CURRENT LITERATURE

It is intended that the current literature of leprosy shall be dealt with in this department. It is a function of the Contributing Editors to provide abstracts of all articles published in their territories, but when necessary such material from other sources is used when procurable.

BANTUG, J. P. The introduction of leprosy into the Philippines. Mo. Bull. Bur. Health **22** (1946) 42.

While the author believes that leprosy existed in the Philippines long before the advent of the Spanish, the first recognizable record of the disease is the description by a missionary named Collins, written in 1603, of the condition of one of his rowers during a visit to Leyte. [Leyte is not so located that it would be infected readily or promptly if leprosy was brought to the Philippines by traders from China.] It was 28 years later, in 1631, during the Christian persecution in Japan, that the emperor sent 150 Japanese Christians with the disease to "test the mettle of the Catholic missionaries in the Philippines." They are said to have been placed in a hospital conducted by the friars of the Franciscan order which had been started as early as 1577 and from which eventually evolved the actual San Lazaro Hospital. —H. W. W.

BURKHOLDER, S. L. & HART, I. History of the San Lazaro Hospital; a relic of Spanish days in the Philippines. Mo. Bull. Bur. Health **22** (1946) 63-80.

As related by the authors the background scene of the San Lazaro Hospital in Manila "is somewhat mystic." It begins—presumably in the 16th century—with the Hacienda Mayhaligue, an area at some distance across the Pasig River from the (walled) city, owned by a wealthy and devout man with leprosy who willed that the rentals should be used exclusively for the benefit of others similarly afflicted. The history of hospitalization in the Philippines begins according to some writers with the arrival in 1577 of one Fray Juan Clemente, a lay brother of the Franciscan Order, who began to treat people with sores and ulcers and who was finally enabled to construct a building for the care of his patients. That place, made of bamboo and nipa, was burned with the rest of the city in 1583, and in the following years it underwent many vicissitudes and several changes of location, the first of which resulted from another disastrous fire in 1603. After that, in other hands, it became the "Hospital de Santa Misericordia" (later the "Hospital de San Juan de Dios"), and in quite another area—outside the Walled City—the Franciscans built a "Hospital de San Lazaro." On two occasions military necessities led to its demolishment, first in 1662 in preparation for an attack by a Chinese pirate, and again in 1783 when the British were expected to repeat their invasion of 1762; and in this period it was moved from place to place. Finally, in 1784, a royal order specified that: "The House and Hacienda of Mayhaligue shall at once be converted into a Leper Hospital, and the old one destroyed as proposed, and as the sanitary requirements of the neighborhood and the defence of the post require;" and then was initiated the institution which still exists. Though it was supposed to have the income of the hacienda

and certain other revenues there were continual difficulties, and in 1859 it was on the verge of closing. Then, in 1863, the deteriorated buildings were almost destroyed by an earthquake. One Rev. Felix Huerta was given the task of rehabilitating the place, and before his death in 1894 he had built it up physically and increased its capacity from 130 to 200. The patients were almost entirely of the poor and destitute class who came without official compulsion, for there was "no comprehensive official policy for the conservation of the public health" and it was considered then, as 260 years before, "the duty of the Church to care for these unfortunates." When the American forces occupied Manila in 1898, the priest then in charge and all others deserted the place save one *practicante* who remained to care for those inmates who could not go; and it was some time before reorganization was effected. During that period outbreaks of cholera and bubonic plague necessitated the establishment of emergency facilities on the grounds of this hospital, and the use of the place as a general infectious disease hospital became established and was continued thereafter. [Today, with the removal of the last of the leprosy patients to the Tala leprosarium, its conversion is complete.] —H. W. W.

[CEYLON] Leprosy campaign in Ceylon. Annual Report for 1947 of the Medical Superintendent, Hendala Leprosy Hospital, Medical Superintendent, Mantivu Leprosy Hospital, and Medical Officer, Leprosy Campaign.

This report deals with the work done in the two leprosy hospitals and in the field, where there are 18 out-door leprosy clinics in the endemic areas (only 15 functioning during the year) and a field organization controlling and observing the noninfectious cases and the contacts. At the Hendala hospital, the oldest one—dating from the Dutch period—on a 26-acre location, there are accommodations for 608 patients. In the two, there were 982 patients at the end of 1946, and 1,003 at the end of 1947; there had been 87 admissions, 13 discharges, and 51 deaths. Only 7 in the hospitals were under 14 years old; 80% were males; 72% were Sinhalese; 466 had had come from the Western Province and 199 from the Southern Province; 687 were lepromatous, 316 neural. Besides these 1,003, there were 1,723 cases on parole and 237 discharged, making a total of 2,963. During the year 11,906 school children had been examined without detecting any case among them. Elsewhere, however, 163 new cases were discovered, of which 35% were infectious; the total number of patients for the island had increased by 110, and 34 cases were awaiting segregation, being "more or less in home segregation."—[From summary in *Lep. India* **20** (1948) 164.]

B.E.L.R.A., INDIA. Report of activities directly under the Indian Council of B.E.L.R.A., 1947. Part II. Lep. India **20** (1948) 190-202.

The research work carried on during 1947 and the results obtained were: (1) An investigation of the therapeutic value of the sulfone drugs, which caused definite improvement in most cases except with respect to nerve pains and other neural symptoms. (2) Attempts to cultivate the leprosy bacillus by Row's method of symbiosis with leishmania, which were not successful. (3) A study of eye lesions, which were found to be much less frequent in India than in other countries. They are of two different kinds, corresponding to the two main types of the disease. In the neural type they are secondary to nerve involvement, whereas in the lepromatous

type there is actual infiltration of the tissues of the anterior segment. An interesting condition not usually reported is the presence of lagophthalmos due to dense infiltration of the eyelids. (4) Correlation of the histology, immunology, and course of the disease in two groups of selected cases, those of "doubtful" classification and those of tuberculoid reaction. In the former the histology was always "doubtful" even after repeated examinations, and in the latter it was tuberculoid although there were atypical features such as the presence of highly vacuolated cells and scanty giant cells, and slightly infiltrated nerves within the granuloma. (5) An investigation of the lepromin test inside and outside the macules of leprosy, with the finding that in lepromatous cases they are similar—and usually negative—in both locations, whereas in most neural cases reaction is stronger inside the macule than outside. (6) Examination of the gut contents of roaches from endemic and nonendemic areas of leprosy, and feeding roaches with different acid-fast bacilli in their feces, did not support the hypothesis of Moiser that cockroaches play an important role in the transmission of leprosy. —DHARMENDRA.

[Reports of much of the work here noted were presented at the Havana Congress, and abstracts of them appeared in the Congress issue of THE JOURNAL. The papers themselves have now appeared in the *Memoria*.—EDITOR.]

B.E.L.R.A., INDIA. Report of the Leprosy Investigation Center, Bankura, for the year 1947. Lep. India **20** (1948) 203-205.

This center, established in 1936 to study the epidemiological features of leprosy in a localized rural area of West Bengal, comprises 42 villages with a total population of 10,000. The work includes, (*a*) recording of new cases arising in or migrated into the area, and removal from the list of those that have died or left the area; (*b*) periodical reexamination of all cases; (*c*) periodical reexamination of all contacts or suspects; (*d*) running a treatment clinic. The total number of cases at the end of the year was 507, of which 435 were neural and 72 lepromatous. New cases detected numbered 24, most of them males, all but one of them of neural type, 5 of them suspects previously under observation. As regards contact, 13 had had obvious contact with lepromatous cases but in all but one of these the disease was neural; the contact cases of 5 were neural; in the other 7 no history of contact was obtained. Of 73 suspects, 5 developed the neural form of the disease, in 30 the lesions remained stationary, in 2 they advanced, while in 16 they faded or disappeared. Reexamination of the 111 arrested cases in whom the lesions had remained dormant for five years or more revealed 3 in which they had become aggravated. Three neural cases changed to lepromatous during the year. The total number of visits to the villages during the year was 187, and the number of cases examined and re-examined was 857. —DHARMENDRA.

LENGAUER, L. Leprosy in the Benin and Warri areas in Nigeria. Lep. Rev. **19** (1948) 14-20.

