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.

SAGHER, F. Leprosy (a review of the literature of the last months of 1952, 1953 and part of 1954). Dermatologica **111** (1955) 244-284.

This is the sixth of the author's sweeping surveys of the literature of the period stated in the title [for previous ones see THE JOURNAL **17** (1949) 155, **19** (1951) 92, **21** (1953) 107, **23** (1955) 338]. This one has no less than 459 numbered references, many of which concern two or more publications. The main subdivisions of the subjects dealt with, after a page of "general considerations," are: etiology; serology; biochemistry; immunology, including the "isopathic phenomenon" of the author and associates, the lepromin reaction, with BCG, and tuberculosis and leprosy; diagnostic and clinical features; pathology; treatment (a lengthy and comprehensive section); lepra reaction and its treatment; history; distribution and statistics; prevention and control; and lastly, classification. These reviews are especially useful for anyone seeking information about articles which would fill lacunae in their knowledge of recent literature. The author evidently has access to an extraordinarily large variety of sources. —H. W. W.

ARNOLD, H. L., JR. Hawaii Medical Association, 1856-1956. Hawaii Med. J. **15** (1956) 313-324.

This issue of the *Hawaii Medical Journal*, commemorating the centennial celebration of the Hawaii Medical Association, whose first charter was granted by the Privy Council of King Kamehameha in 1856, contains thirteen historical articles. The first of them tells of public health measures which began as early as 1836 for the prevention of the introduction of smallpox. The first specific disease discussed is leprosy, which was apparently present as early as 1840, for when in 1853 William Hilldebrand discovered a case near Honolulu, Dwight Baldwin recalled having seen one 13 years before. The Hawaiians soon called it *mai Pake*, the Chinese sickness, probably because it was familiar to the Chinese there from having seen it at home; it may have been brought in "by sailors from Africa, India, Malaya, the Cape Verde Islands or Mexico, quite as easily as from China." Ten years later (1863) Hilldebrand officially called attention to the increasing numbers of cases, and in 1865 the legislature authorized the establishment of a receiving station in Honolulu (Kalihi), and an isolation settlement on Molokai Island (Kalawao, Kalaupapa Peninsula), where the first patients were taken the next year. The average annual case rate for the next 25 years was about 160; for the following 50 years about 80; down to 60 in 1930, to 30 by 1940, and to about 20 by 1951. Roughly 70% of the health funds were used for leprosy in 1865, and about the same proportion in 1890; it still runs close to 50%. "Kalaupapa, once so dreaded that patients on occasion committed murder to avoid going there, is now so beloved that the 1955 legislature, at the patients' insistence, legally required the Department of Health to transfer any patient there at any time upon his own request!" —H. W. W.

[BELGIAN CONGO] Rapport Annuel de la Direction Générale des Services Médicaux, Congo Belge, 1954. [Annual report of the Director General, Medical Services, Belgian Congo, 1954.] Mimeographed, 123 pp.

The 89 leprosaria (of which 6 have more than 1,000 patients, one with 3,167)

had 30,402 patients, of whom 6,730 were new. [These figures are lower than those for 1953; see THE JOURNAL **20** (1954) 474.] The number of cases treated in all medical units was 195,761, of which 105,467 are credited to the itinerant services. The estimate for all cases in the country remains 210,000. Regarding the CIO institutions (Centres d'Isolement Organizées), they were evidently still in the planning stage although it was said in the 1951 report [THE JOURNAL **21** (1953) 108] that three had then been established and 10 others were projected, a statement not repeated in subsequent reports. Estimates are given of the cost of establishing such a center (Fr 24,100,000), and of what is planned to expend in all 13 of them (Fr 238,520,000, ranging from 8 to 24 million each.) —H. W. W.

[FOREAMI] Rapport sur l'activité de la Section "Père Damien." [Report of the Père Damien Section of FOREAMI.] By M. Kivits. Reprinted from the report of FOREAMI for 1954, 8 pp.

When in 1936 the remains of Father Damien were repatriated, there was created the Foundation Père Damien pour la Lutte contre la Lèpre (FOPERDA), to encourage research and antileprosy activities. In 1949 the Fonds du Bien-Etre Indigène (FPI) made FOPERDA its advisor and agent for the utilization of a fund set aside for leprosy institutions in the Belgian Congo, and there was proposed the plan for Communautés d'Isolement Organisées (CIO's), 2 or 3 per province, based on existing leprosaria. Administrative problems led in 1953, to an arrangement with FOREAMI (Fonds Riène Elizabeth pour l'Assistance Médicale au Indigènes) whereby the latter assumed the responsibilities of executing the program of construction and development. FOREAMI was charged by the government virtually to take charge of the antileprosy campaign, and it established the Section Père Damien. In 1954 a survey of the situation was made. Not seen in government reports are the statements that the estimated 213,000 cases (188,420 known) in a population of 12 million is about 1.8%, and that in two provinces (Equator and Orientale, in the hot, humid central basin) the prevalence is about 3.5%; the lowest is 0.6%. (In Ruanda-Urundi it is only 0.12%.) Only about 10% are lepromatous, on the average. Here again appears the figure of 180 for the number of leprosaria against the official 89 [see above], but 20 is the largest number in any other province than Equator. It is credited with 115, but most of them are small agricultural villages [THE JOURNAL **22** (1954) 354] established by local authorities, many with only a few cases. At Kwango (Mosango), Leopoldville, FOREAMI was establishing a "pilot" leprosarium, to be opened in 1955, for the study of methods of control treatment and rehabilitation. The rest of this report is devoted to the plans for development and organization. —H. W. W.

[TANGANYIKA] Annual Report of the Medical Department, 1955. Vol. 1. Dar es Salaam: Government Printer, 1956.

In this narrative report, put out before the statistical data were prepared, it is said that a new leprosarium was opened at Mkunya, Southern Province, on a 600-acre tract which includes a revenue-producing cashew-nut plantation, and connected with it are 16 outpatient centers. There was no indication of change of incidence of leprosy, but an increase of patients under outpatient treatment had resulted from progress in the development of facilities. Outpatient treatment is readily organized where communications are good and the population concentrated, but not where it is scattered. —H. W. W.

[QUEENSLAND.] Annual Report of the Health and Medical Services, Queensland, 1952-53. Brisbane, 1953.

——— *Idem.*, 1953-54. Brisbane, 1954.

——— *Idem.*, 1954-55. Brisbane, 1955.

1. The section on "Hansen's disease (leprosy)" in this report is of interest in

that it contains a brief history of the disease in the state, so far as it is known. The records of the Brisbane Hospital show that a Chinese with the disease was there in 1855, and that a European wardsman was so diagnosed in 1868. Chinese coming into the goldfields were the first to establish the disease, passing it on to both aboriginals and whites, and later the imported Kanakas brought it with them. Wherever these two peoples "settled in large numbers, foci of the disease were set up which persist to this day." A Leprosy Act was passed in 1892, and three other islands were used for isolation until 1907 when all the patients were transferred to Peel Island. In 1908 there were 65 of them there, and 84 in 1910—20 Europeans, 39 Kanakas, 20 aboriginals, and 5 Orientals. Later the numbers averaged 60-70, about two-thirds of them aboriginals, until those people were moved to Fantome Island, one of the Palm Island group about 40 miles north of Townsville, in the care of the Sisters of the Franciscan Missionaries of Mary. In connection with the changed attitude toward leprosy, it is related, "In the early days patients were brought down from the north in kennel-like structures on the poop deck of coastal boats and the patient's food was passed to him on a pole." Afterward the hovel was tipped into the ocean. For the trip over to Peel Island the patients were not allowed to travel on the boat, but were towed in a dinghy "—a miserable journey in wet weather." Treatment with chaulmoogra oil was introduced in 1907 and was used until replaced by the sulfones 40 years later. A few arrested patients were discharged each year, at first after 2 years of bacteriological negativity, the period gradually reduced to 12 months; now they may be released after only 6 monthly negative reports plus a negative biopsy, but no patients have chosen that alternative. The disease is probably declining slowly among the whites, but it remains a problem among the aboriginals, in whom it runs a more acute course. At Peel Island there were only 23 patients in June 1953, against 43 a year before, there having been 21 discharged and only 1 admission. Four sulfones are among the drugs being used, and also INH. Certain specialists visit the island at intervals, and several patients needing special treatment have been sent to the Brisbane Hospital. At Fantome Island the number had decreased during the year from 69 to 61 (8 admissions and 16 discharges). Conditions there had been improved, so that many patients "view their discharge with mixed feelings." No patient discharged from either leprosarium after sulfone treatment had as yet come back relapsed, a thing which happened frequently in the chaulmoogra days.

2. At Peel Island in June 1954 there were 24 patients, including 2 negatives permitted to stay because of crippling. The number of admissions was high, 11, of which 9 were new cases—some discovered early by new medical graduates. One was a relapsed case from the chaulmoogra period. Treatment was much as during the previous year. At Fantome Island, too, the number of admissions was high, 17, with only 12 discharges, bringing the total up from 61 to 65. However, 9 of them were eligible for discharge but were being kept for treatment of ulcerations of the legs.

