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.

[KENYA] Medical Department Annual Report, 1949. Government Printer, Nairobi, Kenya Colony, 1951.

An examination of 53,814 persons by J. Ross Innes, interterritorial leprologist, has revealed a leprosy prevalence of 10.2 per mil.—compared with 39.5 for Uganda and 14.3 for Tanganyika—and an estimated total of some 35,000 cases. Following his report a site for a leprosarium at Itesio, North Nyanza, near the Uganda border, was made available. Preliminary plans have been made to accommodate 500 persons on a settlement basis, for the more severe and infective cases. Most of the cases are of the noninfective kind and could be treated at home if a system of safe medication could be devised. Excellent results have been obtained with sulphetrone, and the simpler sulfone base has been introduced. The establishment of health centers, which has been started, may allow of home treatment. [Compare the view here expressed with that of Dr. A. B. MacDonald, in another abstract in this issue.] —H. W. W.

CHUNG-HOON, E. K. Hansen's disease in Hawaii, 1939-1949. Hawaii Med. J. **9** (1950) 305-309.

An average of 32 new cases of leprosy have been found annually in Hawaii for the past ten years. The annual morbidity has fallen from 9 per 100,000 in 1939 to 6 in 1949, although yearly fluctuations conceal this apparent downward trend. Over one-half of the cases are Hawaiian or part-Hawaiian, with a morbidity rate of 70 (per 100,000 per year) for the former group and 13.9 for the latter. Morbidity among Caucasians is 1.1, in Filipinos 13.6, in Orientals 2.6 to 8.6. One-third of the new cases are under 20 years of age, and one-fourth over 40. Four-fifths have had symptoms for less than a year when diagnosed. Two-fifths are bacteriologically negative at the time of diagnosis, and for the most part they are not isolated. Tuberculoid cases comprise 45%, lepromatous 41%, and indeterminate 14%. Knowledge of any contact with the disease is denied by 60%. The ratio of males to females is nearly 2:1 in lepromatous cases, but only 1.1 to 1 among tuberculoids. The proportion becoming bacteriologically negative and clinically inactive increased from 12% to 22% during the latter half of the 10-year period studied. —H. L. ARNOLD, JR.

GONZALES PRENDES, M. A. & IBARRA PEREZ, R. Epidemiología y profilaxis de la lepra en Matanzas. [Epidemiology and prophylaxis of leprosy in Matanzas.] Rev. Sif. Leprol. y Derm. **6** (1950) 101-118.

After a short note on the origin of leprosy in Matanzas, one of the smallest and least populated of the Cuban provinces, the authors report the finding of 148 nonsegregated cases, or 0.4 per 1,000 inhabitants. Regarding age, 73% are between 15 and 50. There is the usual predominance of males over females. Most of the patients are laborers, and the standard of living is low in more than 50% of them. The lepromatous

type predominates (66%). A majority (60%) are being treated, mostly in the dispensaries of the Patronato (PLECS). —F. R. TIANT

GONZALEZ PRENDES, M. A. & IBARRA PEREZ, R. Estado actual de los enfermos de lepra, provincia de Las Villas. [Status of leprosy patients in the province of Las Villas.] Rev. Sif. Leprol. y Derm. **7** (1951) 29-34.

For this important Cuban province, according to the statistical data of the Patronato (PLECS), there are 635 known cases of leprosy, 88 of them segregated in the 2 leprosaria of the island. This gives an index of 0.58 patients per 1,000 inhabitants. Regarding age and sex, 55.6% are between 20 and 50 years of age, and 58.7% are males. More than 1/3 of the patients are laborers, and the standard of living is decidedly low in 70% of them. As for the form of the disease, 66% are lepromatous. Of the 547 unsegregated cases, 68.7% are under treatment, mostly at the PLECS dispensary in Santa Clara, the capital of the province. —F. R. TIANT

LEPERS' TRUST BOARD. First Conference of the Lepers' Trust Board, Inc., Christchurch, New Zealand, 2nd December, 1950. Mimeographed, 26 pp., with printed paper cover.

This Board gives aid to leprosy work in various ways over a large area of the South Pacific, and this conference was attended by visitors from Fiji and elsewhere.

Report of the Fiji Board.—Sir Henry Scott, chairman of the Fiji auxiliary—the Lepers' Trust Board (Fiji) Inc.—reported on contributions to the government leprosarium on Makogai Island—mainly, it would seem, with funds received from New Zealand. Apart from an x-ray building these consist entirely of patients' facilities: a theater, separate recreation halls for boys, men and women, a workroom for women, a cooperative store building, a technical school for boys (projected), and among other things rehabilitation allowances for selected discharged patients. The inspector general of the South Pacific Commission, the territory of whose jurisdiction extends from New Guinea to Samoa, had proposed the sending of medical officers of the various island administrations to Makogai for special training, and had asked if the Board would aid in this project. This was agreed to.

Use of sulfones at Makogai.—In this report Dr. C. J. Austin, of Makogai, recounted the evidence that sulphetrone exhibits considerable toxicity in the patients of island origin, materially more than in Indians [see THE JOURNAL **18** (1950) 345-349]. Nevertheless, the results obtained had been encouraging although, because the period of healing of ulcers had passed, progress has been less dramatic than at first. The great majority of patients who were able to stand the drug have continued to improve, and 12 cases had become and remained bacteriologically negative, indicating superiority of sulfones over the former chaulmoogra treatment. Trials of DDS and thiacetazone have been started.

British Solomon Islands.—A report from Dr. J. S. McKenzie Pollock, senior medical officer of this Protectorate, was read. To trace the history of leprosy in this region, it is stated, would entail an anthropological thesis on the migrations of the Pacific peoples. Its presence in the Solomons was first recorded by various visitors around the middle of the 18th century. There are now, it is estimated, some 2,000 cases. Ross Innes, in 1938, made pilot surveys of Malaita, Nggela and Guadalcanal which indicated a

prevalence of around 2% in the areas investigated. It would not be practical to hospitalize all sufferers, and to attempt compulsory segregation might tend to concealment. The policy is to use the three existing leprosaria, Tetere (government, under development), Fauaba (mission, 25 beds) and Kukundu (mission, 40 beds) as treatment centers. Each Native Council is being urged to construct special houses near their villages where sufferers can live and yet not be completely out of touch with community life, and "this idea is catching on well" because an inborn fear of the disease exists. Voluntary colonies under government direction are being encouraged, and already two—on Malaita and Santa Isabel—have been formed and are working well. One mission, on Vella Levella, has 3 new dispensaries where good work is being done. There is close cooperation between the government and the missions concerned in this work, the former supplying the antileprosy drugs used.

The Tetere Leprosy Settlement.—This institution—actually the primary subject of Pollock's report—is under development on the coastal plain of Guadalcanal in an area of 4,055 acres where the American army had built roads which are still usable. This location, 2½ hours by launch from Honiara, where the specialist medical services of the protectorate are concentrated, has much arable land and a good water supply. The buildings, constructed of materials salvaged from an old army installation, are set up—so far as patients' housing is concerned—in units of four buildings, each unit to house 24 patients; 5 of them are planned, for a total capacity of 120. Other necessary facilities have been provided. Religious sisters have the immediate care of the patients, and the results of treatment of the first 15 months of operation are encouraging; 8 cases, "clinically arrested and relatively noninfectious," have already been discharged after 12 months treatment. To date £16,000 had been expended, besides a contribution of £6,000 from the New Zealand Board.

Report on Samoa.—In the absence of an expected official report, a brief informal statement was heard. Samoa is a closely-knit, well-organized community where, in the opinion of the chief medical officer, Dr. J. C. Lopdell, it should be possible to effect big inroads into the leprosy problem. The majority of the cases come from a relatively small number of pockets of infection. If they could be thoroughly combed out, it was believed, probably 80% of Samoan cases could be found. A mobile medical unit has recently been organized, staffed entirely by Samoan medical practitioners and nurses, and the possibility of attaching to it a practitioner with special training in leprosy is being entertained.

Leprosy in New Caledonia.—Included in this document is a report on this subject sent by Dr. E. Ragusin, of Noumea, which appears in this issue of THE JOURNAL.

Aspects of nursing in leprosy.—This contribution, by Miss M. I. Lambie, late director of nursing services of the South Pacific Health Board, deals largely with the principles which pertain to the care of leprosy patients who are sent to the isolation units of the hospitals in the area served by that organization, and who often have to be taken care of for months while awaiting transportation to Makogai. It also gives general information regarding the nursing set-up in this vast area. New Zealand's responsibility for nursing supervision there began, before World War I, with the Cook Islands alone; since then it has been extended gradually to numerous areas spread from Western Samoa to the Solomons, including

Fiji. In 1950 there were 100 New Zealand nursing sisters in the service and approximately 300 native nurses, for whom there are 7 training schools in different places. New Zealand nurses also work in several other areas, outside of the regular service.

Not without interest is the last item of this document, which tells of the activities involved in the raising of funds in New Zealand—totalling more than £23,000 for the year, as yet unfinished—and the handling of goods donated for the patients of the leprosaria in Fiji and the Solomons.
—H. W. W.

MISSION TO LEPERS. The Seventy-fifth Annual Report of the Mission to Lepers and Statement of Accounts for the Year ended 31st December, 1949.

This report tells of much encouragement in a situation often full of difficulties. The situation in China was causing particular concern. Selected incidents elsewhere: At Mandalay, in Burma, the leprosy home had for a day been involved in fighting when the rebel forces took cover in the wards. The Rawalpindi home, in the foothills below Kashmir in West Pakistan, was also affected by the local political situation; it was overwhelmed by patients in miserable condition from among the refugees from other areas. At the great Itu colony in Nigeria, a night fire destroyed the hospital with eight wards, and associated facilities. In some places there was a shortage of medical personnel, requiring adjustments and leading to recruiting efforts. In that connection, Dr. Muir had started his two-year term of service in India and Dr. Maxwell had gone to China for a like period in an honorary capacity—which is slightly ancient history. The mission (*a*) owns or manages 30 homes for leprosy sufferers in India, Pakistan and Burma, and 8 in China; (*b*) it also gives aid of one kind or another to homes or clinics at 24 other stations in India and Pakistan, 11 in China, 29 in Africa, and 1 in New Guinea—the institutions of these two categories having in total some 14,000 inmates and 1,200 healthy children—and (*c*) it has other connections with several places in Ceylon, Malaya, Union of South Africa and Paraguay. In this work it works in partnership with no less than 38 other organizations, representing many nationalities and religious denominations. The ordinary income in 1949 totaled £197,609 and the expenditures reached the hitherto unequalled total of £199,375.
—H. W. W.