The incidence of lepromatous leprosy is much higher in these sparsely-populated, low-lying areas in the delta of the Niger than in Eastern Nigeria. Tuberculoid leprosy is very common, and is like that seen elsewhere. Most of the lepromatous cases started with a single depigmented macule, multiple macules appearing soon after but nodules only much

later. In a number of cases macules and tuberculoid and nodular infiltrations were observed at the same time. ["Borderline" tuberculoid cases?] Special features noted as common in these areas are nodules around the mouth and nose which ulcerate and later produce fibrous contractions. Laryngitis is very common, and also ulcerating nodules of the male genitalia with stenosis of the urinary meatus. Heart and kidney complication are frequent. On the other hand blindness and alopecia are uncommon. The writer states that the change of type from tuberculoid to nodular is a very common and bewildering phenomenon. —G. O. TEICHMANN.

RYRIE, G. A. The macular syndrome in Nigeria. Lep. Rev. **19** (1948) 35-39.

The writer, during a tour of Southern Nigeria, observed a type of macular leprosy which was a marked feature of the disease in that area and by far its most common manifestation. The macules, which occur early in the disease, are small discolored patches, not elevated, single or multiple, and often of a cafe-au-lait color with a faint erythema usually underlying the depigmentation. Onset may be insidious or abrupt. These macules are unlike those of juvenile leprosy (Muir) or the prelepromatous macule (Cochrane); they are not like those seen in tuberculoid or lepromatous leprosy, nor are they the "uncharacteristic" lesions of the South American classification. The essential features of this Nigerian macular syndrome are: (*a*) the absence of any sensory deficiency; (*b*) the essentially macular character, which dominates the whole course; (*c*) the marked depigmentation; (*d*) the underlying erythema, faint at first but variable and perhaps most marked in the hazy-edged phase; (*e*) a phenomenon of macular reaction with the abrupt appearance ("almost overnight") of fresh crops but without any marked signs of inflammatory response; (*f*) the frequent thickening of the ulnar and peroneal nerves and the absence of thickened nerves proximal to the skin lesions; (*g*) the absence of bacilli except perhaps during a temporary late phase, or when the case becomes lepromatous, which is exceptional. On the other hand the cases may become tuberculoid, with thermal and later tactile anesthesia. The prognosis seems to be good, especially as regards response to treatment. It is suggested that this may be a third type of leprosy.

—G. O. TEICHMANN.

ROMERO, A. [Leprosy in Costa Rica.] Bol. Of. San. Panamericana **27** (1948) 61 (personal communication).

Data on the leprosy hospital of Costa Rica, the Sanatorio Las Mercedes, show an increase in the number of patients from 75 in 1937 to 120 in 1946, with admissions of less than 20 per year for the early part of that period increasing to 32 in 1946. There is also, in San José, a dermatological dispensary where contacts are examined—114 in 1946 and 116 in the first half of 1947, with 15 and 13 positive cases found. [This would total 28, but it is also stated that the number of contacts examined between July 1945 and June 1947 was 358, with 11 positives found.] The number of existing cases is 194, or 0.25 p.m. for a population of 771,000. —H. W. W.

[COSTA RICA] Special leprosy edition of the Revista Médica de Costa Rica, **8** (1948) 213-308 (Nos. 173-176, Sept.-Dec.); (with summaries in Spanish, English and French).

Besides an introduction and an appendix this publication contains 9 articles, of which 2 are classified as clinical, 5 as therapeutical, and 2 as epidemiological. Four of them were sent to the Havana Congress [see THE JOURNAL **17** (1949) pp. 27 for one of them]; and those of which abstracts did not appear in the Havana issue are dealt with in this one. The introduction, among other things, relates the principal features of the history of leprosy in the country: First case discovered, 1738; a place for patients built on the Rio Virilla, 1826; moved to "La Sabana," near San Jose, 1890; moved to the present building, "Las Mercedes," 1909; the Sisters of Charity of Santa Ana took charge, 1938; the Rotary Club took up the antileprosy campaign and founded a Patronato del Asilo de las Las Mercedes, 1943; Dr. Arturo Mom, Argentinian leprologist, brought in to organize the scientific side of the campaign, 1945; on Dr. Mom's initiative a "Dispensario Dermatologico" established at the Hospital San Juan de Dios and a special section in the central health office, 1946; the first 9 cases paroled, May 1948; name of the leprosarium changed to "Sanatorio Nacional de las Mercedes" (present director, Dr. Abelardo A. Brenes Ibarra), and an Asociación Femenina Pro Bienestar Social de Enfermos de Lepra founded, August 1948; the Departmento de Lucha Contra la Lepra (Dr. Arturo Romero, director), created in the Ministry of Public Health, September 1948. —H. W. W.

CARRANZA AMAYA, A. Lepra en El Salvador; zonas endémicas y su problema social. [Leprosy in El Salvador; the endemic areas and the social problem.] Thesis. Biblioteca Universitaria. Universidad Autónoma de El Salvador, 1947, 99 pp., with photographs and graphs.

This thesis, which received "*mención honorífica*," is a study of leprosy which, in less than a hundred pages, discusses briefly all of the important features of leprology. The South American classification is used, and in the section on therapy the sulfone derivatives are discussed. The epidemiology and the social problem are specifically adapted to the sister republic. —[From abstract in *Rev. argentina Dermatosif.* **31** (1947) 657.]

[EDITORIAL] Leprosy and leprosy research institute. J. Indian Med. Assoc. **18** (1949) 208.

Figures of more than a million cases in India, and 20,000 in West Bengal alone, are cited, and it is said that a general survey has not as yet been undertaken to ferret out the early or nerve type of cases which respond fairly well to early treatment. The need of public health education in the matter is stressed ("there is, at present, so much horror and hatred of leprosy that people try to hide any kind of suspicious skin lesions..."), and also the responsibility of the state in the whole matter of the control of the disease, in coordination with voluntary bodies. The plan for a leprosy research institute dates back to 1941, to a report on leprosy and its control in India by an official committee which recommended that the location should be central, in or near a rural area with satisfactory communications and near a large leprosy institution where adequate clinical material would be available. In the entire eastern belt of high endemicity, from Madras in the south up to Assam in the northeast, this editorial goes on, Calcutta with its Leprosy Research Department of the School of Tropical Medicine [nothing being said of the required

"large leprosy institution"] possesses many advantages for the proposed new institute.—[From a copy of the original, supplied by J. A. Doull.]

JAGADISAN, T. N. "Balance" in leprosy work. The World Dom. & The World To-day, 1947, July-Aug.; Lep. India **20** (1948) 96-99.

The author dwells on the importance of a balance between the "relief" view of missionary endeavors and the "control" view of the government. The people should be educated and their social and economic condition improved, so that home isolation of infective patients may be possible. A liberal attitude should be adopted towards open cases. People should come to recognize the distinction between those whose household circumstances are "dangerous" to others and those whose household conditions are unfavorable to the spread of the disease (e.g., cases who live in a family of adults). —DHARMENDRA.

TEICHMANN, G. O. What of the children? Lep. India **20** (1948) 103-108.

The author traces the history of the children separated from parents with leprosy and brought up in the Healthy Home at the Purulia hospital, and that of those who had already developed leprosy and were treated in the Purulia leprosarium between 1927 and 1942. Although two-thirds of the children in the Healthy Home did at some time show signs of leprosy, only two developed the lepromatous type and the majority are now healthy and many are married. More than one-half of those in the leprosarium who had lepromatous leprosy have died, and of those who remain the majority still have the disease. It is suggested that children removed from infective surroundings may develop an immunity if brought up in healthy surroundings. The need is stressed not only of isolating persons suffering from infective leprosy, but also of removing child contacts to homes where no further infection can take place. —DHARMENDRA.

OTEO DE HOOGH, E. Social work in the campaign against leprosy in Mexico. Med. Woman's J. **5** (1948) 15-25.

In the fight against leprosy the patient should be considered individually, psychologically, socially and economically, and should be treated as a member of human society. Mexican leprologists do not apply any laws of reclusion or complete isolation. They aim to hospitalize infectious patients by means of persuasion, and where possible he is treated or hospitalized in his native state. If freedom is allowed an infectious case the patient must promise to occupy a room separate from others, to have no contacts with children, and to avoid intimate contact with healthy people. The author feels that there should be an "integral diagnosis" of the case, comprising medical classification as to type, sanitary classification as to infectiousness, and social classification as to intellect, adaptability, and economical status. For the campaign it is necessary to have cooperation of all social resources. Everything is being done to rehabilitate the patient therapeutically, economically and socially. This article should be read by those interested in the campaign against leprosy. —F. A. JOHANSEN.

