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Abstracts

The following 26 abstracts are reprinted, with permission, from *Int. J. Lepr.*, **37**, No. 4 and **38**, 1-4.

1. **Primeras manifestaciones clinicas en la lepra. Experiencia personal (Primary clinical manifestations of leprosy. Personal experience),** by EGEA BUENO. *Actas Dermosifilog,* 1968, **59**, 477-486.

Interrogation of patients is of relatively little value in the recognition of initial lesions in leprosy. To determine these as precisely as possible, periodic examination of family and dwelling contacts of patients is essential. The lesions the author has observed most frequently are liprides and achromic macules. These are followed by zones of anaesthesia, and in smaller proportion diffuse infiltrations of the face and later extensive bacilliferous involvement. Finally there are cases in which the only manifestation of the disease is the presence of *M. leprae* in the nasal mucosa—a good reason for not abandoning bacilloscopia in the examination of contacts.

Author's Summary

. **Temperature-linked sensory loss. A unique pattern in leprosy,** by T. D. SABIN. *Arch. Neurol.,* 1969, **20,** 257-262.

A unique pattern is described of sensory loss in the arm in lepromatous leprosy patients, sparing the palm and antecubital fossa, with concomitant dense loss of sensation over the dorsum of the hand and forearm. Determination of sensory thresholds and skin temperature at multiple sites suggests that the relatively cool areas show the most marked sensory loss. It is suggested that in advanced lepromatous leprosy destruction of fine cutaneous nerve endings occurs earliest in relatively cool areas of the skin, leading to a pattern of sensory loss unique to this disease. Attention to this pattern would permit diagnosis of lepromatous leprosy when there are no skin lesions or when a patient has become bacteriologically inactive.

From Author's Summary

Résultat du traitement spécifique de la lèpre par les sulfamides retards à l'Institut Marchoux (Results of specific treatment of leprosy by long-acting sulfonamides at the Marchoux Institute), by J. LANGUILLON. *Acta Leprol.,* 1969, N.S. **34-35**, 45-56.

Since 1958, 490 leprosy cases have been treated at the Marchoux Institute by orally given long-acting sulfonamides, including sulfamethoxypyridazine (Sultirene), sulfamethoxydiazine (Madribon), sulfamethodiazine (Kiron), Depovernil, acetylmethoxypyrazine (Acétylazide) and sulforthomidine (Fanasil). Dosages of the first 4 of these were 750 mg every 2 days, and the last 2 respectively 2.50 g and 1.50 g weekly. Among 235 tuberculoid cases of a type recognized as prone to self-healing, practically 100% cure occurred within 3 years. In lepromatous cases Sultirene gave the best results within 5 years (89%). In practical mass treatment Fanasil proved preferable. No toxic reactions were observed with the sulfonamides.

From Author's Summary

4. **Chirurgie directe des gros troncs nerveux dans la lèpre (Direct surgery of the great nerve trunks in leprosy),** by A. CARAYON. *Acta Leprol.,* 1969, **N.S. 34-35,** 65-91.

We are now in a position to respond to problems feared by Paul Brand in 1966. This work, which should be repeated and controlled by others, in the fight against the habitual failure of medical and orthopaedic treatment in nerve deficits is supported by new documents, and justification of direct nerve surgery. That work, endowed today with effective methods and without danger, gives a reasonable proportion of success if one limits it to strictly selected cases. It has gained the right of choice in the treatment of leprotic disabilities, and its application should be extended with earlier indications. In the face of the motto "without using the knife at all" we believe that direct surgery of the leprotic nerve is now an indispensable link in "preventive rehabilitation".

From Author's Summary

5. **Cell walls from *Mycobacterium tuberculosis* (BCG) as vaccine against *Mycobacterium leprae* infections in mice,** by C. C. SHEPARD and E. RIBI. *Proc. Soc. Exp. Biol. Med.,* 1968, **127,** 517-521.