AMERICAN LEPROSY MISSIONS. (Annual Report, 1950.) Lep. Miss. Digest **4** (1951) No. 1.

Apart from a financial statement, there is only a brief and informal statement under the name of Emory Ross, president, in this "Annual Report Number." Full support, or a major part of it, has been given 67 leprosy institutions, and auxiliary aid to 38 others; their distribution is not indicated. An important part of such aid consists of buildings constructed, but the mission vests ownership in each case to the particular organization which operates the institution. Help was given to the starting of two new colonies, one in Angola and the other in Indo-China. Funds have continued to be sent to China and Korea, almost without interruption. Distribution of diasone had been discontinued in favor of the cheaper sulphetrone, and the dropping of that in turn for DDS was contemplated. With the Mission to Lepers of London, arrangements are being made for a regional conference to be held in India in 1953; the physical side of all

leprosy work being properly the business of governments, consideration will be given to the things that Christian institutions can do better than governments. (Elsewhere in the magazine is reported a conversation with an African patient about a difference between missionary and government leprosaria. The government doctor "works from 9 to 12 and 2 to 5; and don't be sick in the middle of the night," whereas the missionary doctor is always ready.) The financial statement shows a total income of $607,205 for the year, and expenditures of $729,986. The total assets were $1,143,273.

—H. W. W.

[DICHPALLI, INDIA] Victoria Leprosy Hospital, Dichpalli, Hyderabad State, India; Annual Report, 1950.

A steadily increasing deficit caused by the rising cost of living has necessitated releasing some of the staff, with replacements by patients, and reduction of the number of inpatients receiving free treatment to 300 by discharging improved patients, not all of whom had met the criteria of noninfectiousness. The maximum permitted by the present research establishment would be 400. Twice as many infective cases which should be isolated for public health reasons are on the waiting list as in the institution, a hopeless situation. The medical staff consists of Drs. E. J. Currant, (medical superintendent, E. G. Daniel, house surgeon, and A. L. Furniss, pathologist. Sulphetrone (cost per patient per year Rs 22) is the main drug now used; a few patients are receiving promin (Rs·170), more are under diasone (Rs 130), and DDS (Rs 6) is being tried. Only a minority are receiving hydnocarpus oil (intradermal injections), but that drug is not yet outmoded and outpatient clinics throughout the state still need skilled injectors trained at Dichpalli. The physiotherapy department remains one of importance. During the year the farm and gardens supplied 37,000 lbs. of fruit and vegetables and produced 12,000 lbs of rice.

—H. W. W.

LAMPE, P. H. J. & BOENJAMIN, R. Social intercourse with lepers and the subsequent development of manifest leprosy. Doc. Neerl. et Indonesica Morb. Trop. **1** (1949) 289-346.

[The essential features of this lengthy report are included in the article by the junior author which appeared in THE JOURNAL **19** (1951) 277-282.]

DO PÁTEO, J. D., JR. Da lepra incipiente na vigilancia sanitária dos fócos domiciliares (Estudo dos Comunicantes). [Incipient leprosy in the sanitary supervision of domiciliary foci; a study of contacts.] Rev. brasileira Leprol. **17** (1949) 249-263.

In the section of the Leprosy Prophylaxis Department of São Paulo which is responsible for this work, 72,079 contacts had been registered in 24 years of operation to the end of 1945, and among them 796 cases of leprosy had been found. The data are set forth mainly in a series of tables and graphs which have much of interest for anyone concerned with this feature of the epidemiology of the disease. The period of observation before discovery was between 1 and 5 years in 75% of the cases. The type incidence was: indeterminate, 639 (80.3%); lepromatous, 96 (12.1%); and tuberculoid, 61 (7.7%). The sex distribution was: males, 414 (52%); females, 382 (48%). More than one-third (36.2%) were under 16 years of age (none under 2 years) when discovered. This age group had 59% of

the tuberculoid cases (49% being in persons under 10 years of age), but there was little difference with respect to the other types. Persons over 40 constituted 9.4% of the total. The presentation with respect to the cases between these extremes does not permit subdivision along ordinary lines, these data being dealt with according to "bio-physiological periods." A graph drawn on that basis shows a sharp peak (199 cases) in infancy, a marked drop for the prepuberty period, going still farther (52 cases) for puberty, and then a sharp rise for adolescence and the preadult period (134 cases) to the maximum in the period of "increasing virility" (248 cases); after that the curve drops abruptly to the lowest levels of all. Regarding the relationship of sex and type, 61.5% of the lepromatous cases, 52.1% of the undifferentiated, and only 36.1% of the tuberculoid ones occurred in males. Of the cases to which these contacts had been exposed, 80.4% were lepromatous, 19.6% indeterminate, and none tuberculoid. The author concludes that the female sex has a relative immunity to infection, as indicated by the lesser number of cases [although actually the difference is not great] and the greater proportion with the tuberculoid form. There is a close relationship between the time of appearance of lesions and the period of sexual development. The value of periodical examinations of contacts is emphasized. —H. W. W.

MACDONALD, A. B. [Infectiousness of neural cases.] Lep. Rev. **22** (1951) 36-38 (correspondence, without title).

The writer cites an article by Davison, of Pretoria [evidently referring to the one which appeared in THE JOURNAL **17** (1949) 247-252], on the infectivity of neural leprosy, in which it is stated that in "neural or non-lepromatous" cases the bacilli will be found with a frequency in direct proportion to the energy expended in looking for them, and that very high proportions of neural cases studied—those which had not responded to treatment and hence had remained in the leprosarium—had either changed to lepromatous or had shown bacilli in their nasal smears without change of clinical type. This disquieting report, the writer says, is in keeping with his own opinion based on experience at the Itu colony in Nigeria, where there are roughly 800 lepromatous and 2,700 neural or tuberculoid cases. There are many neural parents with neural children, and they—including the intelligent and educated element—say they have had no contact with any other form of the disease; and it is held that not all of them can be wrong. A survey of a tribe in the neighborhood revealed 7% of several thousand individuals examined with leprosy, but only 5% of the cases were lepromatous. "It is difficult to credit that all these [persons] acquired the disease from a relatively few positive cases." Can it be confidently said, it is asked, that cases with obviously active erythematous lesions, spreading or multiplying, are noninfective? To regard neural cases as noninfective, and to leave them—such as will come to dispensaries—to the totally ineffective outpatient treatment, is a convenient and inexpensive policy but one based on an assumption which, in the writer's opinion, will not stand the test of time. [Compare the view here expressed with that of the director of medical services of Kenya, in another abstract in this issue.] —H. W. W.

URRETA ZAVALLA, A. Resultados del examen gonioscopico de los enfermos de lepra. [Results of gonioscopic examination in leprosy patients.] Rev. brasileira Leprol. **17** (1949) 227-236.

The author examined by means of the Goldman crystal the angle of the anterior chamber in 29 leprosy patients. No changes in that region were found in 10 tuberculoid cases, or in 2 of the incharacteristic form, or in 2 in which the disease had transformed from incharacteristic to lepromatous. In 15 lepromatous cases of long duration, changes were seen in the irido-corneal sinus only when there were lesions of the part of the iris which is ordinarily visible. These changes consisted of miliary nodules, goniosynechias, anterior peripheral synechias, and loss of substance of the root of the iris. In only one case were miliary nodules seen in the sinus of one eye which appeared to be free from other leprosy lesions; the other eye showed such lesions in the cornea and the iris.—[From author's summary.]

RECODER FABRE, J. M. [Cyanosis in leprosy.] Rev. Fac. Quím. y Farm. Paraguay (1949) 61 (Nos. 10-11).

The purpose of this study is to ascertain the probable cause of the cyanosis usually seen in the different forms of leprosy. The author found that condition in 75% of lepromatous and 45% of tuberculoid cases. The capillary hemoglobin content is low and is liable to produce cyanosis. The reasons may be: (1) circulatory disturbances of the affected areas, and (2) transformation of the hemoglobin into meta- or sulfohemoglobin derivatives as an outcome of toxic participation on the part of other organisms.—[From abstract in *Bol. Of. San. Panamericana* **29** (1950) 1087.]

FLOCH, H. & DESTOMBES, P. Les lèpres ulcéreuses: "Lèpre lazarine" et "lèpre de Lucio." [Ulcerous leprosy: "lazarine" and "Lucio" leprosy.] Inst. Pasteur Guyane et Terr. Inini, Publ. No. 217, October 1950.

In connection with a case of "lazarine leprosy" seen in a European in French Guiana, the authors have returned to the question of the terms "lazarine leprosy" and "Lucio leprosy." Theoretically, "lazarine leprosy" should be reserved for the diffuse lepromatous form of Latapi, as yet reported only from Mexico and Costa Rica. Wade believes that the term "Lucio leprosy" should be applied to the pure diffuse lepromatous form with acute outbreaks of necrosing vascularitis [of Latapi], and proposes the transfer of "lazarine leprosy" to the bullous acute reactions of tuberculoid leprosy. The first of these propositions appears to be satisfactory. As for the second, which would retain the term "lazarine," confusion would persist since sometimes it would be applied to the lepromatous Lucio form (rule of priority), and sometimes to tuberculoid leprosy—i.e., to the opposed polar forms of the disease. It seems better, therefore, to abandon the term entirely. There are thus two forms of ulcerous leprosy, one a tuberculoid ulcerous reaction and the other a leprotic ulcerous reaction in a truly special form of lepromatous leprosy, and these two forms of Hansen's disease can readily be included in the cadre of the international classification adopted in Havana in 1948. —AUTHORS' ABSTRACT

GOMEZ ORBANEJA, J. & GARCÍA PÉREZ, A. Un caso de lepra lazarina. [A case of lazarine leprosy.] Actas Dermo-Sif. **42** (1950) 47-53.

The authors presented before the Academy a supposed case of spotted leprosy (*lepra manchada*), or the lazarine leprosy of Lucio, which they had studied completely, both clinically and histologically. There was active discussion of this interesting case. —F. CONTRERAS DUEÑAS

GÓMEZ ORBANEJA, J. & GARCÍA PÉREZ, A. Un caso de lepra intermediaria. [A case of intermediate leprosy.] Actas Dermo-Sif. **42** (1950) 45-47.

The authors presented before the Academy of Dermatology a patient 22 years old with contradictory clinical, immunological and bacteriological findings. There were lesions identifiable as tuberculoid, together with others undoubtedly lepromatous. The histological examination revealed vacuolated epithelioid cells without fat but with bacilli, separated from the epidermis by a normal band of collagenous tissue. The authors believe the case to be intermediate leprosy, holding such cases to be of importance because of the great frequency with which they transform to frank lepromatous. —F. CONTRERAS DUEÑAS

GÓMEZ ORBANEJA, J. & GARCÍA PÉREZ, A. Eritema nodoso en la lepra. [Erythema nodosum in leprosy.] Actas Dermo-Sif. **42** (1950) 258-272.