[EDITORIAL] La lepra como problema de gobierno. [Leprosy as a government problem.] Arch. Salud pub. [Buenos Aires] **5** (1949) 243-249.

The number of patients enumerated in a census made by the health authorities in Argentina was 5,714, but the total number is calculated at 12,000, or 0.42 per thousand of the population. The present number of

occupied beds in the leprosaria is 1,470, and the government proposes to increase that number to 4,480 within five years. The antileprosy campaign can be summarized as comprising five points: (1) early isolation of open, contagious forms; (2) outpatient treatment and surveillance of the closed, noncontagious forms; (3) surveillance of contacts; (4) education of the general public in control measures; and (5) scientific investigation of the disease. —G. BASOMBRIO.

CONTRERAS DUEÑAS, F. El tatuaje bubi. [The Bubi tattoo.] Actas Dermosif. **38** (1947) 735.

The purpose of this nontechnical article is to record photographs of the first Spanish preventorium, the so-called orphanage of Ncué, in Guinea, for children who are "orphans" of living parents, under the care of Oblate nuns who themselves are of the colored race. Mention is also made of an asylum for leprosy patients. [No actual data on either place appears in the abstract.]—[From abstract in *Fontilles* **2** (1948) 80.]

ROMERO, A. & BRENES IBARRA, A. A. Edad sexo y lepra. [Age, sex and leprosy.] Rev. méd. Costa Rica **8** (1948) 294-298 (summary in Spanish, English and French).

As usual, leprosy in Costa Rica is more frequent in males (60%) than in females (40%). Judging by the age of onset of the disease, and from the 12 cases observed in patients under 15 years of age, leprosy attacks both sexes with almost equal frequency before that age, females predominating slightly. Infectious cases (bacteriologically positive undifferentiated and lepromatous) occur somewhat more frequently in women than in men. The frequency of ovarian disturbances in leprous women suggests a close relationship between ovarian function and the evolution of the disease. Data on onset show that leprosy develops with special frequency during puberty and the menopause. Amenorrhea and oligomenorrhoea are frequent. Pregnancy, the puerperium and the menopause are often precipitating phenomena in the initiation of leprosy. These facts suggest a folliculin deficiency as a condition in the development of the disease, and the use of folliculin as a coadjuvant treatment.—[From the authors' summary.]

BRENES IBARRA, A. A. & ROMERO, A. Arboles genealógicos de enfermos de lepra. [Geneological trees of leprosy patients.] Rev. méd. Costa Rica **8** (1948) 299-307 (summary in Spanish, English and French).

There are 172 patients among the 733 persons included in these 28 families (23%). Consideration is given to the proportions of infected children in relation to the sex of the parent responsible for the contagion, both in the cases in which only one parent is affected and in those in which both are infected. [No statement of findings is made in the summary.] Probable infection of one spouse by the other was found in 15% of the 47 couples studied. Conjugal infection produces, in the main, undifferentiated and tuberculoid forms, lepromatous forms being in the minority. The latter have an excellent prognosis because these patients have a high index of resistance to the Hansen bacillus.—[From the authors' summary.]

FITE, G. L. Leprosy, its detection and management. Postgrad. Med. **1** (1947) 292-302.

This is an excellent article on diagnostic methods and management in leprosy. It contains a number of pencil drawings showing the common sites of early lesions, areas of the body unaffected, and peripheral nerve involvement, and photographs illustrating lesions found in early and advanced cases. The complications and sulfone therapy are discussed. The author feels that segregation as a preventive measure is unlikely to succeed unless it is nearly total. —F. A. JOHANSEN.

VEGA NUÑEZ, J. Los casos indeterminados de lepra. Revisión general. [The indeterminate cases of leprosy; general review.] Fontilles **2** (1948) 115-160.

After accepting the Panamerican classification, and also with reference to recommendations of the Havana Congress, a quite complete study is made of the indeterminate form, its frequency, pathogenesis, symptomatology, its relation to other clinical forms, and the matter of transformations. In the study of the incharacteristic cases at Fontilles the bacteriological, immunological, serological annd histopathological features were examined repeatedly; and, lastly, the evolution and prognosis of the cases and their treatment are discussed. —F. CONTRERAS DUEÑAS.

BRENES IBARRA, A. A. Estudio de algunas características de la reacción lepromatosa en nuestro medio. [Study of some of the characteristics of the lepromatous reaction in Costa Rica.] Rev. méd. Costa Rica **8** (1948) 228-247 (summary in Spanish, English and French).

The somewhat lengthy summary of this article does little more than enumerate the phases of the subject dealt with. Lepra reaction in its various forms is defined at some length. Special attention is given to the "typical erythema multiforme" condition, with respect to its clinical features (the more favorable forms of the disease being those without history of the occurrence of that condition), its immunological features (difficulties in the interpretation of the lepromin reaction being pointed out), and its laboratory features (bacteriological findings, the hemogram, and the erythrocyte sedimentation test). The etiology of lepra reaction is considered with respect to climate, hormones, intercurrent diseases and drugs, with special reference to the sulfones. The author's personal conception of the evolutive cycle of the lepromatous form is set forth, with reference to the following aspects (in the original wording): (1) characteristics of the erysipelas in the course of the evolution of diffuse lepromatous form; (2) influence of penicillin on the erythema multiforme; (3) relation between necrotic erythema, recurrent erysipelas and erythema multiforme; leprous background and secondary cocci infections; (4) different reaction forms of the diffuse lepromatous form. (The enumeration of other features of the article, being also without conclusions, is no more instructive.) —H. W. W.

DA VEIGA, S. As lesões osteo-articulares da lepra através das imagens radiográficas. [Bone and joint lesions in leprosy, with radiographic illustrations.] An. Inst. Med. Trop. (Lisbon) **4** (1947) 149-160 (summary in English).

The author, in the Central Leprosarium of Goa, took 400 radiograms of the hands and feet of 100 leprosy patients aged between 12 and 67 years, the duration of the disease ranging up to 28 years. The pathological process was chiefly rarefying osteitis and osteoporosis, with cyst-like formation,

and more extensive destruction resulting in multilation. Some of these changes, in particular the osteoporotic ones, would seem to be due primarily to vascular disturbance, whereas those involving the joints as well as the bones result from nerve involvement. Hence the osteoarticular lesions were most common in those with the neural form of the disease, and they were more marked in the feet than in the hands. The article is illustrated with 24 excellent and instructive reproductions of radiograms.—[From abstract in *Trop. Dis. Bull.* **45** (1948) 1091.]

KIRWAN, E. W. O. The eye in leprosy. Trans. Roy. Soc. Trop. Med. & Hyg. **41** (1948) 583-590.

From a large experience in Madras the author discusses the eye affections of leprosy in a paper which those interested in ophthalmology should read in the original. Although very common, their frequency varies in different parts of the world, being low in India where there is a large proportion of mild cases, high in Europe and Japan, and very high in Panama and Cuba. In lepromatous cases these complications are due to direct involvement by lepromas and are serious, whereas in other forms they are secondary to nerve paralysis. Lepromas occur in the upper lid but never in the lower. Madarosis is common, and its absence in advanced cases is a good sign. Lagophthalmos is common in nonlepromatous cases and is often pathognomonic. Leprous nodules never occur in the conjunctiva, but yellowish gelatinous nodules are common in the episcleral tissue at the sclero-corneal junction and tend to spread around the limbus and infiltrate the cornea. The cornea is the most vulnerable of the eye tissues, and all varieties of keratitis are seen. Leproma of the cornea is never primary, but spreads from the limbus. Involvement of the iris and ciliary body is next in frequency. Miliary, nodular and diffuse plastic forms are seen, and atrophy of the iris may be present in varying degrees. Lesions of the posterior segment are uncommon and are due to direct spread from the front. Bacilli have never been found in the choroid. For treatment of lepromatous conditions of the eye he recommends irradiation by Grenz rays or application of carbon dioxide snow or diathermy. Local application of penicillin is advised for conjunctivitis. Subconjunctival medication he has found of little use. The pupils must be kept dilated with atropin if the iris is involved. Tarsorraphy is recommended in lagophthalmos. The slit lamp with the corneal microscope and the electric ophthalmoscope are essential for diagnosis. —G. O. TEICHMANN.