3. At Peel Island, where there had been 7 admissions and 8 discharges (one-third of the 24 left last year), the total was down to 22, including the 2 crippled cases. One of the admissions was an old patient who had had some sulfone treatment but had not taken maintenance doses after discharge because of intolerance. Treatment was as before, except that short courses of ACTH had been used for lepra reaction with very encouraging results. Again several patients had been sent to the Brisbane Hospital for specialist treatment. Occupational therapy was being emphasized. Significant of a matter not otherwise mentioned is the remark that "the decision to remain at Peel Island has resulted in many improvements." At Fantome Island there had been a marked change in that no less than 29 patients (nearly one-half) had been discharged, and only 1 admitted, leaving 36 at the end of the period.

—H. W. W.

[VIET-NAM] Rapport annual sur le fonctionnement technique de l'Institut Pasteur de Saigon, 1955; Dr. J. Fournier. Saigon, 1956.

The numbers of cases registered at the antileprosy dispensary increased during the year from 3,395 to 4,054. Detailed data are given on the 659 new cases, of which 52% were classified as tuberculoid, 9% as undifferentiated, and 38% as lepromatous. All but a few of the 1,531 cases treated during the year received sulfones, mostly DDS. The section on research tells of work by Destombes and Chambon in the treatment of lepra reactions with phenylbutazone [THE JOURNAL **24** (1956) 115], also of a trial of Di-atox argentique, made at the request of the manufacturer, on 6 cases, 5 lepromatous and 1 tuberculoid, the daily dose 150 mgm. Clinical regression of the lesions, including those of the nose and throat, was evident after the 6th month and very clear after a year; improvement of the nerve lesions occurred later. At the end of a year the bacilli were diminished in all, sometimes had disappeared, those that remained being granular and staining poorly. Regression and sclerosis was followed by biopsy specimens taken each six months. It is concluded that the therapeutic effects are not inferior to those of the other sulfones.

—H. W. W.

BONNE, W. M. WHO activities in the field of leprosy. Relaz. Congr. Internaz. Difesa e Riabil. Soc. "Lebbroso," Rome, 1956, 27-32.

Pointing out that the constitution of WHO defines health as "a state of complete physical, mental and *social* well-being, not merely the absence of disease or infirmity," the speaker shows in what ways the organization has taken an interest in leprosy, including relationship with the International Leprosy Association in 1948 and creation in 1950 of a leprosy expert panel from which were drawn the members of the Expert Committee which met in 1952. Application of control measures requires preliminary evaluation of local conditions, and consultants have been supplied to Burma, Ceylon, Ethiopia, Thailand, Turkey, Paraguay, Indonesia, Iran and Iraq. The organization has participated in joint UNICEF/WHO assistance to national control projects in Ceylon, Nigeria, French Equatorial Africa, Thailand, and the Philippines. Information from different countries stresses the importance of the problems of rehabilitation.

—H. W. W.

DAVEY, T. F., ROSS, C. M. AND NICHOLSON, B. Leprosy; a changing situation in Eastern Nigeria. British Med. J. **2** (1956) 65-68.

Little was known about leprosy in Nigeria when the Leprosy Ordinance of 1917 was passed, and that did not even refer to Eastern Nigeria, then an almost unknown territory. Developments after that were rapid, and it soon became evident that in some places the prevalence was "phenomenal," up to even 150 per thousand. Efforts of missionary societies—the first colony was built in 1927, at Itu—were followed by the creation, in 1945, of the Nigeria Leprosy Service. The disease is peculiar in that for the most part it is mild: only about 10% are frank lepromatous, indeterminate cases are common, and among the tuberculoid cases severe ones are infrequent. There is little sex difference, and little respect for age. Response to treatment is unusually good, a fact noted before the introduction of sulfone therapy. Recently there has been a marked decrease in some heavily infected areas, with for one thing a proportionate decline of indeterminate cases and an increase in tuberculoids. In one area the drop has been from 522 active cases in 1943 to only 49 in 1954; in another, from 31 to 5 per thousand; in three provinces with a total of 30,630 under treatment in 1948 to 14,770 in 1954. The causes of the decline, most unusual for leprosy, are discussed. It is suggested that there has been an epidemic (as there was on Nauru) which is now waning; that there may perhaps have been some influence by the spread inland of tuberculosis, with immunological effects; and that improved living conditions has probably helped. It is unlikely, however, that

these factors together could have made so much difference in the space of seven years, and the main influence is ascribed to the active antileprosy measures that have been taken, which are summarized briefly. [No abstract can do justice to this interesting article.] —H. W. W.

DAVEY, T. F. Leprosy and yaws: points of contact. World Health Organization document WHO/VDT/219, WHO/Leprosy/18, 1956 (mimeographed).

This paper was presented when the participants of the Second International Conference on Yaws Control, held in Enugu, Eastern Nigeria, in November 1955 visited the Oji River Leprosy Settlement. In that region leprosy and yaws have flourished side by side, sometimes in the same patient, and certain of their clinical features have similarities. In yaws, minor recurrent skin lesions are mostly the ones that may be confused with leprosy; for the reverse situation are mainly the indeterminate macular lesions of leprosy, which sometimes simulate the macules of yaws —specifically, the erythematous healing and the hypopigmented healed ones—and the multiple circular framboesid. In diffuse lepromatous leprosy there may be small nodules resembling the isolated keratotic papules sometimes seen in yaws; but they would be bacteriologically positive. In early tuberculoid leprosy there may be groups of papules not unlike papulate yaws lesions, and serpiginous lesions that may resemble a lupoid framboesid. Gangosa and certain lesions of the hands also enter the picture. The closest resemblances between the two diseases, however, are in their epidemiological aspects. —H. W. W.

ROSS, C. M. Leprosy control in Northern Nigeria. Lep. Rev. **27** (1956) 64-66.

This report of the beginning of field work in Northern Nigeria is of interest particularly because of the data on dosage. The pilot experiment, designed to ascertain the practicability of the outpatient clinic system and the prevalence of the disease in the region, was begun at a sleeping-sickness dispensary in Zaria Province. The response was slow at first, but soon hundreds of patients appeared—lepromatous ones few until the scheme became popular—and new clinics were established. In the five largest villages, with 7,733 people, 414 patients (5.3% of the population) had registered within a year. Later, in a survey of three areas with 5,704 people, 390 cases were found (6.8%), mostly children or young adults; 42 of them were lepromatous (10.7%). None of these lepromatous cases had failed to register at the clinic. Treatment was given once a week by mouth, and it was found that the people would attend regularly. Because of trouble in the leprosaria where the then-recommended doses were being used, especially with lepra fever, the starting dose in the clinics were low and increase was slow; advanced lepromatous cases were begun on only 50 mgm. weekly (ultimately up to 400 mgm. as the usual maximum), yet clinical response was seen even in cases that had to be kept at the 50 mgm. level. In 1955 some 540 patients were discharged; 40% of them were slight tuberculoid cases in children, none of them lepromatous. —H. W. W.

WADE, H. W. A note on the less familiar forms of leprosy. La Lepro **25** (1956) 61-68 (in Japanese).

———— *Idem.* Lep. India **28** (1956) 41-48.

After pointing out that classification, which it has been agreed must be primarily clinical, has become increasingly complex, the forms and varieties about which there is disagreement or misapprehension are discussed. The "indeterminate" diagnosis should be limited to cases with simple macular lesions that are early with respect to development, if not to time, and uncertain as to future evolution; the author, like the Indian leprologists, prefers "maculoanesthetic" for those whose macules become fixed and persist as such. Regarding tuberculoid cases, it is emphasized that the terms "minor" and "major" properly apply to varieties of the torpid condition, the latter term not necessarily signifying reactional lesions. As for

reactions in this type, the distinction made by certain South American workers between "tuberculoid reactivation (tuberculoid) lepra reaction)" and "reactional tuberculoid leprosy" is held to be valid. Special problems surround the recently-recognized "borderline" form, which commonly develops in tuberculoid cases as a result of repeated or unusually severe reactions that lower or abolish resistance and tend toward or to lepromatous. In lepromatous leprosy there has arisen the problem of distinction between ordinary lepra reaction ("reactivation") and the kind of reaction called "acute infiltration" by Japanese workers (e. g., Tajiri) and "pseudoexacerbation" by de Souza Lima; this condition, which usually results from sulfone treatment, and whose lesions are more or less tuberculoid, probably develops only in lepromatous cases that previously had been borderline. Confusion in classification and statistics results when cases are classified or reclassified on the basis of retrogressive or residual lesions (e. g., when a case previously tuberculoid improves and is reclassified as "simple macular" instead of being retained among the tuberculoids with proper qualification). Finally, emphasis is given the "spectrum" concept of classification, which recognizes that the types and groups are not sharply delimited but that many cases as seen for diagnosis fall somewhere along the line between two adjacent forms. (Incidentally, the Japanese version, translated by Prof. Kanehiko Kitamura, exemplifies the difficulty of discussing such matters by the number of technical terms for which the English words are used.) —AUTHOR'S ABSTRACT

LUCAS, C. J. Leprosy diagnosed as syringomyelia. British Med. J. **2** (1956) 214.