Cell walls from BCG were prepared by the method of Ribi *et al.* (*Bull. Hyg.* **41** (1966), 1146). After lyophilization, 100 mg of the preparation were mixed with 0.48 ml 7-*n*-hexyloctadecane and suspended in 40 ml saline containing 0.2% Tween 80; the mixture was then heated at 65°C for 30 min, and was referred to as the oil-treated vaccine. A similar vaccine was also prepared but without the treatment with oil. Groups of CFW mice were vaccinated either intravenously or intradermally with the oil-treated vaccine, with the vaccine without oil-treatment, or with viable BCG, and after 34 days the mice were inoculated in the foot pad with 5×10^3 *M. leprae.* At 6 months, when the count in unvaccinated control mice had reached more than 10^6 bacilli, the number of bacilli in the vaccinated mice was determined and again 3 months later; these counts were made on pools of up to 8 mice. The results showed that intradermal vaccination with the oil-treated cell wall preparation gave less protection, as judged by depression of multiplication of the leprosy bacilli, than did intravenous vaccination, and that at 6 months the degree of protection was similar to that produced by viable BCG, although at 9 months, it was somewhat inferior. Cell walls without treatment with oil afforded no protection. Local induration from the intradermal vaccination was less with the oil-treated cell wall preparation than that produced by the viable BCG vaccine; the enlargement of the draining lymph glands was also less. Intravenous injection of the oil-treated vaccine and the viable BCG produced pulmonary nodules with a peripheral zone of macrophages.

From abstract by S. R. M. Bushby, Trop. Dis. Bull., 1969, 66, 307-308.

Erythema nodosum leprosum: a clinical manifestation of the Arthus phenomenon, by S. N. C. WEMAMBU, J. L. TURK, M. F. R. WATERS and R. J. W. REES. *Lancet,* 1969, *ii,* 933-935.

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

7. **Osteo-dental alterations and anomalies in children suffering from leprosy,** by R. P. G. MIRANDA. *Publ. Centro Estudos Leprol. (Parana),* 1969, **9**, 17.

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 leprous 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

Evaluation of the earlobe in leprosy. A clinical and histopathological study, by R. E. MANSFIELD, M. A. STORKAN and I. S. CLIFF. *Arch. Dermat.,* 1969, **100**, 407-412.

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 smears and 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

. **Deux cas d'inefficacité antiréactionnelle de la thalidomide dans la lèpre (Two cases of antireactive ineffectiveness of thalidomide treatment of leprosy),** by F. P. MERKLEN and F. COTTENOT. *Bull. Soc. Fr. Dermat. et Syphilig.,* 1968, **75**, 738-739.

A case of major tuberculoid leprosy with reactional exacerbation in an African patient yielded on the first occasion to a daily dose of 400 mg 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. Harter

10. **Human leprosy in normal mice,** by R. J. W. REES, A. G. M. WEDDELL, E. PALMER and J. M. H. PEARSON. *Br. Med. J.,* 1969, **3**, 216-217.

It has now been shown that normal mice can be used as models for studying the early stages in the development of leprosy. Inoculation into the footpads of mice of as few as 10^4 leprosy bacilli leads to infections which spread to distant sites via the bloodstream and after 2 or more years give rise to granulomata and neural damage at the sites of inoculation. Where the tissue response had fully developed it reproduced exactly the histologic features of human leprosy in the borderline range.

Authors' Summary

11. **Correlation with results of mouse footpad inoculation,** by L. LEVY, P. FASAL and L. P. MURRAY. *Arch. Dermat.,* 1969, **100**, 618-620.

The morphologic appearance of *M. leprae* 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. leprae* were demonstrated in 15 of the 16 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. leprae*; viability of the organisms was found to be much reduced in 5 of these 10 specimens. By contrast, of 15 specimens obtained during dapsone therapy from 5 patients proven to harbour dapsone-resistant *M. leprae*, 14 were demonstrated unequivocally to contain viable organisms.