CONTRERAS DUEÑAS, F. & RODRIGUEZ PASCUAL, C. Hemoglobinuria paroxistica coincidiendo con leprorreacción. [Paroxysmal hemoglobinuria accompanying lepra reaction.] Fontilles **1** (1946) 319-324.

This is a report of two female patients whose lepra reactions were usually accompanied by attacks of paroxysmal hemoglobinuria, in one of them recurring frequently. —AUTHORS' ABSTRACT.

MARGAROT, J., RIMBAUD, P. & RAVEIRO, J. Deux cas de lèpre tuberculoïde avec névrite hypertrophique ascendante partant de la plaque. [Two cases of tuberculoid leprosy with ascending hypertrophic neuritis starting from the lesion.] Bull. Soc. franç. Dermat. et Syph. **54** (1947) 11-12.

Both cases were of incipient leprosy manifested only in the form of a raised, infiltrated, erythro-squamous, anesthetic tuberculoid patch from

which ran hard, mobile cords corresponding to hypertrophic nerve fibres infiltrated with giant cells, lymphocytes and histiocytes. Hansen's bacillus could not be found in the patches or in the nerves.—[Abstract from *Excerpta Medica* **3** (1949) 39.]

PIERARD, J. & VAN PRAET. Cas de lèpre. [A case of leprosy.] Arch. Belges Dermat. et Syph. **4** (1948) 80-83.

Description of a case in a Belgian officer, contracted in the Belgian Congo. It was of tuberculoid type, with reaction and few bacilli. Reexamined at the end of 1949, the condition seems to have cleared up under sulfones and carbonic snow. —A. DUBOIS.

GOLD, S. Leprosy in British nationals. British J. Derm. & Syph. **60** (1948) 139-143.

A report of leprosy developing in 2 persons of pure British strain within 18 months of residence in India, without any known contact with leprosy. The first case was a child of 4½ years with purplish-red anesthetic macules on both buttocks, teeming with *M. leprae*. The Wassermann and Kahn reactions were positive. This case was diagnosed as an intermediate form of leprosy, with poor prognosis. The other was a case of neural leprosy in a soldier who showed no macules but wasting of the muscles of the right hand. The possible sources of infection in these cases are discussed. —G. O. TEICHMANN.

EBERT, M. Leprosy, mixed type; case report. Arch. Dermat. & Syph. **57** (1948) 445.

A case in a Chinese woman 34 years of age who emigrated from China to Chicago 10 years ago. Shortly after her arrival a reddish plaque developed on her face and, after a series of intramuscular injections, disappeared in one year. Two years ago reddish-brown plaques appeared on the face, neck and extremities and claw hand developed. She entered a hospital because of swelling of the face and a large necrotic area on the right alveolar ridge extending on to the palate. Acid-fast bacilli were demonstrated in the nasal smears. The patient's husband and 5 children, ranging from 2 to 8 years of age, revealed no evidence of leprosy.—F. A. JOHANSEN.

EBERT, M. & KAGAN, M. S. Neural leprosy; case report. Arch. Dermat. & Syph. **57** (1948) 445-446.

A case report in an American-born Japanese aged 32 years, who had spent 4 years in Japan between the ages of 6 and 10 years. In 1941 [then 25 years old?] he noted loss of sensation of the right thumb. A few months later macular lesions with anesthesia was found by an Army doctor. The patient was transferred to Carville and paroled after 1 year. In 1944 he entered a Chicago hospital with claw-hand, foot-drop and weakness of facial muscles. *M. leprae* was found in the skin and bone marrow. —F. A. JOHANSEN.

MUIR, E. Recent advances in the treatment of leprosy. Trans. Roy. Soc. Trop. Med. & Hyg. **41** (1948) 575-582.

In this, the first of a group of three papers read before the Society [the others, by Kirwan and Adams; see elsewhere in this section] the author states that after using hydnocarpus oil for 30 years he felt pessimistic about its effects, which he believes are largely due to counter irri-

tation. He had had better results with its use in Calcutta than in Trinidad, where the cases of leprosy were much worse. The sulfones are far more efficacious. With diasone by mouth he had seen rapid and remarkable improvement in very severe cases within a few weeks. In almost all cases the disease subsided, blind eyes improved, noses began to clear, and ulcers healed. He had seen equally good results during a visit to Brazil in 400 cases treated with promin or diasone by de Souza Lima. Reports on sulphetrone indicate that it is less toxic and gives quicker results than the other sulfones used. With regard to dosage he advocated caution, especially in severe cases, until the patient's tolerance has been tested, and mention is made of the usual laboratory tests, the treatment of anemia, and the procedure in case of reactions. Davey has reported from Nigeria that in some lepromatous cases the lepromin reaction becomes positive within 5 to 10 months under sulphetrone. Tuberculoid cases, with few bacilli, apparently do not respond as well as lepromatous ones. The mode of action of the sulfones is still uncertain, and the duration of treatment has still to be worked out. Whatever may be the ultimate value of sulfone therapy, there is no doubt that the diminution of symptoms and bacillary count reduces infectivity and so will make room for many more patients who are at present hiding and who will now come for treatment

—G. O. TEICHMANN.

ADAMS, A. R. D. Three cases of leprosy treated with diasone. Trans. Roy. Soc. Trop. Med. & Hyg. **41** (1948) 591-594.

Three male patients, 2 English and 1 Pole, treated by the author in England had improved considerably under diasone but with no obvious diminution of the bacilli. Attention is drawn to the lamentable lack of facilities in England for treating patients with leprosy, apart from one small institution in the south. In consequence, concealment has to be practised by patient and doctor alike. —G. O. TEICHMANN.

CHATTERJEE, S. N. Intramuscular injection of Hydnocarpus oil and its preparations. Lep. India **20** (1948) 109-111.

The various factors responsible for producing pain, induration and abscess formation after intramuscular injection of hydnocarpus oil are discussed. —DHARMENDRA.

RAJAH, Z. J., PAUL RAJ, M. & COCHRANE, R. G. A short note on experimental investigations on the optimum dose of hydnocarpus preparation at the Lady Willingdon Leprosy Sanatorium, Chingleput, S. India. Lep. India **20** (1948) 146-148.

In an investigation of the optimum dose and the most suitable way of administration of hydnocarpus preparations the authors used these drugs in different groups of patients in three doses, viz., high (15-25 cc.), medium (10-15 cc.), and low (10 cc.); and they injected them in three different ways, viz., intradermal, subcutaneous and intradermal, and subcutaneous. The most efficacious method, they found, is with the medium dosage of oil and esters weekly, given by a combination of the intradermal and subcutaneous routes. —DHARMENDRA.

CUTTLE, T. D. Failure of streptomycin in the treatment of leprosy. American J. Med. Sci. **214** (1947) 385-388.

This is a rather complete case history of a Filipino who enlisted in

the Navy as a steward's mate and, four months later, was admitted to the hospital because of areas of dark and of depigmented skin over the legs and trunk. Acid-fast organisms were demonstrated in sections of biopsy material and a diagnosis of leprosy was made. Treatment with streptomycin was attempted, there being no report of its use in leprosy at that time. In a period of 55 days 175 gm. was administered but the depigmented macular and hyperpigmented nodular lesions progressed and the course of the disease was not significantly altered. Biopsy after treatment showed acid-fast bacilli in approximately the same number and distribution as before treatment. —F. A. JOHANSEN.

ROMERO, A. La vitamina A en lepra. [Vitamin A in leprosy.] Rev. méd. Costa Rica **8** (1948) 287-293 (summary in Spanish, English and French).

Vitamin A, 100,000 U. daily by the intramuscular route, was used in the treatment of 54 patients. In more than two-thirds of the lepromatous cases there was observed the production or exacerbation of lepra reaction. A preparation containing 10,000 U. of vitamin A was administered to 12 patients by the intravenous route with the same results, except that the reactions were more prompt and intense. The cause of this phenomenon is not known. However, if the occurrence of lepra reaction is beneficial to the patient, the use of this vitamin would be desirable. On the other hand, if lepra reaction aggravates the patient's condition, its use should be avoided, or else one should determine the dose that would benefit the organic resistance of the patient without provoking reactions.—[From the author's summary.]

