

CURRENT LITERATURE

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

- (SAGHER, F. Leprosy. (A review of the literature of the end of 1947 and part of the literature of 1948.) *Dermatology* **99** (1949) 193-208.

This highly condensed but useful review of the literature for the period indicated is the third one of its kind prepared by the author since the war. The first, in German (*ibid.* **95** (1948) 210-230), covered the war period to the beginning of 1946. The second, in English as is this one [see *THE JOURNAL* **17** (1949) 155], covered the years 1946 and 1947, and part of the literature of 1945. The present one follows the same general line as the second, the topical subdivisions being: general considerations; etiology: bacillus, staining methods, culture, serological investigations; epidemiology, transmission, animal experiments, and tests; diagnostic and clinical considerations; pathology; treatment; history, statistics, prevention, control, classification and name. There are 182 abbreviated references.

—H. W. W.

- (MACARTHUR, W. Mediaeval "leprosy" in the British Isles. *British Med. J.* **1** (1949) 320-321 (reports of societies).

This item is a lengthy summary of a paper read by Lt. Gen. Sir William MacArthur before the Section of the History of Medicine of the Royal Society of Medicine. It is difficult to determine the extent of leprosy in the British Isles in the past, for although there is no question that it existed the word "leprosy" as used had a multiplicity of meanings. Examples of its misuse are given, including the biblical statement that Job was a leper because of his "boils," and the fact that "lazarus" simply meant "without help" but became synonymous with the imaginary disease and survives today in "lazar" and "lazaret." The question of how many "leper houses" existed, and indeed that of the very nature of many places so designated, is clouded with confusion. The story that Robert the Bruce had leprosy is shown to be dubious in the extreme. Contrary to the idea that leprosy disappeared from England because of strict isolation, there is little evidence of any form of real isolation. The custom of regarding persons with leprosy as dead and without civil rights was never followed in England; there is no contemporary evidence that the "leper windows" in churches had anything to do with them; and the so-called "laws" with respect to them are merely extracts from the rules of one or another of the leper houses which had no authority outside their walls, and the people concerned had a legal right to beg in public places. Diagnoses were made by monks and public officials. It is not implied that there was no leprosy, but no statement bearing on the matter should be accepted unless clinical data are given to point the diagnosis.

—H. W. W.

- (MACGREGOR, R. B. Medical history of the war in Malaya. *Med. J. Malaya* **3** (1949) 146-172.

This article gives a vivid over-all account of the activities of the civilian medical service in Malaya as the war progressed down the penin-

sula, and especially the situation in Singapore when it was under attack and during the first days of the occupation. Within a few days the Japanese required the removal of the patients from the civilian hospitals—their equipment and supplies to be left behind—and the inmates of the leprosy institution gave succor, with rice from their stock and vegetables from their gardens, to the evacuated patients who were put into the neighboring mental hospital buildings. One section deals at length with the situation in the Sungei Buloh leprosy settlement near Kuala Lumpur, in part from a report by Ryrie [not the one abstracted in *THE JOURNAL* 15 (1947) 355], and in part by one made by a patient for the period after Ryrie was interned at the end of 1943. [Later information, supplied by the author of this paper, appeared in *THE JOURNAL* 16 (1948) 85-87.]

—H. W. W.

- 6 [BOMBAY] Annual Report of the Executive Health Officer for 1948, in the Administration Report of the Municipal Commissioner for the City of Bombay for the Year 1948-49, Vol. II.

There is no municipal institution for the isolation and treatment of leprosy cases in Bombay, inpatients are not admitted to any municipal institution, and there is urgent need of a proper colony or settlement for the infectious cases of the province. Such cases, whether voluntarily admitted or committed by the police, are cared for at the Ackworth Leper Home at Matunga, which has been in operation for over 50 years and has accommodations for 396 patients, 284 males and 112 females. That institution runs an outpatient clinic, largely supported by the Municipal Corporation, at which the average daily attendance was 202 patients, with 1,215 new cases seen during the year; and other (noninfectious) cases are dealt with at general dispensaries of the municipality. Two health visitors, one supported by the municipality and the other by the Ackworth institution, are engaged in work with patients and contacts at their homes.—[From excerpt in *Lep. India* 22 (1950) 104.]