Authors' Summary

12. **Cell-mediated immunity in patients with leprosy**, by J. L. TURK and M. F. R. WATERS. *Lancet,* 1969, *ii,* 243-246.

Fifty per cent of patients with lepromatous leprosy could not be sensitized to 2,4-dinitrochlorobenzene (DNCB). However, 10 DNCB nonreactors could be induced to show delayed hypersensitivity to keyhole-limpet haemocyanin (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

13. **Cellular immunity in infectious diseases (Editorial)**. *Lancet,* 1969, *ii,* 253-255.

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 co-workers, 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 phytohemagglutin (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—haemocyanin. 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 antimycobacterial antibodies in their serum 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.

14. **BCG vaccination in mycobacterial infections**, by R. J. W. REES. *Br. Med. Bull.*, 1969, **25**, 183-188.

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 antigens 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

15. **An unusual form of lepromatous leprosy**, by S. KUNDU and S. GHOSH. *J. Indian Med. Ass.*, 1969, **52**, 566-578.

Two cases of lazarine leprosy, a form not infrequent in Latin America, were detected in the Leprosy Research Department, School of Medicine, Calcutta. In each case the disease was fulminant, with unusually severe signs and symptoms, and both patients died. The authors note that the disease is in general progressive and the trend is toward fatality even though a patient may at first appear in good health.

E. R. Long

Skeletal muscle changes in leprosy: their relationship to changes in other neurogenic diseases affecting muscle, by P. SLOTWINER, S. K. SONG and P. J. ANDERSON. *J. Path.*, 1969, **97**, 211-217.

The report is based on biopsy studies of 4 leprosy patients (3 females and 1 male) presenting signs of peripheral neuropathy and, in 1 case, myositis. Multiple subcutaneous granulomas were seen in 2 patients, commonly surrounding blood vessels, nerves, hair follicles and sweat glands. Acid-fast bacilli were demonstrated. Extensive granulomatous change, with fragmentation of axons and myelin sheaths, and visible acid-fast bacilli, was noted in peripheral and intramuscular nerves. Inflammation seen in muscles was restricted to perivascular, perineural and intraneural foci and muscle spindles. Segmental atrophy affecting groups of fibres was a consistent change. Sarcoplasmic structural changes included phagocytosis, vacuolar change and

basophilia, chiefly in areas remote from inflammation and associated with regions of segmental atrophy. The evidence supports the view that a concurrent myopathic process need not be invoked to explain the sarcoplasmic changes. It was concluded most of these changes were secondary to leprous neuropathy and consequent denervation.

E. R. Long

17. **Leprosy in twins,** by Y. A. KETKAR, P. N. KULKARNI and P. N. PATIL. *Leprosy in India,* 1969, **41**, 85-88.

A report is made of tuberculoid leprosy in a pair of identical twins, aged 15 years. There was no family history of leprosy, nor was any specific contact recognized. The pair shared the same environment. Blood groups, iris colour and other characteristics were identical. *M. leprae* were not found in either patient. The duration and course of the disease were similar. In each case there was a severe initial response to DDS treatment followed by good response. The observations support views, many times expressed, on the role of genetics in leprosy.

E. R. Long

18. **Preservation of sensation in a cutaneous vascular malformation in lepromatous leprosy,** by T. D. SABIN. *New Engl. Jl Med.,* 1970, **282**, 1084-1085.

A case of leprosy is reported in which a palmar congenital vascular malformation was spared neurologic involvement, although sensation to pinprick was lost over much of the body surface. The temperature in this area as measured by thermography was 7°C warmer than in adjacent parts. The author suggests that the increased vascularity with the increased skin warmth created a relatively unfavourable site for growth of bacilli.

G. L. Fite

19. **Ethambutol en el tratamiento de la lepra. Resultados del tratamiento de 20 pacientes durante 12 meses (Ethambutol in the treatment of leprosy. A twelve-month trial in 20 patients),** by A. SAUL and R. BARCELATA. *Dermatología (Mexico),* 1969, **13**, 152-159.

