

## CURRENT LITERATURE

*It is intended that the current literature 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.*

ARNOLD, H. L., JR. American medicine in Hawaii, 1820-1959. *New England J. Med.* **261** (1959) 694-699.

The author points out that public health measures evolved in response to need. Leprosy may have been first noted in Hawaii in 1840 (by Dr. Dwight Baldwin, a missionary physician from Durham, Connecticut); it was officially diagnosed in 1856; and it swiftly became endemic. The leprosy work in Hawaii still costs well over \$1,000,000 a year (almost a third as much as all other public health expenditures together), but leprosy is now a steadily declining problem in point of numbers. The annual incidence has dropped in the past two decades from 40 to 15, and about one-third of the cases are imported. Active cases under treatment at the Hale Mohalu Hospital were 95 in 1954, and only 72 in 1958; at the Kalaupapa Settlement the drop was from 148 to 76. Bacteriologically negative cases receiving outpatient treatment, many of them on mere maintenance therapy, have increased from 130 in 1954 to 160.—SR. HILARY ROSS

[ETHIOPIA] Report of the First National Leprosy Conference of Ethiopia, Addis Ababa, 1957. Pamphlet, 80 pp.

This conference took place August 29-31, 1957, at the Princess Zenebework Memorial Hospital, the country's central leprosarium, under the chairmanship of Dr. K. F. Schaller, chief of the Leprosy Control Service of Ethiopia and medical director of the hospital. The members included representatives of the United Nations, of WHO, and of Unicef, and also the chief of the Leprosy Control Service of Eritrea (Dr. C. Greppi). From the 24 speeches and papers, and 6 demonstrations, much can be learned of what is known of the leprosy situation, and about the antileprosy activities in the country. According to data presented by Schaller the sex ratio is nearly 3:1, a predominance of males existing even among children. About 25% are lepromatous, 14% tuberculoid, and 61% indeterminate. Estimates of prevalence for the different provinces vary from 5 to 140 per thousand, with a probable average of 15, or 200,000 cases for the country. There are some 1,735 patients in the 4 leprosaria: Princess Zenebework Hospital at Addis Ababa (government, 1,250), St. Anthony's Hospital, at Harar (mission, 208); one at Shashamana, in Arussi Province (mission, 247); and one in Kaffa Province (government, 30). There are 6 segregation villages in as many provinces (government, mission and Ethiopian Church), with 1,754 patients. Of outpatient clinics in operation there were 16 at the time, in 8 provinces, with an enrollment of 26,651 patients. The Institut Pasteur of Ethiopia (Dr. C. Serie) collaborates with the central office in routine work and in research (electrophoresis, the Rubino test, and the Middlebrook-Dubos test). In Ethiopia there is no habit of hiding the disease—fortunately, although that may contribute to its spread—and released patients evidently present no serious social problem. Unicef and WHO were collaborating in the field program, and rapid progress had been made in the previous three years. Although Schaller holds that, from the legal point of view, leprosy control can be handled under the provisions of existing general legislation for the control of communicable diseases, nevertheless the possible need of additional legislation was contemplated [but, we are informed, has not been pursued]. A proposal to organize an

Ethiopian Leprosy Association (including Eritrea) was approved, and Schaller was elected as organizer. [Copies of this report are obtainable from Dr. K. F. Schaller, P. O. Box 1133, Addis Ababa, Ethiopia.]—H. W. W.

WARDEKAR, R. V. Fourth report, Gandhi Memorial Leprosy Foundation. Wardha, 1958, 114 pp.

This report of the secretary of the Foundation, which covers the entire period of operation of this important pioneer activity to the end of 1958, is the first to give statistical information of each of the 10 control units—which have, in total, 27 clinics. Brief narrative statements reveal some of the many difficulties of such an operation. Examples: The experience of two units shows that work done in an uncooperative community cannot be successful. In one area there were difficulties of recording because the people do not live in villages. Workers from the plains had found difficulties in adjusting themselves to work in hill country. An idea of the type rates among the cases found by the different units in the different parts of the country may be obtained from the data of cases registered during the first two years of work in each instance. The numbers of cases varied from 92 and 144 in two of the least cooperative communities to 404 and 479, with a total of 2,961 (average 296). The lepromatous cases, including a few typed as borderline, were from 10-20% among the cases registered except in the uncooperative communities, where the percentages were 32 and 34. The tuberculoid cases ranged from 15% to 50%, and the maculoanesthetics from 21% to 52%. (The over-all averages: L, 16; T, 32; Ma, 36.) The other case groups were indeterminate and polyneuritic (8.0% and 7.5%). Most of the reports indicate changes in the later period after the beginning of the work; proportionately fewer lepromatous and polyneuritic cases and more tuberculoids are now being found, and of macular cases higher proportions with few lesions, and, altogether, smaller proportions of cases with deformities. A training class for social workers set up at the first unit established was later transferred to another unit because of reduction of cases suitable for teaching purposes. The central laboratory for histopathology, because of difficulties in a rural community without electricity, has been transferred to Wardha. Grants of one kind or another have been made to some 16 institutions, including research grants to Bombay and Vellore, and there are summary reports concerning them.

[From later data (compiled for the WHO Inter-Regional Conference held in Tokyo in November 1958) are taken the following points: (1) Of 2,340 cases found in the first surveys (first two years of the units' work) 24% had deformities, but only 8% of the 1,525 cases found subsequently. (2) Of 2,327 cases with no or only slight thickening of the nerves when registered for treatment only 1% had developed deformities later, against 6% of the cases which had had more marked nerve thickening. (3) Regarding the clearing of macular forms (I, Ma and T) under treatment, the results have varied somewhat with the number of macules at the time of registration: 1 macule, 44%; 2 or 3 macules, 37%; 4 or more macules, 31.5%. (The difference between the first and third of these groups the author regards as significant.) (4) Of the cases classified as lepromatous 95% were found bacteriologically positive at the time of registration, whereas on the latest examination in 1958 only 50% of them were positive. Positive by period of treatment: 4-6 years, 22%; 2-4 years, 52%; less than 2 years, 79%.]—H. W. W.

[BELGIAN CONGO] Rapport Annuel de la Direction Générale des Services Médicaux, 1957 (unsigned). Mimeographed, 126 pp.

The extensive antileprosy campaign, undertaken as a program of the Père Damien Section of Foreami, based primarily on ambulatory treatment of noncontagious cases, is continuing throughout the territories of the Belgian Congo. With increase of the numbers of treatment centers, it is believed that all persons with leprosy can now get treatment near their homes. The total number of cases was 271,114, compared with 275,293 at the end of 1956. Selection of cases for segregation has resulted in a marked decrease in the number of cases segregated; in the 9 "centers of segregation" listed (which serve as

regional centers of treatment) there were only 904 cases, 184 of them new in 1957. The Père Damien had created four teams to study the influence of BCG vaccination on the evolution of leprosy. They are working in highly contaminated foci, making tuberculin and lepromin tests to ascertain the changes brought about by BCG. (This report is "dimorphous" in language, *antilépreuse* being used in one paragraph and *antihansénienne* in the next; the words *lepreux* and *hanséniens* both appear twice.)—H. W. W.

[WESTERN AUSTRALIA] Report of the Commissioner of the Public Health for the Year 1957. Perth: Government Printer, 1959.

At the end of the year there were 175 patients in the Derby leprosarium (for aborigines), down somewhat from the average of 185 for the preceding 5 years. There had been 33 admissions or readmissions, about the same as in previous years, but 44 discharges. The tuberculoid form is increasing in relative frequency, although the lepromatous form, still predominates. When leprosy was introduced about 50 years ago it spread rapidly in the nonimmune population, with a heavy preponderance of lepromatous cases. Five leprosy cases (in whites) were also treated in the Wooroloo Tuberculosis Sanitarium during the year, and all but 1—an advanced case present since 1936—were discharged.—H. W. W.

[EAST AFRICAN LEPROSY RESEARCH CENTER] Annual report of the East African Leprosy Research Centre (John Lowe Memorial), 1st July 1957-30th June 1958. Nairobi, Government Printer, 1958.