After a very complete study in which the history of this matter is compiled, the authors conclude that the nodular syndrome seen in lepromatous cases is not an intercurrent one, but rather is related to the disease in its evolution. It is held that the sulfones do not intervene in the determination of this syndrome, although it is sometimes presented in patients treated with these drugs. —F. CONTRERAS DUEÑAS

SIMONS, R. D. G. PH. Een geval van lepra anaesthetica (N_1) na een traumatisch lepreus primair affect (?) waarbij een voorheen nog niet beschreven leucoderma leprosum latens kon worden aangetoond. [A case of anesthetic leprosy with a primary lesion following trauma, with a hitherto undescribed leucoderma leprosum latens.] Geneesk. Tijdschr. v. Nederlandsch-Indië **82** (1942) 353-363.

A case is described in which the first manifestation is supposed to have been an analgesic area on the knee developing some weeks after trauma. This area was still present as an atrophic scar, central in an anesthetic area larger than the palm. No other skin lesions of leprous nature were to be seen. Said not to have been described before is a condition called "leucoderma leprosa latens" which could be made visible as an area of leucoderma in a berlock dermatitis caused by bergamont oil. Sunburn alone could not provoke this phenomenon. —R. BOENJAMIN

ARGUELLES CASALS, D. Una forma clínica de lepra tuberculoide; la lepra arciforme, purpúrica y pigmentada de los miembros inferiores. [A clinical form of tuberculoid leprosy: arciform, purpuric and pigmented leprosy of the lower limbs.] Bol. Soc. cubana Dermat. y Sif. **7** (1950) 192-195.

The author reports a clinical variety of tuberculoid leprosy of which he has seen 5 cases, always in women. The lesions, 2 or 3 in number, occur only in the legs. They are oval shaped, rarely more than 2 inches in diameter, with a well-marked border in which are seen purpuric points and some pigmentation. The center is slightly atrophic and hypopigmented. The usual troubles of sensibility are elicited in the lesions, and their pathology is typically tuberculoid. They have a very slow eccentric evolution. —F. R. TIANT

VILANOVA MONTÍU, X., LLORENS RIBAS, M. & ALVARADO, L. Epitelioma sobre leproma. [Epithelioma on top of a leproma.] Actas Dermo-Sif. **42** (1950) 39-43.

Referring to other cases of this complication previously seen in the same school, the authors report a new observation of a case with a basal cell tumor which was cured by roentgen rays. —F. CONTRERAS DUEÑAS

TAKAHASHI, T. Squamous celled carcinoma on knee. La Lepro **19** (1950) No. 3-4, pp. 31-32 (in Japanese); English abstract, p. 2.

A rare case seen in my hospital was a patient crippled by neural leprosy who had to walk on his knees and developed a cancer in that location, diagnosed as squamous celled carcinoma.—[From abstract.]

RATH DE SOUZA, P. & DE SOUZA LIMA, M. Sôbre o mecanismo da ação terapêutica dos derivados sulfonicos na lepra lepromatosa. [Mechanism of action of the sulfone derivatives in lepromatous leprosy.] Rev. brasileira Leprol. **18** (1950) 59-68 (summary in English).

This presentation of views developed from experience with material from some thousands of cases depends in large measure on 15 photomicrographs which demonstrate first an active lepromatous lesion, and then several which have regressed in varying degrees in cases some of which had been treated with sulfones and others which had not. Several are designed to show the acid-fast bacilli (which usually cannot be made out) while certain others represent the appearance of sections after staining with scharlach R. The authors do not deny that the sulfones may have a direct action on the bacilli, but they are more ready to believe that they do not go farther than to start off, speed up and intensify some mechanism which seems to be present in the Virchow cell-Hansen bacillus complex, acting principally on the cell component in some way so as to alter its metabolism and render it an unsuitable medium for the multiplication and survival of the bacillus. An identical mechanism also occurs, although not so regularly and effectively, as a result of other forms of treatment or even at times under natural conditions, i.e., without treatment. The characteristics of the receding lesions are: swelling of the Virchow cells, pycnosis of the nuclei, vacuolation of the cytoplasm producing the foamy appearance, and presence of lipids in the vacuoles in quantities inversely proportional to the numbers of bacilli—all of these changes evidencing injury of the cells— and diminution in the numbers of bacilli with granular appearance—this a sign of injury of the bacilli. It is believed that the cellular degeneration occurs before that of the bacilli. —H. W. W.

FLOCH, H., LECUILLER, A. & DESTOMBES, P. Mode d'action des sulfones dans la lèpre. Comment agit la succinyl-diamino-diphényl-sulfone (sulfone monosubstituée) administrée par la voie intraveineuses. [Mode of action of sulfones in leprosy. How succinyl diamino-diphenyl sulfone (monosubstituted sulfone) acts when administered intravenously.] Inst. Pasteur Guyane et Terr. Inini, Publ. No. 224, February 1951.

In 2 years experience in the treatment of 60 patients with the monosubstituted product, succinyl diaminodiphenyl sulfone, or 1500F [see THE JOURNAL **19** (1951) 99], the authors have concluded that this drug owes its antimycobacterial action *in vivo*, at the outset to the direct action of its molecule itself; later, to the action of DDS liberated by partial hydrolysis in the organism; finally, to the action of a sulfonated product elaborated by the organism from the monosubstituted sulfone. To confirm and make precise this view they made for several months sulfone determinations of

the blood and urine in many patients who were receiving this drug in daily doses of 1 gm. given intravenously. They found that only a very small part of the dose injected is hydrolysed. The average value of the H/SH ratio was 1.36 for the blood and 1.35 for the urine, figures which indicate that the amount of free DDS is at the most about 10%. With respect to the blood levels found, the free DDS had an average maximum value of 0.15 mgm., an amount entirely insufficient to explain the action of the drug by break-down to the mother substance. At least 90% of the drug is eliminated in the urine unchanged. These results are entirely different from those which the authors have obtained with disubstituted sulfones. They confirm the view that, while these latter drugs act in the organism only when reduced to DDS, the monosubstituted sulfones act directly by their own molecule, a conclusion which had previously been arrived at from other considerations. —AUTHORS' ABSTRACT

FLOCH, H., LECUILLER, A. & DESTOMBES, P. Mode d'action des sulfones dans la lèpre. Comment agit la promin (sulfone disubstituée) administrée par la voie veineuse. [Mode of action of sulfones in leprosy. How promin (disubstituted sulfone) acts when administered intravenously.] Inst. Pasteur Guyane et Terr. Inini, Publ. No. 225, February 1951.

Concerning sulfones injected intravenously in man, Wade has said that "no DDS determinations of bloods and urines of actual patients treated with such drugs parenterally have been seen." In several patients receiving 5 gm. of promin intravenously per day, the authors have sought to determine, for one thing, the variations in blood concentration and urinary elimination during the hours following the injection, and, for another thing, the proportion of the promin which is broken down in the blood and the form in which it is eliminated in the urine. It was found that a large part of the injected drug is eliminated during the first two hours, 100 cc. of urine containing the DDS equivalent of 1.8 gm. of promin, or 36% of the drug injected. The sulfone is found eliminated in the same forms and the same proportions as it exists in the blood at the same moment, i.e., 42% promin and 58% DDS. Later, although one still finds that proportion in the blood (apart from the possibility of the presence of a monosubstituted sulfone derived from promin), only pure DDS is eliminated in the urine. It therefore seems that in the blood itself, and throughout the organism more generally, promin is ultimately transformed entirely into the parent sulfone, more or less rapidly in different cases. Without rejecting entirely the hypothesis of the formation of a monosubstituted sulfone in the organism from promin, the results obtained clearly indicate that the therapeutic effect of the disubstituted sulfones is by means of the parent sulfone. The monosubstituted derivatives resulting from the degradation of promin can at most represent transitory stages of the transformation of the complex sulfone to DDS.

—AUTHORS' ABSTRACT

FLOCH, H., LECUILLER, A. & DESTOMBES, P. Mode d'action des sulfones dans la lèpre. Comment agit la diamino-diphényl-sulfone (sulfone-mère) administrée par les voies buccale et intramusculaire. [Mode of action of sulfones in leprosy. How DDS (the parent sulfone) acts after oral and intravenous administration.] Inst. Pasteur Guyane et Terr. Inini, Publ. No. 226, March 1951.

To determine if DDS occurs in the blood and urine free or in a conjugated form, the authors have made daily determinations by direct diazotization and after hydrolysis according to the technique of Marshall. One group, 7 patients, received 1.20 gm. of DDS per weekly intramuscular injection (10 cc. of a suspension in physiological saline containing 1.25% agar). The other group, 6 patients, received daily 0.2 gm. of DDS by mouth. It was found that after intravenous administration DDS remains unchanged in the blood and urine. When taken by mouth, however, it is found in both fluids partly in a conjugated form, the proportions of which vary quite widely. Nevertheless, even in the latter case it is probably the DDS itself which is active, because of the instability of the derivative and because most of the drug remains free (80% on the average, varying from 68% to 92%). In any case, the behavior of the parent sulfone in the organism differs according to the route of administration, probably due to a function of the liver which is necessarily involved when the drug is administered orally. This difference of behavior may be correlated, without drawing any more precise conclusion, with the authors' previous observation that leprotic reactions are much less frequent when the drug is given intramuscularly (8%) than when the oral route is used (47%).

—AUTHORS' ABSTRACT

FLOCH, H., LECUILLER, A. & DESTOMBES, P. Mode d'action des sulfones dans la lèpre. Comment agit la succinyl-diamino-diphényl-sulfone (sulfone monosubstituée) administrée par la voie buccale. [Mode of action of sulfones in leprosy. How succinyl DDS (monosubstituted sulfone) acts when given orally.] Inst. Pasteur Guyane et Terr. Inini, Publ. No. 227, March 1951.

Previous experiments have shown that this drug (1500F) given intravenously is found only slightly decomposed in the blood and urine. Similar results have been obtained with "1500F-retard," after intramuscular injection. An attempt has been made to ascertain if the results would be different after oral administration, as in the case of DDS, using the same methods as in that study [see preceding abstract]. It was found, contrary to the experience with intravenous administration, that only about 40% of the drug is found as such in the blood. This proportion of the unmodified compound is nevertheless higher than that observed with the disubstituted sulfones when taken by mouth; with cimédone [sulphetrone] about 80% is decomposed. In patients receiving this drug by mouth, 3 gm. per day, determinations made before and after acid hydrolysis gave an average ratio of 1.16. (Smith found this ratio to be 1.69 for the pure product.) Assuming that only the parent sulfone and cimédone are recovered in the blood, one can calculate the proportion of the latter substance in relation to the former at about 20%, or one-half of what the authors have found for 1500F. In any case, it is evident that cimédone is transformed into DDS in the organism, as are the other disubstituted sulfones, particularly promin, and that the parent substance so released is the principal active element. On the other hand, the monosubstituted sulfone 1500F acts directly by its molecule. This is certainly true when it is given intravenously. By the oral route a portion of the drug is, indeed, transformed into DDS. Even in this case the mono-substituted sulfone acts, in large part, directly by its entire molecule. —AUTHOR'S ABSTRACT.