Two cases are reported of leprosy in young Anglo-Indians seen in the neurology department of a hospital in London, to which they had been referred with the diagnosis of syringomyelia, exemplifying how the disease is liable to be misdiagnosed because of its rarity. In leprosy, it is pointed out, the sensory loss usually includes all forms of sensitivity, although at an early stage the anesthesia may appear to be dissociated because temperature discrimination is lost first, and it is often of the glove type. There is no evidence of a spinal cord lesion, as is almost invariably present in syringomyelia by the time wasting of the hand is pronounced, and in the latter disease the glove distribution of sensory loss is uncommon, but there is depression of one or more of the reflexes in the upper limbs, which is not the case in leprosy. [In an abstract in *Trop. Dis. Bull.* **53** (1956) 1351, by E. Muir, it is pointed out that one diagnostic picture of leprosy is not mentioned. When nerves are not thickened enough to be palpable, tingling can generally be elicited by percussion over the nerve supplying the affected cutaneous area.] —H. W. W.

SHUTTLEWORTH, J. S. AND ROSS, SR. HILARY. Secondary amyloidosis in leprosy. Ann. Int. Med. **45** (1956) 23-38.

Secondary amyloidosis is the leading cause of death in lepromatous leprosy at the U. S. national leprosarium, the mortality being directly due to amyloid involvement of the kidneys. The correlation between the duration and degree of the disease and the development of amyloidosis is poor. Amyloid, a protein polysaccharide complex of variable composition, is related to hyperglobulinemia or to some specific fraction of the serum globulins and perhaps to altered connective-tissue structure and disturbed antibody-antigen relationship. The diagnosis of secondary amyloidosis depends largely on the following findings, in order of importance: persistent proteinuria; Congo red absorption, at least 60% and preferably 80% in 1 hour; hepatosplenomegaly; and hyperglobulinemia, with or without hypoalbuminemia and with no consistent alterations in the globulin fractions. Serum protein and lipid changes occur in lepromatous leprosy *per se*, and no further consistent alterations occurred in these cases with amyloidosis. Serial Congo red tests in cases with initial negative findings will often show results approaching 100% absorption before death. The average duration of life after the onset of the proteinuria was approximately 38 months,

with a fairly wide range above and below this figure. The development of anemia and progressive elevation of the nonprotein nitrogen are unfavorable signs. In view of the possible relationship of hyaluronic acid to amyloid, a patient with advanced amyloidosis was given two courses of hyaluronidase intravenously, each course consisting of approximately 250 mgm. of the enzyme in divided doses over a 5-day period. There was a tendency for the abnormality of the globulin fractions to improve and an associated increase in polysaccharide during this treatment. Further studies are necessary to determine the significance of these changes. A limited number of cases with suspected amyloidosis but negative Congo red tests had needle biopsies of the liver performed. This procedure is of value in differentiating amyloidosis from severe lepromatous leprosy involving the liver. The Congo red test (which was performed on 95 patients, 87 lepromatous and 8 tuberculoid), consists of intravenous injection of a 1% aqueous solution, 1 cc./10 lb. body weight. Blood specimens are taken for comparison 2 minutes and 1 hour after the injection, and urine is examined after 1 hour. The correlation between the results of the test and the degree of amyloidosis is poor, hence the high percentages specified.

—AUTHORS' ABSTRACT

PATERSON, D. E. Bone changes in leprosy. Indian J. Radiol. **10** (1956) 90-97.

This report is of radiographic findings in 116 patients at the Christian Medical College, Vellore. The bone changes seen are of three main types: I. Specific destructive, due to lepra reaction in the presence of leproma formation in the bone. 2. Nonspecific destructive and erosive, due to secondary infections in hands and feet which are insensitive. 3. Osteoporotic, due mainly to disuse. These changes are described, and their differential diagnosis from similar changes in other diseases is discussed. Specific destructive changes, found in 45 (41%) of the cases, may be mild, pseudocyst formation; severe bone destruction resulting in an almost explosive process in a phalanx; in most cases it is confined mainly to the subarticular, more vascular, part of the bone, resulting in collapse of the articular surface and joint-cupping deformity; while in some cases reaction in soft tissues may cause subperiosteal erosion, concentric or eccentric. Specific changes may also be found in lepromatous cases without history of lepra reaction: pseudocyst formation, or subarticular honeycombing of metacarpals and phalanges, or enlarged nutrient foramins, or tubular formation of the shafts of metacarpals and metatarsals in children. Nonspecific erosive and destructive changes are ascribed to chronic nonspecific infection, not to neutrotrophic changes. Nearly all of the patients had some loss of sensory or motor function, and 83% showed nonspecific changes. Acute changes of this kind are osteitis, giving the appearance of hazy bone destruction, and osteomyelitis, resulting in destruction of the shaft with subperiosteal involucrum. Chronic changes are concentric erosion of the outer layer and laying-down of new bone within the medulla, and fragmentation of bone. In the healed or quiescent stage there occurs absorption of the terminal phalanges. Osteoporosis, found in only 23% of the cases, is considered to be a nonspecific change associated with disuse. —DHARMENDRA

SOMERSET, E. J. AND SEN, N. R. Leprosy lesions of the fundus oculi. British J. Ophth. **40** (1956) 167-172.

Leprosy lesions occur much less often in the eye than in other organs, and a lesion in the fundus is extremely rare. Leprosy of the eyes is less common in Bengal than in many other parts of the world. The authors describe two cases of leprotic retinitis occurring in relatively young people who had had the disease for at least 25 years. The first case was discovered in the 108th leprosy patient examined, and the second in the 224th patient. Both presented several round, discreet, yellowish nodules in the periphery of the retina which seemed to be identical with similar nodules in the iris. Most of these cleared under general antileprosy treatment.

Neither patient had ocular symptoms from the retinitis, whereas symptoms from lesions in other parts of the eye are quite common.—[Abstract from *American J. Ophth.* **42** (1956) 681, supplied by Sr. Hilary Ross.]

FLOCH, H. Gale norvégienne et lèpre. [Norwegian scabies and leprosy.] Arch. Inst. Pasteur Guyane Française et Inini, Publ. No. 391, 1956.

In these notes on two observations of Norwegian scabies the author remarks on the rarity and difficulty of diagnosis of this malady. The diagnosis is evident when the microscopic examination shows a multitude of Sarcoptes, which are identical with those found in scabies vulgaris. The condition affects persons in poor general health, and who live under miserable conditions of existence. The three classical elements of the affection were complete in both cases: cornified formations, polymorphous eruptive elements, and erythrodermia. As regards the relationship between leprosy and the scabies crustosa of Boeck, one of the patients—who had lived in a leprosy endemic country for 25 years—showed no symptoms of that disease, while the other had leprosy of long duration with marked anesthetic and atrophic disturbances. It is therefore impossible to draw an argument in favor or against an influence of leprosy in favoring the appearance and evolution of Norwegian scabies.
—AUTHOR'S ABSTRACT

TREFOUÉL, J. Chimiothérapie de la lèpre. [Chemotherapy of leprosy.] Atomes **11** (1956) 15-17.

The author reviews his studies on chemotherapy, in collaboration with Fourneau, which led to the development of the sulfones. In work with drugs against protozoa he observed the importance of the position of radicals in the molecule. Thus, the shifting of the methyl group from one benzene nucleus to another may suppress therapeutic activity and increase toxicity. However, in studying Prontosil, it was found that certain modifications of one of the two benzene nuclei, the one bearing two amine radicals, had no influence on the therapeutic activity. Separation of the benzene nuclei resulted in *p*-aminophenylsulfamide (1162F). This substance is more active than Prontosil *in vivo*, and is active *in vitro*. With this product the usual rules applied; any chemical modification nullifies or diminishes the therapeutic activity, with the exception of substitutions on the sulfamide radical. He then proceeded to prepare a series of products in which the S atom was more and more oxidized. Thus was obtained di-(p-aminophenyl)-sulfone, or 1358F—the parent sulfone—which is active against the Koch and Hansen bacilli. Although other products are now being used in tuberculosis, this sulfone has been found remarkably effective in leprosy. It is only slightly toxic, is inexpensive, and now constitutes the basic treatment of leprosy, the prognosis of which it has radically altered. —M. VIETTE

DAVEY, T. F. [Testing of new drugs.] Lep. Rev. **27** (1956) 70-73 (correspondence).