In response to local requests, the name of the location of this center has been changed from Itesio to Alupe. Work during the year had been affected by changes of personnel. Three clinics in Kenya are supervised, and this will be extended to 6 clinics in Uganda. Results of treatment with diphenylthiourea continued to be encouraging, with no more unpleasant reactions than with standard drugs and apparently more uniform effects.—H. W. W.

CHENEVEAU, R. La lutte contre la lèpre en A.E.F. [The campaign against leprosy in French Equatorial Africa.] *Méd. Afrique noire* (Dakar) **5** (1958) 535-538.

Beginning in January 1954, all available agencies were mobilized under the Service Général Mobile d'Hygiène et de Prophylaxie. The Service made a leprosy survey, placed the patients in each region under the care of a doctor, and allotted them for treatment to hospitals, agricultural colonies, treatment centers, or domiciliary treatment in the villages. The census showed the numbers of patients and percentages of population according to territories: Middle Congo 11,188 (1.6%), Gabon 7,057 (1.8%), Oubangui-Chari 56,508 (5.1%), Tchad 40,883 (1.6%)—total 115,636. The type percentages were: lepromatous 7, tuberculoid 54, indeterminate 39. Sulfone treatment is either by tablets given weekly or by injections of a slow-absorption suspension given twice a month. The greatest difficulty results from the distances that have to be traversed, often through country without suitable roads. Many of the patients are gathered together in villages, and these are preferably situated along the main roads so that they can be easily reached by mobile dispensaries. Motors are used when possible, but often the assistant has to travel with his equipment by bicycle. Motors often have to traverse a circuit of 1,500 km. twice a month, and bicycle a circuit of 150 to 200 km. In other parts, where neither motor nor bicycle can pass, it is necessary to travel by horse or ox. Details of finance are given, with acknowledgment of aid received from certain international funds and from missions and charitable societies.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 454.]

WORSFOLD, J. T. The leprosy endemic in Northern Rhodesia, with special reference to sex incidence. *Leprosy Rev.* **29** (1958) 222-226.

✓ The author's intensive survey of the Balovale District of Northern Rhodesia gives a leprosy incidence of 11.85 per 1,000, which roughly corresponds with the results of previous, more extensive surveys in Northern Rhodesia. The familial source of infection

is shown by the fact that 66% of all patients have a near relative with the disease. The sex incidence is unusual in that at Chitokoloki Leprosarium males did not preponderate; there were 1,745 males to 2,281 females, or 1.0:1.3. The author suggests that the emancipation of women in this district and their growing freedom may have caused a temporary increase in leprosy which may be preliminary to a general diminution in the disease. He does not think that it is dependent on any inherent quality in the women themselves.—[From abstract in *Trop. Dis Bull.* **56** (1959) 445.]

KITANO, H. Epidemiological studies on leprosy in Gifu Prefecture. IV. Summary. *La Lepro* **27** (1958) 429-436 (in Japanese; English abstract).

Although the numbers of fresh cases in Gifu prefecture have decreased in recent years, the total number of patients (in the leprosarium and in private homes) has increased slightly due to decrease in mortality. The total number of cases is believed to be 246 (1.58 per 10,000). The number of nonhospitalized patients, treated at home, has decreased by 113 in the past 20 years to only 24 (0.15 per 10,000), most of them old cases whom it would be difficult to induce to enter leprosaria. The small number of home patients with the lepromatous form, the marked shift to the right in the age distribution curve of both the total and new cases, the high proportion of cases of 11 or more years of duration, the type ratio (L:M+N) in new cases, and the reduction in sex ratio, all suggest that the epidemic in this prefecture is nearing the end of its course. Gifu has reached the average level of the whole country, and can no longer be considered a leprosy-prevalent prefecture (except among Koreans living there). It can be assumed that the number of undetected cases has decreased sharply due to the program of early examination and detection. The estimate of about 15,000 leprosy patients in Japan is considered too high; about 13,000 (i.e., 1.46 per 10,000) is probably closer to the actual number.—[From abstract.]

HWANG, MING-YI. Die Bekämpfung der Lepra in Süd-China. [Management of leprosy in South China.] *Dermat. Wehnsehr.* **139** (1959) 360-361.

In China, leprosy is most prevalent in the province of Kwantung. It was reported officially in 1957 that the total number of cases in the whole of China amounted to 380-390 thousand, of which 3,600 were hospitalized. Kwantung now has 5 leprosy colonies, a greater number of ambulatory treatment centers, and the two leprosaria at Santschau (1,025 patients) and Schautam (250-300 patients). Of the Santschau leprosarium it is reported that most of the patients have the lepromatous form; two-thirds of them are men. Men and women are strictly separated, and are occupied with work. Besides the sulfones, thiosemicarbazones and isonicotinic acid preparations are used. Treatment is given twice monthly. The aim is to admit all lepromatous cases to specialized hospitals and to treat tuberculoid cases ambulatorily. People who have been living in contact with leprosy patients undergo BCG vaccination.—E. KEIL

SAÚL, A. La enseñanza actual de la leprología en México. [The present teaching of leprology in Mexico.] *Dermatología (Mexico)* **1** (1957) 343-348.

The author speaks of the still-existing prejudice inspired by leprosy, and of how little the present ideas about the disease have penetrated even the physicians, to say nothing of the general population. In Mexico importance is given to the teaching of leprology; the Mexican physician should have a fuller knowledge of the disease because it is a social problem in this country. The instruction should be extended to the medical students; they should be taught in the departments of dermatology of the universities. The dermatologist should be a leprologist, and should cover both the medical and social aspects. For physicians, the teaching is given in short courses, as in the annual course given by the Sociedad Mexicana de Dermatología, in which the subject of leprosy has a prominent place. For the general public, information is given by means of lectures, pamphlets and magazines, emphasizing the fact that leprosy is not as contagious as it is

believed to be, that it is now curable, and that the patient will not be segregated in leprosaria but will be treated like patients with any other disease.—M. MALACARA

✓ AGUIRRE DE GONZALEZ, A., MEZA, D., SANTILLAN, G., RAMOS, J. and ALVARENGA, A. E. Pesquisas de casos de lepra em Assunção. [Survey of leprosy cases in Asunción.] *Rev. brasileira Leprol.* **29** (1958) 27-31.

A survey of Asunción, the capital of Paraguay, showed among a population of 248,955 a leprosy prevalence of 3 per 1,000. The rate increased with age. The type rates were: tuberculoid, 39.6%; indeterminate, 30.0%; lepromatous, 28.3%; there were also 8 pre-lepromatous cases. During the survey 381 patients were enrolled. Compulsory segregation has been abolished, and the patients are given intensive sulfone treatment at outpatient dispensaries.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 445.]

✓ GONZALEZ PRENDES, M. A. and YBARRA PEREZ, R. Importancia del examen de los convivientes de hansenianos en la búsqueda de nuevos casos de lepra. [Importance of the examination of contacts of leprosy patients in the search for new cases.] *Rev. Sifilog. Leprol. y Dermatol.* **14** (1958) 9-12.

The records of 428 patients of the San Lazaro Hospital who had reported family contacts, in total 2,165, showed that 109, or 25%, of the patients reported 165 infected persons among their contacts, and it is believed that if the contacts had been actually examined the number would have been higher. It is pointed out that the examination of contacts should be regarded as of basic importance in an antileprosy campaign.—H. W. W.

✓ QUAGLIATO, R. and VEITIEKA, J. Revisão dos focos de lepra. Cadastro lepromínico e exames de comunicantes pelo sistema de convocação—viabilidade—rendimento—aspecto económico. [Review of the foci of leprosy; lepromin register and examination of contacts under the convocation system: viability, value and economic aspect.] *Rev. brasileira Leprol.* **26** (1958) 273-293.

The authors tried to examine leprosy contacts by convocation (invitation through letters, sanitation agents, etc.), but the average attendance was only about one-third. The average percentage of new cases found among the contacts examined was about 1.8—which rate would probably be increased if the absent two-thirds of the contacts could have been examined. Home examinations in large areas were very difficult, and the public health visitors have had the same experience. Taking into consideration only the days of work of the workers directly connected with the inquiry, the finding of each new leprosy case cost about Cr.\$6,600. The lepromin test was read in 60% of the new cases, with 50% positive results.—[From authors' summary.]