BRENES IBARRA, A. A. & ROMERO, A. Terapéutica de la reacción lepromatosa. Diversos esquemas de tratamiento experimentados en el Sanatorio Nacional de las Mercedes de Costa Rica. [Treatment of lepromatous reaction; various methods of treatment tried in the Las Mercedes National Sanatorium, Costa Rica.] Rev. méd. Costa Rica **8** (1948) 278-286 (summary in Spanish, English and French).

Six methods of treatment of lepromatous reaction have been tried in 285 instances of that condition. In order to judge the results, a triad consisting of erythema multiforme, fever and various algias was taken as reference. These treatments were: vitamin B complex with ascorbic acid; tartar emetic; vitamin B complex, ascorbic acid and tartar emetic; benadryl; penicillin; and streptomycin. The best results were obtained by the combination of vitamin B complex, ascorbic acid and tartar emetic. The results obtained in the special treatment of certain other manifestations of lepromatous reaction—neuritis, iritis, iridocyclitis, orchitis, mastitis and erythema necrosans—are discussed.—[From the authors' summary.]

SAGHER, F. & MITERSTEIN, B. Effect of Grenz rays on leprous infiltrations; response of lesions of anterior portions of eyeball. Arch. Ophth. **38** (1947) 78-88.

The Grenz rays were applied to lepromatous changes in the anterior segments of the eyeball in 6 patients. Since it was obvious on the basis of experience with irradiation of the skin that only large doses could produce any effect, 3 practically sightless patients were chosen for this treatment. In all of them the lepromas became smaller or disappeared. When the treatment was applied to 3 other patients with fairly good

vision, 2 exhibited a favorable response, whereas in the third the lepromatous part which was irradiated became quiescent or even reduced but the surrounding parts presented rapid growths of new lepromas. The voltages used ranged from 6 to 14 kv, which is equivalent to half-value layers of 0.021 to 0.031 mm. of aluminum. The most effective doses applied at one sitting were from 700 to 1,200 r, the total amounts varying from 5,500 to 11,600 r. These large doses could be applied safely because the external tissues of the eyes are much less sensitive to the rays than is the skin. No damage to the cornea, lens or deeper structures of the eye was observed over periods varying from 2 to 4 years. Although the study indicates that lepromas of the anterior portions of the eyeball cannot be effected by Grenz rays, no definite conclusions can be drawn in view of the small number of observations. —F. A. JOHANSEN

SMITH, M. A pharmacological study of three sulfones. Lep. Rev. **20** (1949) 77-88.

This report of work done by the BELRA Research Unit in Uzuakoli, Nigeria [see Lowe and Smith, THE JOURNAL **17** (1949) pp. 181], deals with the absorption, distribution and excretion of the three sulfones diaminodiphenyl sulfone (the parent substance, DDS, designated "DADPS" in this report), diasone and sulphetrone as determined during the treatment of nearly 300 patients, most of them severe lepromatous cases. The following is the substance of the author's summary. Estimations of sulfones in the feces show that DDS is extremely well absorbed from the gut, diasone is well absorbed, sulphetrone is poorly absorbed. Estimations of urinary excretion show that DDS is excreted slowly but almost completely, diasone more rapidly and less completely, sulphetrone very rapidly but with only 10-20% of the daily oral dose recoverable from the urine. The sulfones are fairly equally distributed in the various body fluids, and no evidence of concentration in the skin has been found. Parenteral administration of sulphetrone is advocated, oral administration being uneconomical. Pharmacologically, DDS has great advantage in that, given orally, it is absorbed well and excreted slowly, and thus only a small amount is needed to establish and maintain a blood level comparable with that obtained by other sulfones. It has the reputation of being too toxic a drug for use in human infections and no previous report of its therapeutic trial in leprosy is available. For the treatment of a chronic disease such as leprosy its dosage may be adjusted to give a blood level comparable in terms of chemical equivalents with that obtained when using the proprietary compounds. —G O. TEICHMANN.

MAURI, A. C., HADLER, W. A. & SOUZA CAMPOS, N. Dosagem das proteinas do sóro em face dos resultados da lepromino-reação. [Partition of serum proteins in relation to the results of the lepromin reaction.] Rev. brasileira Leprol. **15** (1947) 137-162 (English summary).

This biochemical study was made with reference to clinical observations and the results of the lepromin test in 113 children, of which 63 were positive to the lepromin test and 50 were negative. The protein fractions were determined quantitatively by sodium sulfate in different concentrations. On the average, the figures obtained were higher in the lepromin-positive cases than in the negative ones, especially with respect to the globulins and in particular pseudoglobulin I. Increase of globulins

is a common finding in infectious diseases, and it is correlated with the presence of specific antibodies. The authors compare their data with those obtained in other infectious diseases, but draw no final conclusions regarding the presence of specific antibodies in the lepromin-positive cases. The differences found in the two groups could be without relation to immunological properties; the increase of globulin could be a nonspecific reaction of the body.—[From the authors' summary.]

PICCARDI, G. & RADAELI, G. Sulla ricerca e sul comportamento dei composti di molibdeno negli organi leprosi. [On the behavior of molybdenum compounds in leprous tissues.] Spectrochin. Acta **3** (1948) 233-234.

That methylene blue injected into the living body stains electively the tissues and organs attacked by *M. leprae* and the bacteria themselves is well known. It is also known that when solutions of ammonium molybdate and of methylene blue are mixed a dark-blue solid is produced. Hence there arose the idea of localizing, as it were, the molybdate in the affected tissues by means of the methylene blue and obtaining thereby a more energetic action of the drug. A leprous nodule stained with methylene blue in a young patient was extirpated and divided into two parts. One part was immersed for a time in a solution of am. molybdate, the other not. Transferred to 95% alcohol, the latter was rapidly decolorized while the former retained the color, confirming the fixing action of the molybdenum. The patient, who had many lepromata some of which were stained with methylene blue while others were not, was given a series of intravenous injections of 1% am. molybdate. Five days later two nodules were extirpated, one which had been stained and one which had not and was of the normal red color. Treatment of the nodules with fuming nitric acid gave oily residues. Examined spectrosopically, in the UV area, the lines of molybdenum were plain in both residues, and to about the same degree. Five months later two more nodules, one blue and one unstained, were again extirpated and the same procedure was carried out. No traces of molybdenum could be found on spectroscopic examination in either residue. It had been completely eliminated, indicating that the methylene blue had not had the effect of fixing the molybdenum.—[From abstract in *Trop. Dis. Bull.* **45** (1948) 1092.]

FREIRE, S. A. & RAMOS, J. C. Produção de leucofuchsina no *M. leprae* tratado com bogalita. [Production of leucofuchsin in *M. leprae* treated with bogalite.] Arq. mineiros Leprol. **8** (1948) 290-295; *also* Brasil-med. **62** (1948) 281-283 (conclusions in English).

Since bogalite [rongalita] and sodium formaldehyde sulphoxalate decolorize dilute basic fuchsin in the test tube, with the formation of leucofuchsin, and since the original color can be restored by the action of an oxidizing agent such as hydrogen peroxide, it is supposed that the same action takes place *in vivo*. In smears and sections rich in stained bacilli the substances referred to (0.5% solution) decolorize them, but the original color does not reappear under the action of hydrogen peroxide but only after long washing and restaining with fuchsin. Sections of biopsy specimens taken after 14 gm. of bogalite had been administered intravenously during a period of 18 hours showed (after staining by Faraco's technique) a diminution of affinity for fuchsin on the part of the bacilli. The same thing was observed in sections of specimens from untreated cases, im-

mersed for 10 minutes in 0.5% bogalite. The action of bogalite cannot be bactericidal, but merely bacteriostatic. Diasone, which contains sodium formaldehyde sulfoxylate in its molecule, and promin, which contains sodium bisulfite, also decolorize basic fuchsin *in vitro*. In patients treated with bogalite, and possibly also promin and diasone, the bacteriological examination does not afford a reliable indication of therapeutic action since these reducing substances can, of themselves, interfere with the affinity of the bacilli for fuchsin.—[From author's conclusions, supplied by F. A. Johansen.]