- 6 [FIJI] Medical Department (Annual Report for 1949). Legislative Council, Council Paper No. 24, 1950 (J. M. Cruikshank, Director of Medical Services); Appendix III, Fiji Leprosy Hospital, Makogai (C. J. Austin, Medical Superintendent).

With 87 new admissions—35 from the Gilbert Islands—and 5 readmissions the population of the Makogai hospital remained virtually unchanged, 683 at the end of the year. In Fiji alone there were 46 notifications of leprosy, of which a disappointingly large proportion (44%) were rather advanced. Of the 48 patients discharged a disproportionately high percentage (69%) were Indians, who react better to treatment than do the South Sea Islanders. Discharged cases are followed up, and the percentage of readmissions is low. Most of the patients had been treated with sulphethrone during the year, and the hospital wards had been emptied of chronic ulcerated cases. Considerable effects of toxicity have been seen—less in the Indians than in the others—and an itchy desquamative dermatitis developed in 20 (4.5%) of this treatment group. Many had to be given a rest from treatment because of loss of weight. Another appendix is a report by P. E. C. Manson-Bahr of a special study of the mild anemia seen in 20 cases, classed as of microcytic normochromic type as a rule, with some of hypochromic type. The staff has been increased by three Sisters, one from New Zealand and two from the United States; the latter are

medical technicians and are being utilized in the laboratory control of the treatment.

—H. W. W.

- 6 [QUEENSLAND] Annual Report on the Health and Medical Services of the State of Queensland for the Year 1949-50, Brisbane, 1950.

In his introductory statement the director-general, Dr. Abraham Fryberg, tells of visiting the leprosaria of Hawaii and the Carville institution in Louisiana, at which last place he was attached to the resident medical staff for duty. On request of the patients of the Peel Island institution the disease, for the first time in these reports, is designated "Hansen's Disease (Leprosy)." Removal of the institution from that island to the mainland has been approved, and a suitable site is under discussion. The report on Peel Island, written by Dr. V. F. B. Lennon, who replaced the previous medical officer in charge, shows that during the year only 1 new case was admitted, together with 2 readmissions, and the number remaining at the end of the fiscal year was 54, a reduction of 5 from the previous year. The benefits of sulfone treatment are now being seen in the bacteriological findings, it is stated. Conditions for release have been modified, the required period of observation having been shortened; and the number and frequency of visitors by friends are no longer limited. At the Fantome Island institution for aborigines, located in the Palm Island group, there were 10 admissions, bringing the total up to 78 from 73 at the end of the previous year. There has been difficulty with sulphetrone on account of reactions and complications, but reduction of dosage has lessened that trouble.

—H. W. W.

- 6 LARA, C. B. The further role of the Culion Leper Colony. *J. Philippine Med. Assoc.* **23** (1947) 465-471.

The role of this world-renowned institution is discussed from the sanitary, public health, medical and administrative aspects, with consideration of the socio-economic problems of the patients, and the policies and availability of material for fundamental research. The continued maintenance of the colony is recommended.

—J. O. NOLASCO

- 7 [EDITORIAL] The problem of leprosy in Britain. *Lep. Rev.* **21** (1950) 3-5.

The increasing incidence of leprosy in Great Britain has aroused interest, it is stated, and the authorities are considering making the disease notifiable and providing a home for patients in a converted fever hospital in Reigate, near London. Notification is held to be desirable for the protection of children with whom contact might be made, for the opportunity of offering treatment to the patients, and for the epidemiological information that would be derived; but for the measure to be of value the reports would have to be made to an experienced specialist and under conditions that would ensure absolute privacy. It appears, by implication, that the government does not know how many cases there are, or whether any of them are of indigenous origin. The problems involved in any measure to provide for segregation of severe or dangerous cases, whether on a voluntary basis or otherwise, are reviewed. No over-all solution is offered, but it is suggested that the best way of meeting the problem would be the appointment of a full-time leprosy officer with experience and wide powers of discretion.

—H. W. W.

- 6 GARRIDO QUINTANA, F. La nueva lucha antileprosa; esquemas. [New antileprosy campaign: outline.] *Actual. méd. (Granada)* **35** (1949) 159-163.