In this communication (without title) the author offers his views about the testing of new drugs. It does not follow that because a drug has been found safe in short-term trials in tuberculosis it will be safe for use in leprosy, which involves long-term treatment. Although the number of leprosy centers suitable for primary trials is limited, any such trial should be initiated in two or three of them simultaneously, later—if the drug is found safe and promising in 6-9 months—to be extended to less fully-equipped centers. Patients selected for first trials should not be advanced lepromatous cases, for they are in need of the best treatment available (the sulfones) and that should not be delayed for 6 months or more while they are taking a drug of unknown value. Early lepromatous cases would be more suitable. Since they usually respond quickly to sulfone treatment, it would not take so long to arrive at a judgment about the activity of a new drug. Furthermore, active tuberculoid cases can yield rapid information. Under sulfone treatment they usually show signs of resolution within 3 months, and—acknowledging that spontaneous improve-

ment often occurs—failure of an entire trial group to show satisfactory results under a new drug within 3 months would have significance. If, starting with a group of early lepromatous and active tuberculoid cases, signs of drug activity appear, then more advanced lepromatous ones would be added to a total of not less than 16-20 of that type and 8-10 tuberculoids. With such a group 6 months would suffice for proof of activity, and 12 months for a short-term comparison with DDS. The success of sulfone treatment introduces an important ethical aspect in this matter. The multifaceted problem of controls is then discussed, with reference to individual *versus* group controls. Perhaps the accumulated experience with DDS in large numbers of cases of each type might afford a more accurate comparison than the findings in a small group could be. —H. W. W.

DAVEY, T. F. AND CURRIE, G. Clinical trial of diphenyl thiourea compound SU 1906 (Ciba 15095E) in the treatment of leprosy; progress during the first year. Leprosy Rev. **27** (1956) 94-111.

This substance is 4,butoxy-4',dimethylaminodiphenyl thiourea (or thiocarbanilide). The test was begun with a few lepromatous and tuberculoid patients, and as its effectiveness and nontoxicity became evident the number was increased to 40, now treated for 4-16 months. Each patient was matched against a corresponding one on DDS. The dosage was started at 1 gm., daily and increased gradually, while the tuberculoid cases were watched for signs of resolution. These signs appeared at the 1.5 gm. dose, and double that amount was then chosen as the standard maximum dose, which has been well tolerated. All of the lepromatous patients showed clinical improvement, the 12 under treatment for more than 12 months comparing favorably with the corresponding DDS patients. Bacteriological improvement was better on an average than with DDS for the first 9 months, and in several cases it continued without interruption. Improvement in the tuberculoid, borderline and indeterminate cases was similar with the 2 drugs. All of 5 severe lepromatous cases that were not making much progress under DDS showed improvement on a daily dose of 1.5 gm. There was similar improvement in 2 indeterminate cases showing fresh macules after 40 and 50 months of DDS treatment. In 3 cases with persistent neuritis under DDS that trouble has cleared up and they have shown general improvement. It is mentioned that a trial was made by Buu-Hoï *et al.* with a similar preparation, diethyloxythiocarbanilide [THE JOURNAL **24** (1956) 233], with good results. Schwartz *et al.* used yet another preparation in tuberculosis. The promising features found so far are absence of toxicity, infrequence of erythema nodosum, more rapid bacteriological improvement, and the indication that patients intolerant of DDS or ceasing to make further progress with DDS may benefit with SU 1906. It remains a question whether or not drug resistance will develop.—[From abstract in *Trop. Dis. Bull.* **53** (1956) 1435.]

BASSET, A. Peut-on préjuger du mode d'action des sulfones dans la lèpre. Notre expérience actuelle. [On the mode of action of sulfones in leprosy. Our actual experience.] Sem. Hôp. Paris **32** (1956) 143-146.

The complex *thymolée, diargentique* sulfone J.51 is as effective in the treatment of leprosy as the other sulfones, di- or monosubstituted. It is less toxic with respect to the red blood cells, and is indicated for deficient cases. *In vivo* it acts directly, without the production of DDS by hydrolysis.—[From author's summary.]

FLOCH, H. Discussion sur l'injection mensuelle de DDS "gros grains." [Discussion of the monthly injection of large-grain DDS.] Arch. Inst. Pasteur Guyane Française et Inini, Publ. No. 390, 1956.

With reference to the conclusions of a note on the subject by Montestruc *et al.*, the author again emphasizes the value of the use of monthly depot injections of DDS in 0.2% agar water. The sulfone blood level in the third week after an injection

of 1.80 gm. of large-crystal DDS is of the same order as that produced by 50 mgm. daily by mouth. If these sulfone levels are considered of value, so also should be, by analogy, that of the fourth week after an injection of 1.80 gm. of DDS in the agar solution. It is in fact advisable to avoid lowering too greatly the dose of this active drug, since the risk that the Hansen bacillus may acquire sulfone resistance is not negligible. A regular sulfonemia of 0.40 mgm.% of DDS is regarded as certainly more active and more advisable than that around the 0.04 mgm.% level, although the latter is actually recognized as the minimum requirement, and it permits monthly depot injections. —AUTHOR'S ABSTRACT

HUEHNE, W. H., WHANG YONG HI AND SCHMIDT, W. Beobachtungen bei der Behandlung von Lepra mit Thiosemicarbazon (Conteben). [Observations on the treatment of leprosy with thiosemicarbazone (Conteben).] Ztschr. Tropenmed. u. Parasitol. **7** (1956) 358-361.

A group of patients (67 lepromatous and 22 tuberculoid) who did not tolerate or respond to sulfone medication were treated for 1 year with Conteben (thiosemicarbazone), 150 mgm. per week, plus vitamins B_1 and C, and iron. Ulcerations of the skin and mucosa received additional local treatment with nasal emulsions, eyedrops and ointments of Conteben. The results were convincing. Chronic catarrhs of the nasal mucosa, conjunctiva and cornea subsided rapidly in most cases, and even old deep ulcers usually healed within a few weeks. In some cases the Conteben treatment was interrupted or discontinued because of arthritic and neuralgic symptoms, increase of temperature, pruritus, allergic eruptions, or edema of the eyelid. In 3 patients an erythema nodosum reaction developed. In most cases these symptoms were transient, and Conteben was well tolerated afterwards. —ERNST KEIL

TRAPPMANN, R. Behandlung der Lepra mit Oxyprocainpenicillin. [Treatment of lepropsy with oxyprocaine penicillin.] Ztschr. Haut- u. Geschl.-Krankh. **21** (1956) 104-113.

Of 6 patients with lepromatous leprosy who received daily intramuscular injections of 400,000 IU of oxyprocaine penicillin for 3 months, 1 was markedly and 2 were moderately improved; in 3 the treatment was of no avail. Four cases of indeterminate leprosy were considerably improved by this treatment. All 10 patients had been positive for leprosy bacilli prior to treatment. The treatment effected clinical improvement, but no success was seen histologically. Similar results were obtained in 4 comparable controls given parenteral promin treatment during the same period of time. The author thinks that oxyprocaine penicillin may be of use in the treatment of leprosy. —ERNST KEIL

LEIKER, D. L. Note on sulphone activity in malaria infection. Lep. Rev. **27** (1956) 66-67.

It was first noticed that a group of leprosy patients treated with DDS in a public hospital or in a dispensary in a malarial area had been free from that disease for more than a year. Then at the Miei leprosarium, also in a highly endemic area, only one case of malaria had been diagnosed during a year, and that was in a recently-admitted patient who had had only a single dose of DDS. Thick blood drops of all the patients were examined, but none was found positive. The conclusion that DDS has some suppressive action against malaria is regarded as permissible.

—H. W. W.

HANKS, J. H. AND GRAY, C. T. The metabolic properties of mycobacteria and the pathogenesis of mycobacterial disease. Adv. Tuberc. Res. (Basel) **7** (1956) 1-16.

The metabolic problems and properties of cultivable mycobacteria and of the non-cultivated *M. lepraemurium* have been surveyed in relation to the pathogenesis of mycobacterial disease. The metabolic repressions resulting from the evolution of

saprophytes to commensals and intermediate forms, to tubercle and Johne's bacilli and to the rat leprosy bacillus appear to form a continuous spectrum. Laboratory strains of tubercle bacilli recovered directly from animal tissue, for example, exhibit many of the metabolic properties of the non-cultivated *M. lepraemurium*. The trend toward strictly intracellular parasitism is characterized not only by increasing limitations of ability to gain energy from substrates *in vitro* but also by increasing susceptibility to certain intermediary metabolites and to tissue derivatives and serum and body fluids. Meanwhile the capacity to survive in intracellular environment is associated with low requirements for oxygen, the toxicity of lipids which disrupt cellular metabolism and oxygen demand, and with a persistent endogenous metabolism. The latter is an important determinant of infectiousness. The metabolic processes which shift the intracellular relationships in favor of the mycobacteria or of tissue cells remain challenging questions for investigation.—[Authors' summary.]

BERGEL, M. Patogénesis de la lepra. [Pathogenesis of leprosy.] Semana Méd. **109** (1956) 215-225 and 321-335.