FLOCH, H. & DESTOMBES, P. Rôle de la thérapeutique sulfonée sur l'apparition et l'évolution des réactions lépreuses: réaction léprotiques et tuberculoïdes réactionnelles. [The rôle of sulfone therapy in the appearance and evolution of lepra reactions: leprotic reactions and reactional tuberculoids.] Inst. Pasteur Guyane et Terr. Inini, Publ. No. 218, October 1950.

The sulfone therapy of leprosy has fixed attention on the reactions of leprosy, for these drugs unquestionably favor their occurrence. They are very frequent in the first months of treatment, in the authors' experience in 40% of the cases. In some patients the first reaction appears only after the beginning of the treatment; in others, there exists a veritable threshold, above which the reaction is precipitated. With DDS, the daily dose of 200 mgm. in adults has a definitely more constant activity and toxicity than the disubstituted sulfones, apparently regardless of the route of administration. However, with this drug reactions are notably more frequent with the oral route (47%) than with the intramuscular one (8%). A similar difference has been observed with the monosubstituted succinyl compound (1500F): 44% by mouth, 7% intramuscular or intravenous. Since only the route of introduction varied, not the dosage, it is logical to think that the liver, involved much more actively with the drugs when they are given by mouth, plays an important role in the pathogenesis of leprotic reactions. The intramuscular route is therefore indicated. For reactional eye lesions the intramuscular route, and better still the intravenous one (with 1500F), is preferable. The antimonial and synthetic antihistamine compounds are only useful adjuvants. Combining streptomycin with sulfones has given no significant results. In tuberculoid reactions (reactional tuberculoid *ab initio*, or "tuberculoid in reaction"), vitamin D_2 in massive doses has given interesting results although inferior to those reported by Capurro and Guillot. The tuberculoid reactions are quite sensitive to sulfone therapy (DDS and 1500F), their evolution being clearly shortened.
—AUTHORS' ABSTRACT

TRESPALACIOS, F. & PIÑEYRO, R. Reacción leprótica tuberculoide. (Estudio de un caso con neuritis nodular colicuativa tratado por la diasona.) [Tuberculoid lepra reaction; study of a case with nodular colliquative neuritis treated with diasone.] Bol. Soc. cubana Derm. y Sif. **7** (1950) 21-31.

The authors emphasize Souza Campos' distinction between the exacerbation of preexisting tuberculoid lesions (tuberculoid lepra reaction) and the development of tuberculoid lesions in an apparently healthy patient (reactional tuberculoid leprosy). A case of the former kind is reported in a 12-year-old Negro boy of healthy parents who had lived with his grandmother who had lepromatous leprosy. The boy reported the appearance of dark patches on the face and other regions one year before examination. Seven months later the patches had reddened, and after another 3 months a swelling developed on the inner aspect of the right elbow. He was treated with chaulmoogra oil until recently. On examination there were found more or less scaly erythemato-pigmented patches surrounded by achromic halos, and an egg sized, slightly fluctuating swelling in the right ulnar region. Biopsy of a patch showed tuberculoid structure. After 6 months of treatment with diasone the skin lesions were greatly ameliorated, and no trace of the ulnar swelling could be found. —F. R. TIANT

DUBOIS, A. Sulfones et prophylaxie de la lèpre au Congo Belge. [Sulfones and the prophylaxis of leprosy in the Belgian Congo.] Inst. Roy. Col. belge, Bull. Séances **21** (1950) 205-211.

The author wonders if the introduction of the sulfones in treatment will not lead the Belgian Congo leprologists to a modification of their antileprosy scheme. This is to say, to insist on stricter isolation, but limited to lepromatous cases, which are no more than 15% of the total. Strict isolation of such cases would aid the realization of an active treatment of real prophylactic and individual value. It is suggested that the workers in the Congo should observe to what extent sulfone treatment would prevent the development of mutilations in neural (tuberculoid) cases, which condition is frequent and often requires hospitalization. Four favorable cases in Europeans treated with sulfones are reported.

—AUTHOR'S ABSTRACT

JACONO, G. & COLUCCI, C. F. Prime osservazioni sull'impiego del tiosemicarbazone nella lebbra. [Thiosemicarbazone in the treatment of leprosy.] Acta Med. Italica **5** (1950) 301-304.

The authors have made trial of thiosemicarbazone with small dosage starting with 12.5 mgm. Two cases are detailed, both of which had previously been treated with sulphonamides and PAS. For one the dose was raised gradually to 120 mgm. on the 8th day, for the other to 50 mgm. on the 6th and 7th days. In neither were the immediate results satisfactory; there was rise of temperature, lighting up of old lesions and appearance of fresh ones, with nausea and vomiting, sweating and pain. The treatment was stopped, but after this recrudescence the condition showed a little improvement and bacilli were fewer.—[From abstract in *Trop. Dis. Bull.* **48** (1951) 166.]

GROSCH, W. & KALIEBE, H. J. Uber einen Fall von Lepra. [A case of leprosy treated with Tb I/698.] Ztschr. f. Haut- u. Geschlechtskr. **9** (1950) 281.

Little attention has been paid to leprosy in Germany since the war, other problems being more important. However, a few cases have been observed, and much sensational matter has appeared in the lay press. The present report is a very full one of a case in a young man, 25 years of age, whose family went to Brazil when he was only 6 months old and returned 14 years later. The disease was of lepromatous form. Prolonged treatment —apparently more than a year—with conteben gave good results, described in detail. —H. W. W.

HEILMEYER, L. [Nonspecific action of thiosemicarbazone.] Beitr. Klin. Tuberk. **102** (1950) 583-

The tuberculostatic action of thiosemicarbazone *in vitro* is considerably less than that of other substances, such as of para-aminosalicylic acid, but in clinical application it is active in smaller doses. The law of mass applies for most other chemotherapeutic substances—i.e., the higher the concentration in the blood the greater the effect—but it does not apply to thiosemicarbazone. Small doses (0.1 to 0.3 gm. daily) are more effective than massive doses. These and other observations seem to indicate that the action of this drug is not due entirely to its effect on the tubercle bacillus. The effect on the sedimentation rate is noteworthy; it subsides more rapidly than does the curative process, and may even decrease when

there is a clinical exacerbation. This effect on the sedimentation rate is also seen in rheumatic polyarthritis, gonorrheal arthritis or tumor metastases. Since sedimentation is a manifestation of the colloidal structure of the plasma colloids, the changes that take place in them under the influence of thiosemicarbazone were investigated. It was found that this effect represents something new and unique, since it cannot be produced with other drugs. Conditions that are accompanied with a great increase in the sedimentation rate are decisively influenced by thiosemicarbazone. In chronic articular rheumatism, normalization of the colloid structure of the plasma accompanies a decrease in the inflammatory manifestations, but if the administration of thiosemicarbazone is interrupted the symptoms recur. Similar effects have been observed in erythema nodosum, exudative pleurisy, and some nephroses. It is peculiar that such effects cannot be produced in all cases. The therapeutic importance of thiosemicarbazone is not limited to tuberculosis.—[From abstract in *J. American Med. Assoc.* **144** (1950) 427.]

GARDUÑO, D. M. & DE LEON, D. M. Streptomycin in leprosy, early cutaneous type. J. Philippine Med. Assoc. **27** (1951) 93-101.

A case said to be an early one of lepromatous leprosy of three years duration, the patient also suffering from minimal, exudative, bilateral pulmonary tuberculosis and chronic tertian malaria, both of six years duration, was treated intermittently over a period of 6 months with dihydrostreptomycin. The treatment days totalled 130, the dosage being 0.5 gm. a day in 3 divided doses given intramuscularly; the total amount of the drug given was 65 grams. The treatment resulted in the resolution of the lesions in the face and upper extremities, leaving only faint brownish discolorations level with the skin. The site of a lesion on the right leg became thin, atrophic, shiny, with brownish discoloration on the borders and hypopigmentation in the center. All lesions became bacteriologically negative. —J. O. NOLASCO

ROUSSET, J. & MARIE-SUZANNE (SOEUR). Action sur le lépromes des injections sousjacentes d'huile de chaulmoogra hydrogenée. [The effect of injecting hydrogenated chaulmoogra oil beneath lepromas.] Bull. Soc. française Derm. et Syph. **56** (1949) 306.

Injections of hydrogenated chaulmoogra oil immediately under the lesions produced a rapid subsidence and retrogression of the lepromas. Apparently this is a local action of the agent, independent of its general effect. It was excellently tolerated.—[Abstract from *Excerpta Med.* **4** (1950) 400.]

GATÉ, J. & ROUSSET, J. Action remarquablement rapide de la bisdihydrochaulmogroyl 4-4' diamino diphényl-sulfone dans un cas de lèpre lépromateuse. [Remarkably rapid action of a chaulmoogra-sulfone compound in a case of lepromatous leprosy.] Bull. Soc. française Dermat. Syph. **58** (1951) 191.

The brief case presentation concerns an 11 year old girl with lepromatous leprosy who at first had been treated with PAS (15 gm. daily) for more than 3 months with no effect. Treatment with the chaulmoogra-sulfone compound was begun with injections increasing from 1.5 cc. once a week to 4 cc. twice a week. In 2 months, after the 13th injection, definite changes in the lesions were evident, and these were more marked a month

later although treatment had been interrupted for a period of 3 weeks because of technical difficulties in preparing the product. The remarkably rapid clinical results, obtained with a total dose of 201 cc., are held to illustrate the extraordinary activity of this product, a report on which was in press. —H. W. W.

HEMPEL, G. Uber den Wirkungsmechanismus des Chaulmoograöls. [On the mode of action of chaulmoogra oil.] Ztschr. f. Immunitätsf. u. Exper. Therap. **106** (1949) 154-163.

The inhibitory effect of chaulmoogra derivatives and 3,5 di-iodine-salicylic sodium on acid-fast bacteria (so-called leprosy species) is neutralized or weakened *in vitro* by the addition of non-toxic alkaline salts of fatty acids. That interference phenomenon can be regarded as a proof of the specific effect of chaulmoogra oil in the treatment of leprosy; it coincides with the clinical experience that only a long-lasting treatment is successful.—[Abstract from *Trop. Dis. Bull.* **48** (1951) 267-268.]