ASH, J. E. The lymph node in tropical diseases. American J. Trop. Med. **27** (1947) 483-491.

The author believes that the lymph node has diagnostic potentialities in many tropical diseases. With regard to leprosy, he recalls that peripheral lymph-node involvement is one of the most constant features of the disease, and that bacilli may be obtained from them—commonly the inguinals—by aspiration or biopsy when the usual sources fail. Histologically, the picture is sufficiently specific to be suggestive through the distribution of the lepra cells, and is confirmed by the large numbers of bacilli present. In the early stage the pigmented foam cells are scattered near the cortex but contain bacilli. In the later stages they are diffused throughout the node. Involvement of the lymph node occurs in both lepromatous and neural types. —F. A. JOHANSEN.

ALVAREZ LOWELL, L., RODRIGUEZ PEREZ, A. P. & RODRIGUEZ PUCHOL, J. La participación de los centros nerviosos en el sustratum histopatológico de la lepra. [The participation of the central nerves in the histopathological substratum in leprosy.] Fontilles **2** (1948) 101-114.

The authors discuss the concept of Klingmüller that the lesions of the central tracts of the nervous system in leprosy are always secondary to the peripheral lesions, and that the former do not represent a specific response but are of general nature. In their own study they have found medullary perivascular infiltrations and degenerative neurological changes leading to clasmatodendrosis, and they also found degenerative alterations of the microglia and oligodendroglia. The morphologic picture observed corresponds to degenerative toxic changes of the centers. They also found various degenerative changes in the optic nerve which have not been described before. They conclude that almost all of the lesions probably have their origin in the ganglia and in the nerves by toxic affection, and are very similar to those usually encountered in other chronic diseases, without any specific characteristics. —F. CONTRERAS DUEÑAS.

DE FARIA, J. L. Estudo da reação a lepromin (Mitsuda) em cães. Histopatologia. Significaçao. (Resumo; conclusões.) [Lepromin reaction in dogs; histopathology; significance.] Rev. brasileira Leprol. **15** (1947) 195-201 (summary and conclusions only, in both Portuguese and English).

This communication is a three-page summary (in each language) followed by conclusions as follows: Adult dogs from nonleprous communities give positive late lepromin reactions, the nodules histologically of tuberculoid structure, without early reactions. The author agrees with Wade that the increase in the injection papule in the first hour is not specific, but disagrees with the view that the late reaction is allergic in

nature. He believes it to result from the natural resistance these animals present against the inoculation of lepromin, a foreign substance, and to be mainly caused by the lipids of the bacilli. The occurrence or non-occurrence of the reaction in animals does not permit any conclusion as to whether those animals are or are not resistant to leprosy infection. In this study, in which the amount of lepromin used was kept as 0.1 ml., it was necessary to take into account the age of the animals and the histopathologic changes at different intervals after the lepromin injections. A normal skin antigen prepared by the lepromin (Mitsuda) technique caused, in 2 dogs of the 10 used, slight nodular cutaneous reactions of tuberculoid structure.—[From the author's summary and conclusions.]

KAHN, R. L., BARIBEAU, B. J. & VILLALON, F. T. Universal serological reaction with lipid antigen. IV. In lepromatous leprosy. American J. Clin. Path. **19** (1949) 408-413.

Sera from 55 lepromatous cases were examined by the universal technique, and typical results are demonstrated. Marked precipitation occurred before incubation, strongest in reduced NaCl concentration; after 4 hours in the ice-box almost all dilutions showed precipitation, complete in zones I and III, nearly complete in zone II; after 24 hours incubation all zones showed complete precipitation. In contrast, in tuberculoid leprosy there were no differences in precipitation in the 4- and 24-hour tests. It is suggested that in lepromatous leprosy there is not only an increase over normal in the liberation of tissue lipoids, but also liberation of distinctive lipoids; serological patterns vary with the activity of the disease, differing according to whether it is active or "burnt out." These differences may serve to distinguish between forms of the disease and as an index of response to treatment. [From abstract in *Trop. Dis. Bull.* **46** (1949) 944, supplied by F. A. Johansen.]

[Comment by Sister Hilary Ross: At the National Leprosarium, Carville, this universal serological technique was used in examining 140 cases, lepromatous, tuberculoid and neural, in the various stages of activity of the disease. The test is time-consuming, taking 90 test tubes for each serum. We find the standard Kahn test, and more recently the cardiolipin antigen used by Kahn, to be of more value than this unpractical universal serological technique.]

MUÑOZ RIVAS, G. Longevidad de un bacilo ácido-alcohol resistente. [Longevity of an acid-alcohol-fast bacillus.] Editorial Cromos, Bogotá, Colombia, 1947, 8 pp.

The author made an experimental study on the longevity of the acid-alcohol-fast bacillus outside of the living organism, and concluded that "the infection of houses which have been occupied by tuberculosis and leprosy patients is generally accepted by the mass and denied by the epidemiologists, but the data found in this experimental study on the longevity of some mycobacterias give the idea a serious aspect of truth." —[From abstract in *Arq. mineiros Leprol.* **8** (1948) 99.]

ROW, R. Further observation on symbiosis of microorganisms in culture with special reference to mycobacterium in leprosy. Indian Physician (Bombay) **7** (1948) 255-258.

The author first states that he has repeated his isolation in pure culture of acid-fast bacilli from leprosy lesions in symbiosis with Leishmania

organisms [see THE JOURNAL **16** (1948) 109], and goes on to report attempts at its cultivation in symbiosis with other, nonpathogenic, acid-fasts. First, he planted in hemoglobinized saline a few drops of leproma fluid together with a trace of an acid-fast bacillus culture, and obtained a mixed growth of long and short acid-fast bacilli which formed heaped-up, orange-colored colonies like those of the tubercle bacillus; but separation of the two forms proved difficult. He then cultivated the tubercle bacillus in Sauton's fluid medium and introduced a sterile filter bougie containing a fragment of spleen of a mouse well infected with the rat leprosy bacillus, so that the diffusible substances generated by the tubercle bacilli could reach the bacilli within the bougie without the latter being contaminated. After four weeks at 37°C. the sparse, longish acid-fast bacilli within the bougie were planted out on glycerinated potato and, for control, on Sauton fluid. After eight weeks a small yellow patch developed on the surface as a pure culture of an acid-fast bacillus, now perhaps a little shorter than the original. A control test showed the bougie to be bacteria-proof. The author concludes that acid-fast mycobacteria can be isolated in culture by symbiosing leprous material with cultivable microorganisms, whether they be mycobacteria or protoza. The author believes that, by his symbiosis techniques, he has cultivated both the Hansen and the Stefansky bacilli. How far the cultures which have been isolated in this manner will satisfy Koch's postulates is left for future investigation.—[Mainly from abstract in *Trop. Dis. Bull.* **46** (1949) 264.]

ROW, R. On the experimental transmission of rat leprosy in the mouse with the culture of *Mycobacterium stefanski* isolated by symbiosis. Indian Physician (Bombay) **8** (1949) 145-149.

With reference to the cultivation work, it is pointed out that it is essential to start with an actual fragment of leproma, to permit the preliminary proliferation (and adaptation) to occur in the leprous tissue; the symbiosis "played only a secondary role, however helpful," because isolated colonies could be obtained on glycerinated potato even before submitting the material to symbiosis. The present report is of a single inoculation experiment with a culture obtained from infected mouse spleen by the filter bougie method (details given). A culture on potato from the bougie made one month after the set-up was prepared showed growth 2½ months later; a subculture from it was "well established" some 7 weeks later, and a second subculture was made; and material from it, taken about 3 weeks later, was inoculated intraperitoneally into 2 mice. One of them died after 11 days, probably accidentally. The second was killed 6 months after inoculation, and the liver and spleen were found to be much affected, and a smear from the spleen revealed "enormous numbers of long fine acid-fast bacilli and innumerable globi of all sizes." The author concludes that "most of Koch's postulates" have been satisfied. [He does not evidence consideration of the possibility that the culture obtained, a chromogen, may be just one more of the many cultures of unprovable nature grown out from human and rodent lesions, and that the infection of the mouse might have been due to pathogenic microorganisms carried along through the very limited series of subcultures from the original inoculum.]

—H. W. W.

