CURRENT LITERATURE

This department carries selected abstracts of articles, published in current medical journals, dealing with leprosy and other mycobacterial diseases. Abstracts are supplied by members of the Editorial Board and Contributing Editors, or are reproduced, with permission, from other abstracting journals.

Terencio de las Aguas, J. and Contreras Dueñas, F. Curación de la lepra. [Cure of leprosy.] Rev. Leprol. (Fontilles) 6 (1965) 345-359.

The concept of curability of leprosy has changed radically since that prevailing prior to knowledge of the sulfones. Unquestionably the situation has improved since new and incomparably more effective drugs became available, but realistically we still have to distinguish between leprosy diagnosed early, when it could be designated as in the "prediagnostic period," from that diagnosed currently, and late, in a period that could be called the "postdiagnostic period." Attention may be called ostensibly to the "prediagnostic period" when authors are really reporting data and statistics that represent late diagnosis. In such cases, when the history is complete and thorough, it is evident that the disease commenced several years previously. In cases designated as in the prediagnostic period, a new distinction must be made, taking account of the fact that lepra reactions constitute a primordial factor in the evaluation and prognosis of the disease, and also in the possibility of its cure. Graphs and statistics are presented on deaths at Fontilles, in relation to earliness or lateness of diagnosis, travel time and distance from the sanatorium, and time elapsed between admission to the sanatorium and attainment of an arrested state and cure. From the data at hand the following conclusions are reached: Leprosy is easily cured when it is diagnosed early. Indeterminate and tuberculoid forms even heal spontaneously. Lepromatous leprosy, usually diagnosed after more than three years, is healed only with difficulty and slowly. When invasion of the reticuloendothelial system is very extensive, with frequent lepra reactions and significant visceral involvement, cure is extremely difficult; to attain best results it is essential to utilize specialized clinics in which all facilities for case study are available. Patients diagnosed with initial forms heal without scars or sequelae, but in many who suffer from advanced forms, when bacteriologic cure is attained, physiotherapy and surgery for deformities are required for rehabilitation. It is essential, too, that cure be not only somatic but psychologic as well.—F. Contreras D.

Labusquiere, M. Critères de blanchiment et de guérison pour les lépreux. [Criteria of arrest and cure of leprosy.] Méd. Trop. (Marseilles) 26 (1966) 130-133.

During the first Technical Conference of OCCGEAC (Organisation de Coordination et de Coopération pour la Lutte contre les Grandes Endémies en Afrique Centrale) held at Yaoundé in December 1965, the criteria of arrest and cure of leprosy as laid down by successive conferences and meetings of experts of WHO, were reviewed. It was agreed that since these criteria could not be, and have not been, applied to mass campaigns in the Frenchspeaking countries of West Africa represented at Yaoundé, the statistics of patients who are still regarded as being under treatment for leprosy were inflated and misleading. It is therefore recommended that bacterioscopic examination of the skin and nasal mucosa in a patient who has had adequate treatment for tuberculoid leprosy, being both unnecessary and impracticable, should not be required before discharge. Clinical criteria of arrest and cure are laid down. For malign leprosy, which includes bacilliferous borderline leprosy as well as lepromatous leprosy, bacterioscopic examination in addition to clinical evidence is necessary to establish inactivity. While such patients may be declared arrested (blanchis), a patient who has had lepromatous leprosy "may never be said to be cured." [Abstract by S. G. Browne, *Trop. Dis. Bull.* **63** (1966) 1096.]

Languillon, J. Les classifications de la lèpre. Pour une classification immunologique. [Classification of leprosy. Toward an immunologic classification.] Med. trop. (Marseilles) 26 (1966) 115-123.

After a brief historic review of the main pronouncements on the classification of leprosy by international conferences (Manila, 1931; Cairo, 1938; Madrid, 1953) and of the systems proposed by the South American and the Indian leprologists, the author stresses the importance of the immunologic basis for classification. While unimportant differences of opinion exist regarding the lepromatous and tuberculoid polar types, controversy continues in respect to the precise nomenclature to be used for patients exhibiting lesions in the broad unstable intermediate zone. The author considers that the indeterminate stage is essentially transient, and that persistently achromic and inactive macules (sometimes referred to as indeterminate) should be regarded as scars indicating healed lesions. Patients who have had adequate and regular treatment for polar tuberculoid leprosy may safely be placed on observation without treatment; but treatment for life is advocated both for those with lepromatous leprosy who have, necessarily, a persistently negative Mitsuda reaction, and for those with the type of borderline leprosy the authors refer to as interpolar unstable leprosy. [Abstract by S. G. Browne, Trop. Dis. Bull. 63 (1966) 1095-1096.]

Barsky, S. and Brual, G. C. Lepromatous leprosy. (Transactions: Chicago Dermatological Society, 20 October 1965.) Arch. Dermat. 94 (1966) 242-244.

Leprosy in an adult Philippine male is described in which treatment with dapsone (50 mgm. weekly) and ferrous sulfate was started 19 months after the presenting sign (a keloid-like lesion on the shoulder) was noted. This patient arrived in the United States and soon discontinued medication after a total of four months' treatment. Two

weeks later acute lesions appeared, involving the face, ear lobes, shoulder, and extremities, accompanied by nasal obstruction, epistaxis, joint pains, weakness and fatigue, without cephalgia, nausea, vomiting, chills or fever. The patient presently is receiving one-half tablet of sulfoxone sodium twice weekly, ferrous sulfate, vitamin B complex, and a high protein diet. Large nodules and the infiltrations on the shoulder have decreased in size. In the ensuing case discussion Dr. Leon Goldman questioned if the "classification is only lepromatous in spite of the positive lepromin test," since the biopsy showed "some beginning epithelioid cell formation and it is a question whether it ought to be put in the dimorphous or some intermediary group. . . ." He stated further that "the nonreactive serology" was in favor of this case "being a little bit different from the ordinary type of lepromatous leprosy." Dr. Irene Neuhauser pointed out that a number of factors, such as resistance and sensitivity, determine the type of lesion found in the patient with leprosy, and the interrupted treatment must be kept in mind. The variety of lesions suggested a highly unstable situation. Dr. Harold O. Perry made the point that ". . . in these days we are going to see patients with leprosy" and that Canizares "has outlined an orderly progression from the indeterminate to the dimorphous type, and then into either the pure tuberculoid or pure lepromatous types. It seems a reasonable classification to me." Dr. Perry further stated, "We have had experience recently in seeing . . . ten cases of previously undiagnosed leprosy since 1951." Not all the patients originated in areas where leprosy is common; some cases occurred in persons born and raised in the USA, who had traveled. For this reason, one must be on the lookout for leprosy, which is a great imitator of other diseases. Earlier misdiagnosis occurred in 9 of the 10 cases. Dr. Harold Rodin emphasized the laxity in physical examinations at the point of entry. He stated "not only the dermatologists should be alerted but also the U. S. Public Health officials whose function it is to prevent these patients from entering the country."-J. A. ROBERTSEN

Porto, J. A., Netto, N. H. and Posse, A. M. /Languillon, J. La régression tuberculoide Filho. Lepra nodular infantil. [Infantile] nodular leprosy.] Bol. Centro. Estud. Hosp. Serv. Estado (Rio) 16 (1964) 115. Summary in Dermatol. Iber. Lat. Amer. 6 (1964) 236.

The authors comment briefly on infantile nodular leprosy, considered as a tuberculoid form of the disease and characterized by a nodular lesion, usually single, localized in the face, and which regresses spontaneously. The histologic structure is that of tuberculoid granuloma, and the Mitsuda reaction is positive. They emphasize the importance of the diagnosis in this type of leprosy because, according to the current concept, there should be a carrier of the lepromatous type of the disease among those living with the patient.—N. DE SOUZA Campos

Souza Campos, N. de Aspectos clínicos, epidemiológicos e profiláticos de determinadas formas do tipo tuberculóide da lepra. [Clinical, epidemiologic and preventive aspects of some forms of the tuberculoid type of leprosy.] Summary in Proc. 7th Internat. Congr. Trop. Med. & Malaria, Rio de Janeiro, 1-11 September 1963. Vol. 3, pp. 53-54.

The author studied several forms of tuberculoid leprosy, separating them from other forms of this type. He analyzed the clinical aspects, activity, and prognosis of the so-called infantile nodular and sarcoid forms of leprosy, which show fixed evolutional and regressive characteristics, bacilloscopic negativity, and immunologic positivity. These forms heal independently of therapy, never present involvements of the nervous system, and therefore, never show any deformity. In spite of efforts made by leprologists, there is still a stigma attached to the diagnosis of leprosy. The nodular and sarcoid cases need only be observed from the epidemiologic and not the preventive point of view. These two groups of lesions, much more frequent than the borderline forms, could constitute a subgroup of the tuberculoid type and are of interest only from an epidemiologic point of view, which is the only reason justifying their recording.—N. DE SOUZA CAMPOS

dans la lèpre lépromateuse. [Tuberculoid regression in lepromatous leprosy.] Bull. Soc. Path. exot. 58 (1965) 780-788.

The author reports five cases of tuberculoid regression in acute lepromatous leprosy. After a week a regressive phase appears, with decrease in infiltration of skin lesions and nerve trunks, disappearance of pain, and decrease in number of bacilli. The term tuberculoid regression is convenient for such an evolution.-[From author's summary]

Cave, L., Fustec, R. and Basset, A. Radiologie de la lèpre. [Radiology of leprosy.] Ann. Radiol. 8 (1965) 61-76.