✓ MONTEL, M. L. R. Les "inconnues" du problème de la lèpre. [The "unknowns" of the leprosy problem.] *Bull. Soc. Path. exot.* **51** (1958) 698-708.

This discourse, presented during the celebration of the 50th anniversary of the Society, held in Paris, November 18 and 19, 1958, is not readily susceptible to summarization. The unknowns were discussed under the following headings: the bacillus, the granular forms of the bacillus (with pictures), tuberculoid leprosy, the Fernandez and Mitsuda reactions, BCG and the Mitsuda reaction, the "isopathie phenomenon" of Sagher, puncture biopsy of the liver, electrophoresis, lepra reaction, and therapy (uncertainty about the mode of action of the sulfones) and about actual cure.—H. W. W.

✓ BRESANI SILVA, F. El síndrome neural leproso; ensayo de sistematización. [The neural syndrome of leprosy; an attempt at systematization.] *Rev. peruana de Salud publ.* (Lima) **5** (1956) 85-340; 381-502 (Nos. 2, 3 & 4); **6** (1957) 3-116 (No. 1.). Reprinted, with serial pagination, 1958.

This exhaustive monograph of 470 pages, plus a 4-page laudatory introduction by Pesce, with 368 tables, is the result of an exceptional study by the medical superintendent



of the Colonia de San Pablo at Loreto, Peru, of the neural manifestations of the 400 patients in that institution—of whom, it is said, 95% showed both skin and nerve disorders, 3.5% were exclusively of the nerve type (primary or secondary), and 1.5% were of the cutaneous type. It is divided systematically into three parts: material and methods, neurologic observations, and neurologic evolution, with a total of 14 chapters, besides which there is a general summary and a section on conclusions reported in English and French. Presumably, copies can be obtained from the Division of Leprosy, Ministry of Health, Lima, Peru.—H. W. W.

TARABINI C., G. and TERCENIO, J. Consideraciones patogénicas acerca de los momentos de origen de la enfermedad de Hansen. [Pathogenic considerations regarding the origin of leprosy.] *Rev. Leprol. Fontilles* **4** (1958) 345-353.

The authors propound a hypothesis regarding the determining factors in the onset of leprosy, showing in a group of 25 patients studied that onset was connected with various circumstances of stress, such as the death of a spouse, grave economic difficulties, emotional distress, serious illnesses, childbirth, etc. All these conditions are liable to have an adverse effect on hormonal secretions. Another consideration is the size of the adrenals during early childhood. These glands increase in intrauterine life up to the sixth month, when they are larger than the kidneys; after that they diminish and do not regain their former size until the child is 12 years old. The authors suggest that this may account for the greater susceptibility of children to leprosy, and that spontaneous recovery from early leprosy may be connected with increase in size or function of the adrenals. They also refer to the theory already propounded that severe lepra reaction and exacerbations of leprosy are connected with adrenal insufficiency. On these considerations they found the hypothesis that resistance to leprosy is closely connected with the function of the adrenals.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 446.]

SAÚL, A. Lepra infantil; estudio de un caso tuberculoide. [Infantile leprosy; study of a tubercloid case.] *Dermatología (Mexico)* **2** (1958) 45-55.

A general discussion of infantile leprosy, with a report of a case in a child 3½ years old who for more than a year had lived in the same house with a lepromatous patient. There were two plaques on the right cheek, proved tubercloid by biopsy, which subsided markedly in 6 months without treatment. The child was lepromin positive while the other members of the family, without evidence of infection, were lepromin negative.—H. W. W.

JONQUIERES, E. D. L. Lepra tuberculoide, variedad nodular de Souza Campos en un niño de 2 años. [Tubercloid leprosy; the nodular variety of de Souza Campos in a child 2 years old.] *Rev. argentina Dermatol.* **42** (1958) 191-195.

A case of tubercloid leprosy of the nodular childhood variety of de Souza Campos is reported. From that author's observations the "self-healing" nature of this form is assumed. The immunity mechanisms which are responsible for its appearance and expected spontaneous resolution are discussed. This last phenomenon seems to be peculiar to childhood below the age of three years.—[From author's summary, supplied by G. Basombrio.]

JONQUIERES, E. D. L. Control de las reacciones leprosas tuberculoides con prednisona. [Control of tubercloid lepra reactions with prednisone.] *Rev. argentina Dermatol.* **42** (1958) 173.

From experience with 17 cases of reactional tubercloid leprosy the author believes that prednisone, easy to use and not dangerous in the proposed dosage, is the corticoid of choice for the control of the hyperergic dysreactive phenomena in this condition. It seems probable that this hormone, used in combination with DDS, will increase both the tolerance to that drug and its therapeutic effect on the granuloma, hastening its resorption.—[From author's summary, supplied by G. Basombrio.]

- ✓ CHAMBON, L., PESTEL, M. and NGUYEN-VAN-AN. Contribution a l'étude de la réaction d'inversion dans la lèpre. [Contribution to the study of the reversal reaction.] Bull. Soc. Path. exot. **51** (1958) 554-562.

Of 20 patients with lepromatous leprosy treated with D-cycloserine, 12 underwent marked reactions of the reactional tuberculoid (or reactional borderline) type, the regression of which was marked by the appearance of cutaneous lesions having characters proper to the transitional and tuberculoid forms. The inflammation of this reversal process should be controlled by appropriate drugs to limit the harmful effects of too great production of fibroblasts. The condition is independent of reactivity to lepromin. It seems to be due to a disturbance of the metabolism of the Hansen bacilli by the cycloserine, which in certain conditions can traverse the walls of the histiocytes. The effect of this reaction is beneficial.—AUTHORS' ABSTRACT

- ✓ SUSMAN, I. A. Clinical observations on erythema nodosum leprosum (E.N.L.). Leprosy Rev. **29** (1958) 227-231.

Of the 328 lepromatous patients at the Ankaful Leprosarium in Ghana, during a 4-year period 174 suffered from 906 attacks of erythema nodosum leprosum (ENL), with cutaneous eruptions, fever and pain. In most cases the ENL was cyclic, with a cycle of 1 to 6 months. It was especially common in those with high bacteriologic indices. It was not related to the drug used (DDS, Sulphetrone [solapsone] or thiacetazone), nor was there any correlation with the stage of the disease or the season (52% in the wet 6 months, 48% in the dry 6 months). Stibophen was only a palliative, but doses of 25 I. U. of corticotropin intramuscularly gave dramatic improvement, and it was generally not necessary to continue it for more than 3-10 days.—[From abstract in *Trop. Dis Bull.* **56** (1959) 452-453.]

- ✓ CARBONI, E., MERCAU, A. R. and SERIAL, A. Reacciones tuberculoides a lesion única. [Tuberculoid reactions with single lesion.] *Leprológia* **3** (1958) 53-56.

The authors present three cases of tuberculoid leprosy reaction, all in adults, each with a single lesion located on the face. In two of them the lesion appeared in apparently healthy skin; in the third one it was on the site of a previous lesion. Clinically and histologically the lesions were the same as the reacting elements in cases with multiple lesions; the bacteriologic examinations were negative, and the lepromin reactions were strongly positive. Two of the patients were released after 3 and 5 years of treatment, resp., and they showed no subsequent changes during a further observation period of 5 years.—[From authors' summary, supplied by G. Basombrio.]

- ✓ MELAMED, A. J. La reacción leprosa. [Leprea reaction.] *Med. Panamericana* **12** (1959) 55-74.