FERNANDEZ BAQUERO, G. Resultado extraordinario de un nuevo método de tratamiento para la lepra lepromatosa. [Extraordinary results of a new method of treatment of lepromatous leprosy.] Bol. Soc. cubana Dermat. y. Sif. **6** (1949) 133.

A preliminary report of the marked clinical improvement observed in a case of lepromatous leprosy treated with whole blood transfusions (150 cc. once a week for 5 weeks) from a brother suffering from tuberculoid leprosy. —F. R. TIANT

ARRUDA GENÚ, J. O., DE OLIVEIRA LIMA, S. & SANTOS, M. A bota de Unna no tratamento das úlceras lepróticas. [Unna's boot in the treatment of leprotic ulcer of the foot.] Rev. brasileira Leprol. **17** (1949) 191-194.

This seems to be merely another example of "cure by local rest." Eighteen women and 22 men with leprotic ulcers [presumably perforating ulcers of the sole] were treated by the Unna boot, which checks the edema and chances of secondary infection and trauma. It would appear that after 8 days the smell resulting from "organic decomposition" is almost intolerable; though it can be masked by deodorants or materials "of a sweet-smelling savor." After another week this malodor diminishes and the boot is worn for 2 months altogether. Of 179 ulcers so treated 100 healed and cicatrized firmly; 50 others improved greatly and it is thought that further application of the boot will cure these also; 15 remained unaffected and 14 became worse. The method has the advantage that patients can get about and do their work.—[Abstract from *Trop. Dis. Bull.* **47** (1950) 551.]

ISHIHARA, S. Studies on serum protein of leprosy. First report. La Lepro **19** (1950), No. 5, pp. 3-11 (in Japanese); English abstract, p. 1.

Examination of the serum proteins of leprous patients with the biuret reaction and colorimetry gave the following results: (1) In tubercular leprosy the albumin decreases and the globulin increases, compared with normal sera. In neural and macular leprosy no change was found. (2) The albumin/globulin ratio was more than 1.0 in neural and macular leprosy, and less than 1.0 in tubercular leprosy. (3) The volumes of α and β globulins did not differ in the different types, but α-globulin increased in tubercular leprosy. (4) One factor which accelerates the red blood cell sedimentation in leprosy is globulin. (5) The chief factor of the

positive of Takada reaction in leprosy is the increase of γ globulin.—[From abstract.]

ISHIHARA, S. Studies on serum protein of leprosy. Second report. La Lepro **19** (1950), No. 5, pp. 12-18 (in Japanese); English abstract, p. 1.

The electro-flocculation method was employed with the same sera as in the previous experiments, comparing the results with those obtained by colorimetry. The serum proteins of cases of erythema nodosum leprosum were also examined with colorimetry. (1) The results obtained with the flocculation method corresponded fairly well with the results of colorimetry. The marked difference of the serum fractions between the nervosa and maculosa forms and lepra tuberosa was the increase of globulin on account of increasing of γ-globulin in lepra tuberosa. (2) Albumin/globulin ratio in erythema nodosum leprosum was less than 1.0 on the average, and did not differ much from ordinary lepra tuberosa. (3) In this condition there was no remarkable difference in the fractions of serum protein. The fractions of the serum proteins in the early stage of erythema nodosum leprosum do not differ from those after its recession.—[From abstract.]

TANIOKU, K. The general and local blood pictures of leprosy. La Lepro **19** (1950), No. 3-4, pp. 27-30 (in Japanese); English abstract, p. 1.

A survey of the general and local blood pictures has been made in 80 leprosy patients. (1) In the case of the general blood picture, the monocytes, shift-type and neutrophil staff cells are increased in both maculosa and tuberosa leprosy. In the maculosa type, eosinophil cells were found increased. In both types, among advanced cases eosinophil cells were increased and lymphocytes decreased. (2) In the local blood picture, eosinophil cells and lymphocytes were found increased, and neutrophil segmentocytes decreased.—[From abstract.]

PIERINI, D. C., SÁNCHEZ NAVARRO, J. Anetodermia secundaria (leprosa) del tipo Schweninger-Buzi. [Secondary leprous anetodermia of the Schweninger-Buzi type.] Rev. argentina Dermatosif. **34** (1950) 267-272.

This is a report of a case of lepromatous leprosy, bacteriologically positive and Mitsuda negative, with lepromatous infiltrations and nodular and cord-like lesions. In their evolution these lesions give rise to elevated, wrinkled and atrophic plaques with central depression. Histologically, although clearly lepromatous, there was also atrophodermia of the Schweninger-Buzi type. —G. BASOMBRIO

PORTUGAL, H. & AZULAY, R. D. Vantagens de coloração pelo método de Gram-Weigert dos cortes de lesoes lepromatosas. [Advantages of the Gram-Weigert method in the staining of sections of lepromatous lesions.] Rev. brasileira Leprol. **18** (1950) 206.

The authors employ this method in parallel with that of Ziehl-Neelsen in the study of lepromatous lesions. The method used is that given by Mallory: Stain for 10 minutes in Carazzi or Delafield hematoxylin, then for 15 minutes in eosin in the paraffin oven, and finally in phenol-crystal violet for one hour, after which treat with lugol for 2 minutes. (Wash after each of these steps.) The section is then dried carefully with filter paper and differentiated in aniline oil-xylol, 50:50. This is the only delicate step of the operation, since differentiation should be neither

insufficient nor excessive. Finally, wash with pure xylol and mount in cedar oil. The bacilli remain stained for 24 hours. There is no reason for the use of this method with tuberculoid or undifferentiated lesions, for the simpler Ziehl-Neelsen process gives the same results. With lepromatous lesions, on the other hand, the Gram-positive germs are always much more numerous than acid-fast forms. With lesions of the erythema nodosum or multiforme type in lepromatous leprosy there are cases in which acid-fast germs are few or absent but which show innumerable bacilli after the Gram-Weigert technique. Four cases are cited in which, after treatment with sulfones, the sections showed no acid-fasts but more or less numerous Gram-positive bacilli. —H. W. W.

OIKE, Y. & SUZUKI, M. On the staining of tubercle bacilli in tissues. Sci. Rep. Res. Inst. Tohoku Univ., Ser. C, **1** (1949) 9-13.

Treatment of smears of tubercle bacilli with 10% formalin for prolonged periods reduces the numbers that remain acid-fast, but pH 5.4-6.0 is less harmful than other levels. Tissues should be examined promptly after fixation, but if they must be stored it should be at the pH stated. The various fat solvents usually used in the embedding series (alcohol, xylene, chloroform and "ether benzine") are deleterious to the bacilli in sections or smears, whereas toluene has no such effect. The sequence recommended is alcohol—the time not prolonged more than necessary—toluene and paraffin. Toluene is also better than the other reagents for removing paraffin from the sections. In cut sections mounted on slides and exposed to the air for periods of 50-86 days, the numbers of fuchin-retentive bacilli were materially reduced, and there was also reduction in paraffin blocks stored for a long time. Fite's formaldehyde method [see THE JOURNAL **9** (1941) 264] was found superior to others used. In counterstaining, preparations treated with aqueous methylene blue (2%) showed fewer bacilli than controls, whereas with Bismark brown or malachite green (also 2% aqueous) there was no such effect. —H. W. W.

DE FARIA, J. L. Sobre a natureza de reação de Mitsuda. [The nature of the Mitsuda reaction.] Rev. brasileira Leprol. **17** (1949) 237-247 (including English translation).

This article is a summary of investigations to be published as a monograph. A study of the reaction in dogs [see THE JOURNAL **18** (1950) 124], in which there is no early reaction, led to the hypothesis that in that animal the Mitsuda response is not one of allergy but a nonspecific phenomenon due to natural resistance. It is caused mainly by the bacillary lipids, and can be produced by the lipid fraction of the Mitsuda antigen but not by the water-soluble proteins or polysaccharides. Because the extracted lipids are free, the response to them develops early, without a latent period; and the reaction lesion, a nodule of tuberculoid structure, is of more rapid evolution and smaller than with the normal antigen. In the latter material the lipids are bound in the bacilli and liberated only as they break down, hence in the dog there is a latent period of 7 to 21 days and the reaction is of longer duration and greater intensity, always with ulceration. In the tuberculoid leprosy patient there is no latent period, the late reaction begining on the 4th day, and ulceration is rare. Microscopically, the reaction in these patients is partly hyperergic in nature; the granulomatous changes are apparent in 48 hours (against the

4th day in the dog), perhaps because of the earlier liberation of lipids due to greater initial inflammation; it lasts longer than in the dog, because of slower disintegration of the bacilli consequent on the lesser degree of natural resistance; and there is less phagocytosis of bacilli in the earlier phase and they persist longer. Only the early reaction is allergic; the late one in the tuberculoid patient, as in tuberculin-negative normal persons and the dog, is due to a natural resistance which is responsible for the breaking down of the bacilli and liberation of the granuloma-inducing lipids. Further evidence that the Mitsuda reaction is of nonspecific nature, independent of an antigen-antibody mechanism, is its production with other acid-fasts and with a normal skin extract. Theoretically, however, it is possible to admit that an immunity or acquired resistance may result from the infection and operate in the same way as natural resistance. This may perhaps explain the positive reactions obtained in subsided or healed lepromatous cases; and it is possible that the same occurs in the patient with tuberculoid leprosy, with allergic hypersensitiveness disclosed by the early reaction, who may later develop immunity. Thus the thesis of the role of natural resistance is applied "indirectly," because the hypothesis of acquired resistance appearing in the course of the infection cannot be ruled out with certainty. The author disagrees with Dharmendra's view that the proteins are responsible for both early and late reactions, but agrees with Harrell and Horne who attribute the former to soluble (protein or polysaccharide) elements of the antigen and the late one to an insoluble (lipid) fraction. The mild degree and rapid evolution of the response to the lipids may erroneously be taken for negative, and histological demonstration of the granulomatous nature of the response is important. The other substances in the Mitsuda antigen which are absorbed with difficulty (collagen and elastic fibers, horny substance and melanin) also participate in the pathogenesis of the Mitsuda reaction. The instances of discordance between the early and late reactions are explained on the ground of the presence of natural resistance without allergic hypersensitivity, or vice versa, a relationship of the two conditions hitherto unknown. Finally, for the reading of the Mitsuda reaction in doubtful or anomalous cases the histological examination is indispensable. The positive result shows the tuberculoid change, while pseudopositive reactions show the lepromatous structure. There are apparently positive reactions in lepromatous patients which show the latter structure, and this may perhaps occur in such cases when other acid-fasts are used as antigens. Consequently, the histological examination offers the only reliable way of reading the reaction and verifying the presence of acquired resistance in lepromatous leprosy. This examination would also be important in children made lepromin-positive by BCG.