A program is suggested to increase the efficiency of the struggle against leprosy.—[From *Excerpta Med.* **4** (1950) 154.]

- 8 RODRIGUEZ, E. Resumen y comentario bio-estadístico apartado por los 100 primeros enfermos de lepra fichados en el Departamento de Concepción. [Biostatistical summary and comments on the first 100 leprosy patients examined in the Department of Concepción.] *Rev. Derm. Sif. y Lep. (Paraguay)* **1** (1949) 55-58.

It is concluded, from a study of 100 cases and 176 contacts, that leprosy in this area is of long standing, dangerous and progressive.—[From author's summary.]

- 8 COOK, C. E. The native in relation to the public health. *Med. J. Australia* **1** (1949) 569-571.

After a general discussion of the status of the Australian aboriginal, his importance—and that of his mixed-stock descendants—with respect to the white community, and the irrational and unpractical "protection" policy applied to him, the author, who is the commissioner of public health of Western Australia, deals briefly with various diseases prevalent among these people. With respect to leprosy the following is said: "A quarter of a century ago there was no leprosy problem in this State's Kimberley division. Today the estimated incidence in the native population there is 1 in 50, with no sign of abatement notwithstanding efforts at rigorous control. The employment of natives in white households in intimate domestic contact with children, the intermarriage of natives with the white race and the raising of a generation of hybrid children having contact elsewhere with children of European stock, create a situation threatening the wide dissemination of leprosy from the coloured to the white race and imperil the security of the white population." —H. W. W.

- 8 WHEATE, H. W. An intensive leprosy survey in the Teso District, Uganda. *East African Med. J.* **27** (1950) 274-277.

The author, in charge of the Kumi Leprosarium, Eastern Province, Uganda Protectorate, reports on a leprosy survey made in a small area close to the leprosarium, in which he examined 586 persons, which was 85% of the population. It is noted that 3 infectious cases of this area had been long segregated and treated by the leprosarium, but 19 tuberculoid and indeterminate cases had remained and were found in this survey. The leprosy prevalence rate for this area is 32.1 per thousand. This survey is the first to be recorded in East Africa for some time, of the type done by a leprosy institution in adjacent country. —J. ROSS INNES

- 8 BERTACCINI, G. A proposito di nuove classificazioni e orientamenti nella lebbra. [New classifications and orientation in leprosy.] *Rass. Clinico-Scientifica (Milan)* **25** (1949) 205-209.

The author holds conservative views in regard to several new classifications of leprosy based on histological and bacteriological criteria. It is maintained that the old clinical separation of leprosy into cutaneous (nodular) and anesthetic (neural) forms has still such practical value that its retention is recommended.—[Abstract from *Excerpta Med.* **4** (1950) 389.]

- 6 LAVIRON, P. La classification de la lèpre et les nouvelles directives dans le traitement de la maladie. Leur application dans les secteurs du S. G. H. M. P. [The classification of leprosy and new indications for the treatment of this disease. Their application in the sectors of the S. G. H. M. P.] Bull. Méd. A. O. F. (Dakar), (1949), Spec. No. pp. 113-120.

A general survey of the classifications of leprosy at the Manila Conference (1931), the Cairo Congress (1938) and the Havana Congress (1948). The present-day methods of treatment are reviewed—chaulmoogra and the sulfones, with details of dosage and technique—but no new ideas are offered.—[From abstract in *Excerpta Med.* 4 (1950) 390.]

- 7 ZIRILLI, L. Sul valore diagnostico della intradermo-resorcino-reazione nella lepra. [The diagnostic value of the intradermal resorcin reaction for leprosy.] Riforma Med. (Naples) 63 (1949) 994-996.

The intradermal reaction with resorcinol may be of good diagnostic value in cases of leprosy in which tuberculosis can be excluded. Only 1 out of 19 cases was negative.—[From abstract in *Excerpta Med.* 4 (1950) 394.]

- 8 CASIANO, A. Sul valore diagnostico della intradermoreazione istaminica nella lebbra. [The diagnostic importance of the histamine intradermal reaction in leprosy.] Riforma Med. (Naples) 63 (1949) 887-889.