A synthesis of the material presented is as follows: (1) Leprea reaction is constituted of acute and subacute inflammatory phenomena basically localized in the preexisting granulomatous lesions and subsidiarily outside of them. (2) These phenomena are conditioned by the global disturbances of all the elements of the connective tissue (extrinsic and intrinsic) which occur in the leprotic foci, and they are precipitated by agents which exacerbate or aggravate that disturbance, quantitatively or qualitatively. (3) The acute inflammation (vascular phenomenon) and the necrosis of the leprotic foci are intimately bound by relationships of cause and effect, in such a manner that the inflammation or necrosis can be the original and apparently only phenomenon in mild cases, although they are two links of a long and indefinite chain in the more grave cases of lepra reaction. (4) The factors of most importance in the conditioning and precipitation of lepra reaction are: (a) vascular ataxia of neural origin, (b) disturbance of the permeability of the fundamental substance (capillary permeability, precipitated colloids, anoxia), (c) phenomena of autoimmune antibodies, (d) variations of the antiphlogistic hormones in relation with stress situations, and (e) dysproteinemia and particularly hypoalbuminemia.—[From author's summary, supplied by G. Basombrio.]

MELAMED, A. J. Los tiocianatos en la reacción leprosa. [The thiocyanates and lepra reaction.] *Leprología* **3** (1958) 44-52.

In a previous study it was found that phenylbutazone has a special capacity of precipitating or aggravating lepra reaction, apparently due to its effect on capillary and cellular permeability and the amount of disposable fluid. Potassium thiocyanate has now been studied because of a theoretic possibility that it may also modify the collagen. It has been found to have the same effect of usually provoking and/or aggravating lepra reaction. Combining the two drugs strengthened this effect, although not constantly. Modifications of the cellular, vascular and interstitial permeability are the principal factors which provoke lepra reaction, but the author does not exclude complementary factors such as sensitivity phenomena, in relation with the collagenosis. The mechanism of action of thiocyanate in lepra reaction may explain the enigma of the sensitiveness of leprosy to iodides, considering the equal capacity of both drugs to affect the collagen.—[From author's summary, supplied by G. Basombrio.]

MELAMED, A. J. and BARCIA, A. El proteinograma seriado en la reacción leprosa tratada con hormonas antiflogísticas. [The serial proteinogram in lepra reaction treated by antiphlogistic hormones.] *Leprología* **3** (1958) 57-67.

The variations of proteins in two patients with lepra reaction, under treatment with prednisone and ACTH, were studied by means of electrophoresis on paper. The most important modifications while the hormones were being given and the reactions were being controlled were increase of albumin and diminution of alpha-2-globulin. When the dose of hormone diminished and the lepra reaction recrudesced, however, there occurred diminution of albumin and increase of alpha-2-globulin. The proteinogram showed, as a whole, a tendency to normalization during the steroid therapy. The well-known diminution of serum albumin and the increase of alpha-2-globulin in leprosy, and especially in lepra reaction, is correlated with similar changes in the nephrotic syndrome, and also in other processes of very different etiology although probably of common physiopathogenesis.—[From authors' summary, supplied by G. Basombrio.]

CONTRERAS, F., GUILLÉN, J., TERCENIO, J. and TARABINI C., G. Pronóstico de las leproreacciones. [The prognosis in lepra reaction.] *Rev. Leprol. Fontilles* **4** (1958) 317-323.

The authors consider that when there is any "stress" on the body an alarm is sounded against the aggressor, whatever it is, and in the first phase this is accompanied by a discharge of corticotropin which acts on the adrenals so that they liberate defensive hormones. In the second phase, that of resistance, the suprarenal hyperfunction stimulates all the metabolic functions of the economy and by its antiphlogistic action repels the inflammatory condition. When the aggressor is overcome the reaction disappears. In the third phase, that of exhaustion, the organism can no longer resist the aggressor and a state of lepromatization occurs and causes constant infiltrations and ulcerations and leads to fatal amyloidosis and cachexia. The authors therefore divide cases with lepra reaction into groups according to the numbers of reactions they have had. Since 1946 the number of patients at Fontilles has increased from 267 to 301, but the number of reactions has decreased from 197 to 99, and the number of deaths from 25 to 8. The diminution of deaths is held to be a result of the diminished reactions.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 446.]

CHATTERJEE, K. R. and PODDAR, R. K. Autoradiographic observations on the uptake of diaminodiphenyl sulphone in tissues of leprosy patients. *Bull. Calcutta Sch. Trop. Med.* **5** (1957) 158-159.

Biopsy specimens of healthy and affected tissues from leprosy cases were taken after a single oral dose of 4  $\mu$ c./kgm. of DDS tagged with S-35. Frozen sections of the formalin-fixed specimens were mounted, dehydrated, and covered with autoradiographic



emulsion. These preparations were sealed against moisture and light and stored at 4°C for periods varying from 8 to 12 months as indicated by the activity of each as ascertained by the Geiger-Müller counter. They were finally developed and examined with the phase-contrast microscope. Blackened photographic grains, indicating the presence of the radioactive drug, were found to be more dense in the affected tissues than in the normal ones. In the latter their distribution was more or less general, in the former they were more densely aggregated around the various appendages of the skin and also in the infiltrated zones. Such grains were found particularly in histiocytes, epithelioid and foamy cells, Schwann cells, and nerve fibers.—N. MUKERJEE

[For an abstract of a more general report of this study, see *THE JOURNAL* **25** (1957) 299. This particular report was not known about at that time, but this abstract is used now because the investigation reported was so unusual.—EDITOR.]

GATÉ, J., ROUSSET, J. and COUDERT, J. Essai de traitement de la lèpre par la diphenylthiourée (15.095 Ciba). [Trial of treatment of leprosy by diphenylthiourea (Ciba 15,095).] *Bull. Soc. française Derm. et Syph.* **65** (1958) 164-185.

Beginning in March 1957 the authors used Ciba 1906 in 11 cases of leprosy, in 3 cases simply to see how well it was tolerated, therapeutically in the 8 other cases. The initial dose was usually 1.5 gm. daily, usually maintained at that level (or 2 gm.), but if necessary increased to as much as 4.5 gm. daily. The drug is so well tolerated that courses of treatment can be extended over prolonged periods without need for interruptions. The results were encouraging, both clinically and bacteriologically. In one case a combination of Ciba 1906 and prednisone yielded good results.—[From abstract in *Lit. Rev. (Ciba)* **4** (1959) 12.]

ALONSO, A. M. Nossas observações sobre a difenil-tiouréa no tratamento da lepra. [Observations on the treatment of leprosy with diphenyl thiourea.] *Bol. Serv. nac. Lepra* **17** (1958) 5-11.

Report of experience with Ciba 1906 over a period of 16 months in 7 leprosy cases, 1 tuberculoid and 6 lepromatous. The usual dosage was 3 gm. daily by mouth, in 3 fractional doses. The drug was well tolerated; even when administered uninterruptedly for more than a year, there were no side effects or toxic reactions. The therapeutic results are referred to as very satisfactory. Especially interesting is the case of a patient who had undergone a partial gastrectomy and was unable to tolerate either oral sulfone treatment or intramuscular thiosemicarbazone injections; he tolerated the Ciba 1906 well, and the response was so good that the lesions regressing markedly within only 12 months.—[From abstract in *Lit. Rev. (Ciba)* **4** (1959) 13.]

SCHMID, K. and TRIPOD, J. Experimental investigation of the absorption and excretion of Ciba-1906 (DPT). *Leprosy Rev.* **30** (1959) 85-97.

Different batches of Ciba 1906 (DPT) were tagged with radioactive carbon ( $C^{14}$ ) and sulfur ( $S^{35}$ ), and their metabolism in rabbits and dogs was studied. It was clearly demonstrated that in these animals there is good absorption after oral administration, in spite of failure to demonstrate DPT in the blood or urine by color reactions, and it is probable that this holds true for man as well. Very little is excreted in the urine unchanged, the drug being rapidly and completely metabolized after absorption; but where and how degradation takes place is not known because of definite metabolites have not yet been identified in blood, urine or bile. It therefore remains a question whether the therapeutic action is due to the drug itself or to its metabolites.—H. W. W.

DAVEY, T. F. and HOGERZEIL, L. M. Diethyl dithiolisophthalate in the treatment of leprosy. (ETIP or 'Etisul'); a progress report. *Leprosy Rev.* **30** (1959) 61-72.