Comment.—It is impossible to evaluate the conclusions of this writer because only summaries of his findings have been published, apart from a report of a lepromatous case which had developed tuberculoid manifestations and positivity to lepromin [see THE JOURNAL **18** (1950) 443]. Such was the report referred to on the work in dogs, and that with a normal skin suspension has only been mentioned as "in press." This condensation of the present summary has been held a full year in anticipation of the monograph, publication of which seems to have been delayed. The reveiwer refrains from further comment except to recall, in connection with the positive results with the lipid fraction, that Raffel [*American Rev.*

Tuberc. **54** (1946) 564] concluded from his work with the supposedly purified "wax" of the tubercle bacillus that it contained proteins carried over in the extraction, and they were essential for the immunological effects of that fraction when used alone. —H. W. W.

NEYRA RAMIREZ, J. Las correlaciones inmunológicas de la lepra con la tuberculosis. Su applicación práctica: la vacunación BCG en la profilaxia de la lepra. [The immunological relationship of leprosy and tuberculosis. Its practical application: BCG vaccination in leprosy control.] Rev. San. Pol. (Lima) **11** (1951) 519-552.

The lepromin reaction, generally a sign of leprosy infection, should be properly interpreted as to its sensitivity and specificity. The early reaction is an expression of hypersensitivity, the late one an expression of immunity. The author has made observations regarding the immunological relationships of leprosy and tuberculosis. Lepromatous leprosy has an energizing or depressing effect on the tuberculin reaction; of 22 such cases only 77% were positive to the maximum dose (1/10 dilution). On the other hand, tuberculous infection has an important sensitizing effect with respect to the lepromin reaction; of 100 such patients from nonleprous areas 45% gave the Fernandez reaction and 56% the Mitsuda response, whereas among 100 tuberculin-negative healthy persons only 15% reacted positively to lepromin. In 53 healthy persons negative to both tests, the lepromin reaction was made positive by means of BCG vaccination in 81%; in 24 children up to 16 years of age, positive early reactions were seen in 96% and late ones in 87%, while in 29 older individuals the corresponding percentages were 69 and 76. BCG vaccinations should be extended to leprous areas of the country to reinforce the antileprosy campaign. The Mitsuda reaction should be investigated in tuberculous patients with respect to its prognostic significance in that disease. It would be of national, scientific and practical interest to study the tuberculin and lepromin reactions in aboriginal populations from remote areas which are supposed to be virgin to both infections.—[Mainly from the author's conclusions.]

DANBOLT, N. On the skin test with sarcoid-tissue-suspension (Kveims reaction). Acta Dermato-Venereol. **31** (1951) 185-193.

This reaction was applied, in the Dermatological Clinic in Oslo, to 175 individuals in the period 1945-1947. (1) Of 25 healthy persons, none gave reactions which met the requirements of positivity, i.e., that the papule be distinct after one month and remain so for another month or more. (2) In 51 patients with diseases other than sarcoid, 5 gave results which had to be regarded as unspecific positive; so, taking these two groups together, 6.5% gave false positives. (3) Of 46 definite sarcoid cases, 5 were negative, indicating a positivity rate of about 90% in Boeck's sarcoid. (4) Of a heterogeneous group of 65 patients sent in because of pulmonary alterations which might possibly have been due to sarcoid, the reaction was positive in 24. These cases were not followed up, but in a previous study of similar patients good agreement had been found between the results of the skin test and the clinical findings. In an effort to elucidate the pathogenesis of the reaction, experiments were made with tissue suspensions from lymphogranuloma inguinale, lymphogranuloma maligna, and normal spleen and brain tissues. All were negative, as were those with mineral particles and catgut. Intracutaneous injection of BCG and killed tubercle bacilli in sarcoid patients had not induced reactions

which could not be obtained in tuberculin-negative controls. It must therefore be assumed that there are special substances in sarcoid tissue suspensions which are responsible for the development of the reaction papule. It seems improbable that the Kveim reaction is a Köbner phenomenon; more probably it is of an allergic nature. Because of its high degree of specificity it must be regarded as a valuable diagnostic implement.

—H. W. W.

OKA, S., YAMADA, S. & NIITSU, Y. Immunization against tuberculosis with dead tubercle bacilli. Sci. Rep. Res. Inst. Tohoku Univ., Ser. C, **1** (1949) 14-21.

Heat-killed tubercle bacilli suspended in oily substances, such as paraffin oil, olive oil or lanolin, not only established tuberculin sensitivity in high degree in guinea-pigs but also conferred to them a state of acquired resistance, or immunity. Such bacilli in paraffin oil injected into the testis of the rabbit gave rise to lesions in distant organs which, histologically, were like those produced by living bacilli. On the other hand, dead acid-fast saprophytes under similar conditions did not induce skin allergy to tuberculin, or acquired resistance, nor were visceral lesions produced. Other observations are related. It is believed that immunization of man by killed tubercle bacilli is possible, although the matter requires further study.

—H. W. W.

ISHIHARA, S. On complement fixation reaction of lepra serum. La Lepro **19** (1950), No. 3-4, pp. 11-26 (in Japanese); English abstract, p. 1.

The complement fixation reaction has been made with sera of leprosy patients, using as antigens an aqueous emulsion of leprous nodules and an alcohol extract. (1) In lepra tuberosa most patients gave positive reactions, whereas in lepra nervosa and lepra maculosa most of them were negative. (2) In positive cases there was a certain relation between the strength of the complement fixation reaction and the severity of the case. (3) The results of the complement fixation reaction corresponded well with those of the Mitsuda test. (4) The antigens involved in these reactions are regarded as of lipoid and not of protein nature.—[From abstract.]

CHOUCROUN, N. Réaction de précipitation permettant de déceler, dans le sérum du tuberculeux, et aussi de lépreux, des anticorps précipités par un polysaccharide du bacilli tuberculeux. [A precipitation reaction permitting the detection of antibodies, precipitated by a polysaccharide from the tubercle bacillus, in the serum of tuberculous and leprous persons.] Compt. rend. Acad. Sci. **229** (1949) 145-147.

A precipitation reaction with a polysaccharide antigen prepared from tubercle bacilli was worked out and tested for its specificity. Positive results seem to occur especially in persons who are combating tuberculous infection successfully. In five cases of leprosy high antibody titers were also found.—[Abstract from *Excerpta Med.* **4** (1950) 15.]

SATO, S. Contribution to the study on cultivation of the leprosy bacilli. A re-examination of Prof. Nakamura's method and on the behavior of bacilli implanted in various nutrient liquid media with some accessory substances. Sci. Rep. Res. Inst. Tohoku Univ., Ser. C, **2** (1950) No. 2, pp. 1-7.

In his many and varied attempts—all unsuccessful—to cultivate the human and rat leprosy bacilli, including tissue cultures and chick embryos,

the author has employed certain special methods described by others. One was the symbiosis method of Toda with various other bacteria in fluid media, in which a Chamberland bougie containing one microorganism is inserted in a large tube containing the other. A supposed leprosy culture obtained by Yoshi (1948) with cultivated chicken monocytes is held to have been a nonpathogen; the author obtained no multiplication of the leprosy bacilli. Urabe and M. Nakamura (1948) claimed success with a modified Kichner medium; 50 attempts to confirm that result all failed. Special attention is given the method of K. Nakamura (1949, 1950), with which other workers have had at most only limited success. Nakamura claimed multiplication in the culture fluid in all attempts; the human bacillus in growing formed globi, and the rat leprosy bacillus gave growths evident with a magnifying glass or even the naked eye after 4 weeks or more and inoculations in rats always proved successful. Subcultivation was easy with both microorganisms, and at the beginning of 1950 he had a 9th subculture of the human bacillus and a 14th one of the rat bacillus. In a previous article the author and Nishimura had reported almost complete failure to obtain multiplication even in the first generation. Details are given of the Nakamura method, with information concerning the mucins and phthiocols used in the further work here reported, done over a period of 1½ years with 31 lepromas from 12 leprosy patients and 35 nodules from rats. Using the small inocula recommended by Nakamura—with suspensions containing 2 or 3 isolated bacilli per field—bacilli were very difficult to find in smears from the cultures; multiplication was not confirmed, and subcultures failed. Using much heavier inocula—50 to 100 or more scattered, single bacilli per field—smears from the cultures showed numerous bacilli, scattered or grouped. The human bacilli were often in aggregations which suggested globi—"in round and unstained spaces or wrapped in masses of mucin"—but this appearance is held to represent only spontaneous aggregation, particularly since it also occurred with killed bacilli. Bacilli were much fewer in the first subcultures, and could not be found in the second ones. Furthermore, in the original cultures the bacilli in time became fewer and degenerated. Inoculation tests with the rat-bacillus cultures made after 21 or more days of incubation all gave negative results. It is concluded that neither type of bacillus is cultivable by Nakamura's method. In other experiments made with various more ordinary fluid media in a specially-devised capillary culture tube, again masses of bacilli were seen when the heavier inoculum was used, in the case of the human bacillus resembling globi and suggesting growth and colony formation; but again it was concluded that the aggregation was spontaneous and that actual multiplication had not occurred. Noting that it is generally considered that leprosy bacillus can live and multiply only in living cells, especially the lepra cells, the author holds that it is questionable if it can multiply, "although microscopically it may," in highly nutrient media with accessory ingredients. —H. W. W.

YOSHINAGA, T. Influence of lecithin and kephalin on growth of acid-fast bacilli. La Lepro **19** (1950), No. 3-4, pp. 3-10 (in Japanese); English abstract, p. 1.

(1) Brain and yolk lecithin and kephalin made in my laboratory have been tested with respect to their influence on the growth of human and avian tubercle bacilli. It was found that lecithin strongly controls their

growth, whereas kephalin is apt to help rather than control it. (2) Yolk lecithin made by Merck, and soya-bean lecithin made by Takeda, as well as lecithin fatty acid and kephalin fatty acid have been found to control the growth of acid-fast bacilli.—[From abstract.]

LEVADITI, C., VAISMAN, A. & BARRAT, L. Virulence du bacille de Stefanski inoculé par voie cérebrale au rat et à la souris. [The virulence of Stefansky's bacillus inoculated in rats and mice by the cerebral route.] Compt. rend. Soc. Biol. **145** (1949) 1429-1432.

When Stefansky's bacillus is inoculated in mice and rats by the transcranial route, alterations of the meninges and plexus appear which contain acid-fast bacteria. The exact technique and a detailed analysis of the results are presented.—[From abstract in *Excerpta Med.* **4** (1950) 393.]