The radiologic aspects of leprosy are discussed with reference to bones, blood vessels, and nerves. An analysis was made of 210 bone x-ray examinations, 10 arteriographs, and 30 cubital neurographs in Senegalese leprosy patients. The osseous lesions were classified on the basis of the graduated severity of changes, ranging from nodular lesions of the epiphyseal spongy bone to major degenerations combining osteitis, osteoarthritis and neurotrophic disturbances. Arteriography discloses the existence of authentic severe arteritis in leprosy that is sometimes only slightly advanced, and focuses attention on the importance of vascular lesions in the pathogenesis of lesions of the limbs in leprosy. Cubital neurography with the aid of liquid lipiodol yields variable results for the morphologic analysis of the cubital nerve. Yet in some cases these results are sufficiently encouraging to warrant continued studies of this type, preferably with ultrafluid lipiodol. [From authors' summary]

Sakai, T. Statistical study on anomalies of teeth in leprosy patients. Shikwa Gakuho **65** (1965) 153-160; 257-265; 342-349; 405-415. (In Japanese)

The author studied a variety of anomalies of the teeth in leprosy patients, including abnormal localization, such as displaced and malplaced teeth, abnormal number of teeth, including persisting deciduous teeth, unerupted wisdom teeth, and abnormal forms, such as microdontia and Carabelli's tubercle, in 749 leprosy patients at the National Leprosarium Ogu-Komyoen in Japan. The group included 490 males and 259 females, of whom 561 were lepromatous and 188 tuberculoid. All were over 15 years of age. The anomalies of the teeth found in leprosy patients were not essentially different from those to be seen in normal persons, but their frequency among leprosy patients (33.07% \pm 0.99%) was comparatively higher than that found in normal persons. In the great majority of cases with some anomalies of the teeth the disease occurred before 10-30 years of age, i.e., in the ages in which the teeth grow or complete their growth. Anomalies were found more frequently in lepromatous cases $(34.29\% \pm 1.16\%)$ than in tuberculoid cases (29.43% \pm 1.92%). These facts suggest some relation between anomalies of the teeth and leprosy.-K. KITAMURA

Stein, A. A. and Nikolaeva, M. N. Caries of the teeth in leprosy patients. Collection of articles on "Pathogenesis and therapy of dermatosis." IVth Scientific Conference, Llov, 1966, pp. 270-273.

The authors found caries in 77% of leprosy patients. In the lepromatous type it was present in 81.4% and in the indeterminate type in 92.9%. It occurs more often in patients aged 40-50 years. Teeth in the upper jaw are affected more frequently, especially the molar teeth; next come the premolars. Cutting teeth are rarely affected. Caries grades I and II are prevalent. Gangrene and pulpitis occur less in relation to the premolars. Cutting teeth are ground off less. Sometimes teeth are ground off to a half crown. Tooth stone was found in 4% of nonleprotic persons, and in 67% of leprosy patients; it was soft, light and rapid in growth. When teeth are drilled, the leprosy patients, although anesthetic in the gums, feel pain just as normal persons do.— N. Torsuev

Pierini, L. A., Abulafia, J. and Wainfeld, S. Las hipodermitis. [Types of hypodermitis.] Arch. argentinos Dermat. 15 (1965) 1-38. (1st part)

X

In this first part perniosis, the erythema nodosum group, and the migrant subacute nodular hypodermitis of Vilanova and Piñol

Aguadé are reviewed. Twenty-two cases of symmetric supramalleolar erythrocyanosis are reported. Three clinico-histopathologic forms are pointed out: (1) pure supramalleolar erythrocyanosis, with cyanosis due to a diffuse venous vascular stasis, and pure edema due to mucoidosis of the connective tissue and folliculosis due to atrophy or pilosebaceous adnexa; (2) supramalleolar erythrocyanosis with perniosis, presenting soft, infiltrated cyanotic plaques, with diffuse outlines due to the presence of an important perivascular lymphocytic infiltration added to the above picture, sometimes with bullae due to papillary edema; and (3) supramalleolar erythrocyanosis with purpura, with lesions of necrotizing angiitis and thrombosis resulting in necrosis, purpura and dermoepidermic bullous formations that heal with superficial scars. This last form suggests a pathogenesis of hypersensitivity. It usually predominates in patients with sequelae of poliomyelitis. For erythema nodosum the following findings are quoted. Typical erythema nodosum develops in children and adolescents, is of possible tuberculous origin, and evolves approximately in one month without recurrences. An atypical form consists of plaques or nodes of long duration and tendency to recurrence. It is related to ingestion of drugs or septic foci, and develops principally in adults. Histopathologically, lesions of vasculitis, predominantly in the hypodermis, are pointed out. Infiltrates of lymphocytes and neutrophils occur. Three histologic types of erythema nodosum are described, according to the type of vessel altered: type 1, with hypodermic universal capillaritis; type 2, with phlebocapillaritis and Miescher's radiating granuloma; and type 3, with necrotizing angiitis in hypodermic muscular arteries simulating Kussmaul-Maier disease. No parallelism was demonstrated between the clinical and the histopathologic picture. Multiple etiologies are suggested, with a common pathogenesis of hypersensitivity, the hypodermic vessels being the predominant shock organs. Miescher's radiating granuloma is interpreted as a hyperplasia of endothelial cells in venules, related to the vascular irritation phenomenon. Vilanova's and Piñol's migrating subacute nodular hypodermitis is a peculiar entity with histologic characteristics defined by the development of granulation tissue with giant cells, which causes atrophy of the adipose lobules and thickening of the hypodermic connective tissue walls; clinically it is represented by migrant or nonmigrant subacute nodules which are cured by potassium iodide intake. Its relationship with erythema nodosum is discussed, and it is believed that some of these cases have been described as atrophic erythema nodosum or as erythema nodosum migrans by Bäfverstedt.—Authors' Summary

Pierini, L. A., Abulafia, J. and Wainfeld, S. Las hipodermitis. [Hypodermitis.] Arch. argentinos Dermat. 15 (1965) 105-128.

In this issue "relapsing lepromatous nodular hypodermitis" (erythema nodosum leproticum), and the erythema nodosum of sarcoidosis are described. Nineteen cases of ENL were studied. This form is related to erythema nodosum with atypical characteristics. It differs from typical erythema nodosum by its recurrences and tendency to fusion. In these aspects ENL is nearer to the erythema induratum of Bazin than to typical erythema nodosum. The suggestive term given by Ramos e Silva to ENL, i.e., relapsing nodular lepromatous hypodermitis, seems preferable. From the histopathologic standpoint this picture shows two types of infiltration: a chronic one, formed by the typical lepromatous granuloma, and an acute one, superimposed, with vascularitis, polymorphonuclear leucocytes (predominantly neutrophils), with common occurrence of leucocytic destruction, and lymphocytes predominating in the phase of decline of the outbreak. Capillary and venous alterations are frequent. Arteriolar lesions are less common. Endothelial hyperplasia is an important finding. The granuloma radiatum of Miescher could be found. Erythema nodosum seen in sarcoidosis proved to have histopathologically two different pictures: one is identical with that described before as typical erythema nodosum; the other represents merely a sarcoid nodule of hypodermic location.-E. D. L. JONQUIÈRES

Chaudhury, D. S. and Chaudhury, M. A case report of gangrenous balanitis in progressive reaction in leprosy. Leprosy Rev. 37 (1966) 225-226.

Case report of a young African patient with gangrenous balanitis as a complication of ulceration arising in a subcutaneous nodule during progressive reaction in leprosy.—Authors' Summary

Parikh, A. C., Ganapati, R., Kapadia, B. I. and Naik, S. S. Acetylcholine test for anhydrosis in leprosy. Leprosy Rev. 37 (1966) 231-237.

Ever since Father Joseph Damien de Veuster's observations in 1899 that on the early macules of leprosy which appeared on his own skin, perspiration did not appear, many authors have been stimulated to investigate this localized anhidrosis in early patches of leprosy and also utilize this phenomenon for early diagnosis of the disease, especially where examination for the cardinal signs of leprosy gives doubtful results. A simple method to detect anhidrosis using 0.1% acetylcholine and bromophenol blue paper is described. In a study of 159 patients, anhidrosis was demonstrated by use of this test in 96.6% of lesions caused by leprosy diagnosed by routine standard methods, and in 79.4% of those clinically and histopathologically suggestive of leprosy, but without definite sensory impairment. As histologic changes in relation to the sweat glands have been observed in the majority of hypopigmented lesions suggestive of leprosy in which anhidrosis could be demonstrated, it may be concluded that abnormal sweat response resulting from denervation of sweat glands due to leprotic neuritis probably precedes the development of demonstrable sensory changes.—N. D. Fraser

Kandhari, K. C. and Sehgal, V. N. Electromyographic studies in leprosy and dermatomyositis. Dermatologica Internat. 4 (1965) 96-101.

Electromyographic studies were conducted on 37 patients with leprosy and three cases of dermatomyositis. Results obtained were compared with 23 normal controls. Five of the leprosy patients

showed a complete nerve lesion with isoelectric recordings, even on muscular contraction, while others showed a partial nerve lesion with a specific mixed pattern, with poly- and biphasic waves. Dermatomyositis patients showed a specific pattern of their own. The significance of these findings in the prognosis for such cases is discussed.—Authors' Summary

Jopling, W. H. The use of a dermojet injector for skin biopsies. Leprosy Rev. 37 (1966) 219-220.