After an intradermal injection of histamine (0.1-1.0 cc. per thousand) into skin affected with leprosy anesthesia no reflex erythema occurs, in contrast with the effect in normal skin or other anesthetic conditions. This fact is considered to be of great importance in the differential diagnosis of leprosy.—[From abstract in *Excerpta Med.* 4 (1950) 230.]

- 9 PAVLOV, N. F. [The phenomenon of "inflammation and edema" produced by nicotinic acid in the early diagnosis of leprosy.] Vjestnik Venereol. i Dermatol. (Moscow) 5 (1949) 45-51.

This phenomenon was first described by Sinelnikov in cases of syphilitic rash; under the influence of nicotinic acid (5 cc. of a 0.5% solution given intravenously) the roseola spots became lighter and sometimes elevated. This intervention was tried in 27 cases of leprosy. Macular patches, erythematous spots and the anesthetic periphery became inflamed and partly elevated. Nicotinic acid was helpful in the diagnosis of early leprosy when the spots were not yet defined; following a 1% nicotinic acid injection discoid patches appeared and remained for 18 to 25 minutes. In other skin diseases only hyperemia of the face and ears was seen after such injections.—[From abstract in *Excerpta Med.* 4 (1950) 392.]

- 10 HEINEMANN, H. Akute Lepra-Reaktion. (Bericht eines Krankheitsfalles mit Bemerkungen zum Auftreten von Lepra in Europa.) [Acute lepra reaction; report of a case, with remarks on leprosy in Europe.] Acta Tropica 6 (1949) 268-269.

A patient seen by the author in Switzerland, who had suffered with pulmonary tuberculosis with hemoptysis on two occasions within 20 years and had returned to Europe after a stay of 14 years in the tropics, presented reddish blotches on the right cheek and breast. These were proved by biopsy to be leprosy, and he has been treated since 1947 with chaulmoogra oil. On a hot summer day in 1948 he developed high fever and a papular efflorescence on the face, back and arms and a localized

bronchitis on the left side. Moist sounds were audible in the left lung and acid-fast bacilli present in the sputum were proved by animal inoculation to be *M. tuberculosis*. Eight days later, after a time of improvement under treatment with thiocalcium and antistin "Ciba," the fever returned and fresh infiltrations appeared, and the moist sounds in the lungs were more extensive, involving the whole of the left lung and the upper two-thirds of the right. The Mitsuda reaction was negative. The question whether the bronchiolitis was due to an extension of the tuberculosis or to edema from the weak heart action, or was a symptom of the leprosy reaction is left unanswered. The case is recorded because, now that men who have served abroad have returned, cases of leprosy are liable to be encountered but overlooked.—[From abstract in *Trop. Dis. Bull.* **47** (1950) 248.]

- Y VAN OYE, E. and BALLION, M. Fautra-t-il tenir compte d'une nouvelle affection à bacilles acido-résistants en Afrique? (Note préliminaire.) [Is there a new disease due to acid-fast bacilli in Africa? Preliminary note.] *Ann. Soc. belge Méd. Trop.* **30** (1950) 619.

Description of a case of chronic ulceration, of 4 months duration, on the dorsum of the foot of an American child 6 years of age living in the Belgian Congo. The bottom of the ulcer was covered with a gelatinous mass; there was no pain, and the general condition was good. Examination of the exudate showed numerous acid-fast bacilli on the nature of which the authors are not, for the present, able to express an opinion, but they suspect that it may be identical with the cases of a new mycobacterial infection described in Australia by MacCallum and associates in Australia [see *THE JOURNAL* **18** (1950) 127]. Further observations of this child, who was taken back to America for treatment, will be published later. Considering the thermophobia of these microbes in culture, the application of heat to the lesion proved to be very effective and brought about complete recovery.

In discussion, P. Janssens stated that since 1942 he has known of a similar affection observed in the N. E. Belgian Congo. With Lubicz he observed 81 such cases in the Tora area, in Logo and Zande natives. He succeeded in infecting male white rats but failed to cultivate the bacilli, perhaps because of the temperatures employed (20°, 37° and 45°C.). Until now it has not been possible to identify this affection with the Australian condition, and there are some differences: in the Congo, the ulcers may be multiple and of rather short duration, and experimental lesions in rats are not similar to those observed in Australia. —A. DUBOIS

- Y AGUIRRE, A. El examen de piel en colectividades. [Mass examination of the skin.] *Arch. uruguayos Med. Cir. y Espec.* **34** (1949) 139-142.