KIKUTH, W. & MUDROW-REICHENOW, L. Ueber die Diamidine und ihre Wirksamkeit auf die experimentelle Leprainfektion der Ratte. [The activity of diamidines in rat leprosy.] Ztschr. f. Immununitätsf. u. Exper. Therap. **107** (1950) 139-151.

The authors review the chemotherapeutic activities of the diamidines and describe the effect of stilbamidine and pentamidine in experimental rat leprosy. It appeared that the rate of development of lepromata in animals treated with stilbamidine was much slower than in control animals, but the general state of infection was not appreciably influenced. Pentamidine possessed a comparable activity.—[Abstract from *Trop. Dis. Bull.* **48** (1951) 271.]

URABE, K. The effects of photodynamic substance on rat leprosy. La Lepro **19** (1950) No. 5, pp. 19-20 (in Japanese); English abstract, p. 1.

The results of application of photodynamic substances to rats at the sites of inoculation of murine leprosy bacilli were as follows: Eosin and erythrosin accelerated a little the development of granuloma, but hematoporphyrin, fluorescein and bergamot oil had no influence on it.—[From abstract.]

N. Y. ACADEMY OF SCIENCES SYMPOSIUM

The New York Academy of Sciences held a two-day symposium on leprosy on November 10 and 11, 1950, at which fifteen papers were presented. These have been published as the first issue of Vol. **54**, 1951, of the *Annals* of the Academy. Abstracts of these papers were supplied by Dr. F. A. Johansen.

BADGER, L. F. History of leprosy in the United States. Pp. 6-11.

Evidence is cited which indicates that leprosy may have existed in the United States for 200 years or longer; it was definitely reported to exist in Florida in 1776 and in the Mississippi delta at about the same time. Imported cases have come from many regions, from Europe and Africa to the Pacific Islands and Asia. During the approximately 30 years of operation of the national leprosarium, patients have been admitted who were born in 52 countries throughout the world. The disease is considered endemic in four of the states, where it appears to be static. The extent of its prevalence is difficult to determine. The national leprosarium has received approximately 1,500 cases from 41 states and the District of

Columbia. Efforts to establish a national leprosarium were made as early as 1908, when only 2 states, Louisiana and Massachusetts, provided institutions for the care of leprous patients. In the other states, patients were hounded from place to place, and isolated on the outskirts of cities or in huts in the woods. Recently there has been some change in the attitude towards isolation, and selective isolation is recommended based on infectiousness, although the laws of some states still require that every case be isolated. There is an increased interest at present to control the disease by case finding, treating cases early in the disease, keeping contact with infectious cases to a minimum, and by not too radical relaxation of the control measures.

HANKS, J. H. Bacteriology of leprosy. Pp. 12-19.

Two major pitfalls have confused the literature on this subject. Claims are made, (*a*) that cultivable organisms—rapidly growing acid-fast bacteria, diphtheroids, fungi, or actinomyces—are the etiological agent, and (*b*) that *in vitro* leprosy bacilli are capable of limited, but not continuous, multiplication in fragments of lepromatous tissue and in or on various bacteriological media. These are held to represent erroneous findings. All of the cultures studied by the author are believed to have been saprophytes. Errors in microscopic studies arise from the fact that bacilli in fresh nodules are encased in intact cells, while those in autolyzed tissues are largely freed because of cell disintegration; also, lack of cell debris after autolysis produces smears in which most of the stainable material appears to be bacilli, which increases the illusion that they have grown. Another source of error is that pseudocolonies are at times formed within incubated tissues. The Ziehl-Neelsen method enables one only to enumerate the number of acid-fast bodies which persist, and affords no measure of the metabolic quality of the bacilli. Recent studies with the murine bacillus have shown that they are incapable of surviving *in vitro* —as do other mycobacteria—by metabolizing their endogenously stored nutrients, that their biochemical ability to carry on dehydrogenation deteriorates with remarkable rapidity, and that their respiration is not enhanced by any of a wide variety of organic compounds. This last has been shown by a survey of all classes of substrates which are known to be assimilated by, or to stimulate the respiration of, the cultivable mycobacteria, made by a biochemist working with the author. There are several graphs which show the influence of pH, temperature and certain ions on the murine bacilli in a buffered solution, and a table giving the influence of purified bovine albumin and of rat serum on the quality of these bacilli.

KLUTH, F. C. The epidemiology of leprosy. Pp. 20-27.

The author discusses the history and distribution of leprosy, the sources of infection and mode of transmission, the environmental factors influencing transmission, and those which influence susceptibility. Cases of active lepromatous leprosy are generally recognized as the principal, if not the only, source of the infection. Studies in the Philippines have indicated that persons living in a household with a lepromatous case had a risk of infection four times greater than that of persons living in a household with a tuberculoid case, and eight times greater than that of persons living in a household containing no known patients. The usual views are expressed regarding the mode of transmission and environmental

factors. Age and sex influence susceptibility. The estimated risk of attack of children under 15 years of age in the household of a lepromatous case is 1 in 70, against 1 in 600 for older persons. The disease is more common in males than in females. No race is immune. It is said that the initial lesion may be either the site of inoculation or an area of weakness in which the disease first manifests itself. The principal conclusion is that there is no well-supported theory which can explain adequately the history and the selectivity of the disease.

FITE, G. L. The pathology and pathogenesis of leprosy. Pp. 28-33.

The tissue reactions to the leprosy bacillus are conditioned principally by the type of the disease, the sensitivity of the tissues to the organism, and the stage and extent of the process. The "lepra cell" is a macrophage, a histiocyte or a reticuloendothelial cell depending only upon the school of cellular histoanatomy to which one subscribes. Extremely early lesions may show only banal inflammatory changes with very few bacilli. As the first few bacilli that the lepra cell phagocytizes increase in numbers, they appear as clumps arranged in parallel columns. When growing most actively, the columns appear to radiate from a common center, best seen in silvered preparations. Later, cytoplasmic vacuoles separate bundles of bacilli, producing the foamy appearance. Lipids are seen in the earliest-bacillus-containing cells. Coalescence of these cells may result in the formation of globi. Globi are a degeneration phenomenon rather than an expression of activity of the disease, and hardly contributory to the pathogenesis of leprosy. They are of some significance in its treatment, however, because they become inert foreign bodies and are little amenable to therapy, persisting in regressive cases long after other refuges of bacilli have lost their organisms. Tuberculoid leprosy is simply leprosy in the individual specifically sensitized to the bacillus. The tissue reaction is chiefly a proliferative one, with production of epithelioid cells and loose tubercles in which giant cells are not striking. Bacilli may be moderately plentiful in the early phases of these lesions, but never to the point of abundance as in the lepromatous form. An interesting difference between these types concerns the nerves. To the histopathologist all leprosy is neural leprosy. All leprosy lesions show some involvement of the terminal nerves, and spread of the infection along branches to larger nerves follows to a variable degree. In lepromatous leprosy bacilli are seen in every part of the nerve fiber, as is dramatically shown during acute reactions; in tuberculoid leprosy they occur in fair numbers. The visceral changes in tuberculoid leprosy, apart from those in the lymph nodes, are not known for want of autopsy material. Various intermediate forms are discussed, including clinically lepromatous cases in which traces of tuberculoid changes are found, cases positive to lepromin while the histologic changes are mixtures of lepromatous and chronic inflammatory, and those in which the clinical appearance and the course of the disease are typically lepromatous but histologically there is a striking variant, the bacillus-containing cell being epithelioid in type with no vacuoles.

SOULE, M. H. The laboratory diagnosis of leprosy. Pp. 34-39.

The laboratory, it is pointed out, merely confirms the clinical diagnosis of leprosy, and, for lack of a specific serological test and a susceptible animal, the procedures are reduced to microscopic examinations of stained specimens. The techniques of examination are discussed, from the selection

of sites to the recording of findings, they being the ones usually followed by personnel working with leprosy.

KAHN, R. L. Universal serological reaction in leprosy. Pp. 40-47.

The author concludes that the serologic pattern of his universal reaction is distinctive in lepromatous leprosy and different from that seen in other diseases, although in practice intercurrent diseases, especially syphilis, will change the pattern. The pattern is believed to be the result of a reaction between particular antigenic lipids and autoantibodies. These lipids, it is assumed, are liberated in the course of the tissue-destructive processes in lepromatous leprosy, and they possess the capacity of calling forth autoantibodies which react *in vitro* with reactive lipids present in the antigen. No distinctive pattern has been observed in tuberculoid leprosy and in the undifferentiated form. Qualitatively the results in lepromatous leprosy seem unaffected by the activity of the disease, but quantitatively—i.e., with respect to the intensity of the precipitation—the results show such a relationship; it is low when activity is at a low level, and increased when activity is increased, but when the activity becomes so marked as to interfere with the patient's capacity to produce antibodies precipitation drops to a low level, as is also seen in other diseases. The author feels that this reaction may prove to be of value in lepromatous leprosy, especially as a serologic guide to therapy, provided it is made periodically and the results are correlated with clinical findings.

THIERS PINTO, J & ZEO, A. Universal serologic reaction in leprosy. Pp. 48-52.

The authors applied the universal reaction of Kahn to 75 leprosy patients in Rio de Janeiro, all of whom had received treatment. They state that the distinctive serologic pattern described by Kahn in lepromatous leprosy was often not evident, apparently due to syphilis and other intercurrent diseases. They observed that treatment of these conditions may change an atypical serologic pattern to a typical one.

FELDMAN, W. H., KARLSON, A. G. & GRINDLAY, J. H. Lepromin: Mitsuda's reaction, with experimental observations in dogs. Pp. 53-71.