Following the work of Del Pianto who found that a mixture of certain thiol compounds prevented the development of tuberculosis in guinea-pigs, the authors decided

to test the effects of diethyl dithiolisophthalate (ETIP, or Etisul) in the treatment of leprosy. The ester formed from isophthalic acid and ethyl mercaptan is a bland pale yellow oily liquid with a disagreeable garlic-like smell. The first trial on 9 lepromatous patients, when 3 cc. of a 70% cream was rubbed over a large area of the body once a week, proved self-limiting because the smell on the patients' breath proved too offensive. In a second trial with 22 patients, using a more effectively perfumed ETIP preparation, of which 6 cc. was rubbed twice a week only over parts of the body not covered by clothes, the treatment was more acceptable, and with some difficulty patients were persuaded to continue for periods up to 5 months. In a third group of patients, 10 lepromatous and 5 nonlepromatous, the drug was rubbed over a large area of the body [special reference to the back]. It was found (1) that when ETIP was associated with DDS, the disease took a particularly advantageous course; and patients in whom there was a macular element in their clinical picture did particularly well. Also (2) that contrary to the usual sequence, bacteriologic progress preceded clinical progress. (The bacterial index graph of the treated cases is compared with a standard graph of cases treated with DDS, a comparison which the author regards more reliable than the use of an individual control group.) There is evidence that drug resistance may develop quite quickly if the drug is used alone. Thus this one cannot be included among the basic leprosy remedies, but it appears to have a place as an adjunct to oral chemotherapy.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 542-543.]

DE ALMEIDA NETO, E. and PAREJA REVELLES, J. O emprego da D-cycloserina no tratamento de lepra. (Resultados preliminares.) [The use of D-cycloserine in the treatment of leprosy; preliminary results.] *Rev. brasileira Leprol.* **26** (1958) 63-102.

The authors have used D-cycloserine in the treatment of 20 lepromatous patients, most of them either untreated advanced cases or else sulfone resistant. The maximum dose was 4 to 6 250 mgm. tablets daily; treatment lasted 1-11 months. In 4 cases sulfones were added to the treatment, and in 1 case thiosemicarbazone was given. The results are given in full detail, with photographs. The clinical results were rapid and striking. None of the patients had as yet become bacteriologically negative but there was marked improvement, especially in the nasal smears. It is believed that the drug acts in a different manner from the sulfones, directly on the bacillus, and that consequently there is a great advantage in the combined treatment. Side-effects and serious reactions are uncommon, and signs of drug resistance have not been encountered; consequently, the drug should be used especially on patients intolerant of or unresponsive to sulfones. Longer trials are, however, necessary.—[From authors' summary.]

BECKETT, D. W. A trial of antigen marianum as an adjunct of D.D.S. in the treatment of lepromatous leprosy. *Leprosy Rev.* **29** (1958) 209-214.

In this trial 84 lepromatous-type patients were treated with "antigen marianum" in addition to DDS, over a period of 3 years. The antigen was given 0.1 cc. intradermally once a month for 6 months; three of these 6-month courses were given with a 6-month interval between. Controls on DDS alone were 21 lepromatous patients in whom on the whole the disease was rather more active than in the trial group. Lepromin positivity of the 84 was 15% at the beginning, and 82% at the end of the trial—at which time 31% had been discharged, 43% others were improved, while 26% were stationary or worse. The figures for the controls were: 19% discharged, 57% improved and 24% no better. It is concluded that conversion of the lepromin reaction did not necessarily indicate that the patient had become more resistant to the infection, or that the type of disease had changed from lepromatous to tuberculoid. "It is concluded that antigen marianum was of no value when given as an adjunct to DDS in the treatment of lepromatous leprosy."—[From abstract in *Trop. Dis. Bull.* **56** (1959) 453-454.]

BOUZAS, A. Quelques manifestations inaccoutumées consecutives à l'infection sous-conjonctivale des corticostéroïdes chez les lépreux. [Unusual manifestations following subconjunctival cortisone injections in leprosy patients.] Bull. Mem. Soc. française Ophth. **71** (1958) 540-550.

Subconjunctival injections of cortisone acetate and hydrocortisone acetate are well tolerated in ordinary patients, and only occasionally has slow absorption of the drug been noticed, although animal experiments—especially in monkeys—have shown transitory foreign-body nodule formations at the place of the injection. The eyes of 22 leprosy patients reacted quite differently. Resorption of the subconjunctival depot was much slower, and in the conjunctiva there were observed local atrophy, temporary surface ruptures, discoloration, or nodule formation; also transitory groove formation of the marginal cornea without epithelial defects. These unusual reactions could be explained by a decreased resistance of the local tissue or by specific reactions to the hormones. In view of the potentially severe ocular complications of leprosy, response of the cornea, sclera and conjunctiva toward corticoids deserves continued attention.—[From abstract in *American J. Ophth.* **48** (1959) 408-409, supplied by Sr. Hilary Ross.]

MUFTIC, M. K. Advances in the pharmacological study of cerase—a new anti-tuberculous agent. *British J. Tuberc.* **52** (1958) 308-312.

Cerase is an enzyme, present in crude extracts of whole larvae of the wax moth (*Galleria mellonella*), which decomposes waxy membranes of *M. tuberculosis*. It is a constitutional enzyme present in different microorganisms and insects, representing a part of their digestive systems. It changes osmotic conditions on cell membranes by oxidizing and decomposing wax-like substances. Fifty-six human cases of tuberculosis have been treated with cerase and followed up from 1-10 years. In all cases the sputum had become negative in 14-60 days, and clinical improvement was marked; 39 of them had resumed their regular activities. Two patients died of hyperpyrexia, but during the first week of treatment their sputum had become negative. Death is ascribed to hepatic failure caused by tuberculous involvement of the liver, precipitated by sudden tuberculinization and hyperpyrexia. These cases demonstrate the close relationship between cerase administration and its pyrogenic properties, and the violent reaction of a hypersensitive organism induced by sudden lysis of the mycobacteria and the release of tuberculin or tuberculin-like substances. The low toxicity and highly specific antibacterial—and antituberculosis activity of cerase justify larger scale clinical trials, which are in progress.—[From abstract in *American Rev. Tuberc. & Pulmon. Dis.* **79** (1959) 721.]

BOYD, D. H. A., STEWART, S. M., SOMNER, A. R., CROFTON, J. W. and REES, R. J. W. Macrocyclon in the treatment of pulmonary tuberculosis. *Tubercle* (London) **40** (1959) 369-376.

Of a series of nonionic, surface-active polyoxyethylene ethers (detergents) which, although not bacteriostatic or bacteriocidal to the tubercle bacillus *in vitro*, suppress tuberculous infection in mice by an effect on the host, macrocyclon is the most active and least toxic. This article is a report on a pilot trial of this substance in 10 cases of far-advanced pulmonary tuberculosis not suitable for or responsive to ordinary methods of treatment. No effect on the patients' condition or the positivity of their sputa was observed. The failure is probably due to the fact that monocytes containing bacilli are rare in the lesions of chronic tuberculosis in man. [There is no scarcity of monocytes containing bacilli in lepromatous leprosy.]—H. W. W.

PANSE, M. V. and GOKHALE, S. K. Blood glutathione and its relation with haemoglobin and red blood cell count in tuberculosis, leprosy and diabetes. Part II. *Indian J. Med. Res.* **46** (1958) 159-170.

In this study the authors examined bloods from 91 leprosy cases, all outpatients of the Sasson Hospital, Poona. In most cases oxalated fasting blood was examined immediately after drawing. Glutathione, total and reduced, was determined by the method of

Woodward and Fry. The average values were as follows: red blood cells, 4.16 millions; hemoglobin, 13.06 gm.; glutathione; total 45.33 mgm., reduced 39.68 mgm., and oxidized 5.65 mgm. The mean values of these constituents in 102 normal individuals was, respectively: 4.86; 14.57; 41.25; 36.50; and 4.75. The increase of glutathione in the blood of leprosy cases was found to be statistically significant.—N. MUKERJEE

DESFORGES, J. F., THAYER, W. W. and DAWSON, J. P. Hemolytic anemia induced by sulfoxone therapy, with investigations into the mechanisms of its production. *American J. Med.* **27** (1959) 132-136.