An analytical study is made of the etiologic, epidemiologic, histopathologic and chemotherapeutic factors which could serve as a basis for the biochemical definition of the leprous state and for the interpretation of the pathogenesis of this disease. One can deduct from the illness that the leprous state is defined in terms of a favored auto-oxidation of lipids. The pathogenic factors of lepromatosis would consequently be those which favor the auto-oxidation of lipids. The author indicates studies to be made in order to supply a more complete experimental demonstration of this concept of pathogenesis.—[From author's summary, supplied by G. Basombrio.]

RAMOS E. SILVA, J. L'innervation de la peau ne paraît jouer aucun rôle dans le mécanisme de la sensibilization de la peau au dinitro-chlorobenzene; expériences sur des malades atteints de lèpre anesthésique. [The innervation of the skin plays no part in the mechanism of sensitization of the skin to dinitrochlorobenzene; experiments on patients with anesthetic leprosy.] Dermatologica (Basel) **111** (1955) 1-8.

Charpy has reported that integrity of the peripheral sensory pathway is essential to production of eczematous contact-type sensitivity to dinitrochlorobenzene in the guinea-pig, and that such sensitivity can be induced by application of the chemical to any portion of the sensory pathway up to and including the cerebral cortex. In the human, however, such sensitivity can be induced as readily in totally anesthetic areas of the skin of leprous patients as in skin areas in which sensation is intact. The intact peripheral sensory pathway is therefore not essential to the production of such sensitivity in the human. —HARRY L. ARNOLD, JR.

RODRIGUES VIEIRA, I. As formas polares de lepra à luz da histopathologia. [The polar forms of leprosy from the histological aspect.] Arq. mineiros Leprol. **16** (1956) 11-29 [English summary].

There are numerous and various histopathological aspects of leprosy lesions in which there exist at the same time structures and cellular elements common to both of the two polar forms, a phenomenon which has become more frequent since the advent of sulfone therapy. The author therefore concludes that there exists a single pathogenic line extending from the extreme lepromatous to the extreme tuberculoid, with a great variety of intermediate stages. Sometimes there is a greater or lesser predominance of the lepromatous element, or tuberculoid element may be similarly predominant; and at times there are doubtful stages equidistant between the two. All of this runs parallel to the immunoallergic condition of the organism. It is suggested that the Panamerican classification be revised to make it more malleable, more adaptable to these aspects of pathogenic continuity.—[From summary.]

[To illustrate this thesis, which is based on histopathology findings, the article has 12 photomicrographs which for the most part, affected by the processes of

reproduction, are not very helpful. One of them shows the extreme of the lepromatous condition, and in the legend it is pointed out that there can be no tuberculoid element there, that it is used to illustrate the concept that leprosy ranges in a single line of pathogenesis from this extreme (pure) lepromatous condition to a similarly extreme tuberculoid one, with an almost endless gamut of intermediate stages. Many cases regarded as lepromatous are far from pure because, when they acquire the slightest degree of immunoallergy, they lose their typical physiognomy and little by little show admixture of features related to organized tissue defence, which tends however remotely toward the tuberculoid configuration.—H. W. W.]

RICHTER, H. Bemerkungen zur Histologie der Leprareaktion nach Conteben. [Remarks on the histology of the lepra reaction after Conteben.] Dermat. Wchnschr. **134** (1956) 1071-1077.

During a febrile lepra reaction, nodules resembling erythema nodosum developed in a lepromin-negative patient with lepromatous leprosy who had been treated with Conteben (thiosemicarbazone), INH and DDS. Although Conteben treatment was continued, the reaction subsided after a few days. Histological examinations of a fresh reaction nodule revealed, as the most important finding, fibrinoid degeneration of the collagenous connective tissue as it is only found in very fresh foci. The fibrinoid degeneration is followed by fibrosis in the form of keloid-like proliferation. These changes bear a great resemblance to those seen in rheumatism and acute lupus erythematosus. At the border of the cutis and the subcutis, miliary granulomas consisting of infiltration-envelopes develop around the smaller vessels. At the same time large amounts of PAS-reactive material are deposited in the vascular wall. All these changes are reversible. —ERNST KEIL

ORTMANN, R. AND STEIGLEDER, G. K. Fettablagerungen in Granulom der Lepra lepromatosa. [Fat deposits in the granuloma of lepromatous leprosy.] Arch. klin. u. exper. Dermat. **202** (1956) 349-356.

Histological examination of a granuloma from a 62-year-old patient who had had lepromatous leprosy for 4 years was carried out, using the modern techniques of lipid demonstration according to Barker and polysaccharide staining with Schiff's periodic acid reagent. In the practically collagen-free nodule 2 types of storage cells were found in relatively large numbers. (1) Large epithelioid cells, rich in cytoplasm, containing deposits of lipid granules. These cells showed an eccentrically situated nucleus and a large nucleolus. (2) Cells containing inclusions so large that the nucleus was flattened against the border of the cytoplasm. The cellular inclusions consisted mainly of lipids and also contained polysaccharide and probably protein components. Numerous mitoses were discernible in the granuloma, usually in the close neighborhood of the vascular adventitia. —ERNST KEIL

CRAXI, P. Mucosclerosi del miccardio nella lebbra. [Mucosclerosis of the myocardium in leprosy.] Med. Sper. **24** (1953) 155-159.

Histological examination of the heart in 3 cases of leprosy revealed a diffuse increase of the interstitial connective tissue between the individual muscle fibers. The connective tissue did not have the solid aspect as in sclerosis; the phenomenon is called mucosclerosis, i. e., changes in the mucopolysaccharides of the ground substance which are brought about by changes in the plasma proteins, increased capillary permeability, and increased protein content of the interstitial fluid.—[Abstract from *Excerpta Med.* **9** (1955) 423.]

ROTBERG, A. Simpósio sôbre lepromino-reação e imunidade na lepra. 1933-1953. [Review of the lepromin reaction and immunity in leprosy, 1933-1953.] Rev. brasileira Leprol. **23** (1955) 1-22.

This is an extremely condensed review of the subject with 98 references, not including the literature on the nature of the reaction and experimentation with

animals, which has been dealt with by de Faria [THE JOURNAL **24** (1956) 121], or changes of the reaction (especially by BCG), reviewed by de Souza Campos [THE JOURNAL **23** (1955) 351]. Although it is not entirely complete or up to date (e. g., concerning the reading of the reaction only the schedule adopted by the Second Pan-American Conference, held in 1946, is given, and not the recommendations of the WHO committee or of the Madrid congress), it should be available in a more widely-understood language for anyone who might wish to inform themselves of the developments in this field. For the beginner, however, the profusion of older material of purely historical interest might prove a bit confusing. —H. W. W.

FLOCH, H. Utilisation de lépromines diluées. (IV) Résultats de l'injection intradermique d'extrait phéniqué de peau normale chez des malades atteints des différentes formes de la lèpre. [The usefulness of diluted lepromins. IV. Results of the intradermal injection of phenolized normal skin extract in patients with different forms of leprosy.] Arch. Inst. Pasteur Guyane Française et Inini, Publ. No. 394, 1956.

The Hayashi-Mitsuda integral leprosy antigen is composed of heterogeneous elements, each of which plays a part in the positivity or negativity of the intradermal reactions. These elements are, principally, the Hansen bacilli, the leprous tissue, and the nonleprous cutaneous tissue. In tuberculoid cases, habituated to react to a very poor antigen (the leprosy bacillus), the organism naturally reacts (late reading) to the Hansen bacillus in the intradermal injection of an integral leprosy antigen (90% of positivity). It also reacts to the intradermal injection of normal skin tissue (in this instance in only 54%; 67 tuberculoid patients). The organism of the lepromatous patient, on the contrary, is absolutely indifferent to the presence of the Hansen bacillus and does not react to it, and naturally it does not react to the introduction of integral lepromin. Consequently it should not do so to any of the different components of the latter, especially to the normal tissue, and the author has found this to be so in all of the 12 lepromatous cases tested. In the indeterminate cases the results are, as might be expected, intermediate: 72% of positivity to the integral antigen, and 55% of positivity to the normal skin antigen (76 patients). One cannot distinguish integral lepromin and normal skin extract. —AUTHOR'S ABSTRACT

DINIZ, O. AND ABRAHAO NETO, H. Reação de Mitsuda com antígeno preparado de lesões de lepra tuberculoide. [Mitsuda test with antigen prepared from tuberculoid leprosy lesions.] Arq. mineiros Leprol. **16** (1956) 30-41 [English summary].

This study of antigens prepared from tuberculoid skin lesions was made on 148 inmates of the São Tarcizio preventorium, of whom 88% were positive to the regular Mitsuda-Hayashi lepromin. With the tuberculoid antigens (readings made after 48 hours and 21 days) the Fernandez reaction was positive in only 25%, the Mitsuda reaction in 57%. In view of these results the authors agree with Wade that the findings in the Fernandez reaction with tuberculoid antigen are of little significance, because in this antigen there is so little bacillary protein, on which reactions of the tuberculin type depend.—[From summary.]

DE SOUZA CAMPOS, N., ROSEMBERG, J. AND AUN, J. N. Correlação tuberculina-lepromina. [Tuberculin-lepromin correlation.] Rev. brasileira Leprol. **23** (1955) 23-40 (summary and conclusions in English).