The problem was to find the best way of delivering the local anesthetic into the skin, using the minimum number of applications. It was soon found that the actual region of skin injected was of no value to the histologist because of tissue disruption. By a process of trial and error a successful method was evolved, which consisted of cleaning the skin with ether, drawing a circle 1 cm. in diameter around the biopsy site with a skin-marking pencil, and then administering a jet of local anesthetic at eight points around, yet close to the circle. It is simple enough to space the eight insertions of local anesthetic outside the circle, as a wheal appears immediately at each site, and after a wait of a minute or two the region within the circle is ready for biopsy. Slight discomfort may be experienced when the deepest part of the tissue is removed, but it is no worse than with the standard methods of anesthesia.-N. D. Fraser

Williams, H. W. G. The leprosy thumb. Brit. J. Plast. Surg. 19 (1966) 136-139.

The author found that the standard operation in which a sublimis tendon is used to produce abduction-opposition of the thumb, fell short of the ideal. He, therefore, considered the possibility of using the flexor pollicis longus as the transferred tendon and reports thirty cases that were operated on by this procedure with gratifying results. The methods of correcting the deformity of the leprosy thumb are reviewed and the new approach is described. The author's discussion and summary indicate that obviously a single tendon cannot perfectly reproduce the action of half a dozen paralyzed ones, but the flexor polli-

cis longus is a powerful one, capable of a strong pull through both transferred divisions. Its normal function is solely in flexion of the terminal phalanx, and in the leprosy thumb this is a disadvantage rather than an asset. The final result is a thumb that can be well opposed to the fingers, although movements at the interphalangeal joint are lost. Accurate routing of the tendon is vital because, if the line of traction falls proximal to the metacarpophalangeal joint, extension, rather than abduction is obtained. As stated by the pioneers in this field, if web contracture is present it must be corrected before tendon transfer.—N. D. Fraser

Abreu, L. B. Cirurgia reparadora de mão nas lesões nervosas da lepra. [Reconstructive surgery of the hand for the treatment of neural leprosy lesions.] Rev. Hosp. Clin. Fac. Med. (S. Paulo) 18 (1963) 305-314.

Leprosy is a disease that has been known for centuries. It is a disease of the skin and nerves. Clinical treatment heals the cutaneous lesions, but the nerve lesions continue. M. leprae is sometimes found in a caseous mass in nerves. Diagnosis is not difficult. Surgical treatment is directed toward relief of pain and improvement of function through correction of claw hand. There are many types of operations, indicated according to the case, including neurolysis, tendon transplants, tenodesis, arthrodesis, capsuloplasties, etc. The author reports preliminary results of five cases treated with eight operations. He believes that rehabilitation of the leprosy patient represents team work, in which physiotherapy, occupational therapy, vocational orientation and psychologic treatment all play an important part. Surgery is only a part of the treatment, and not always the most important one.-N. DE SOUZA CAMPOS

Reginato, L. E. and Belda, W. Ensaio de correção das deformidades amiotroficas do dorso da mão por novos metodos; retalhos dermogordurosos, enxertos de fascia lata e inclusões de silicone. [Attemps to correct amyotrophic deformities of the dorsum of the hand Ly new meth-

ods; skin fat flaps, fascia lata grafts and implantation of silicone.] Rev. brasileira Leprol. 32 (1964) 49-53.

Three new methods for restoration of the hand deformed by leprous amyotrophy of the interosseous muscles are described: fat flaps, fascial grafts, and liquid silicone implants. Results are described. Epineurectomy of the ulnar and median nerves is suggested, as well as the administration of peripheral vasodilator drugs for improvement of the neurotrophic state of the tissues to be repaired.—[From author's summary]

Belda, W. Tratamento do mal perfurante plantar leprótico com extrato de sangue desproteinizado (Solcoseryl). [Treatment of plantar ulcer in leprosy with extract of deproteinized blood (Solcoseryl).] Dept. of Dermatology, 11 August 1964 session. Summary in Rev. paulista Med. 65 (1964) 347.

The author reviews the theories of etiology of the plantar ulcer, analyzing in particular the concept of the Rehabilitation Service of the Department of Leprosy Control in Brazil, which considers the plantar ulcer as a late complication of the pathologic process of leprosy. It develops whenever profound trophic, paralytic and anesthetic changes alter the somatic structures of the distal extremities of the lower limbs. With this approach, the author reviews the therapeutic procedures used, from immobilization to arthrodesis. In an attempt to improve trophism of the affected areas the author uses extract of deproteinized blood of young animals (Solcoseryl) in local infiltrations, together with the jelly of the same product. Five patients, with nine ulcers, were treated without the use of accessory procedures or decrease of activity. The lesions of the five patients (2 lepromatous, 1 tuberculoid and 2 indeterminate) were treated on an average for 20 days. The author concludes that the product is highly useful in the complex of therapeutic factors basic in the treatment of plantar ulcers.-N. DE SOUZA CAMPOS

Mukherjee, S. M. Management of uncomplicated plantar ulcers in the field. Leprosy in India 38 (1966) 107-115.

The problem of plantar ulcer remains unsolved. The important role of paramedical personnel in solving it is discussed. They can and should deal with the early and uncomplicated ulcers. Necessary for this are: (1) to protect the ulcer from injury and infection by means of antiseptic dressings, and (2) to put the foot to rest by means of a plaster-of-paris cast.—Author's Summary

Tio, H. and Santoso, K. Ambulatory treatment of plantar leprosy ulcers. Leprosy Rev. 37 (1966) 239-244.

The authors found it difficult to apply the recommended treatment for plantar ulcers. Absolute bedrest is not practical for patients of the poorer classes, and plaster casts are both inconvenient to the patient and a burden to medical personnel. Their studies led them to conclude that pressurized rubbing is the causative external factor, and that treatment should aim to rest ulcers while allowing the patients to walk freely, but in such a way that pressure is not concentrated on the normal pressure points. Zincoil (75% zinc oxide, 25% cod liver oil) was used to plug the ulcers, with the result that the patients had to walk with a different push-off point. The therapeutic way of walking depended on the site of the ulcers, and each patient was taught or encouraged to adopt the gait suited to his condition. Out of 71 ulcers on anatomically normal feet, 56 were healed within 5 weeks, and the remaining 15 within 9 weeks. Anatomic deviations interfered with the healing of 22 ulcers. The procedure constitutes a simple and cheap ambulatory treatment for leprosy ulcers, especially suitable for rural areas.— N. D. Fraser

Amendola, F. Present status of ocular leprosy. Ophthalmol. Iber. Amer. 24 (1963) 1-22. (In English, Portuguese summary.)

The author discusses the orientation of the ophthalmologist in the diagnosis of ocular leprosy. Leprosy patients attending ophthalmologic clinics can be divided in two classes, i.e., those who ignore the etiology of their ocular condition, and others who are misled, reporting symptoms of a

different disease, e.g., allergic disorders, intoxication, syphilis, etc., based on diagnoses made by physicians who do not know leprosy. Because of the serious symptoms of their visual deficiency and acute pain they look for assistance and cure of their visual illness. The clinician may be misled by an incorrect anamnesis, but the ophthalmologist, through the objective symptoms characteristic of ocular leprosy, will make the etiologic diagnosis. Patients rarely inform him they have leprosy. After diagnosis of diffuse scleritis, infiltration in the form of pannus (generally localized in the superexternal region) localized or diffuse keratitis (superficial or parenchymatous), granuloma or leproma of the eveball, iridocyclitis, acute serous iritis, iridian miliary nodules, etc., topical antiphlogistic medications used routinely in acute ocular infections are administered, and either the case is reported or referred to a specialized public health service, or the ophthalmologist assumes responsibility for the treatment, administering the sulfones according to the dosages usually established, varying according to the tolerance of the patients and results of the treatment.—N. DE SOUZA Campos

Warren, A. G. A method of medial tarsorraphy for correction of lagophthalmos and ectropion. Leprosy Rev. 37 (1966) 217-218.

The author has devised a simple operation for the correction of lagophthalmos, which consists of the insertion of monofilament nylon to take up the slack resulting from paralysis of the orbicularis oculi. Success depends on the correct placing and correct tension of the suture. "This procedure has been used on over 25 patients; some previously failed by other methods. The first patient was in December 1960 and is still functioning with the nylon in situ. . . . This method generally gives better functional and cosmetic results than more conventional procedures. The patency of the lachrymal apparatus has been checked in a number of cases after surgery and found patent. Many patients claim marked relief from watering, which is often the original complaint; this is easily explained

as the lower punctum is brought into better apposition with the eyeball."—N. D. Fraser

Perquis, P. and Muret, G. Ulcères tropix caux a mycobactéries. A propos de 2 observations. [Report of two cases of tropical ulcer due to mycobacteria.] Bull. Soc. Páth. exot. 58 (1965) 789-795.

Two cases of tropical ulcer due to *M. ulcerans* are reported. Bacteriologic, radiologic and clinical data for the diagnosis are presented. Therapy is still under study. Surgical excision, followed by skin graft, appears to be the most effective procedure. Fungal antibiotics, streptomycin, PAS, and isoniazid, proved ineffective.—[From authors' summary]

Souza Lima, L. Novos conceitos sôbre a terapêutica da lepra. [New concepts on the therapy of leprosy.] Summary in Proc. 7th Internat. Congr. Trop. Med. & Malaria, Rio de Janeiro, 1-11 September 1963. Vol. 3, pp. 48-49.