This study is of an adult male patient who was started on 150 mgm. of sulfoxone daily; gradually increased to 1.2 gm., and who 4 months after treatment began took 2.4 gm. daily in error and thereupon developed nausea, weakness and malaise, and mild anemia with 12.0 mgm./% hemoglobin (of which 17% was methemoglobin). After the drug was withdrawn for 6 weeks, studies were made with the use of radioactive iron to demonstrate the hemolytic effect of sulfoxone. Tagging the red cells of a single age group, it was shown that the susceptibility to hemolysis was related to cell age. Only after the cells had been in the circulation for about 50 days were they subject to the hemolytic effects of the drug. No significant biochemical defect of the erythrocytes could be demonstrated. However, the decline in activity of glucose-6-phosphate dehydrogenase and glutathione reductase in the aging red cell, and the reported sensitivity to this drug of patients with red cell deficiency of the former enzyme, suggest that the hemolytic mechanism is related to this enzyme system. The case demonstrates that drug-induced hemolytic anemia of this type may occur without demonstrable enzymatic defect of the erythrocytes. The observation that patients appear to compensate for the hemolytic anemia and methemoglobinemia if maintained on this drug may be explained by the fact that the older cells containing less adequate enzyme systems are removed from the circulation and an equilibrium is maintained by increased production of red cells with a shorter age span.—SR. HILARY ROSS

TARABINI C., G. Ideas sobre la immunoalergia hanseniana. [Ideas on the immunoallergy of leprosy.] *Rev. Leprol. Fontilles* **4** (1958) 355-362.

Speculations concerning the factors which have a decisive influence on the reticulo-endothelial system, with the conclusion that the protein antigens of the leprosy bacillus determine the antiprotein antibodies of the serum and the early reaction to lepromin, while the lipid antigens determine the antilipoid antibodies and the late reaction to lepromin.—H. W. W.

TARABINI C., G. Breves consideraciones sobre la patogenia de los trastornos lipoideos en la enfermedad de Hansen. [Brief consideration of the pathogenesis of the lipid disturbances of leprosy.] *Rev. Leprol. Fontilles* **4** (1958) 363-364.

The author holds that all alterations of lipid metabolism in leprosy patients of the lepromatous type are related. The presence of pathologic lipoids in the tissues, or their facility of being absorbed, is the cause of the negativity of the late lepromin reaction, and of the formation of the antilipoidic antibodies in the serum which, acting on the serum lipoids, probably determine the characteristic hypocholesterolemia.—[From author's summary.]

BRU, P. and ROLLIER, R. La ponction-biopsie du foie dans la lepre. Étude de 38 cas traités ou non traités. [Puncture biopsies of the liver in 38 treated and untreated leprosy patients.] *Maroc Med.* **36** (1957) 1194-1205.

Puncture biopsies of the liver were made in 38 cases: 32 lepromatous, 5 tuberculoid and 1 indeterminate; all but 10 had been treated. Manifest lesions were seen in all specimens, those in the lepromatous cases different from those in the tuberculoids. The lesions were all in the mesenchymal element, the "noble" tissue being spared, and all indicated hematogenous origin. Bacilli were found in 33 of the specimens, including 2 of

the 5 from tuberculoid cases. The histologic findings are discussed at length, with illustrations.—H. W. W.

ASANO, M. Leprous pink spots of the tooth. *La Lepro* **27** (1958) 398-401 (in Japanese; English abstract).

Leprous pink spots of the tooth is a condition found in the upper incisors of lepromatous leprosy patients, not neural ones, and is a coloration of the tooth caused indirectly by the leprosy bacilli. There are usually no defects in the teeth, and no subjective symptoms can be elicited. Histologically, there is in the dental pulp initially hyperemia and inflammation, and increase in lepra cells together with proliferation of leprosy bacilli. This is followed by degeneration of the pulp and disappearance of the lepra cells and bacilli, with an increase in lipoid material and hyaline and lipoid degeneration of the pulp. At this stage the tooth becomes discolored a red tone, due to combination of the lipoid with lipofuscin which is produced by destruction of the bacilli. This condition is unique to leprosy.—[From abstract.]

GRIEBEN, L. Contribución al estudio de la lepra del sistema nervioso central; absceso lepromatoso cerebral. [Contribution to the study of leprosy of the central nervous system; lepromatous cerebral abscess.] *An. Neuro-Cirujía* (1958) 93-107.

This study, which contains a lengthy bibliography, is based on the case of a 48-year-old woman whose disease began with a dermatosis diagnosed as Besnier-Boeck disease (sarcoidosis). Histologically a cutaneous lesion showed a tuberculoid structure. The results of the Mitsuda and tuberculin tests were negative. An illness of two months' duration, with febrile onset and accelerated sedimentation rate, and with hemiparesis and speech aphasia, indicated a cerebral lesion of the left frontal lobe which could be seen by x-ray. Treatment with antibiotics gave no results. Surgical intervention revealed an abscess in which were found acid-fast bacilli of the appearance of *M. leprae*, not cultivable and not pathogenic, and Virchow cells. The patient died 45 days after the operation.—G. BASOMBRIO

PRICE, E. W. The innervation of the hand in relation to leprosy. *Leprosy Rev.* **29** (1958) 215-221.

In 20% of the muscles of hands the innervation is anomalous, due to shunting of nerve bundles from one main nerve to another. Weakness of a muscle may indicate a lesion of the normal nerve supply, a lesion of a nerve which gives an anomalous supply, or a lesion of a nerve bundle of the normal nerve which has become involved in the lesion of a second nerve along which it is being shunted. Similarly, the normal and anomalous sensory innervations of the hand are described. The author has found in the literature no studies correlating motor and sensory innervation of the hand. Where sensation has been lost its restoration may be due to one of two factors or to both: renewed innervation or renewed function of the original nerve, or spread from healthy nerves in the surrounding skin areas. In the former event, function is restored proximally and laterally; in the latter, the gain of sensation occurs all around the area simultaneously.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 445-446.]

MASANTI, J. G. Nefropatía amiloidea: insuficiencia renal e hipertensión asociadas con amiloidosis renal secundaria en enfermos de lepra. [Amyloid kidney pathology; renal insufficiency and hypertension associated with secondary renal amyloidosis in leprosy patients.] *Medicina* (Buenos Aires) **18** (1958) 61-70.

In 22 cases of generalized secondary amyloidosis in leprosy patients, renal localization was found to be frequent (82%). Uremia was not infrequent (36%). All patients with renal insufficiency aggravated by amyloidosis had hypertension. The evolution toward uremia and hypertension seemed to depend less on the duration of the renal



amyloidosis than upon other factors, such as the number of glomeruli affected and the consequent interference with glomerular circulation.—[From author's conclusions.]

✓ **OLMOS CASTRO, N.** Concepto de hipersensibilidad y resistencia referido particularmente a lepra. [Concept of hypersensitivity and resistance, with special reference to leprosy.] *Leprológia* **3** (1958) 34-39.

**Hypersensitivity:** The introduction of *M. leprae*, live or dead, into the tissues of a sensitive organism prepares that organism to react more strongly and rapidly to a new introduction of the bacillus or of its protein derivatives. In this state of hypersensitivity the bacillus or its protein derivatives, which are relatively innocuous to normal persons, become highly toxic. Little is known of the mechanism of this condition or of its role in leprosy. Studies have revealed the sensitizing capability of heat-killed leprosy bacilli in most normal person and in adult dogs. The author has observed that: (1) The hypersensitivity of infection in leprosy disappears with time. Tuberculoid cases which react to lepromin gradually lose their hypersensitivity to the protein derivatives, but regain it quickly after a new accession of the bacilli. (2) Testing of the hypersensitivity threshold in tuberculoid leprosy with graduated dilutions of total protein leprolin (TPL) indicates that there is no direct relation between intensity of the hypersensitivity and the evolution of the skin lesions. (3) Testing of healthy contacts for hypersensitivity with the protein antigen makes it possible to determine the influence of the focus; i.e., positive Fernandez reactions are much more frequent among contacts of lepromatous patients than those of tuberculoid patients. (4) Experimental studies in man have shown that *M. leprae* can create hypersensitivity for other acid-fast bacilli or their protein derivatives, or vice versa (group specific hypersensitivity).