The authors' findings with BCG-vaccinated persons have been the same as they have reported previously; their results in other groups parallel those reported by various other authors. In summary: there is a high degree of agreement between the two reactions in (*a*) healthy persons without exposure to leprosy but with tuberculous infection, (*b*) healthy persons exposed to leprosy and with primary tuberculous infection, and (*c*) tuberculous patients; also (*d*) in BCG-vaccinated persons,

at least early after vaccination. On the other hand, lepromatous patients with the Koch infection present an almost complete disagreement, tuberculin positive but lepromin negative. The factors mainly responsible for lepromin positivity are infection by the Hansen bacillus, or by the Koch bacillus, or BCG vaccination. An organism infected by the Hansen bacillus and Mitsuda positive will be negative to tuberculin while it is not infected by the Koch bacillus, contrary to those infected by the Koch bacillus (or BCG) who will regularly be positive to both reactions. Mitsuda reactivity is irreversible, while tuberculin positivity may disappear spontaneously (although immunity remains), which would explain why in places without leprosy there are found people who are positive to lepromin but negative to tuberculin. Persons with lepromatous leprosy do not develop immunity and they remain nonreactive to lepromin, hence Koch-bacillus infection can induce only reactivity to tuberculin. The high degree of correlation between the two reactions seen in certain populations expresses only a more or less temporary parallelism between the manifestations of two phenomena, one the state of sensitivity to tuberculous infection, the other a state of resistance to leprosy infection. This is a matter of two dissociable and independent phenomena. —H. W. W.

LOWE, J. AND MCFADZEAN, J. A. Tuberculosis and leprosy—further immunological studies. Leprosy Rev. **27** (1956) 140-147.

This is a report of work done during the last months of Lowe's period in Nigeria, after he had become aware of the views of Carroll Palmer and associates regarding the nonspecificity of reactions to large doses of tuberculin. The subjects were 621 healthy children aged 5-16 years in schools near Uzuakoli, an area where clinical tuberculosis is uncommon but leprosy is common. The tuberculin used was of the PPD type; the lepromin was made and "standardized biologically" at Uzuakoli. The primary tuberculin tests were with 5 TU, and all individuals giving reactions less than 6 mm. were retested with 100 TU. With the smaller dose 32.2% were positive, while 53.2% of the 421 retested with the larger dose reacted positively. With the lepromin test counting 2-3 mm. or more as positive only 45% were positive. There was a significant correlation between the two reactions. The tuberculin-positive rates were regarded as higher than could be explained by the prevalence of tuberculosis in the area, the results of that test being similar to those reported for regions where a nonspecific factor is regarded as responsible for high-dose reactions. The possibility that, in leprosy-endemic countries, infection may contribute to such nonspecific reactions was one of the things in mind when this work was undertaken, but no conclusion on that point was possible. In the comparison of the results with low and high doses of tuberculin, the findings reported from four other areas and those in Nigeria are set forth in a tabulation which is condensed as follows: —H. W. W.

Country (investigated region of)	Age group (total)	Low dose			High dose[a]		
		Dose TU	No. of tests	Reactions 6 mm. or more	Dose TU	No. of tests	Reactions 6 mm. or more
Denmark	5–16	10	9,842	5%	100	8,874	6%
Mexico	5–15	10	1,727	37%	100	1,017	16%
Egypt	5–16	10	3,012	49%	100	1,237	57%
India	5–15	5	2,130	19%	100	1,121	63%
Nigeria	5–16	5	621	32%	100	421	53%

a In persons showing 5 mm. or less response in the low-dose test. —H. W. W.

Silva, D. and Chaves Rodrigues, A. B. C. G. e lepra. [BCG and leprosy.] Arq. mineiros Leprol. **16** (1956) 42-49 [English summary].

The authors administered heavy doses of BCG orally by the concurrent method of Arlindo d'Assis, a total of 1,200 mgm. In this way they succeeded in changing the Mitsuda reaction in 71 of 101 nonreactive cases, or 70%. This low percentage they attributed to the BCG, which was nearly always at the limit of validity. They consider, however, that this vaccination is of great value to strengthen immunity against leprosy.—[From summary.]

Kraus, E. and Dvorak, J. Allergie et immunité des nourrissons vaccinés par des doses massives de BCG "per os" selon la technique de de Assis. [Allergy and immunity in infants vaccinated with massive doses of BCG orally by the method of de Assis.] Presse méd. **62** (1954) 1680-1682.

Allergy to tuberculin should not be confused with true immunity in a person vaccinated against tuberculosis. A positive reaction to the BCG test is indicative of immunity; combined with a negative tuberculin reactivity, it is the most desirable condition. The authors consider persons with positive tuberculin and negative BCG-test reactions susceptible to tuberculosis. They have had a large experience with vaccination of infants with orally-administered massive doses of the Moreau strain of BCG (de Assis' method). Monthly revaccinations increased [to a certain point] the number of tuberculin reactors, from which it appears that the negatives after the first vaccination were slightly allergic but too weakly so to be detectable by the test (below-threshold allergy). After revaccination there is an increase in the number of subjects reacting positively to the BCG test, it appearing that in the ones who had negative reactions after their initial vaccination there was immunity but too slight to cause reaction (below-threshold immunity). Among infants revaccinated every month up to the sixth month of life, the proportion with positive tuberculin reactions decreases to 30%, while those with acquired immunity increase to 100%, i. e., they all react positively to the BCG test. There are no complications with these repeated vaccinations; the children gain weight normally, and they have no more minor infections and ailments than nonvaccinated children or children vaccinated intradermally.—[From abstract in *J. American Med. Assoc.* **157** (1955) 970. See also the following.]

Contrary to the general opinion, de Assis believes that the culminating point of immunization is the secondary tuberculin anergy (immunoanergy of Fourestier). In that case the BCG-test would give positive, and the Mantoux tuberculin test negative, reactions. The positive reaction to the BCG test is held by some to be an index of an infra-tuberculinic allergy (de Assis, Oliveira, etc.), but by others as proof of tuberculosis immunity (Sula). The authors have performed both tests simultaneously in healthy children, the BCG test to investigate antituberculosis immunity. Tuberculin, being mainly of protein nature, is distinguished from the bacillary bodies used in the BCG test, which consist chiefly of lipoids. These lipoids much first undergo hydrolysis within the histiocytes in order to liberate the tuberculin-type substances. The local infiltration of the tuberculin reaction is lympho-monocytic; the lesion provoked by the BCG test is composed exclusively of specific granulation tissue. The former resolves quickly, the latter cicatrices only after some time. There are persons hypersensitive to tuberculin who are negative to the BCG test. On the other hand, there are persons negative to tuberculin who are positive to the BCG test. This stage can be created artificially by administering massive, repeated doses of BCG by mouth. This shows that the positive tuberculin and BCG-test reactions are not of identical nature. The lympho-monocytic reaction provoked by tuberculin in the allergic organism has nothing in common with immunity. On the contrary, tuberculosis immunity is based on the formation of specific granulation tissue. In a group of children 6-14 years old, all Mantoux positive either

spontaneously or because of BCG vaccination, 3% did not react to the BCG test; and these are regarded as not immunized and candidates for oral BCG. On the other hand, among 667 children vaccinated with BCG, 24% were Mantoux negative but nevertheless reacted positively to the BCG test; and these are regarded as immunized. In Czechoslovakia the law requires that the BCG test be made before vaccination of persons whose tuberculin reaction has changed (*redevenus*) to negative, because persons with tuberculin reversion after BCG vaccination but positive to the BCG test exhibit violent local reactions if they are revaccinated. The authors believe that the state of tuberculin allergy is a harmful one. The ideal model of immunity would be that in which an individual reacts negatively to tuberculin and promptly (but not violently) to the BCG test. In 1951-1952 they followed-up 730 infants who at birth received a single 100 mgm. dose of BCG (Moreau). Six months later, 45% of these reacted positively to tuberculin and 75% to the BCG test. The negatives were given another 100 mgm. dose, and 6 months later 57% were positive to tuberculin and 97% to BCG. Thus, after an oral dose of 100 mgm. at least 25% of newborns do not acquire immunity. It follows that repeated administration of BCG in large doses by mouth is more effective than a single dose. In fact, after a third monthly dose of 100 mgm. all the subjects are positive to the BCG test, which means that all have acquired immunity. At the same time, 90% of them become negative to tuberculin. After a single oral vaccination, the BCG-test reaction reaches its greatest intensity about the fifth day, whereas in revaccinated subjects the maximum occurs in 48 hours. In some hyperimmunized babies they even found desensitization to the BCG test. However, none of the children thus vaccinated has become tuberculous. The authors used for these massive oral vaccinations the Moreau (Brazilian) strain of BCG, which they find has a weaker virulence and allergizing potency than the original strain.—[Abstract by F. van Deinse, supplied by M. Viette. The latter reports that in a footnote to the article reviewed, Fouriester wrote that in Czechoslovakia the BCG test is made by intradermal injection (presumably 0.1 cc.) of killed BCG diluted 15-20 times, whereas in France it is made by application of 20-25 mgm. of live BCG to a 2 cm scarification, and that this may explain why the Czechoslovakian workers obtained fewer positive reactions to the BCG test than to tuberculin.—EDITOR.]