This preliminary trial of ethambutol involved the treatment of 20 leprosy patients: 16 lepromatous, 3 tuberculoid and 1 borderline. A single daily dose of 800 mg was given to all patients for 6 months in tuberculoid cases and for 12 months in the lepromatous. Complete regression of tuberculoid lesions was observed after 6 months of treatment. In lepromatous cases improvement began after the first 15 days followed by flattening and atrophy of nodules, and healings of ulcers. At 12 months clinical cure was evident in 4 cases, improvement in 3 and relapse in 5. Although bacteriologic changes were observed in all patients, smears remained positive in 9 cases after 12 months. Histologic modifications were also noted. Neither lepra reaction nor side-effects were observed. Ethambutol seems to work more quickly than other drugs, but the evidence of bacillary resistance suggests need for further trials.

A. Saúl

20. **Experimental and clinical studies on Rifampicin in treatment of leprosy,** by R. J. W. REES, J. M. H. PEARSON and M. F. R. WATERS. *Br. Med. J.,* 1970, **1**, 89-92.

Rifampicin showed high activity against experimental leprosy, inhibiting the multiplication of dapsone-sensitive and dapsone-resistant strains, of *M. leprae* in mice fed 5 mg/kg body weight. In a formal pilot-type trial on 6 previously untreated patients with active lepromatous leprosy, Rifampicin (600 mg daily by mouth) was as effective as standard treatment with dapsone. *M.*

leprae, however, appeared to be killed more rapidly by Rifampicin than by dapsone or other antileprosy drugs so far studied. This was confirmed on another 10 patients, including 2 with dapsone resistance, and from the infectivity in mice of bacilli recovered from patients during treatment with Rifampicin or dapsone. These results are consistent with the bactericidal activity of Rifampicin against other microorganisms, which could be important to the chemotherapy of leprosy, since all antileprosy drugs in current use are bacteriostatic. The final place of Rifampicin alone or in combination with other antileprosy drugs must await more knowledge gained from larger and long-term studies.

Authors' Summary

21. **The elusive diagnosis of leprosy**, by J. G. SINKOVICS and M. L. IBANEZ. *Postgrad. Med.*, 1970, **47**, 109-115.

As the incidence of tuberculosis decreased the last 10 years, new cases of leprosy increased. The highest incidence of new cases in the United States was reported in Texas. It may be said that with the decline of tuberculosis, the natural ecology of mycobacteria is reversed, and if measures are not taken, the leprosy/tuberculosis ratio may again favour leprosy. In a patient with a lesion of the nasopharynx, the first histologic diagnosis was compatible with rhinoscleroma. Acid-fast stains showed that the lesion was a leprous infectious granuloma. In a patient with lipofibrosarcoma of the leg, lepromatous leprosy was not apparent until injury of the amputation stump and probable septicaemia with *E. coli* occurred. During treatment with antibiotics, metaraminol and hydrocortisone, livid haemorrhagic skin eruptions appeared and later sloughed off. Acid-fast staining of nasal scrapings and tissue biopsy specimens established the diagnosis of lepromatous leprosy.

Authors' Summary

22. **El bacilo de Hansen en algunas formas de neuritis de lepra tuberculoide (Bacilli in certain types of neuritis in tuberculoid leprosy),** by M. M. GIMÉNEZ, H. I. RISSO, C. A. MOGLIA, J. J. RIBICHINI and R. WAISMAN. *Leprologia,* 1969, **14**, 11-16.

The authors present 4 cases of tuberculoid leprosy, all Mitsuda positive, and all without bacilli in cutaneous lesions. In these cases painful ascending neural lesions developed, in which bacilli were readily demonstrated in granulomatous tissues from the nerves, some with a little caseation, and some groups of organisms as globi. Treatment with sulphones and vitamins A, B_1, B_{12}, and D proved effective. The authors suggest that the hypersensitization in these cases is somehow related to the pathogenesis of these lesions.