Examinations with special regard to the frequency of syphilis and leprosy were made of 4,868 persons. Leprosy was found in 2.5, syphilis in 3.7, and scabies in 25 per 1,000. In all these examinations only the visible lesions of the skin and the mucosa were recorded, though, as far as syphilis was concerned, the use of Chediak's test should have been the ideal; that reaction years ago gave about 10% positive results. The percentages of the dermatoses are also mentioned.—[From abstract in *Excerpta Med.* **4** (1950) 285.]

- 400 Y JOHANSEN, F. A. and ERICKSON, P. T. Current status of therapy in leprosy. *J. American Med. Assoc.* **144** (1950) 985-989.

This summary review deals primarily with sulfone treatment, and includes brief mention of experiments with certain drugs not yet in general use. Unfamiliar terms, now official in the United States, are used to designate some of the sulfones: "glucosulfone sodium" for promin, "sulfoxone sodium" for diasone, and "thiazolsulfone" for promizole. The beneficial effects, advantages, deficiencies and general principles of treatment are considered in a general way. The deficiencies are the very slow elimination of the bacilli from the tissues even after visible lesions have cleared up, the tendency to relapse after treatment is discontinued, the resistance of advanced eye and nerve lesions to the treatment, and the fact that episodes of acute neuritis continue to occur during treatment. In the search for a faster acting and more effective remedy, promacatin has been found useful but apparently not materially superior to other sulfones, and HES (4-amino-4'-beta-hydroxyethylaminodiphenylsulfone, a monosubstituted product) has shown beneficial effects in the 6 months it has been used. Streptomycin, now replaced by dihydrostreptomycin, has been found to be a useful adjunct in sulfone treatment, especially where improvement has become retarded; its effect on lesions of the mucous membranes is especially rapid, probably in large part because of action on secondary invaders, and acute iridocyclitis often responds favorably. Aureomycin, used in 5 cases for 1 year, seems to be of promise. The early results obtained with amithiozone (tibione, or TB-1) in a small group of patients suggest that this drug [another sulfur-bearing compound, but not of the sulfone class] suggest that it may prove to be especially promising. Of other drugs under trial, *p*-aminosalicylic acid (PAS) may be able to produce retrogressive changes in lesions. Cortisone seems promising for lepra reaction and iridocyclitis. The antihistaminics have not been of much value when given by the mouth in ordinary doses, but diphenhydramine hydrochloride given intravenously (50 mgm. per day) gives symptomatic relief from erythema nodosum and the deep form of pruritus sometimes associated with leprosy.

—H. W. W.

DHARMENDRA. The present status of sulphones in the treatment of leprosy. *Indian Med. Gaz.* **85** (1950) 348-360.

This is a special review article which deals comprehensively with the subject of the sulfones employed in the treatment of leprosy and their practical use, with over 60 references to the literature, which does not lend itself to abstracting. A useful tabulation gives the chemical names and formulae, and the proprietary names and manufacturers, of avlosulphone or diphone (the mother substance, or DDS), promin, diasone or diamidin, sulphetrone or novotrone, promacatin, and promizole—the names diphone and novotrone being those given products made in India. One section deals with the mode of action of these drugs, and a longer one with the results of treatment and the complications seen. The last one is a plea for the use of these drugs on a wider scale, since they are no longer experimental and since the cost of treatment can be greatly reduced by administering parenterally certain proprietary sulfones originally given by mouth or by employing DDS—although the use of that substance is still in the experimental stage. If necessary, after the more severe changes have been mitigated by several months of treatment, the patients may be returned to hydnocarpus drugs. Some emphasis is laid on the improved prospects for the control of the disease since the acquisition of more effective drugs.

—H. W. W.

- 6 FLOCH, H. and DESTOMBES, P. Traitement de la lèpre par le diamino-diphényl-sulfone. [The treatment of leprosy with diamino-diphenyl-sulfone.] Bull. Soc. Path. exot. **42** (1949) 434-439.

Traitement de la lèpre par la diamino-diphényl-sulfone (1358F). [Treatment of leprosy with diamino-diphenyl sulfone (1358F).] Bull Acad. nat. Méd. **133** (1949) 568-571.