MACCALLUM, P., TOLHURST, J. C., BUCKLE, G. & SISSONS, H. A. A new mycobacterial infection in man. I. Clinical aspects (P. MacCallum). II. Experimental investigations in laboratory animals. (J. C. Tolhurst & G. Buckle). III. Pathology of the experimental lesions in the rat (H. A. Sissons). IV. Cultivation of the new mycobacterium (G. Buckle & J. C. Tolhurst). J. Path. & Bact. **60** (1948) 93-122.

This study, from Melbourne, Australia, has to do with 6 cases of an indolent ulcerative condition occurring in rural districts of Victoria—5 cases in Bairnsdale and 1 in Colac, 200 miles away—of which biopsy specimens teemed with an acid-fast bacillus of unknown source which proved to be pathogenic in rats and mice and which, after repeated failures, was grown in cultures. I. The patients, 3 males and 3 females aged from 2½ to 51 years, presented solitary lesions on the extremities (the leg in 4 cases, the forearm in 2 cases). The condition was thought to be tuberculous until doubt arose because of the abundance and grouping of the bacilli in sections, the absence of the histological picture of tuberculosis, and failure to cultivate the bacillus. Leprosy was also considered but was eliminated (with the agreement of R. G. Cochrane, who saw one of the patients). Beginning with an inconspicuous induration, with histories of abrasions in two cases and an insect bite in one, the lesions ulcerated and extended indolently and often eccentrically, proved intractable to or were aggravated by the treatments employed, and denuded large areas by marginal sloughing without systemic reactions in the absence of secondary infection. Occasionally spread occurred beneath the surface to produce secondary nodules of infiltration or even ulcerations. Histologically the essential element was the macrophage, with lymphoid and plasma cells. Necrosis was conspicuous, especially in the fatty tissue beneath the dermal edge of the ulcer, and in and about the necrotic areas tenaciously acid-fast bacilli were found in enormous numbers, many of them grouped in oval or rounded masses suggesting that they were in distended phagocytes, although nuclei often could not be seen. The findings indicate that this microorganism is very slow to produce tissue sensitivity. It is recalled that, in writing of leprosy, Cilento (Tropical Diseases in Austrialia, 2nd edit., Brisbane, 1942, p. 305) told of cases seen in Queensland with single tiny nonanesthetic ulcers, clinically indolent and intractable, with bacilli indistinguishable from *M. leprae* which were not tubercle bacilli. II. Animal experimentation, beginning with biopsy material from three of the cases, revealed high or complete resistance on the part of guinea-pigs, rabbits, a cockerel, and lizards (thus eliminating the various types of tubercle bacillus), whereas rats and mice were susceptible. After subcutaneous inoculation of rats only local lesions were produced. After intraperitoneal inoculation of males the first sign of disease was swelling of the scrotum after 2 to 9 months (usually 4 or 5 months), followed by marked ascites and, sooner or later, ulceration of the scrotum. Those surviving the ascites (by rupture of the abdominal wall and escape of the fluid) subsequently developed swelling and ulceration of the tail or feet; and ultimately, about 12 months after inoculation, the animals died. The cells of the ascitic fluid were chiefly large phagocytes containing varying numbers, up to hundreds, of acid-fast bacilli; and bacillus-containing lesions were found on the peritoneal surfaces of the epididymis and scrotum and elsewhere. Ascites never occurred in female rats, but ulcerations developed in some of them. The condition in mice was quite different, the most striking

feature being gross subcutaneous edema. As many as eight consecutive passage inoculations had been carried out in rats, without significant shortening of the course of the disease. The morphology and staining characteristics of the bacillus, and its appearance in the cells, are described and depicted. That beading is influenced by staining technique, as reported by Yegian and associates for the tubercle bacillus, was found true with this one. III. The lesions start on the peritoneal surfaces, mostly of the scrotum and the epididymis, the testis being rarely involved, and extend into the deeper tissues. Most of the bacillus-containing cells are macrophages, many of which have vacuolated ("foamy") cytoplasm, but neither globi nor rosettes are seen; and it is uncertain whether the bacilli multiply within the cells or have all been phagocytosed. Necrosis is an essential part of the picture; giant cells are not found. It is pointed out that the initial localization in the epididymis and scrotum, and the tissue changes which follow, resemble what has been reported to occur in the male rat after intraperitoneal injection of barium sulfate. IV. Many and varied attempts to cultivate this mycobacterium failed—except apparently fortuitously a few times—until the occurrence of the human lesions on the extremities and of the principal rat lesions in the scrotum and on the limbs suggested trial of a temperature lower than 37°C. At 33° growths were obtained directly from one of the patients and from several of a number of stored fluids. Strains from three patients were thus obtained, one directly and two indirectly, from rat peritoneal fluids. Growth also occurs at 30° and 35°, seldom at 37°, not at all at 41° or at room temperature. At best the growth is slower and scantier than that of the human tubercle bacillus. On yolk agar there is little or no pigment production, but on Petragnani's medium the growth is usually lemon-colored. The cultures are pathogenic for rats and are recoverable from them. The organism is killed by heating to 60°C for 30 minutes, withstands treatment with sulfuric acid, and can be stored in rat peritoneal fluid up to nine months. No name had been given to this new mycobacterium. —H. W. W.

[Reprinting of this paper was contemplated, for its general interest and because of the possibility that such cases might be taken for "monosymptomatic lazarine leprosy" (Pardo-Castelló), but that is not allowed by the rules of the periodical in which it appeared. In a personal communication Dr. Tolhurst says that since the report was published two more cases from Bairnsdale have been seen—one of them unique in having multiple ulcers, on both legs and one arm—and that the same bacillus has been cultivated by Dr. B. R. V. Forbes of Sydney from a case from Queensland. This microorganism has now been named *Mycobacterium ulcerans*.—EDITOR.]

ASHBEL, R. & POLJAKOFF, A. In vitro cultivation of the rat leprosy organisms. J. Inf. Dis. **83** (1948) 279-282.

The material used in these experiments was taken from 10 rats infected with a strain obtained from the National Institute of Medical Research in London. It was sown on simple media such as egg slants to which was added Locke's solution, and on semisolid agar to which was added rabbit blood or serum. Positive cultures of acid-fast bacteria were obtained after periods ranging from a few weeks to 1½ years, the better results being obtained after the longer periods. Subcultures of these strains grew well. The principal factors contributing to the success of this attempt were the

long periods of incubation and perhaps the drying out of the medium, for the cultures had been permitted to dry (from 269 to 510 days). After they became dry, saline was added and subcultures were made on flooded egg slants. Identification was established by inoculation of 100 rats with primary cultures and various subcultures. Of 53 of these rats, killed from 2 days to 1½ years after inoculation, 22 were positive. Of 47 rats killed between 1 and 3 years after inoculation, 9 had developed various neoplasms and 10 had typical rat leprosy. It is concluded that cultivation of the Stefansky bacillus has been achieved. —F. A. JOHANSEN.

(*Thiosemicarbozones abstracts*)

BEHNISH, R., MEITZSCH, F. & SCHMIDT, H. Chemical studies on thiosemicarbozones with particular reference to antituberculous activity. American Rev. Tuberc. **61** (1950) 1-7.

Besides streptomycin and para-aminosalicylic acid, particular importance in the treatment of tuberculosis has been gained of late—in Germany —by a group of compounds called the thiosemicarbozones, developed by the authors in cooperative work with Domagk in the Bayer laboratories. After new hopes were awakened by the sulfones, which showed a limited therapeutic activity, it was found that an open, chain-like arrangement of the nitrogen and sulfur atoms constituted a much more active basic principle. Of many compounds of this type the thiosemicarbozones proved to be the most efficacious. The sulfur atom plays an essential role, for semicarbozones and other substances of similar structure are inactive. Aldehyde compounds are better than ketones, especially if the aldehyde is of aromatic nature. Acylation leads to particularly effective compounds, and the best of them has proved to be 4-acetylaminobenzaldehyde-thiosemicarbozone ("conteben"; laboratory designation Tb I/698, Schmidt No. 1641X). This substance, $C_{10}H_{12}ON_4S$, otherwise expressed as

$$CH_3CONH \cdot C_6H_4 \cdot CH{:}N \cdot NH \cdot CS \cdot NH_2,$$

or as $CH_3CONH-C_6H_4-CH{=}N{:}NH \cdot CS \cdot NH_2$,

is a pale yellow, finely crystalline powder of bitter taste, almost insoluble in water but somewhat more so in serum and several times as much so in urine. The methods of its determination in body fluids are discussed. Administration is usually by mouth but not limited to that route; by the addition of solubilizing agents, or by solution in glycols or other suitable substances, it can be used for injection therapy. —H. W. W.