**Resistance:** It is assumed that in leprosy, as in other transmissible diseases, the infection by *M. leprae* or the injection of killed bacilli creates, along with hypersensitivity, acquired resistance. We have no knowledge of its intimate mechanism or its duration. There also exists a natural resistance or natural immunity, the intimate mechanism of which we also do not know. Nor is it known whether acquired resistance is equal to the natural one, or perhaps better. The author believes that the fundamental basis of natural immunity is effective phagocytosis (Metchnikoff type of immunity). He finds that these reactional conditions, including the formation of the tuberculoid granuloma, may occur in the absence of hypersensitivity, at least demonstrable with available tests.

**Hypersensitivity and resistance:** The crucial problem, as in other infectious diseases, is whether hypersensitivity is independent of acquired resistance or a manifestation of it. The author believes that they are phenomena of different expressions and effects.

**Concept of allergy:** Discussing this matter at some length, the author proposes that the term "allergy" be not used in the broader sense, to comprise all the phenomena of altered reactivity provoked by *M. leprae*, but (following Rich with respect to tuberculosis), that it be limited to the reactions of hypersensitivity, thus making allergy and hypersensitivity synonymous.—G. BASOMBRIO

✓ **OLMOS CASTRO, N., ARCURI, P., USANDIVARAS, R., CONEJOS, M., BONATI, A. A., LEBRON, E. and TORANZOS, L.** Prednisolona y fenómeno de Wade. [Prednisolone and the Wade phenomenon.] *Arch. argentinos Dermatol.* **9** (1959) 53-59.

Experimenting with two dogs, the authors studied the inhibitory effect of prednisolone on the development of hypersensitivity to *M. leprae* caused by the intradermal injection of lepromin. The inhibitory action occurred only while the hormone treatment was continued, but as soon as the administration of the drug was stopped—thanks to the permanency *in situ* of the injected bacilli—the dogs developed hypersensitivity to them (Wade's phenomenon) in the same time as in normal dogs.—G. BASOMBRIO

- ✓ CHAUSSINAND, R. La problème de la nature et de la signification de la réaction a la lépromine de Mitsuda. [The problem of the nature and significance of the Mitsuda reaction to lepromin.] *Ann. Inst. Pasteur* **97** (1959) 125-134.

An attempt is made to define the nature and significance of the Mitsuda reaction by studying the clinical and immunologic data of leprosy and tuberculosis. Sensitivity to lepromin is regarded as an allergic phenomenon, associated with a foreign-body reaction. This sensitivity does not necessarily evidence immunity, and should have immunologic significance only in individuals already contaminated by living Hansen bacilli. The current theory, considering the early or Fernandez reaction to be a sign of sensitization and the late Mitsuda reaction as a test of immunity, should be revised. However, the parallelism to the Hansen bacillus observed in tuberculous or BCG-vaccinated individuals may also be related to a certain degree of resistance to leprosy infection. Only by clinical study will a conclusion be reached. The allergic Mitsuda reaction induced by repeated injections of lepromin (i.e., dead Hansen bacilli) seems to be due exclusively to cutaneous sensitization, without immunological significance.—[From author's summary.]

- ✓ KOVÁTS, F. and BÖSZ, R. Die Leprominempfindlichkeit bei den verschiedenen Formen der Lungentuberkulose. [Lepromin reactivity in the various forms of lung tuberculosis.] *Tuberk. Arzt.* **13** (1959) 385-387.

The authors, working in Budapest, made lepromin tests of 4 groups of patients, as follows: (1) 20 of pulmonary tuberculosis, (2) 20 of hematogenous tuberculosis, (3) 6 of pleurisy (all 46 tuberculin positive); and (4) 9 of sarcoid and 2 of Hodgkins disease (tuberculin negative). Of the first group 18, and of the second group only 10, were lepromin positive. The third and fourth groups were lepromin negative. The results are considered significant with respect to the degree of immunity in these different conditions which may be of prognostic significance. [It is not stated if the regular Hayashi-Mitsuda lepromin was used.]—E. KEIL

- ✓ ARVELO, J. de J., MOLINENGO, L. and PÉREZ PÉREZ, B. Estudio sobre el empleo de leprominas diluidas para el control inmunológico de contactos Mitsuda positivos. Experiencia realizada en la Leprosia de Providencia y el servicio antileprosy del Estado Zulia. [The use of lepromin dilutions for the immunologic control of Mitsuda-positive contacts. Results obtained in the Providencia leprosy and in the antileprosy service of the State of Zulia.] *Rev. San. y Asist. Social (Caracas)* **23** (1958) 29-38.

The objective of this study with 92 contacts was to effect economy in the use of lepromin because of the limited amount available. Three dilutions of standard lepromin were used: 1 in 400, 1 in 9,600, and 1 in 19,200. With these dilutions the early (Fernandez) reaction was obtained only in a few instances, but the late (Mitsuda) reaction was obtained in most. Some of the subjects were from the town and some from the country; all were known to give 2+ or 3+ Mitsuda reactions. The 47 2+ contacts were injected intradermally with 0.1 cc. of standard and of the first dilution simultaneously; the 45 with 3+ reactions were injected with the same amounts of the second and third dilutions. In the former group, 11.3% of the 44 Mitsuda readings were negative. In the second group, the weaker dilutions failed to give reactions in 33.3% and 58.3% respectively of 36 readings. The authors suggest using the standard lepromin only for first tests, and subsequently using 1 in 400 dilutions for subjects with a 2-plus reaction, and 1 in 9,600 dilution for those with a 3-plus reaction.—[From abstract in *Trop. Dis. Bull.* **30** (1959) 622.]

- ✓ AZULAY, R. D. and NEVES, R. G. Comportamento do teste lepromínico em cobaias becegeizadas por via oral. [Behavior of the lepromin test in guinea-pigs vaccinated orally with BCG.] *Rev. Brasileira Leprol.* **26** (1958) 103-106.

Guinea-pigs were given BCG by mouth and tested intradermally with lepromin.

The degree of positivity of the reactions varied according to the dose of BCG. The highest percentage of positivity (87.5) was obtained in the group which was given 30 mgm/kgm, i.e., the same amount that is commonly given to newborn children in Brazil.—[From authors' summary.]

MARIANO, J. Teste de vacina de tuberculose irradiada em leprologia. [The use of irradiated tuberculosis vaccine in leprology.] *Arq. mineiros Leprol.* **18** (1958) 73-80.

In lepromin-negative leprosy contacts, the administration of irradiated tuberculosis vaccine (Parke, Davis) succeeded in converting the lepromin reaction to positive in 95% of cases. The lepromin test should be done 30-60 days after the third injection of vaccine.—[From abstract in *American Rev. Resp. Dis.* **80** (1959) 479, supplied by Sr. Hilary Ross.]

HANKS, J. H. The magnitude of the immune response incited by killed and attenuated mycobacteria. *J. Immunol.* **81** (1958) 297-301.

In the experiment here discussed mice had been infected with living BCG or RIRv1, with or without heat-killed *M. leprae murium*, and challenged later with that micro-organism or with virulent tubercle bacilli. Assessment of the immune response is based on the observation that a linear relationship exists between the log of an infecting dose and the median response, measured for instance by the incubation period or the survival time. For example, the lengthening by 1 month of the time in which the murine leprosy lesions become palpable in 50% of the animals is equivalent to decreasing the challenge dose by 10X. Immunization with BCG alone, or with heat-killed murine bacilli, 63 days before challenge extended the median incubation period by 2X, while the addition of a small quantity (1/14th) of dead murine bacilli to the BCG vaccine extended the time by 3X (the BCG probably acting as an adjuvant). These extensions are equivalent to increasing the dose by 10<sup>5</sup>X and 10<sup>11</sup>X, respectively, indicating a high degree of protection. Specific protection by BCG against H37Rv was greater than nonspecific protection against the murine bacillus for the median survival time was 4X. In spite of the high degree of protection afforded by these vaccines, the true assessment of the role of such vaccines in chronic mycobacterial infections is impossible because, in the unimmunized animals, immunity from the challenge dose begins to operate before the end-points are reached; there are therefore no unimmunized animals for comparison. A second complicating factor in making these assessments is the overlap which occurs in the responses of animals in the unimmunized and the control groups, due to the differences between individuals being greater than the differences between the groups; assessment must therefore be based on the "average" individual, i.e., the 50% response. In general the problem of giving protection against mycobacteria would not appear to be due to the antigens failing to incite a high immunity response in the "average" person or animal, but rather to the very high protection needed against these particular bacteria and to the difficulty of producing such levels in persons or animals unable to make an "average" response.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 456-457.]