[The first of these papers, whose titles are virtually identical, would appear to be a preliminary one written when only 49 cases had been treated. The second one deals with 101 treated cases, the same number as is involved in the report which appeared in THE JOURNAL **17** (1949) 367-377, and the material is evidently the same.—EDITOR.]

- 317 6 FLOCH, H. and DESTOMBES, P. Manifestations cutanées et nerveuses de type réactionnel constatées au cours du traitement sulfoné de la lèpre. [Cutaneous and neural manifestations of reactional nature observed in sulfone treatment.] Publication No. 192 de l'Institut Pasteur de la Guyane et du Territoire de l'Inini, May 1949.

Reviewing 9 observations, the authors conclude that the acute reactions which frequently occur in the course of sulfone treatment of lepromatous cases (in 50% or more according to some reports) are leprotic reactions, and that the terms erythema nodosum and erythema multiforme are inadequate to qualify them. They usually occur in patients who had experienced them before the institution of sulfone treatment, although that treatment undoubtedly influences their occurrence. At the same time they can be regarded as an index of the activity of these drugs. The treatment should, if possible, not be interrupted during the reactions, but if it is suspended because of serious reactions—notably those with fever or affecting the eyes—that should be only temporarily. If after resumption the condition recurs to a serious degree, it may be well to reduce the dosage when the treatment can be started again. —AUTHORS' ABSTRACT

- 6 FLOCH, H. and DESTOMBES, P. La vitaminothérapie D2 a hautes doses (traitement de Charpy) dans les formes tuberculoïdes et indifférenciées de la lèpre. [High dose vitamin D2 therapy (Charpy treatment) in the tuberculoid and undifferentiated forms of leprosy.] Publication No. 195 de l'Institut Pasteur de la Guyane et du Territoire de l'Inini, August 1949.

The authors have employed the Charpy treatment in cases of tuberculoid leprosy, using a preparation called sterogyl 15 in doses for adults of 360 mgm. in 3 months. Of 9 minor tuberculoid cases, 2 showed improvement, 2 grew worse, and 5 remained stationary. In 4 reactional tuberculoid cases the cutaneous lesions were quickly influenced, the regression usually occurring much more quickly than occurs spontaneously, while the neuritic disturbances were not ameliorated. These results are less favorable than those reported from Argentina by Capurro and Guillot [THE JOURNAL **16** (1948) 283]. In 8 cases of the undifferentiated forms the results were of little significance: 1 case improved, 1 was aggravated, and the other 6 remained stationary. Apart from the possible general effect of this treatment, the authors believe that it merits further trial in reactional tuberculoid cases. —AUTHORS' ABSTRACT

- 316 6 FLOCH, H. and DESTOMBES, P. Utilisation d'une sulfone monosubstituée (la succinyl-diamino-diphényl-sulfone ou 1500F) dans le traitement de la lèpre. [Use of a monosubstituted sulfone (succinyl-diamino-

diphenyl sulfone, 1500F) in the treatment of leprosy.] Publication No. 200 de l'Institut Pasteur de la Guyane et du Territoire de l'Inini, Nov. 30, 1949.

A preliminary report of the results of the treatment of 37 cases—28 lepromatous, 4 undifferentiated, and 5 tuberculoid—with the monosubstituted sulfone designated 1500F. In less than 2 months remarkable improvement was seen, especially in the "incipient" lepromatous form; after 8 months there was 87% improvement. On the whole this sulfone is well tolerated, provided the dosage is increased progressively beginning with 1 gm. per day. Lepra reactions are produced, however, but more often when the drug is administered by mouth (28%) than when it is given parenterally (7%). Certain cases improved with doses as small as 0.1 gm. per day.

—AUTHORS' ABSTRACT

326 FLOCH, H. and DESTOMBES, P. Emploi de la sulfone-mère et du 1500F par voies buccale et injectables (sulfones-retard) dans le traitement de la lèpre en Guyane française. [Use of the parent sulfone and of 1500F by mouth and by injection.] Publication No. 206 de l'Institut Pasteur de la Guyane et du Territoire de l'Inini, March, 1950.