PALMER, C. E. Tuberculin sensitivity and contact with tuberculosis. Further evidence of nonspecific sensitivity. American Rev. Tuberc. **68** (1953) 678-694.

More than 22,000 young women who entered 76 schools of nursing throughout the United States between 1943 and 1949 were tuberculin-tested with two doses of PPD (0.0001 and 0.005 mgm., = 5 and 250 TU) and were questioned regarding history of contact with tuberculosis, and also about places of residence since birth. The data show, as expected, that the frequency of first-dose reactors increases with increasing degree of contact with tuberculosis: from approximately 10% positives among those reporting no contact, to 20% in those with intermediate and 40% with close contact. Yet, the average sizes of the reactions did not vary with degree of contact. Increased exposure simply affects the frequency, not the intensity, on first-dose sensitivity. Moreover, place of residence does not affect the relation between contact and first-dose sensitivity. In contrast, the frequency of second-dose reactions, expressed as a percentage of those negative to the first-dose test, is shown to be entirely independent of degree of contact, but closely related to place of residence. Nearly 70% of the permanent residents of the southeastern states were positive to the second dose, compared with less than 30% in the rest of the country, regardless of whether they were classified as having had close, intermediate, or no contact with tuberculosis. Furthermore, 40% of those from the southeast had reactions 10 mm. or more in diameter, compared with 12% from the north and west. These results, together with previously-published material, are consistent with the hypothesis that

tuberculin sensitivity in human beings can no longer be regarded as being derived from a single source. Most reactions elicited by a low-dose intradermal test undoubtedly indicate specific tubercle-bacillus infection, spread by personal contact. Low degrees of sensitivity brought out only by large doses apparently represent infection by a different organism with a different mode of transmission. The latter (unidentified) organism must be antigenically related to the tubercle bacillus, highly prevalent in certain geographic areas, and apparently nonpathogenic for human beings. —[From abstract in *Leprosy Briefs* **7** (1956) 24.]

[Council, Medical Research.] B. C. G. and vole bacillus vaccines in the prevention of tuberculosis in adolescents. First (progress) report to the Medical Research Council by their Tuberculosis Vaccines Clinical Trials Committee. British M. J. **1** (1956) 413-427.

This lengthy progress report tells of a controlled study which involved the testing, beginning in 1950, of some 56,700 school children around 15 years of age in London, Birmingham and Manchester; then the vaccination of certain groups of them; and—this being the bulk of the report—follow-up examinations for evidence of tuberculosis over a period of 30 months (this work still continuing). The first tests, with 3 TU of OT, brought out some 16,000 reactors, and retests with 100 TU another 6,600, i. e., 28% and 12%, respectively, of the total. Of the 34,100 negatives, 14,100 were vaccinated with BCG and 6,700 with the vole bacillus, while 13,300 were left unvaccinated. The annual incidence of tuberculosis per 1,000 in the BCG group was only 0.37 and in the vole-bacillus group 0.44, while in the negative unvaccinated group it was 1.94. Among the participants who reacted to 3 TU the rate was 1.75, while among the high-dose reactors it was only 0.74. The vaccines each "conferred a substantial and similar degree of protection" during 2½-year period of adolescence covered by the follow-up to the time of the report. Regarding the results in the group that reacted only to 100 TU, mention is made of the view of certain workers that such reactions are nonspecific, with the statement that if "they were *all* nonspecific, the incidence of tuberculosis among [them] and that in the negative unvaccinated group might be expected to be similar (unless the non-tuberculous allergy is associated with some protection against tuberculosis)." Later it is pointed out that the difference between the tuberculosis rates of the nonreactors who were not vaccinated (1.94) and the high-dose reactors (0.74) is not what "would be expected if positive reactions to 100 T. U. only were non-specific for tuberculous infection. The interpretation of weak reactions to tuberculin requires further investigation." [Apart from the parenthetical statement quoted, nothing is said of a possibility that some other factor with an antigenic but not pathogenic relationship to the tubercle bacillus might possibly cause, by cross-effect, weak sensitivity to tuberculin but substantial protection from infection by that bacillus.] —H. W. W.

Honda, H., Oshima, T., Morita, Y., Shirai, S., Sakurai, H. and Iguchi, K. Studies on serum reaction for leprosy. Comparison of Ogata's agglutination method with Honda's complement fixation method. La Lepro **25** (1956) 45-49 (in Japanese; English abstract p. 45).

Subsequent to the introduction of the antigen for complement-fixation test in 1951, Ogata reported his agglutination method. The authors have made a comparative study of that method and Honda's complement-fixation method. In 62 lepromatous cases the complement-fixation test was positive in 55 and the agglutination test in 44; in 29 neural cases the former was positive in 16 and the latter in 9; in 5 macular cases complement fixation was positive in 3 while agglutination was not observed. Both methods were negative in all nonleprous cases examined. From these results the authors believe that Honda's complement-fixation method is more favorable than the method of Ogata.—[From abstract.]

FLOCH, H. AND ANDRE, J. Sérologie de la lèpre; la réaction d'Ogata. [Serology of leprosy; the Ogata reaction.] Arch. Inst. Pasteur Guyane Française et Inini, Publ. No. 393, 1956; *also* Ann. Dermat. et Syphiligr. **83** (1956) 405-408.

While the Ogata reaction with the "syphilitic antigen" (cardiolipin:lecithin = 1:10) has always enabled the authors to detect unmistakably syphilis sera, yet on the other hand it seems that the same reaction with the "leprous antigen" (cardiolipin:lecithin = 1:1) cannot be regarded as specific for leprosy. This negative finding is in line with a previous report by the authors on the Kahn universal reaction, which also was presented as specific for leprosy. —AUTHORS' ABSTRACT

BRIEGER, E. M. AND GLAUERT, A. M. Electron microscopy of the leprosy bacillus; a study of submicroscopical structure. Tubercle (London) **37** (1956) 195-206.

Conclusions drawn from electron micrograms of whole bacteria may be deceptive unless the evidence is supplemented by examination of ultra-thin sections, and such sections of leprosy bacilli were examined in the hope that by that means it would be possible to decide whether differences seen in electron micrograms of unsectioned bacilli are due to genuine differences in internal organization. It was also thought that information might be gained about the structure of the "globi" or lepra cells. At a leprosarium in the Belgian Congo tissue juices from lepromatous lesions of 6 cases were embedded in agar, and punch specimens from three with the tuberculoid or macular lesions were also obtained. These specimens, fixed in osmic acid, were transported to England by air and embedded in methacrylate. The tissue specimens yielded no information. The bacilli of the tissue-juice preparations seen in electron micrograms ranged from short bipolar rods to filaments of different thicknesses and densities, and dense spherical forms are also seen; the bacilli also occurred in groups, or "globi." The relationship of these forms cannot be ascertained from a series of fixed preparations, but it was concluded that if the pleomorphism observed is not due to degeneration, the leprosy bacillus must have a complex life history. In the bacillus masses the bacilli are distinguishable as individual organism. In the globus they lie end-to-end, in parallel array, and are so tightly packed that it is not possible to distinguish them individually. Also seen were groups of bacilli contained within a limiting membrane, similar to the globi as described by Denney. The nature of this membrane cannot be deduced, but the possibility that it is the cell membrane of a disintegrating leukocyte is suggested. It cannot be said if the bacilli within these clumps are viable, although some have the density of apparently healthy organisms. —[From abstract in *J. American Med. Assoc.* **162** (1956) 253, supplied by Sr. Hilary Ross.]

[The original article, of which this abstract (here considerably condensed) was prepared faithfully although apparently by a nonleprologist (another has appeared in *Trop. Dis. Bull.* **53** (1956) 1432), is extremely interesting but decidedly confusing in the choice of terms employed. Thus "filament" is evidently applied to the whole bacillary rod as seen by ordinary optics, and "rod" to a small dense element sometimes seen, either within it or free-lying, in the micrograms. It is not clear if "lepra cell" is applied to the entire macrophage (histiocyte) containing the bacillary mass, or to the latter with perhaps some of the cytoplasm surrounding it (the "lepra cell' concept is apparently connected with Babes rather than Virchow); and there is uncertainty as to what was considered a "globus." The material was obtained from deep incisions into the lepromas, but the further manipulation involved in obtaining it is not stated. At all events it was apparently of the order of what is examined in ordinary smears, and certainly not of the leproma cells in their original location and relationships. As stated, the study was a preliminary one, primarily for purposes of orientation.—EDITOR.]

[South Pacific Commission] Tuberculosis investigations in the South Pacific (1950-1951). Technical Paper No. 12, May 1951, by E. L. Massal. Mimeographed, 74 pp.

