowed with energetic and biosynthetic pathways, and able to utilize available added substrates. Liberation of bacterial cells from host cells transfers critically important pool elements to the diluents used. Cytoplasmic components provide soluble factors (vitamins, proteins, et al.), reestablishing oxidation and phosphorylation. "Leakiness" is a two-way street in rigorously washed cells, loss being partly balanced by supplementations, with reestablishment of respiratory capacity. The acceptance by *in vivo* grown mycobacteria of simple and complex supplements offers a unique type of experimental material.


The colostrum-deprived germ-free piglet obtained by hysterectomy furnishes a model for differentiation of both active and passive acquired immunity, possibly suitable for mycobacterial studies. The germ-free animal seems to be an "immunologic virgin," but is highly competent when exposed to antigen and therefore ideal for studying the development of antibodies as well as nonspecific immunity.


As in the case of the preceding paper, facts learned have not been used extensively in the study of mycobacteria, but may prove useful in that field. The last two decades have seen a burst of immunologic research on humoral antibodies. Some of the results are reviewed under the headings of primary, secondary and tertiary manifestations of antigen-antibody interaction, and 7 tests employing 15 selected human antiserums are analyzed. Quantitative and qualitative binding tests are described.


Mycobacterial phosphatides can now be discussed in terms of well characterized chemical compounds. Among strains studied glycerol phosphatides may constitute a third to half of the total phosphatides. Lecithin is absent, but phosphatidyl-ethanolamine has been identified
in *M. lepra*, *M. avium* and several other tuberculosis strains. Principal differences among the mycobacterial species occur in the phosphatide-linked fatty acids. A second group, phospholipid vitamins, are discussed, with indication of their structure. A crude mannoside mixture fixed complement with sera from tuberculous patients. By combining solvent fractionation and column chromatography it was possible to separate and characterize 4 different mannosides accounting for most of an original phospholipid mixture.

**Guinto, R. S.** Skin tests in leprosy. *Ibid.* 149-150.

The general population of Cebu (Philippines) is highly reactive to lepromin; sensitivity increases from negativity in infancy to almost universal positivity in adults. This reactivity is nonspecific and therefore not diagnostic of leprosy infection. Mycobacterial infections other than leprosy appear to account for much of the reactivity in the general population. Lepromin positivity apparently may occur from some unknown natural cause in the absence of infection by *M. lepra*, *M. tuberculos*, or other known mycobacteria. Lepromin negativity in lepromatous leprosy is associated with general impairment of capacity for delayed-type hypersensitivity; there is partial suppression of reactivity to tuberculosis and other antigens.


Intratracheal injection of BCG caused an increase in the rate of oxygen uptake of alveolar macrophages. Injection of BCG also led to increase in glucose oxidation by the hexose monophosphate shunt pathway (HMS). Organisms more readily destroyed than BCG by macrophages increased HMS activity more rapidly. The rate of digestion of phagocytized bacteria appears to determine the pattern of HMS activity, probably because of the presence of some microbial moiety.


Since *M. lepra* cannot be grown in vitro, experimental models for studying leprosy have had to be undertaken in vitro. Use of *M. lepraemurium* aided in development of indirect methods for determining the viability of leprosy bacilli without growing them in vitro, particularly through recognition of differences in the staining characteristics of living and dead bacilli in tissue (morphologic index). The method of foot pad inoculation, yielding limited tissue growth of *M. lepra* provided models for determination of generation time, and assessment of drug action and drug sensitivity. Notable advance came with the production of progressive infection by *M. lepra* in immunologically deficient (thymectomized and x-irradiated mice, leading to disease comparable to lepromatous leprosy in man. Replacement of competent lymphoid tissue in such animals induced resistance to challenge, with resultant pathologic pictures resembling tuberculoid, or borderline, rather than lepromatous leprosy.


A large scale trial of BCG vaccination was commenced in 1960 among child contacts and relatives of known cases of leprosy in an area of eastern Uganda where the prevalence of the disease was high, and concentration was possible on enough children up to 10 years of age. A number of reports on the success of the trial have been made and need not be repeated here. It is evident that BCG vaccination has had a noteworthy effect on leprosy in Uganda, but the ultimate importance of the finding is still not clear. Since most of the leprosy in Uganda is of the tuberculoid rather than lepromatous type, the information available does not determine if BCG vaccination is effective against the development of the serious lepromatous disease. The findings, however, provide ample leads for further research, both on the immunologic effects of BCG and on the nature of leprosy itself.