HALL, C. H., JR. and ATKINS, E. Studies on tuberculin fever. I. The mechanism of fever in tuberculin hypersensitivity. *J. Exper. Med.* **109** (1959) 339-359.

Considering the unsettled question of the pathogenesis of fever, it is noted that pyrogenic material has been obtained from sterile exudates and in extracts of circulating granulocytes; and there is a similar pyrogen, apparently released from damaged cells, in the serum of patients with fever due to various factors. Evidence is presented that the fever elicited by intravenous injection of old tuberculin into BCG-infected rabbits is of such origin. The circulating pyrogen caused fever in normal recipients, which OT itself did not. Daily injections soon led to tolerance to the pyrogenic effect—evidently due to desensitization, because there coincidentally developed skin-test negativity. It is

postulated that in this experiment the pyrogen was released by specific action of the OT on sensitized cells of the host. [This leads to speculation regarding the possibility that such a mechanism is at work during the febrile episodes in leprosy.]—H. W. W.

✓ TERENCIO DE LAS AGUAS, J. La proteína C reactiva en la lepra. [C-reactive protein in leprosy.] *Rev. Leprol. Fontilles* **4** (1958) 445-453.

C-reactive protein is a specific protein which appears in the blood serum as a result of inflammatory changes and which gives a reaction of precipitation with substance C, a polysaccharide extracted from the body of the pneumococcus. The sera of 41% of 58 lepromatous patients were positive, the positivity being proportionate to the advance of the disease and decreasing as the patient advanced towards recovery. Of 2 tuberculoid cases tested, 1 was positive.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 842.]

✓ TARABINI C. G. and GUILLEN P. J. Formolgelificación modificada por Linke y col. en enfermos hansenianos. [The formol-gel test as modified by Linke *et al.* in leprosy patients.] *Rev. Leprol. Fontilles* **4** (1958) 461-468.

This modification of the formol-gel test consists in adding 14% calcium chloride in equal parts to the formalin before adding it to the serum. The test is recommended because of its simplicity and speed. Positivity is measured by the speed of gelification: 4+ in 2 minutes, 3+ up to 4 minutes, 2+ up to 6 minutes, and 1+ up to 8 minutes. It reveals an increase of gamma globulins in the blood, and also of alpha and beta globulins. High positivity indicates renal complications, hepatic disturbances and lepra reactions. In cured patients it may be used to indicate the total disappearance of dysproteinemia.—[From abstract in *Trop. Dis. Bull.* **56** (1959) 842.]

✓ PARLETT, R. C., YOUNG, G. P., REHR, C. and LESTER, W. The detection of antibodies in the serum of tuberculous patients by an agar double-diffusion precipitation technique. *American Rev. Tuberc. & Pulmon. Dis.* **77** (1958) 462-472.

The technique employed in this study is a marked departure from the original gel diffusion test done in petri dishes, positive reactions being evidenced by bands of precipitate in columns of agar in tubes of 3 mm. inside diameter. The reactions with sera from tuberculous patients were highly specific, occurring only with the tuberculosis antigen, not with those of a saprophytic mycobacterium or three fungi used, including a noecardia. Sera from 13 leprosy patients were tested, and all were found negative to all of these antigens. [A revised technique will be published as a technical note in a forthcoming issue of *THE JOURNAL*, for it might be profitable to apply this test to leprosy sera on a large scale, using as an antigen—among other things—lepromin (or its filtrate or supernatant).]—H. W. W.

✓ BERGEL, M. Investigación de bacilos ácido-resistentes en esputo por el método de la extracción etérea. [Detection of acid-fast bacilli in sputum by the ether extraction method.] *Arch. argentinos Tisiol. y Neumonol.* **34** (1958) 45-48.

Technique of detection of acid-fast bacilli in sputum based on ether extraction. The sputum is shaken with ether and glass fragments until totally disintegrated, and then the ether is centrifuged. The sediment is smeared, stained and examined as usual. This method is more simple and sensible than those generally in use.—[From author's summary, supplied by G. Basombrio.]

✓ MUKERJEE, N., CHATTERJEE, K. R. and BOSE, P. Enhancement of virulence of *Mycobacterium leprae* after passage through hybrid black mouse. *Bull. Calcutta Sch. Trop. Med.* **6** (1958) 15-16.

A strain of the rat leprosy bacillus which had been maintained in white rats for about 20 years was found to have decreased in virulence and infectivity for those animals. By passing it through the hybrid black mice which had been developed at the Calcutta

School, which strain was found to be very susceptible to this organism, the infectivity for white rats seemed to have been restored.—AUTHORS' ABSTRACT

KASAMATSU, S., TOMIZAWA, T. and NAKAMURA, K. Studies on the delayed type allergy by murine leprosy bacillus. I. Relation between lepromin test and tuberculin test. *La Lepro* **27** (1958) 402-408 (in Japanese; English abstract).

The present investigation, using the allergic skin reaction in guinea-pigs, was undertaken to show that an antigen similar to PPD would be contained in murine leprosy bacilli. Groups of animals were sensitized with phenol-killed tubercle bacilli (H37RV), BCG, and suspensions of murine bacilli, the bacilli in each case being suspended in paraffin oil. Old tuberculin, PPD, and a suspension of murine bacilli prepared by the Dharmendra method, gave definite 24-48-hour allergic reactions in all of the sensitized groups, indicating cross-reactions between the tubercle and murine bacilli. Similar allergic skin reactions were observed in guinea-pigs passively sensitized with peritoneal cells from the actively-sensitized animals, but not in the guinea-pigs to which immune sera had been given. Also, the corneal reaction characteristic of this delayed-type allergy was elicited by the intracorneal injection of OT or PPD to guinea-pigs sensitized with the murine bacilli. It became obvious that the murine leprosy bacillus contains an antigen similar to tuberculo-protein.—[From abstract.]

OSHIMA, S., TAKAHASHI, T., MORIYA, M., NOJIMA, T., YANAGISAWA, K., TAKAHASHI, H., NISHIMURA, S. and YASUKAWA, T. Studies on the maintenance of immunity against murine leprosy in BCG inoculated rates. *La Lepro* **27** (1958) 409-416 (in Japanese; English abstract).

Rats were inoculated intraperitoneally with BCG vaccine and then challenged with murine leprosy bacilli after 1, 5, 10 and 20 weeks, to determine the duration of immunity and the fate of BCG in the organs. Onset of leproma development was delayed in degree commensurate with the interval, but delay was evident even in the 1-week animals. Compared with the controls, the weights of the lepromas were less, and the numbers of bacilli in the inguinal and axillary lymph nodes were smaller in the vaccinated groups. Cultivation of the BCG organism from the organs showed proliferation up to 5 weeks, a sharp decrease thereafter, and for the most part disappearance at 26 weeks. The time of maximum immunity could not be determined. It is shown that the growth of the murine leprosy bacillus is slower than that of the tubercle bacillus, and on this account the duration of immunity is somewhat longer.—[From abstract.]

NISHIMURA, S., MASUDA, T., KOSAKA, K. and YASUKAWA, T. Studies on the chemotherapy of leprosy (XXI). Onset suppressing action of antitumor agents and antibacterials in murine leprosy. *La Lepro* **27** (1958) 419-422 (in Japanese; English abstract).

Various substances used [9 are listed] had no suppressive effect on the onset of murine leprosy; but a derivative of INH, saleylaldehyde isonicotinylhydrazone, completely suppressed onset when administered in the large dose of 150 mgm./kgm.—[From abstract.]