The author reviews the various drugs used at present in the treatment of leprosy, emphasizing the benefits from their use, not only in relation to medical but also to public health aspects, with chief reference to the sulfone drugs. He points out the limitations of this therapy, the most serious being the long time necessary for the apparent sterilization of infectious foci and the need to continue treatment for an indefinite period, with the objective of preventing relapses, not always attained. Conditions that favor development of mutants resistant to antileprosy chemotherapeutic agents with the present schemes of treatment are cited, particularly with the sulfone drugs. This resistance can discredit them, from both the medical and public health points of view, since it involves the risk of transmission of leprosy by resistant mutants. The author suggests a scheme of triple treatment, based on the association of more potent drugs, presenting the results obtained with this therapy in pilot groups in the Pirapitingui and Aimorés Sanatoriums of the State of São Paulo.-N. DE SOUZA CAMPOS

Terencia de las Aguas, J. Leproreacciones. Su tratamiento. [Lepra reactions. Their treatment.] Rev. Leprol. (Fontilles) 6 (1966) 431-448.

A detailed review is presented of drugs employed in the treatment of lepra reactions. The drugs are classified in the following groups: (1) antiallergic and desensitizing agents, (2) modifiers of the internal environment, (3) reactivators of the reticuloendothelial system, (4) anti-infectious agents, (5) antipyretic drugs, (6) vitamins, (7) biologicals, (8) hormones, and (9) other treatments.— F. Contreas D.

Santos, H. S. and Nogueira, F. G. Sulfonémia na lepra. Estudo dos niveis sanguineos de DDS em doentes internados no Hospital Rovisco Pais. [Sulfonemia in leprosy. Study of blood levels of DDS in patients in the Hospital Rovisco Pais.] Rovisco Pais 5 (1966) 3-8. No. 16.

The concentration of DDS in the blood of 49 patients treated with weekly intramuscular injection, was studied. A graph of the 330 estimations made shows that for 16 days out of 28 the concentration of DDS in the blood was less than 0.15 mgm. per cent.—Authors' Summary

Adams, A. R. D. and Waters, M. F. R. Dapsone-resistant lepromatous leprosy in England. British Med. J. 2 (1966) 872.

The authors report the detailed history of a 33 year old Anglo-Indian from Bengal whose deterioration despite treatment led to investigations which revealed dapsone resistance. They add the following comment: Dapsone-resistant leprosy is rare. Moreover, the three patients of Pettit and Rees (1964) had all received sulfones for many years, as also, despite his stated history, had our own patient. The application of the mouse foot pad test not only confirmed our clinical diagnosis of drug resistance, but also provided guidance of the patient's future management. Although Hirako and Sakurai (1963) have suggested that long-acting sulfonamides may be of value in sulfone resistance, we were not surprised to find that partial cross-resistance had occurred with sulfadimethoxine,

as the sulfones and sulfonamides are chemically so closely related. However, resistance to thiambutosine had not developed, and the patient had responded well to a further course of this drug, combined with Vadrine (an oxydiazoline compound) and subsequently with thiacetazone.—N. D. Fraser

Castro, I., Almeida, S. and Castro, N. Contrôle da absorção de antilépricos nas campanhas de saúde pública. [Control of absorption of antileprosy drugs in public health campaigns.] Summary in Proc. 7th Internat. Congr. Trop. Med. & Malaria, Rio de Janeiro, 1-11 September 1963. Vol. 3, p. 53.

The author believed it important to control the absorption of antileprosy drugs in view of the results of a systematic investigation of the sulfonuria of patients treated with DDS in the form of coated enteric pills. This study, carried out in the Institute of Leprology at the request of Dr. J. B. Risi, then Director of the National Leprosy Service, demonstrated that inadequate preparation of the coated pill partially or totally impairs absorption of the drug. Apparently it is a pharmaceutical error, but in view of the amount of coated pills to be used over a long period of time, by a great number of patients, this error acquires a significant public health and economic importance. The capability of pharmaceutical manufacturers, the honesty of intermediaries, and the trust that auxiliaries and patients place in public health officials, are important factors, but insufficient in the search for the best therapy at lowest cost. The methods described, which result from the work of many, are not precise, but are useful for the purpose at which they are aimed. All were selected under clinical and experimental control, taking into consideration the essential requirements of applicability to public health campaigns, viz., rapidity of execution, accessible material and reagents, low cost, and sufficient precision.—N. de Souza Campos

Schneider, J. and Languillon, J. Le traitement de la lèpre par un sulfamide-retard, l'acétylsulfaméthoxypyrazine. [Treatment of leprosy by a long acting sulfonamide, acetylsulfamethoxypyrazine.] Bull. Soc. Path. exot. **58** (1965) 771-780.

A new sulfanilamide, N₁-acetylsulfanilamido-2-methoxy-pyrazine, administered by mouth in a weekly dose of 2.5 gm., yields a sufficient blood level of sulfonamide for a week. The treatment proved highly efficient in 79 new patients for a period lasting between 18 and 36 months. An apparent recovery was observed in 58 patients out of 79 (73%).—[From authors' summary]

Currie, G. A clinical trial of sulforthomidine ('Fanasil' Roche) in lepromatous leprosy. Leprosy Rev. 37 (1966) 205-208.

Sixteen lepromatous leprosy patients in Malawi were submitted to a six month clinical trial of sulforthomidine (Fanasil, Roche) (4-sulfanilamido-5,6-dimethoxypyrimidine), a long-acting sulfonamide of low toxicity and good antibacterial efficacy, administered orally in a dosage schedule of 1 gm. once a week. (The name approved by the B. P. Commission is sulphormethoxine.) A control group of 14 patients received dapsone in a dosage of 0.3 gm. twice a week. The clinical and bacteriologic progress of the patients on sulforthomidine was as good as that achieved by dapsone. The incidence and severity of ENL reactions and the incidence of side effects attributable to the drug were much less in the sulforthomidine group than in the dapsone group. From this limited trial it appears that sulforthomidine is an effective antileprosy drug singularly free from side effects and reactions. [From author's summary]-N. D. Fraser

Martins M. G., Filho. Nossos ensaios com a inclusão de silicônio líquido em doentes de lepra, no Instituto Educational "Padre Bento Dias Pacheco." Nota prévia. [Our experiments with the injection of liquid silicone in leprosy patients in the Educational Institute "Padre Bento Dias Pacheco." (Preliminary note).] Rev. brasileira Leprol. 32 (1964) 47-48.

The author describes the use of liquid silicone in leprosy patients, employed for the first time in Brazil, for the correction of amyotrophies of the hand, and presents the technic used in five cases. Results were good, but admittedly the number of patients was small.—N. DE SOUZA CAMPOS

Behl, P. N. and Bedi, B. M. S. New indigenous drug in the treatment of lepra reaction and lepromatous leprosy. Indian J. Dermat. 11 (1966) 153-157.

In their search for a drug for effective treatment of reaction in lepromatous leprosy that would "act as a double edged weapon," i.e., "prevent mutiplication of lepra bacilli as well as control reactions," the authors chose a new indigenous drug, Capyna Compound, which was originally recommended for the treatment of tuberculosis. This drug was tried in 25 cases of lepromatous leprosy with reaction and cases of active lepromatous leprosy, most of which "were intolerant to sulphone and recalcitrant to known therapeutic measures." The drug was administered three times a day with the following results: The reaction was controlled within 15 days to six months. Patients whose reaction could be controlled previously only with cortisone were successfully switched over to this indigenous drug. The authors conclude that the drug has a definite place in the management and control of reaction in leprosy.—K. Ramanujam

Ojha, D. Nimbadi Lepa in the treatment of leprosy. A preliminary report. Indian J. Med. Sci. 20 (1966) 217-221.

The author reports his experience with Nimbadi Lepa in the treatment of lepromatous leprosy. Nimbadi Lepa, one of the several lepas (drugs administered by the percutaneous route) indicated in the treatment of leprosy in the Ayurvedic system of medicine was selected by the author for the trial. No less than 13 ingredients comprised of bark, root, woody portion, leaves, etc., of herbal plants make up the drug, which was made available in powder form. Two groups of subjects were selected consisting of six advanced uncomplicated, untreated lepromatous cases in each. The investigation group received DDS orally in a dose of 100 mgm. a day for six days of the week. In addition they were given

10 gm. of Nimbadi Lepa mixed with butter milk for application and rubbing into the skin once a day after preliminary application of mustard oil. This inunction was also given six days in the week. After application of the lepa, the patients kept it on for three hours and then took a bath with soap and water. The control groups received only 100 mgm. DDS/day for six days of the week. The cases in each group were assessed clinically and bacteriologically at the end of six months. The author concludes that the Nimbadi Lepa seems to have some value in the therapy of leprosy as "evidenced by speedy reduction of external symptoms, such as decrease in size of nodules and skin lesion, promotion of pigmentation and marked reduction in bacillary index."-K. RAMANUJAM

Mathur, J. S., Sehgal, V. N. and Rao, N. S. N. Perineural Priscol injections in leprosy ulcers. Leprosy Rev. 37 (1966) 249-253.

Twenty-five leprosy patients with ulcers were treated with Priscol injections. Ulcers of small size or of short duration healed early. Trophic ulcers in the sole healed with prolonged treatment. All the treated ulcers except one healed or decreased in size. No fresh ulcers were reported in the regions after healing.—Authors' Summary

Ranade, S. N., Joshi, P. B., Deshpande, S. M., Kotnis, M. G. and Apte, A. N. Tolrivizin in the treatment of trophic ulcers in leprosy. Indian J. Dermat. 11 (1965) 17-20.