The parent substance has been used in doses of 200 mgm. per day with excellent results, given by mouth and intramuscularly—the latter being called "*sulfone-retard*" because of the insolubility of the material. The dosages employed of the 1500F, an agent of remarkable therapeutic efficacy, when administered by the different routes are as follows: By mouth, daily except Sundays, 0.2 gm. for the first week, 0.4 gm. the second, 0.6 gm. the third, 0.8 gm. the fourth, and 1.0 gm. the fifth week and thereafter, the capsules being given before meals. Intramuscularly (using an aqueous solution containing 25% of the salt of methylglucamine of the 1500F, with 25% of subtosan), given, in adults, every other day, 3 injections per week, 1 cc. (0.25 gm.) the first week, 3 cc. the second, 4 cc. the third, 6 cc. the fourth, 8 cc. the fifth and thereafter. Intravenously (the same solution), daily except Sundays, 1 cc. the first week, 2 cc. the second, 3 cc. the third, 4 cc. the fourth. Whatever the route, 1 week of rest every 2 months. The tolerance of these doses given intravenously is excellent, and many of the cases have received 2.0 or even 2.5 gm. (10 cc.) daily for many weeks without trouble. The essential conditions for good tolerance with both drugs is to take 4 or 5 weeks for reaching the therapeutic dose and the adjuvant use of iron. The only serious trouble is the appearance of lepra reaction, which occurred in 25% of the cases treated with the mother substance and 28% of those receiving 1500F by mouth; the frequency is much less with parenteral administration. Choice between the two drugs can be made only on the grounds of cost, the mother substance being much the less expensive, but 1500F given intravenously is to be recommended in case of lepra reaction and for the treatment of leprosy eye lesions. —AUTHORS' ABSTRACT

323 FLOCH, H. and DESTOMBES, P. La thérapeutique de la lèpre par une sulfone monosubstituée la succinyl-diamino-diphényl sulfone ou 1500F. [Treatment of leprosy by a monosubstituted sulfone, succinyl diaminodiphenyl sulfone or 1500F.] Publication No. 211 de l'Institut Pasteur de la Guyane et du Territoire de l'Inini, June 1950.

The results with the monosubstituted drug have been excellent, with 100% improvement of the clinical, bacteriological and histological features after 12 months treatment. It has the advantage that it can be given by

mouth as well as by the intramuscular and intravenous routes. On the whole it is more irregularly tolerated in the dosages used than is the mother substance, and it is also less well borne by the parenteral route than by mouth, whereas with the mother substance no such difference is seen; and analogous observations have been made with the disubstituted sulfones. It is therefore suspected that 1500F is more or less broken down in the organism to the toxic and active DDS; but on the other hand the activity of small doses—on the order of those of DDS—indicates that it has a direct antibacterial action not possessed by the disubstituted drugs, which have to be broken down to be effective. It is in the field of the monosubstituted products that work should be pursued to obtain new derivatives of greater activity and less toxicity.

—AUTHOR'S ABSTRACT

- 8 FLOCH, H. and RIST, N. Action thérapeutique anti-lépreuse de la sulfone-mère et des sulfones complexes. [Therapeutic action of the parent sulfone and the sulfone compounds.] Fifth Internat. Congr. Microbiol., Rio de Janeiro, August 17-24, 1950.

Promin and diasone are more toxic given orally than intramuscularly. Rist, in 1945, concluded that promin is toxic and active in the degree to which it liberates the parent sulfone (DDS), as shown by the facts that when disubstituted sulfones are hydrolyzed their bacteriostatic effects are enhanced and approach those of DDS; that paper chromatography shows that this increase of effect accompanies the presence of liberated parent sulfone; and that the urines of rabbits which have ingested disubstituted sulfones contain the liberated parent sulfone. Clinically, DDS is at least as active as the disubstituted sulfones and in considerably smaller doses. There is a certain parallelism between the toxic and active doses of the different disubstituted sulfones and DDS. The advantages of the latter are several, including more certain control of toxicity (inconstant hydrolysis of disubstituted sulfones makes their toxicity irregular); ready determination of the concentration and excretion rates of the active and toxic drug; uniformity of the effects of the same dosage in different patients; similarity of activity and toxicity regardless of the route of introduction; delayed absorption due to the insolubility of the drug, which permits treatment with three or even two injections weekly; and the relatively low cost. Furthermore, it affords a base for a comparison of new sulfones.—[From the authors' pre-congress abstract.]