DOMAGK, G. Investigations on the antituberculous activity of the thiosemicarbozones *in vitro* and *in vivo*. American Rev. Tuberc. **61** (1950) 8-19.

In the twenty years of systematic investigations since the sulfanilamides were discovered, the conditions affecting the action of various chemotherapeutic agents have been determined. Those like sulfathiazole, para-aminosalicylic acid (PAS), the thiosemicarbozones and streptomycin act differently. For one thing, the first two are strongly inhibited by the presence of para-aminobenzoic acid while the other two are not. In a culture experiment Tb I (as a powder, or in formamide, or in a combination of formamide and a glycol) inhibited growth completely in a dilution of 1:200,000 (incompletely at 1:300,000), and streptomycin did so at 1:25,000 (incompletely at 1:50,000); PAS alone inhibited completely at 1:300,000,

but not at 1:5,000 in the presence of para-aminobenzoic acid—whereas with that substance present Tb I was fully effective at 1:300,000 and streptomycin at 1:100,000. The author believes that the thiosemicarbozones have a direct action on the tubercle bacillus rather than a theoretical indirect action upon the host. Although *in vitro* 1% streptomycin does not destroy the infective power of tubercle bacilli after 4 or even 8 weeks, and whereas 1% PAS takes 4 to 8 weeks to produce that effect, 1% Tb I in ethylene glycol rendered them noninfective "after a short period of action." In various animal experiments the effects in guinea-pig tuberculosis of streptomycin, PAS, and Tb I—and sometimes certain variants of the last—were compared. Tb I and streptomycin exerted an effect in adequate dosage. A combination of Tb I and PAS had no greater effect than the former alone. Besides inhibiting multiplication of the bacilli in lesions, Tb I causes degenerative morphological changes, including loss first of acid-fastness and then of gram-positiveness, after which they can be detected only by the fluorescent microscope. Histologically, epithelioid nodules show peculiar regressive phenomena under Tb I treatment; those cells shrink and finally are destroyed, and the centers become surrounded and infiltrated with connective tissue. Caseous centers become encapsulated. It is pointed out that if in Tb I therapy resistant strains of bacilli are bred, as may occur with streptomycin, "the present blessing could grow into a curse"; and for this reason these drugs have as yet been used principally in cases beyond help by other methods. Now, however, after 2 or 3 years experience, the basis of experience can gradually be broadened.

—H. W. W.

MERTENS, A. & BUNGE, R. The present status of the chemotherapy of tuberculosis with conteben, a substance of the thiocarbozone series. American Rev. Tuberc. **61** (1950) 20-38.

Thus far, more than 10,000 patients with different forms and stages of tuberculosis have been treated with this drug, and over 60 clinical reports have been published or are in press. The authors have been responsible for the allocation of the drug and for the collection and analysis of the reports of the various investigators; and this article, which has a bibliography of nearly 100 items, is a comprehensive and summary review which can be abstracted only selectively. The more labile the process of the disease and the better the blood supply of the lesions, the more promising this therapy seems to be. In chronic, stabilized pulmonary tuberculosis the prospects are poorer. However, cavernous processes often respond impressively to oral treatment, and good results have been obtained by supplementing Monaldi drainage with local instillation of conteben; and local treatment of empyema has also given good results. The best tendency toward healing is seen in affections of the mucous membranes (larynx, trachea, bronchi, intestines, and bladder), and much is said of this. Judgment regarding tuberculosis of the kidneys, bones and joints is not yet possible; on the other hand in tuberculosis of the soft parts, especially when there are fistulas, conteben therapy is indicated. In tuberculosis of the skin, especially lupus vulgaris—for which condition the drug was first used—there has been extensive and favorable experience. This treatment is not indicated for miliary or meningeal tuberculosis. In pulmonary disease the sputum frequently becomes negative, usually after some three months of treatment, but the fluorescent microscope may still give positive results long after

the findings with the Ziehl-Neelsen stain are negative. As yet, drug-resistant bacilli have not been detected. The dosage which must be strictly individualized, is extraordinarily small, about one-tenth that of streptomycin. Treatment should be started with 12.5 to 25 mgm. daily and increased gradually within the limits of tolerance; 200 mgm. is the usual maximum in adults exceptionally 300 mgm. The average daily dose in current use is about 2 mgm. per kgm. of body weight. The rule applicable in sulfonamide and penicillin therapy, that high blood levels should be attained as rapidly as possible, does not apply. The matter of toxicity is discussed at length, with note that many of the troubles were seen early in the work, when excessive doses were being used; also, that some which are seen under proper dosage tend to disappear with continuation of the treatment. The topics discussed are: gastric irritation, conjunctivitis and exanthemata, the hematopoietic system (anemias relatively rare with the recommended dosage), agranulocytosis and granulocytopenia (mostly in females; total and differential counts to be made frequently), and the effects on the liver and liver function (fatty degeneration, which often exists in tuberculosis, seems liable to be increased but is reversible). The effect of the treatment upon tuberculin sensitivity of the skin cannot yet be evaluated. Conteben inactivates tuberculin salves, whereas PAS and streptomycin do not. It seems that conteben, PAS, and streptomycin all have different modes of action against the bacillus and the infection, hence the possibilities of combinations are obvious. —H. W. W.

HINSHAW, H. C. & MCDERMOTT, W. Thiosemicarbozone therapy of tuberculosis in man. American Rev. Tuberc. **61** (1950) 145-157.

This is a report rendered to a committee of the American Trudeau Society (one by that committee is to appear later) of a survey made in Germany during September 1949. The party visited 10 of the more than 300 institutions in the western zone in which patients had been treated with conteben during the past two years, and examined the data of some 2,000 patients. Practice with respect to dosage varied but, they found, the initial dose generally used is 50 mgm. a day for one or two weeks, with gradual increase to 200 mgm., oral doses being given from one to four times daily. The average length of treatment was perhaps six months, although some patients had been treated continuously for more than a year. The various manifestations of toxicity and the fields of therapeutic effectiveness are dealt with in much the same way and to much the same effect as in the article of Mertens and Bunge, and the points here noted should be correlated with those in the preceding abstract. Particular attention is given the matter of liver disturbances, that being left an open question with, however, the assumption that "the drug is capable of inducing hepatitis until evidence to the contrary is available." Eight instances of agranulocytosis had occurred among the 2,000 cases reviewed, in some of which aminopyrine had also been given. Effects as regards anemia were not serious within proper dosage limits. The drug has a "strange and potentially deceiving effect" in an impressive but nonspecific decrease in the blood sedimentation rate. Headache and dizziness are the principal manifestations referable to the central nervous system; no observation of peripheral neuritis was elicited. The effects on tuberculosis of the larynx were uniformly impressive, resembling those of streptomycin, and they are accepted as evidence that conteben has a definite effect on tuberculosis.

Every investigator interviewed said that 100% of all patients with symptoms of intestinal tuberculosis—which seems unusually common in German sanatoria— obtained relief, and this effect is also accepted as positive evidence. Certain conditions existing in Germany during the treatment period make it difficult to evaluate the influence on pulmonary tuberculosis, especially since few actual controls were set up, so the roentgenographic evidence of clearing in many patients under prolonged treatment—i. e., 4 to 6 or 9 months—are taken only as "suggestive." Everyone agreed that conteben, like streptomycin, represents but one phase of the medical treatment of tuberculosis. It was also agreed that it is neither as dependable nor as rapid in its effects on pulmonary lesions as streptomycin; but there is an opinion that it can be used more frequently, and it is much cheaper than either streptomycin or PAS. There was little evidence that bacillus resistance may appear, but no bacteriological studies in that field have been made. It is concluded that conteben appears to have antituberculous activity of the same general order as PAS and is an important addition to the available antimicrobial agents; and that although it will not replace streptomycin it may be used together with that substance. It is held that this drug "can no longer be ignored in America" and should be subjected promptly to a thorough series of experimental and clinical trials there, for which procedures are outlined. —H. W. W.