Review of articles on the treatment of trophic ulcers, and the improvement described in the neurologic changes of diabetic patients with Tolrivizin (a hypoglycemic agent) led the authors to try this indigenous drug in nine cases of trophic ulcer. The drug was continued for 118 days (on the average) orally. During this period of observation six cases showed complete healing without any anticipated side effects, such as hypoglycemia.—S. Ghosh

Griffiths, P. G. Notes on the treatment of ulcers in leprosy patients with Polybactrin. Leprosy Rev. 37 (1966) 227-229.

Two patients suffering from lepromatous leprosy complicated by ulcers of the thigh and leg were treated with Polybactrin spray, Cicatrin powder and Cicatrin cream (Calmic, Ltd., Crewe, England) with very satisfactory healing of the ulcers.—Author's Summary

Terencio de las Aguas, J. and Contreras Dueñas, F. Primeros resultados del tratamiento de las lepro-reacciones con Talidomida. [First results in the treatment of lepra reactions with Thalidomide.] Rev. Leprol. (Fontilles) 6 (1966) 449-455.

Six lepromatous patients (two males and four females) with frequent lepra reactions over a period of several years, were treated with Thalidomide (Softenon) in initial maximum doses of 100 mgm. daily, which were decreased gradually to 50 or 25 mgm. as the picture improved. Lepra reaction disappeared in five patients. In one patient it was necessary to suspend treatment because of allergic reaction of moderate intensity. The time of disappearance of fever varied from two to 11 days. One patient, a woman, had remained in continual reactional state, under corticosteroid treatment, for four years.—Authors' SUMMARY

Anonymous. Diaminodiphenylsulfone authorized for troops. Trop. Med. & Hyg. News 15 (1966) 12 (No. 5).

The U. S. Army Surgeon General's office has authorized the use of DDS as an antimalarial among U. S. troops in Vietnam. They will be given "one 25 milligram pill' each day and will continue this for one month after leaving the area. Recent Army field tests showed that DDS halved the number of men stricken by malaria. Drug recipients who do contract malaria should now be able to return to duty in 2 or 3 weeks instead of the former 6-8 weeks. Relapse chances should be cut from 40 per cent to 4 per cent. DDS is aimed specifically at a resistant strain of P. falciparum malaria first reported in South America in 1960 and confirmed among U. S. soldiers in Vietnam in mid-1964.—J. A. ROBERTSEN

Anonymous. Leprosy drug tested as an antimalarial. Trop. Med. & Hyg. News 15 (1966) 12 (No. 3).

Dapsone is said to have protected patients against the resistant strain of *Plasmodium falciparum* in a test on several hundred U. S. soldiers in the South Vietnamese highlands. Last year almost 1,000 American soldiers were stricken by that strain, which has proved resistant to the chloroquine and primaquine antimalarials regularly taken by Americans in Southeast Asia.—J. A. ROBERTSEN

Rees, R. J. W. Enhanced susceptibility of thymectomized and irradiated mice to infection with *Mycobacterium leprae*. Nature (London) 211 (1966) 657-658.

At least one factor limiting multiplication of M. leprae in the mouse foot pad is the development of immunity during the course of infection. The impaired immune response following thymectomy plus irradiation resulted in only limited multiplication of M. leprae, although at a ten to a hundred times higher level than obtained in normal mice, and there was no spread of infection beyond the foot pad. Failure to obtain under these conditions a completely progressive infection with systemic spread may be comparable with the similar significant, but only partial depression of the ability of thymectomized-irradiated mice to reject the more foreign skin grafts. Thus thymectomy plus irradiation provides a means for significantly increasing the yield of M. leprae in the mouse foot pad infection. Further experiments must be undertaken to determine if similar treatment will sufficiently diminish the resistance of animals to allow larger inocula (not less than 106 bacilli/foot pad) to multiply or to allow intravenous inocula to multiply systematically.-E. R. Long

Ghosh, S. Histochemical changes in the tissues of different types of leprous lesions. 2. Indian J. Dermat. 11 (1965) 11-16 (cont'd.).

Procedures for the detection of simple proteins by the methods of Danielli, Bonhag and Chevremont and Frederic were described, with their respective findings. Aldehyde and nonaldehyde stains for nucleic acids were discussed. The reason for the metachromatic reaction with toluidine blue was reviewed, with description of the procedure and results.—S. Ghosh

Ghosh, S. Histochemical changes in the tissues of different types of leprous lesions. 3. Indian J. Dermat. 11 (1966) 51-57 (cont'd.).

The results of study of fifteen active untreated generalized lepromatous cases are presented in the paper. Histologically, in addition to the well recognized changes found in this type of leprosy, large empty spaces having an endothelial lining and often filled with bacilli were encountered in the granulomatous areas of the dermis. It has been suggested that these areas are lymphatic spaces; the localization of bacilli in these spaces indicates that infection may spread along large dermal lymphatics. Histochemical investigation revealed the presence of neutral fat in the histiocytes, limited to the area where leprosy bacilli were present, phospholipids in lepra cells, fatty acids only in the leprosy bacilli, hyalinresistant PAS-positive material in the lepra cells (which was found to be neutral mucopolysaccharide and limited to M. leprae), and alkaline and acidphosphatase in the cells of the granuloma, the latter being more conspicuous in the nerves. The distribution and concentration of lipid in the lepra cells were strictly in conformity with that of the bacilli. The presence of lipids only in the bacillus-laden lepra cells, their absence in the bacteria-free cells or in the extracellular areas, and the close parallelism of the nature, extent and localization of the lipids in the two, viz., the bacilli and the lepra cells, strongly suggested that the accumulation of fatty substance in the latter indicates the presence of the former and not any fatty infiltration or degeneration.-S. Ghosh

Ogawa, J. Electron microscopic study of Mitsuda reaction. Acta Dermat. (Kyoto) 60 (1965) 309-353. (In English)

Mitsuda antigen reveals electronmicroscopically an admixture of various cytoplas-

mic organelles derived from tissue cells, although such admixture of tissue elements does not seem to interfere with the results of the reaction. At the site of negative reaction bacilli derived from antigen are floating in edematous collagen layers. In the foci of positive reaction 48 hours after the injection many bacilli are taken into the cytoplasm of polymorphonuclear leucocytes. Seven to 22 days after the injection bacilli are found in phagocytic vesicles of macrophages. Epithelioid cells have increased mitochondria, an evidence of cellular defense activity against bacilli. The damage to blood vessels, manifested by shrunken and electron-dense endothelial and adventitial cells and the dilation of blood vessels, apparently is caused by some toxic substance released from epithelioid cells in which leprosy bacilli of Mitsuda antigen are destroyed. In cases of weakly or moderately positive reaction in borderline cases the ultrastructural features resemble those of positive reaction in tuberculoid leprosy. There are epithelioid and giant cells. The vascular changes, however, are mild as compared with those in positive reaction.—K. KITAMURA

Girling, J. A. (for Qvist, G.). Leprosy and carcinoma of the bladder. Proc. Roy. Soc. Med. 59 (1966) 424-425.

This is a brief report on the case of an obese white man, aged 69, who in 1935 while working as a marine engineer in India developed skin lesions on his chest which were diagnosed as leprosy in 1940. He was treated with sulfones for ten years after 1945, but developed anesthesia of the hands and feet, which led to multiple injuries and severe trophic ulceration. He had bilateral amputations above the knees and multiple amputations of fingers. In 1960 hematuria developed. In 1961 a large papillary tumor of the bladder was treated by suprapubic diathermy. In 1965 a total cystectomy was performed, with bilateral ureterosigmoidostomy for extensive but superficial carcinoma of the bladder, from which he made a satisfactory recovery. He has good tone of his anal sphincter, is continent by day and night, and has been able to resume his preoperative activities.-N. D. Fraser

Barbosa, Américo, Sousa e Silva and Beja, M. Carcinoma do pulmão multimetástico em doente de Hansen. [Multimetastatic carcinoma of the lung in a leprosy patient.] Rovisco Pais 5 (1966) 9-33. No. 16.

The case history of a male patient who died in the Hospital Rovisco Pais is described. He was found to have an epidermoid carcinoma of the left lung, with necrosis and cavitation and massive metastases in the pancreas and lumbar vertebrae, liver, kidneys and right lung.—Authors' Summary

Prabhakaran, H. and Kirchheimer, W. F. Use of 3,4-dihydroxyphenylalanine oxidation in the identification of *Mycobacterium leprae*. J. Bact. 92 (1966) 1267-1268.

Identification of M. leprae now depends on two time-consuming tests, that of Shepard using the mouse foot pad, and that of Shepard and Guinto, using simultaneous injections of heat-killed unknown and of standard lepromin in leprosy patients. In the first test, several thousand leprosy bacilli multiply within 6 to 9 months to maximal numbers of several million, and gross lesions or invasion of adjacent or remote tissues are absent. In the second, leprosy bacilli are the only known mycobacteria failing to evoke dermal responses in Mitsuda-negative leprosy patients. Since culture of *M. leprae* is now widely attempted, methods for rapid screening are desirable. Prabhakaran had previously found that M. leprae from lepromatous skin nodules, oxidizes 3,4-dihydroxyphenylalanine (dopa) to colored products within 15-30 minutes, but cultivable strains formed no color. Because skin itself contains dopa oxidase, the studies now reported used bacilli separated from spleen, which is devoid of this enzyme. Bacilli were separated from spleen tissue homogenate by the differential centrifugation method of Prabhakaran and Braganca, and were incubated with dopa and its structural analogs, epinephrine and norepinephrine. (Protein concentration of bacilli, 2 mgm.; pH 6.8; 37°C; in 3 ml.) The reaction products, after centrifugation for 45 minutes at 15,000 x g were read spectrophotometrically at 540, 480 and 480 mp respectively. Dopa was oxidized by unheated but not by heated (100 C°/15 min.) M. leprae, nor by human spleen, mouse spleen, M. lepraemurium, M. balnei, nor five isolates from the American Type Culture Collection once thought to be leprosy bacilli. These findings indicate a high degree of specificity for dopa oxidase in M. leprae.—John A. Robertsen

Ghosh, S. and Chakraborty, B. K. Observation on the morphological changes in Myco. leprae in leprosy. Bull. Calcutta Sch. Trop. Med. 13 (1965) 135-136.