In the course of the bacteriological studies it was concluded that for the finding of the tubercle bacillus direct examination by fluorescence microscopy after phenol-auramine staining was best. Nasal smears from leprosy patients were first examined by that method, then restained by Ziehl-Neelsen. Of 112 smears so examined, 4 were positive after Ziehl-Neelsen that had been found negative with auramine, and 1 gave the opposite result. —H. W. W.

De Souza Araujo, H. C. Isolamento e estudo experimental de duas novas culturas de bacilos ácido-álcool resistentes de muco nasal de leprosos. [Isolation and experimental studies of two new strains of acid-alcohol-fast bacilli from the nasal mucosa of leprosy patients.] Mem. VI Congr. Internac. Leprol., 1953; Madrid, 1954, pp. 837-842; *also* Mem. Inst. Oswaldo Cruz **52** (1954) 11-15.

Two strains of chromogenic acid-fast bacilli were isolated from the nasal mucosa of two girls with lepromatous leprosy. These strains showed growth at 37°C in Loewenstein medium, one in two weeks and the other in 25 days.—[Mainly from abstract in *Bull. Inst. Pasteur* **54** (1956) 2698.]

De Souza Araujo, H. C. Lepra experimental em *Macacos*. Ação patogenica de bacilos ácido-álcool resistentes isolados de leprosos (amostras "Chaves" e "Emilia") para a *Macaca mulatta* e o *Cebus fatuellus*. [Experimental leprosy in monkeys. Pathogenicity of acid-alcohol-fast bacilli isolated from leprosy patients ("Chaves" and "Emilia" strains) for *Macaca mulatta* and *Cebus fatuellus*.] Mem. Inst. Oswaldo Cruz **52** (1954) 619-652; (in English, pp. 653-673).

Inoculation of the hairless skin of the rhesus monkey with cultures of acid-fast bacilli isolated from leprosy patients gave rise to nodular lesions which were similar to lepromas, without generalization to either the hairy skin or the viscera, although there was elimination of bacilli in the feces and nasal mucosa. The histopathology of these nodules revealed, in some instances, a lepromatous structure followed by a tuberculoid one in reinoculations, which is a proof that there exists a certain degree of immunity. Bacilli were always re-isolated from primary lesions, and as a rule these retrocultures were found to be more virulent for monkeys than the suspensions of the respective nodules.—[From author's conclusions.]

Nishimura, S. and Iwasa, K. Basic studies on the screening test for chemotherapeutic agents for murine leprosy. Part III. Comparative studies on the subcutaneous inoculation method and Chang's intraperitoneal inoculation method and discussion of screening. La Lepro **25** (1956) 1-14 (in Japanese; English abstract p. 1).

This study is a comparison of the authors' subcutaneous inoculation method using dilute leproma suspensions and Chang's intraperitoneal method using a concentrated suspension as regards the time relation, technique, trustworthiness, quantitative relationship, and reproducibility. Various therapeutic agents tested by the two. Screening tests by intravenous, corneal, subdural, intraperitoneal and other inoculation methods used by other investigators are also discussed. It is concluded: (1) The time required for evaluation is the same with either method, but by using a 10^{-3} suspension subcutaneously it is possible to shorten the time. (2) With the subcutaneous method evaluation is limited to a single point, the site of inoculation, and since measurement can be made accurately with a gauge the technique is simple and accurate. (3) The subcutaneous method reveals the limits of the onset-inhibiting action of known agents, as INH, SM and DDS, with both the dilute and concentrated suspensions. It is believed that this finding is sufficient evidence for trusting the accuracy

of the evaluations. (4) For screening very small quantities of synthetic or extracted samples, subcutaneous inoculation of 0.2 cc. of a 10^{-4} suspension is more suitable than the intraperitoneal method. (5) Reproducibility is more accurate with the subcutaneous method, which is technically simpler, and evaluation is more objective and accurate.—[From abstract.]

FUJITA, Y., ICHIHARA, T. AND ICHIHARA, T. Studies on the susceptibility of mice to murine leprosy. Report I. The influence of mouse strain on susceptibility. La Lepro **25** (1956) 36-39 (in Japanese; English abstract p. 36).

The susceptibility of the experimental animal greatly influences the experimental results, and the accuracy of the results in the study of murine leprosy will no doubt be greatly enhanced if the white rats or mice used are of a highly susceptible strain. From this point of view a comparative study of the susceptibility to murine leprosy was conducted with four strains of mice, C57 EL/6, C_3H, dd and the Wistar strain of white rat. No significant difference in the degree of susceptibility was observed between the different strains.—[From abstract.]

FUJITA, Y., ICHIHARA, T. AND ICHIHARA, T. Studies on the susceptibility of mice to murine leprosy. Report II. The influence of sex and age of the dd strain mouse on susceptibility to murine leprosy. La Lepro **25** (1956) 40-44 (in Japanese; English abstract p. 40).

The influence of age and sex of the experimental animal on susceptibility to murine leprosy was studied in the dd strain (uniform strain) mouse. The animals were divided into four groups, immature, mature, male, and female. No significant difference in susceptibility was noted between the groups.—[From abstract.]

YOSHINAGA, T. On the influence on murine leprosy of DDS and promin. The study on the chemotherapy of murine leprosy. (Report III.) La Lepro **25** (1956) 31-35 (in Japanese; English abstract p. 31).

DDS prevents tolerably the development of murine leprosy. Its effect is almost the same as that of Promin, when the same dose of free DDS is used as the amount of DDS which is contained in Promin.—[From abstract.]

YOSHINAGA, T. AND KAKU, T. On the synthesis of N′-ethyl-p-aminobenzensulfonamide and N′,N′-diethyl-p-aminobenzensulfonamide, and its influence on murine leprosy, and therapeutic test of Pashydrazide. The studies on the chemotherapy of murine leprosy. (Report II.) La. Lepro **25** (1956) 25-30 (in Japanese; English abstract p. 25).

These drugs, synthesized by the authors for the treatment of leprosy, prevent tolerably the development of murine leprosy. Their effectiveness is of almost the same degree. Pashydrazide is pretty good in the therapeutic test with murine leprosy. —[From abstract.]

URABE, K., MATSUO, Y. HIRAMOTO, T. AND USHIO, K. Studies on the *in vivo* cultivation of murine leprosy bacilli. (Part 1.) La. Lepro **25** (1956) 15-24 (in Japanese; English abstract p. 15).

Cultivation of the murine leprosy bacillus *in vitro* has not proved entirely satisfactory. Studies were conducted on *in vivo* cultivation as an indirect aid in clarifying the mode of propagation of the bacilli. In order to avoid the partial observations resulting from *in vivo* methods used heretofore, phase contrast microscopy and the slide culture method *in vivo* were utilized. It was found that the bacilli show elongation, branching and granule formation, similar to the growth of other acid-fast bacilli, on the slide inserted under the skin of the white rat. It is suggested that the bacilli will multiply even in the absence of body cells if there is adequate infusion of body fluid in a susceptible animal (white rat) under conditions where invasion of body

cells is obstructed. Propagation of the bacilli in white rats sensitized to the bacilli is slow and very slight compared to the nonsensitized control.—[From abstract.]

Miscellaneous

The following references are from the *Current List of Medical Literature* of the Armed Forces Medical Library, Washington, D. C. The publications are not available to us, nor do we have Contributing Editors from whom abstracts can be requested, so it is not known whether or not they contain actual contributions.

RUDCHENKO, S. H., TUMASHEVA, N. I. AND SLUVKO, Z. A. Primenenie tibone pri lepre. [Application of TB-1 in leprosy.] Vest. Venerol. i Dermat. (Moscow) No. **2** (1955) 34-36.

BULKIN, A. K. Uskorenaia leprominovaia reaktsiia. [Rapid lepromin reaction.] Ibid. No. **4**, pp. 38-39.

TORSUEV, N. A. K voprosu o lechenii lepry. [Treatment of leprosy.] Ibid. No. **6** pp. 37-41.

LOGINOV, V. K. K voprosu o narusheniiakh obmena steroidnykh gormonov u bol'nykh leproi. [Disorders of steriod metabolism in leprosy.] Probl. Endokr. i Gormonoter. (Moscow) **1** (1955) 60-63.

OERIU, S. Contributii la prepararea de substante cu actiune inhibitoare asupra dezvoltării rezistentei microbiene in tratamentul tuberculozei si cu activitate in tratamentul leprei. (Preparation of substances inhibiting the development of bacterial resistance during therapy of tuberculosis and active in therapy of leprosy.) Stud. Cercet. inframicrobiol. si Parazit. (Bucharest) **6** (1955) 187-197.

JEZIL, V. Diagnostikované onemochnení leprou nervovou. [Diagnosis of neural leprosy.] Casopis Lékarú Ceskych (Prague) **94** (1955) 144-147.

With reference to the Torsuev item, we have recently received from this author a considerable number of reprints and two books, one of them of 582 pages, all on the subject of leprosy, all entirely in Russian before which we are helpless. —EDITOR