G. L. Fite

23. **Sarcoidosis.** *Postgrad. Med. J.*, 1970, **46**, 465-541.

At the Central Middlesex Hospital (London) a Conference on Sarcoidosis was held 29 September, 1969. The *Postgraduate Medical Journal* records the presentations, 17 of them formal, together with many less formal discussions, consuming an entire issue. Although much material would be found only of indirect interest to students of leprosy, some articles such as that of Cronin on skin changes in sarcoidosis (with its nice illustrations in colour, pp. 507-509) deserve recognition. This issue should be found in all leprologists' archives. Rees' "Kveim test in leprosy" is treated separately.

G. L. Fite

Studies toward the standardization of lepromin, by J. H. HANKS, M. ABE, T. NAKAYAMA, L. M. BECHELLI and V. MARTÍNEZ DOMINGUEZ. *Bull. WHO,* 1970, **42**, 703-709.

Because of the wide range of concentrations of *M. leprae* in existing lepromins the authors studied methods of producing a standardizable lepromin containing 160 million bacilli/ml. The effects of using different dilutions of lepromin on the incidence of false-positive reactions were also studied. Progress reported includes a convenient method for preparing large batches of nonsedimenting lepromin, which is directly suitable for microscopic counting of *M. leprae* cells; and a validation of current methods for microscopic enumeration of *M. leprae.* Skin tests with diluted lepromins have demonstrated that dilutions up to 1 : 16 increase progressively the ability to distinguish between lepromatous and tuberculoid leprosy. This work has provided further evidence that 20 million bacilli/ml (a 1 : 8 dilution of the initial lepromin) should produce adequate Mitsuda reactions in general populations, provided that 3 mm reactions are taken as the criterion for 1+ positivity. The net effect of these findings is equivalent to expanding the world supply of lepromin by 8 times. Recommendations for further research are proposed.

Authors' Summary

25. **Serology in leprosy,** by OLIVEIRA DE ALMEIDA. *Bull. WHO,* 1970, **42,** 673-702.

A critical survey of the literature on serology in leprosy has shown that sera taken from lepromatous patients display some striking differences in comparison with sera from tuberculoid patients. The tests most frequently employed were complement-fixation, hemagglutination, electrophoresis, precipitation and immunofluorescence, together with a variety of antigens not only from lepromas but also from *M. tuberculosis* and other actinomycetales. With the exception of the Rubino test, all these serologic tests are lacking in specificity for leprosy since leprous sera have a broad range of reactivity with different antigens, including those employed in the serologic diagnosis of syphilis. Some features of the leprous sera could be related to a hypersensitivity state involving circulating immune complexes, low levels of complement and the presence of antibodies similar to those found in sera from patients with autoimmune diseases.

Author's Summary

[It should be added that this is a useful detailed review of the topic, which includes an elegant bibliography of 300 or more citations.—*G.L.F.*]

26. **Considerações sôbre o real valor da sulfonoterapia nos programas de profilaxia da lepra (The value of sulfone treatment in programs of prophylaxis against leprosy),** by L. de SOUZA LIMA. *Rev. brasileira Leprol.,* 1968-69, **36,** 31-36.

The author considers the real value of sulphone therapy in the programmes of control of leprosy based on the results of the sulphone treatment of cases of lepromatous, borderline and indeterminate leprosy. He points out that the regular sulphone treatment of the cases of the indeterminate group is the most efficient procedure for the control of leprosy, because of the capacity of this drug to prevent transformation of these noninfectious into infectious cases of the lepromatous type or of the borderline group. Emphasis is given to the possible development of sulphone-resistance and the author advises the use of a triple association of drugs (parent-sulphone, thiambutostine, long-acting sulphonamides) in order to avoid this occurrence.

G. L. Fite