Thirty active untreated lepromatous cases were divided into three groups based on their degree of positivity. Another group of lepromatous patients who were taking DDS for varying periods with good results were also taken for observation, five in each group. The proportion of irregularly stained bacilli was 60%, 58%, and 55% in the 2+, 3+ and 4+ groups respectively, whereas in the treated group, the percentage of irregularly stained bacilli varied and showed rapid increase of irregularly stained bacilli with treatment up to six months and then remained almost stationary.—S. Ghosh

Manzullo, A., Manzi, R. O., Lefevre, H. and Oteiza, M. L. Investigación de bacilos ácido-resistentes en el contenido digestivo de enfermos de lepra. [Investigation of acid-fast bacilli in the digestive tracts of leprosy patients.] Leprología 10 (1965) 14-16.

Acid-fast bacilli were found in 7 of 20 samples of biliary secretion, and in two of seven samples of feces. The author speculates on the possibility of dissemination of mycobacteria by this means in countries where sanitary facilities are inadequate.— E. D. L. Jonquières

Kato, L. and Gozsy, B. Limited multiplication of Mycobacterium lepraemurium in parabiotic culture, as influenced by osmolarity of an alkaline-galactomannan medium. J. Bact. 91 (1966) 1859-1862.
During a study of factors affecting the

multiplication of M. lepraemurium in vitro it was found that limited multiplication could be obtained in a medium containing a mucopolysaccharide, galactomannan, at pH 8.4. This substance was not metabolized but appeared to be necessary for the high viscosity which it produced and upon which growth depended. The necessity for the high alkalinity has not been explained. The physical properties of the medium appeared to be as important as its chemical constitution. The optimum concentration of sodium chloride in the medium was 2.0%; and growth was further enhanced when Torula minuta was added to the medium, although in the presence of 2.0% NACl the torula cells were lysed. Organisms were inoculated into rats after four and eight weeks of culture and produced lesions typical of murine leprosy. [Abstract by D. S. Ridley, *Trop. Dis. Bull.* **63** (1966) 1097.]

Sodhi, H. S., Salles, C. A., Sharma, V. N. and Chowdhry, G. A. "Anonymous" mycobacteria, a clinical and bacteriological study. Ghana Med. J. 5 (1966) 88-94.

The morphologic, cultural, and biochemical characteristics of 12 strains of anonymous mycobacteria, isolated from patients attending the Chest Clinic for Greater Accra were studied. Six cultures were considered "significant," as the same organism was isolated repeatedly and/or no other organism was incriminated. The clinical picture of five patients was observed for varying periods under standard antituberculous therapy. All cases had advanced lesions in the lungs characterized by fibrosis and cavitation. No case showed favorable response under medical treatment.—[From authors' summary]

Norlin, M., Navalkar, R. G., Ouchterlony,
O. and Lind, A. Characterization of leprosy sera with various mycobacterial antigens using double diffusion-in-gel.
III. Festskrift, Thomas M. Vogelsang,
1 August 1966. Preprinted from Acta Path. e microbiol. scandinavica. Pp. 116-123

Precipitating antibodies against two antigens, β and δ , common to many mycobac-

terial species, have been demonstrated in sera from cases of leprosy. Of 54 sera tested 78 per cent were precipitin-positive. The anti- δ precipitin was found in sera from 76 per cent of the cases and anti- β in 44 per cent. The frequency of these antibodies in relation to the bacillary status of the patients and the type of the disease is given. The possibility of leprosy serodiagnosis based on the presence on the anti- β and anti- δ precipitins is discussed.—Authors' Summary

Bechelli, L. M. Contribution to the study of the immunoallergic relationship between tuberculosis and leprosy by correlation of the Mantoux and Fernández reactions. Acta Leprol. No. 25 (1966) 5-107.

Publication in extenso of thesis submitted for the competitive examination for the Chair of Dermatology at the Ribeirão Preto Faculty of Medicine, University of São Paulo, Ribeirão Preto, State of São Paulo, December 1960. The present publication carries more recent material in the form of footnotes. The summary and conclusions of this monograph were published in the International Journal of Leprosy 33 (1965) 875-880.—E. R. Long

Melamed, A. J. and Melamed, M. Sensibilidad leprolínica y lepromínica en enfermos de lepra, en sujetos afectados por tuberculosis pulmonar y en individuos sin lepra ni tuberculosis. Correlaciones con la sensibilidad a la tuberculina. [Leprolin and lepromin sensitivity in patients with leprosy, in subjects with pulmonary tuberculosis and in individuals without leprosy or tuberculosis. Correlations with tuberculin sensitivity.] Arch. argentinos Dermat. 14 (1964) 194-201.

Three groups were tested: Group 1, consisting of 27 tuberculoid leprosy patients; Group 2, of 61 individuals without leprosy or tuberculosis; and Group 3, of 66 subjects with pulmonary tuberculosis. Group 1 patients were tested simultaneously with LPT (Olmos Castro's leprolin) and with integral lepromin. Group 2 patients were first tested with raw tuberculin in 1 per cent dilution (Mantoux test). A week later

the group was submitted to the first injection of LPT and of integral lepromin, in homologous sites. Ninety days later the subjects were retested with LPT and lepromin. Group 3 patients were first tested with tuberculin in 1/10,000 dilution; negative cases were retested with tuberculin in a dilution of 1 per cent. A week later LPT and lepromin were injected. A second inoculation was performed 70 days later. The conclusions were: (1) The LPT antigen showed less activity in revealing sensitivity of the tuberculin type (Fernández reaction) than integral lepromin; (2) lepromin showed an evident sensitizing action; (3) tuberculin hypersensitivity favored the production and intensification of the phenomenom described in (2); (4) the facts referred to in conclusions (2) and (3) might be related with the mechanism of Freund's coadjuvant; (5) the very high percentage of adults reacting positively in the Mitsuda test suggests that the incapacity to react to this antigen might be related to a congenital or acquired inmunologic disturbance such as a possible leprosy infection during the intrauterine period or in very early infancy.—E. D. L. Jonquières

Souza Campos, N. de and Lobo, O. P. Considerações em tôrno da sensibilização tuberculínica entre os doentes de lepra do tipo lepromatoso. [Comments on tuberculin sensitivity among leprosy patients with lepromatous type disease.] Rev. brasileira Leprol. 32 (1964) 23-32.

More than 80% of patients with lepromatous type disease, all adults, did not react to tuberculin in a dilution of 1/100. This rate of positive reaction in the adult population of the Capital is only 20%, varying according to the investigator and the nature of the material. The authors plan to compare the tuberculin sensitivity curves of hospitalized patients and ambulatory cases, in order to find out if environment could have any influence on the incidence of sensitivity.—N. DE SOUZA CAMPOS

Ghosh, S. and Bose, R. Vole bacillus vaccine as an immunizing agent in leprosy. Bull. Calcutta Sch. Trop. Med. 13 (1965) 134-135.

The demonstration that an extract of vole bacillus gave skin reactions similar to those given by lepromin suggested that the vole bacillus might be used as a vaccine in leprosy. Accordingly 10 guinea pigs were vaccinated to see if the vole bacillus caused conversion of their lepromin reactions; all the animals were lepromin- and tuberculinnegative before vaccination. One month after vaccination they were retested. Nine animals had become lepromin- but not tuberculin-positive (the 10th animal died). After a second vaccination they gave strong lepromin reactions. Four unvaccinated control animals remained lepromin-negative after repeated testing. The conclusion is drawn that vole vaccine might be a useful immunizing agent in leprosy. [Abstract by D. S. Ridley, Trop. Dis. Bull. 63 (1966) 1098.

Ghosh, S. and Bose, R. Sensitization to lepromin induced experimentally with a vole bacillus vaccine. Indian J. Med. Res. 53 (1965) 1025-1026.

One mgm. of vole bacillus vaccine was given subcutaneously to ten guinea pigs negative to PPD. Positive reaction to Dharmendra's lepromin but not to tuberculin was observed in these animals after only four weeks. In a control group of four guinea pigs none showed positive reaction even after repeated tests with lepromin and tuberculin. So it was concluded that the vole bacillus may confer some degree of immunity against leprous infection. — S. GHOSH

Waldorf, D. S., Sheagren, J. N., Trautman, J. R. and Block, J. B. Impaired delayed hypersensitivity in patients with lepromatous leprosy. Lancet 2 (1966) 773-775.