The first part of this communication deals with certain general aspects of the lepromin test, familiar to leprosy workers. The importance of recognizing that reciprocal sensitization may be due to other mycobacteria than *M. leprae* is emphasized, as is the paucity of immunologically acceptable facts explanatory of the complex and little-understood processes involved in a positive reaction to lepromin. The second portion is a report of the authors' results with human lepromin and other related antigens in 22 adult and presumably normal dogs raised in an area of the U. S. where leprosy is not known to exist. The experiments involved: (1) dogs that received a single or two simultaneous injections of lepromin, (2) dogs that received one subsequent injection of lepromin several months after the first tests, and (3) dogs that received, during a period of 12 days, four different injections of human lepromin, rat lepromin, a suspension of a so-called leprosy bacillus culture, and a suspension of a saprophytic acid-fast bacillus isolated from the soil. Among the 16 dogs of the first group, only 6 reacted positively. Of the 9 animals that received a second injection of lepromin, 5 were recorded as positive, although only 3 of them had reacted previously. All of the 6 dogs of the third experiment reacted

positively. The authors' conclusions are as follows: 1. The capacity to develop hypersensitivity to lepromin varies markedly in different dogs. What factor or factors control the essential mechanism that results in a local tissue response in some animals and not in others is unknown. 2. The initial injection of lepromin often provokes a state of enhanced reactivity that may accelerate the reaction to subsequent injections of the antigen. 3. Repeated injections of lepromin provoke a vigorous activation of the reactive mechanism and, as a consequence, more positive reactions occur than would be true if only a single dose of lepromin were given. 4. The occurrence, following injections of lepromin subsequent to an initial dose of the antigen, of an exaggerated local tissue response which occurs without the period of latency characteristic of the response to a single injection, implies the elaboration and influence of circulating activating substances. 5. Whether or not dogs react positively to an intracutaneous injection of lepromin is not necessarily dependent on previous environmental contact with *M. leprae.* 6. Lepromin injected on one occasion or on repeated occasions in dogs did not sensitize the animals to a diagnostic dose of Old Tuberculin. There are seven photomicrographs showing the cellular reaction resulting from intradermal injections of lepromin, and other illustrations.

REISS, F. The detection of leprosy by the dermatologist. Pp. 73-83.

The author discusses briefly the cutaneous aspects of early lesions in children, which are of importance where suspicion of the disease is indicated, and then at greater length the varied lesions as they occur in the different types of leprosy, using the Cairo classification rather than the one adopted by the Havana Congress. The characteristics of lepra reactions are mentioned. Since leprosy may mimic many of the cutaneous diseases, differential diagnosis is outlined. Nineteen photographs are used, three of which are of primary lesions.

ELLIOTT, D. C. An interpretation of the ocular manifestations of leprosy. Pp. 84-100.

The introduction of slit-lamp biomicroscopy has resulted in new descriptions of distinctive characteristics of ocular leprosy which some authors regard as pathognomonic. These are illustrated diagramatically. Objective ocular symptoms may precede or parallel other symptoms in the course of the disease. A wider understanding of the significance of the ocular pathology is not only essential for early diagnosis and management of patients, but is also a valuable aid in estimating the efficacy of treatment. Ophthalmologists should be alerted to the diagnostic probabilities in patients such as veterans formerly stationed in endemic areas, as an aid in early diagnosis. A time scale developed from observation of limited ocular lesions in a group of children and the advanced pathology in patients of older age groups indicates a periodicity in the appearance of certain ocular lesions of leprosy. These bear a distinct relationship to the duration of the infection. It is suggested that studies of treatment effectiveness should be revised, using the ocular manifestations time scale as an objective device for placing patients in comparable groups according to the duration of the infection.

CARPENTER, C. M. Murine leprosy; its usefulness as an experimental infection. Pp. 101-105.

Experimental murine leprosy remains, in the author's conviction, the most suitable tool with which to investigate the unsolved problems of the human infection. Its similarities to human leprosy from the viewpoints of bacteriology, pathology, clinical manifestations and therapy are emphasized. The various attempts to cultivate *M. leprae murine* are discussed; successes recently reported from three different sources have not been confirmed by other workers. Histologically the murine leproma, it is said, resembles the nodular human leproma, although there are certain minor differences in the pathology of the two types of infection. Another common factor is that neither has yielded to therapy until recently. In human leprosy marked progress has been made with the sulfones, but they only suppress the disease and a cure has not been found. The results in experimental murine leprosy parallel those in the human disease. Cowdry and Ruangsiri reported that promin had "no consistent effect" on the leproma. The author and associates also failed to cure the disease; promin only prolonged the life of the animals while diasone had no effect. These results and others obtained with streptomycin, it is said, show that the response of the two kinds of infection to these drugs is "ostensible similar," and bespeak the value of murine leprosy as a most useful experimental infection for the evaluation of new drugs for the treatment of human leprosy.

376 GRUNBERG, E. & SCHNITZER, R. J. Chemotherapy of murine leprosy. Pp. 107-114.

The work of others who have used murine leprosy in rats and mice to study the antileprosy activity of drugs is surveyed briefly. In their own work the authors have used the Hawaiian strain of *M. leprae murine* which, having been kept in Wistar rats for many years, would not produce lepromas weighing more than 2 gm. The Wiersing breed proved more susceptible, producing lepromas weighing 25-40 gm. in 3-5 months. The material so obtained has been used for large-scale chemotherapy experiments in white mice. The local (subcutaneous) lesion is unsatisfactory for the purpose because it involves long observation periods, and so is the intravenous route for producing generalized infection because many animals die even with single doses. The intraperitoneal route was therefore adopted; small nodules with many bacilli develop throughout the cavity in 21 days. In the treatment experiments the test drug was given for 28 days, beginning immediately after inoculation. No differences were observed in the extent of the lesions in the treated mice and the controls, so it was necessary to resort to microscopic determinations of the numbers of bacilli in smears of peritoneal nodules which had been "disintegrated with slides." Altogether, 200 drugs of many chemical groups have been tested, but none has shown an activity superior to promin. The smears of the promin animals are rated as 1.7 (3.0 being the maximum), against 2.6 for the controls; tibione has the same rating as promin. On the other hand, diasone and DDS were without effect, rated 2.9 and 3.0, respectively; and PAS and streptomycin are also ineffective. In another experiment with three selected drugs the treatment period was extended to 56 days, two strains of mice being used. With the white mice promin was again the only one to show effect (rating 1.6); PAS and streptomycin rated with the controls (2.6, 2.2 and 2.4, respectively). In the more susceptible DBA mice none of these drugs showed any inhibitory effect at the end of this longer period. The authors admit that their report offers more technical

information than real chemotherapeutic results. However, they hold that since their observations with white mice agree with the findings of other experimenters with rats, the method used by them (intraperitoneal inoculation of white mice, treatment for 28 days, the effects estimated on the basis of the number of organisms found in smears of the lesions) is indicated for use in testing new drugs.

ERICKSON, P. T. The treatment of leprosy. Pp. 115-125.

Considering the various therapeutic agents employed during the past two decades, the author concludes that the most important advance has been the introduction of the sulfone drugs. Some consideration is given the value of chaulmoogra oil—the only remedy available in many parts of the world—in mild cases and in the early stages of the disease. The most serious deficiency of sulfone treatment is the slow elimination of the bacillus from the skin and nerves. Of 460 lepromatous cases treated at Carville with sulfones for from 1 to 9 years, arrest of the disease has been secured in 109, based on one-year clinical and bacteriological negativity with monthly examinations. From this experience a modified life table method has been utilized for determining the probability of arrest of the disease. The following shows the calculated chances of arrest per 100 cases.

0.0	chances by end of	1st	year, based on	460 cases
3.6	chances by end of	2nd	year, based on	410 cases
10.0	chances by end of	3rd	year, based on	340 cases
19.2	chances by end of	4th	year, based on	271 cases
28.7	chances by end of	5th	year, based on	193 cases
37.0	chances by end of	6th	year, based on	128 cases
44.7	chances by end of	7th	year, based on	66 cases
62.2	chances by end of	8th	year, based on	42 cases
73.0	chances by end of	9th	year, based on	6 cases

The duration of treatment required for arrest is governed by the type of the lesions. Nodules require more treatment than diffuse infiltrations, and macules less than either: 43 patients with macules required 31 months; 21 with infiltrations required 44 months; and 45 with nodules required 65 months. Short courses of dihydrostreptomycin, in combination with a sulfone or in alternation, are recommended in certain leprous conditions. From the public health point of view, patients who are clinically improved but still positive for *M. leprae* are "open cases," the chances of their transmitting the infection increased by the fact that those whose lesions are no longer visible are more prone than others to carry on a normal life and increase the frequency of contact with susceptible individuals. Because of the tendency to relapse, maintenance doses of sulfone should be given indefinitely. Among the experimental drugs being evaluated at Carville, amithiozone (tibione) is considered the most promising. Limited experience with cortisone has shown that it may be of value in lepra reactions.

This paper was discussed by Dr. Marcel Roche of Venezuela, who had recently collaborated in a trial of ACTH in lepra reaction, with encouraging results [see THE JOURNAL **19** (1951) 137-146.]

KELLERSBERGER, E. R. The social stigma of leprosy. Pp. 126-133.

The social stigma connected with leprosy, the author points out, makes it different from all other diseases. He relates his varied experiences in travels throughout the world and the ideas held by various peoples. The

change of the title of the American Mission to Lepers to American Leprosy Missions was made because of the handicap in seeking office space and objections to the letterheads when writing to patients. It is believed that the Bible is not the cause of the stigma, nor is it due to Christian attitudes. Many instances of inhumane attitudes toward persons with leprosy in the United States are cited. It is held that the medical profession will never be able to control the disease until the social stigma has been eradicated and a new social outlook and attitude have been established. It is held possible for this age-old disease to be eradicated from the earth in our generation, but along with medical and physical therapy and research there must be mental, psychological, and spiritual therapy as well. The whole man must be treated.

DOULL, J. A. The control of leprosy. Pp. 134-141.

The control of leprosy depends upon the interruption of transmission of the infection from the source to the susceptible contact. The only measure which has any scientific basis in the control of the bacteriologically positive cases, the reduction of exposure to them on the part of healthy persons. Segregation of such cases undoubtedly would cause the decline of leprosy wherever that measure could be successfully administered, but there are practical limitations to its applicability. Recourse must therefore be had to other possible means of reducing exposure: (1) education of patients; (2) raising of economic levels, with better housing; and (3) chemotherapy. With regard to therapy in reducing patient-years of infectiousness, there are many practical requirements which must be met before control by this means can be looked upon with optimism. Some of them are: (1) Adequate staffs and proper organization of the health departments in areas of high prevalence. The cost of sulfones is not the chief obstacle to their use, but the lack of the machinery for their effective distribution. (2) Leprosy surveys must be made to ascertain the prevalence of the disease. (3) If the objective is the control of the disease, only lepromatous (open) cases should be treated; other cases are not of importance in spreading the disease, and their relative frequency may demand much more time and drugs than those of the lepromatous type. (4) Districts and clusters of households with higher prevalence should be selected for first attention, and, within these districts, patients who are exposing young children to risk of infection. (5) A plan for control should envisage continuance of intensive efforts for many years. The health officer is in a particularly difficult position in respect to leprosy. Fear of the disease is great, and not likely to be abated soon. In consequence, popular demand for strict isolation is very strong, and he may be subjected to criticism for taking lesser measures. He must weigh the low attack rate of the disease against its seriousness, protect children against exposure wherever possible, and obtain for the patients the treatment most likely to shorten the period of infectiousness.