Delayed hypersensitivity in leprosy was evaluated by testing 34 patients with leprosy with 2,4-dinitrochlorobenzene (DNCB), a chemical that sensitized 95 per cent of 43 controls. Seventeen (50%) of the 34 patients with leprosy were non-reactive to DNCB. This impaired responsiveness was limited to patients with lepro-

matous leprosy who did not have erythema nodosum leprosum (ENL). Patients with lepromatous leprosy who had ENL, those with dimorphous leprosy, and those with inactive disease, had a normal incidence of sensitization. These findings suggest a generalized impairment in the ability to develop delayed hypersensitivity in patients with active uncomplicated lepromatous leprosy which may be significant in understanding the clinical course of the disease. Concurrent tuberculin testing revealed six patients who were reactive to tuberculin but could not be sensitized to DNCB, a fact suggesting that previously developed delayed hypersensitivity might persist despite the demonstration of anergy to a new allergen. The relationship of this observation to the concept of long-lived immunologically committed lymphocytes is discussed. [Editor's Note: In a letter to The Lancet (24 December 1966, p. 1419) W. E. Bullock of the University of Rochester, Rochester, N. N., formerly with a U. S. Naval Medical Research Unit in Taiwan, takes issue with some of the conclusions reached by Waldorf and his colleagues.] AUTHORS' SUMMARY-N. D. FRASER

Ramanujam, K. and Ramu, G. Smallpox vaccination and acute exacerbation of leprosy. Leprosy in India 38 (1966) 3-9.

Vaccination against smallpox in a leprosy population seems to be a definite provocative factor for precipitation of acute exacerbation of the disease, especially in lepromatous cases. It is significant that a fairly large percentage of cases (48%) developed acute exacerbation for the first time following vaccination. In the light of our experience this occurrence of the "first reaction" may be the forerunner of several such episodes. There is a direct relationship between the intensity of the local reaction to vaccination and the chances of occurrence and severity of the acute exacerbation of leprosy. The treatment of acute exacerbation following vaccination is very much the same as of that arising spontaneously or from other causes, except that antibiotics could be employed with advantage. This is recommended in view of the occurrence of local pustulation and regional lymph adenopathy. Since there appears to be definite correlation between local reaction to vaccination, and the onset of acute exacerbation, the leprosy population in sanatoria located in areas endemic for smallpox should be revaccinated periodically. This would perhaps ensure less and less severe local reaction to vaccination and thereby reduce the incidence of acute exacerbation.—Authors' Summary

Sehgal, V. N., Mathur, J. S. and Rao, N. S. N. A. B. O. blood groups in leprosy. Leprosy Rev. 37 (1966) 221-224.

The exact mode of transmission of leprosy is still controversial, despite numerous epidemiologic studies. It has been shown beyond doubt that exposure to the infection is not the sole factor in the spread of the disease since a number of individuals exposed to an open patient do not develop the disease. Genetic factors have been considered significant by a number of workers. The authors studied 623 patients with leprosy and 615 normal controls in the Varabasi district of Uttar Pradesh, India, in order to evaluate the observations made by earlier workers. The distribution of ABO blood groups in relation to leprosy was analyzed and there seemed to be an association between leprosy and these blood groups. An appendix to the article compares the results of the present series with those of Hsuen et al. (1963) in South India, and with those of Verma et al. (1965) in the Baroda District of India.-N. D. Fraser

Bechelli, L. M. and Martinez Dominguez, V. The leprosy problem in the world. Bull. WHO 34 (1966) 811-826.

There is at present a lack of accurate data on the prevalence of leprosy in the different countries of the world, primarily because case-finding has not reached the desired level in many of them. The authors have attempted to provide more realistic figures, using information obtained from several sources and various criteria for calculating estimated prevalence rates. In

all there are 2,831,775 registered patients and 10,786,000 estimated cases; the latter figure may well be an underestimate. The number of treated patients is about 1,928,-000, some 68 per cent of the registered cases and 18 per cent of the estimated. About 2,097 million people live in areas with prevalence rates of 0.5 per 1,000 or higher; in these areas nearly one million new cases of leprosy can be expected within the next five years. The estimated number of disabled patients is 3,872,000, of whom 1,961,000 are in disability grades 2-5 (excluding anesthesia to pain). The data represent an attempt, made with many reservations, to give an indication of the magnitude of the leprosy problem throughout the world.—Authors' Summary

Newell, K. W. An epidemiologist's view of leprosy. Bull. WHO 34 (1966) 827-857.

While leprosy has been studied exhaustively by leprologists, it is only recently that persons in other disciplines have given this disease the attention it deserves. Various methods for its prevention and control are now being advocated and tested in the field, and it appears reasonable for an epidemiologist to review the bases of current theories and to examine the evidence for existing hypotheses. This has been done by a review of some of the more recent literature. The conclusion is reached that the anergic, or factor N, hypothesis that has been evolved to relate the lepromin test to the findings in clinical leprosy appears to be the most promising, and that, if this hypothesis can be substantiated, it is unlikely that BCG vaccination can be a very useful tool for prevention. Many possibilities exist for epidemiologic and laboratory research into this disease, which in many ways appear to be unique. [EDITOR'S Note: This article is discussed at length in an editorial in The Lancet (21 January 1967, p. 145.] Authors' Summary

Christian, E. B., Shamrao, A., Christian, L. R., Christian, J. J. and Christian, I. V. A study of the transmission of leprosy in families. Leprosy in India 38 (1966) 9-17.

Study of transmission of leprosy in families indicates that the most favorable condition for transmission exists in families where there is close, intimate and prolonged contact with a lepromatous case (a parent or a close relation). Casual contact may also infrequently result in infection. Thus lepromatous cases play the most important role in the spread of infection. The infection, when it occurs, is perhaps due to the index case becoming temporarily "open" during an acute exacerbation or reaction. However, the possibility cannot be excluded, that in some instances the infection in families with nonlepromatous cases only had been caused by contact with "open" cases outside the family. It can be concluded that the nonlepromatous cases play a very limited role in the transmission of the disease, much less than the lepromatous cases. In our study the infection has generally taken place in childhood. It is believed that, in endemic countries childhood appears to be the most susceptible age. This, however, does not mean that adults are altogether immune. If an adult is exposed to infection for the first time, he is equally liable to be infected and to get the disease. Children in close or casual contact with nonlepromatous cases are sometimes but very infrequently infected. The study indicates that where there was no leprosy in the families in the first and second generations (grandparents and parents), some of the children in the third and fourth generations (grandchildren and great grandchildren) developed leprosy. However, in the third generation the incidence of the lepromatous cases was much higher (14%) than that of the nonlepromatous (9%). In the fourth generation the situation was reversed, the incidence of lepromatous cases being 4% and that of nonlepromatous cases 16%. On careful investigations and follow-up of the above cases in the families with no cases in the first and second generations, it was found that the children who had developed the disease in the third generations had been in close, but occasional and repeated contact with lepromatous cases in their maternal relations. Although the lepromatous cases are the most potential sources of infection, only about 30% of the children ex-

posed to them in the family get the disease, and the remaining 70% escape. This confirms the normally held views that leprosy is only feebly infective, and that infection with M. leprae is only one of the factors in the transmission of the disease. The other factor or factors are concerned with the susceptibility or immunity of the individuals exposed to infection. The nature of this susceptibility or immunity is not clear and is a subject for study. However, the findings in the present study regarding the difference in the incidence and especially in the lepromatous rate in the third and fourth generation of children, in whose families there were no leprosy cases in the previous two generations, would tend to indicate that inheritance of acquired immunity perhaps plays some role in this connection. The study confirms the generally held view about the infrequency of conjugal infection. In the present study conjugal infection was extremely infrequent, while the incidence of the disease in the children of couples, one of whom was suffering from leprosy, was of the same order as in the investigation as a whole.—[From authors' summary]

Leprosy in Britain. (Editorial) Brit. Med. J. 1 (1966) 560-561.

In a leading article the Brit. Med. J. records the arrangements made by the Ministry of Health making leprosy notifiable to the local medical officers of health but retaining the confidential aspects. In addition to the appointment of an adviser in leprosy, a panel has been formed of 16 practitioners designated to assist medical officers of health and doctors in clinical charge of patients with problems of diagnosis, potential infectivity and management of the cases and their immediate contacts. After noting the history of leprosy in Britain the article reviews the problem today. Accurate figures for England and Wales have been available only since 1951. Up to the end of 1964 the number of patients who had been registered was 578, and 340 still remained on the register. Apparently no indigenous cases have been reported since 1951, and the only three recorded cases of this century were discovered in children who had never been abroad but

had contracted the disease from a close relative with leprosy. Leprosy in Britain is, therefore, not numerically important, but represents one of the many exotic diseases which the general practitioner must be aware of when confronted with immigrant patients from tropical countries where leprosy is an endemic disease. Progress on the medical side will be of little avail unless the fear and social stigma of leprosy are broken down. General educational programs, together with the cooperation of the press, will be required to overcome these prejudices.—N. D. Fraser

Floch, H. and Duchassin, M. La situation de l'endémie lépreuse en Guyane Française en 1965. [Leprosy in French Guiana in 1965.] Bull. Soc. Path. exot. 58 (1965) 401-409.

The senior author refers to his intimate knowledge of the leprosy situation in French Guiana since 1938. With Duchassin, he now reviews the present state of leprosy control in the territory. Since mid-1964, a town leprosy clinic has catered for certain categories of patients: those suffering from recently diagnosed lepromatous leprosy, or from the more serious kinds of borderline leprosy; those with bacillarypositive tuberculoid lesions passing through reactional episodes; leprosy patients suffering from acute intercurrent illnesses; and those requiring surgical treatment for residual paralysis or neuropathic ulceration. The standard treatment is dapsone, either by mouth or by intramuscular injection. A long-acting sulfonamide has proved to be slower in action than dapsone and shows no superiority over dapsone in the incidence of acute exacerbation. The antileprosy campaign has halved the prevalence of leprosy (2.3% in a population of 36,670) since 1949. The authors are satisfied with the system of survey and diagnosis of leprosy among school children, in whom indeterminate and tuberculoid leprosy is diagnosed at an early stage, and in whom cases of serious lepromatous disease are not seen. It would appear that adequate treatment of patients in the early stages of leprosy will prevent the development of bacilliferous forms. They give a warning, however, against premature optimism,

especially in view of the fact that adults with unsuspected and untreated advanced lepromatous leprosy are now being discovered. They plead for a restoration of legal powers (such as insistence on a certificate of noninfectivity for food handlers and others brought into contact with the public) both at the national and at the communal levels, and express some regret that the excellent methods of survey and control which were a feature of the French colonial system, have been abandoned. [Abstract by S. G. Browne, *Trop. Dis. Bull.* 63 (1966) 1094-1095.]

Ghosh, B. N., Veeraraghavan, M. and Zacharia, Miss. A note on the results of investigation on clinical attendance rate of leprosy cases in an urban community. Leprosy in India 38 (1966) 103-106.

A population of 5,113 in an urban health center area was screened for leprosy cases, and their post-detection clinic attendance rates were investigated. A total of 64 cases were detected, giving a prevalence rate of 1.25 per cent. Forty-four patients (70% of the detected cases) started taking treatment at the beginning; another 12 (20%) could be induced to start taking treatment. The largest number of cases (39 or 61%) preferred joint clinics, and the feasibility of their treatment from the primary health center is discussed. Fifty-three patients (82%) of the cases knew that the disease is curable. Understanding by the patients as regard causation, spread, value of isolation, susceptible age and the effect of concealment of the disease was found to be very poor.—[From authors' summary]

Chakravarty, A. K. Climate and reaction in leprosy. Leprosy in India 38 (1966) 99-102.

Many workers believe that climate has some effect on lepra reaction. The present study confirms this view and shows a relationship of climate with the frequency of reactions. In this study one great advantage is that people from different states of India with different climates were observed in the climate of Delhi. On the other hand, a drawback has been that in the group studied there is no indigenous case from Delhi. However, it can be said with some

certainty that extremes of climate precipitate reaction.—Author's Summary

Nutting, W. B., Kirchheimer, W. F. and Pfaltzgraff, R. E. Demodicidiasis and leprosy. Review and proposal. Leprosy Rev. 37 (1966) 209-216.

The authors note that despite a wealth of speculation there is no proof that any arthropod serves as a transmission agent for human leprosy (Dungal, 1961). As a suspect vector the acarine Demodex folliculorum is in some respects unique, since it (1) is apparently ubiquitous with an incidence of 100% (Fuss, 1933), (2) is found in intimate association with M. leprae in the skin (Borrel, 1908), and (3) is probably passed from mother to young during the nursing process. Furthermore, Spickett (1961) reported the presence of acid-fast bacteria in the gut of D. folliculorum and noted that the gut contents of the mite can be regurgitated. These observations point up the need for continuing reevaluation and for further studies on the possible causal relationship between demodicidiasis and leprosy. The literature on Demodex folliculorum pertinent to the problem of the possible transmission of M. leprae and the initiation of leprosy is reviewed. Information on other demodicids (especially D. canis, D. caprae and D. aurati) is also presented with an eye to its use in resolving the suspect relationship of D. folliculorum and M. leprae. A number of suggestions are made which would materially aid an attempt to settle the problem of whether or not there is any casual relationship between D. folliculorum and leprosy.—N. D. Fraser

Maeda, M., Hazama, S., Kobayashi, S., Ishiwara, S., Arakawa, I., Minato, J. and Murohashi, T. Epidemiological meaning of reaction due to Dharmendra antigen on survey of leprosy. La Lepro 35 (1966) 65-70. (In Japanese, English summary)

It has been reported previously that guinea pigs sensitized with *M. leprae* were converted to positive reactivity to Dharmendra antigen and also to tuberculin, and that guinea pigs sensitized with human type tubercle bacilli or BCG were similarly converted in reactivity. On the other hand,

investigation of the results of reaction due to Dharmendra antigen in the general population, showed that positive conversion of reaction to Dharmendra antigen was primarily effected by BCG vaccination and secondarily by natural tuberculous infection. More recent investigation of the use of Dharmendra antigen in detecting leprosy infection has shown (1) that the ratio of the Dharmendra-positive rate to the tuberculin-positive rate, and the rate of positive reaction to Dharmendra antigen among tuberculin negative subjects, were higher in persons in leprosy households than in other populations; and (2) that the positive rate of reaction due to Dharmendra antigen among tuberculin-negative reactors was also significantly higher. Thus it appears that positive conversion of reaction due to Dharmendra antigen can be brought about by leprosy infection. Reaction to Dharmendra antigen may be useful for the detection of immunity against leprosy and for the discovery of leprosy epidemiologically.—[From authors' summary]

Stein, A. A. Leprosy penetration and first attempts at its registration in the Ukraine before the Great October Socialist Revolution. Collection of articles on "Pathogenesis and therapy of Dermatosis." IVth Scientific Conference, Lvov, 1966, pp. 3-5.

As far back as the ninth century leprosy was disseminated throughout the Ukraine, as can be noted in the Slav translation of the Bible, where the Slav word was taken in place of the word "leper" (prokaza). The infection might have been brought from ancient Greece in both war time and commerce. It should be noted that the distribution of leprosy had been promoted by the Greek colonies, such as Panticopea, Khersones, Olvia and Tyre. Herodotus stated that the Egyptian troops headed by the pharoahs Rameses and Sesotris had traveled as far as the Scythian land. The first documentary data concerning leprosy went back to 1883, when H. Munkh found six leprosy patients in the Kherson district. It is clear that the registration of patients was not total. From 1884 to 1914 1,545 leprosy patients were registered in the Ukraine.—N. Torsuev

Prevention of Leprosy. (Editorial) Lancet 1 (1966) 354-355.

This editorial reviews the work of Kinnear Brown and Stone (British Med. J. 1 (1966) 7-14) on BCG vaccination of children (relatives or contacts of known leprosy patients) in Uganda, and of Dharmendra and his coworkers (Dharmendra, Mohamed Ali, Noordeen and Ramanujam. Leprosy in India 38 (1965) 447-467) on the use of dapsone as a prophylactic. After commending the conception, careful planning and execution of the investigations, it calls attention to some of the questions that remain unanswered, and then turns to clinical application and medical economics. "Granted that leprosy is a major crippling disease of great economic importance to the developing countries of the world, is it anywhere financially practicable to provide a service in which one auxiliary supervises a handful of contacts twice weekly for several years? Four out of every five leprosy patients are not at present being treated at all, medical services being too 'thin on the ground', or too preoccupied with killingdiseases to cope with the problem. If BCG vaccination should prove as effective a prophylactic as dapsone, and if BCG can be brought to the millions of contacts now needing it, then BCG would be preferable in many ways. Thus, we are challenged by three possible measures, each of which might eventually suffice to control leprosy: adequate treatment of patients with multibacillary disease; and either BCG vaccination or prophylactic administration of dapsone to contacts. The tools may exist; will the job be finished?"-N. D. Fraser

Møller-Christensen, V. and Hughes, D. R. An early case of leprosy from Nubia. Man 1 (1966) 242-243.

In the course of an examination of Egyptian osteologic material preserved at the Duckworth Laboratory in Cambridge (representing some 1,194 individuals), the writers studied a previously described cranium from Nubia. They agreed with the published description of inflammatory changes in the nasal and palatal regions, and noted a number of additional pathologic changes, viz.: (1) total resorption in vivo of the anterior nasal spine; (2) sec-

ond degree resorption of the anterior portion of maxillary alveolar bone extending laterally so as to expose the roots of the upper incisors, and possibly those of the right upper canine, to such an extent as to make the loosening of one or more of these teeth probable. The identification of the point known as prosthion or alveolare could no longer be made with any reliability. The complex pathologic changes, viz., chronic infection in the hard palate, atrophy of the anterior nasal spine, loosening of the median incisors, and early and medially-situated atrophy of the maxillary aveolar process, are strongly indicative of facies leprosa. The combination has in fact hitherto been found only in cases of lepromatous leprosy. This cranium from Nubia, therefore, may, with no small justification. be considered that of a person with leprosy. The rediscovery of this Nubian cranium, and the possibility of making a diagnosis of leprosy, are of great interest in the history of the disease. There are now known to be two cases of leprosy from the same period of Egyptian history and from the same part of old Egypt.—E. R. Long

Anonymous. Leprosy booklet for overseas visitors. Trop. Med. & Hyg. News 15 (1966) 15 (No. 3).

A pocket-sized booklet designed to acquaint travelers to foreign countries with the basic facts about leprosy has been produced by American Leprosy Missions. Prepared by ALM's president, Oliver W. Hasselblad, M.D., the booklet, entitled Leprosy, A Present Day Understanding, presents a comprehensive survey of the extent of the disease, its cause, signs and symptoms, and its treatment and prevention. It also includes lists of voluntary organizations concerned with leprosy, journals, periodicals and books. The booklet was written primarily to meet the needs of lay overseas personnel of mission boards and voluntary agencies, but it also offers useful material for furloughing missionaries in deputation work and for mission study groups. Free copies of the booklet are available at American Leprosy Missions national headquarters, 297 Park Avenue South, New York, N. Y. 10010.—J. A. ROBERTSEN