- 102 BASSET, A., SCHNEIDER, J. and BALLE, M. Essai de traitement de la lèpre par le 3,668 R. P. (p-di (aminophényl) di (y-phényl N-propylamino) phényl-tétrasulfonate de sodium) au Pavillon de Malte de l'Hôpital Saint-Louis. [The treatment of leprosy with 3,668 R. P. in the Saint Louis Hospital.] Bull. Soc. française Derm. et Syphilig. 56 (1949) 188-191.

This paper records a trial of 3,668 R. P. [equivalent to sulphetrone] in the treatment of leprosy. In comparatively small doses for a sulfone, good results—comparable with those with other sulfones—have been obtained without toxic effects. Details are given of 5 out of 20 cases and the following encouraging results are noted: Improvement occurred after six weeks to six months, with healing of ulcers and drying up of nasal and laryngeal secretions. In some cases circumscribed lepromas necrosed and healed. In neural cases the influence of the drug was slight, and pain

seemed to be exacerbated. The rarity of undesirable reactions is attributed to the small doses used. [From abstract in *Trop. Dis. Bull.* **47** (1950) 549.]

- 6 CANNATA, C. Il trattamento della lepra con i composti sulfo-glucosidici. [Treatment of leprosy with sulfo-glycoside compounds.] *Arch. italiano Derm., Sifilog. e Venereol.* **22** (1949) 29-48.

A report of personal observations in treating 19 leprosy patients with the De Angeli sulfone. The drug was injected intravenously in doses of from 12 to 18 gm. daily, in courses of 25 to 30 days each, separated by 15 to 20 days rest, for periods of 18 to 24 months, no other treatment being given. The cases were of the nodular type, most of them bacteriologically positive, and had previously been subjected to routine therapeutic methods without success. On the whole, the treatment was well tolerated except for mild anemia and leucopenia, which subsided quickly as soon as the treatment was discontinued. Intramuscular injections caused severe local pain, and administration by mouth gave rise to considerable toxic manifestations involving the liver. Therapeutically, the results were satisfactory as regards the resorption and the disappearance of infiltrative manifestations, subsidence of numerous symptoms and of rhinopharyngeal, corneal and other complications. The antibacterial action was good, leading to negative findings in the nasal secretion often after only 4 or 5 courses. The preparation had little or no effect on neural manifestations.—[From abstract in *Excerpta Med.* **4** (1950) 232.]

- ✓ HOHENNER, K. Ein Behandlungsversuch der Lepra mit dem Thiosemicarbazone TB 1/698. [The treatment of leprosy with thiosemicarbazone TB 1/698.] *Med. Klin.* **44** (1949) 1378-1381.

The thiosemicarbazone TB-1/698 was used in the treatment of a patient, a man of 20 known to have had lepromatous leprosy for a number of years. After 6 months of treatment the disease was found to be stationary. The appearance of increased inflammatory manifestations in the anterior chamber of the eye and the ciliary body with each new exhibition of the tablets was interpreted as being the effect of toxic products of bacterial disintegration. Lepromata of the skin resolved rapidly, but a fresh development of lepromata was not prevented. Study of the humoral blood elements suggested that the drug influenced the course of the disease and indicated some similarity with its effect on the course of human tuberculosis.—[From translation of the author's summary in *Trop. Dis. Bull.* **47** (1950) 374.]

- ✓ RYRIE, G. A. Thiosemicarbazone in the treatment of leprosy. *Lancet* **2** (1950) 286-288.

This is a preliminary report on the use of thiacetazone (*p*-acetylmaninobenzaldehyde thiosemicarbazone) in 10 cases of leprosy in England during 4 months. Eight of the cases were of a virulent lepromatous type and two were chronic tuberculoid. Dosage started with 50 mgm. (2 tablets) and gradually increased to 150 mgm., by mouth in divided daily doses. Although the author is very cautious in assessing the value of this drug after only 4 months use, the results he records are truly remarkable. Three of the lepromatous patients who had had the disease for several years and in whom many bacilli were found became bacteriologically negative in 4 months, and the others all showed much improvement. The author says that thiacetazone seems to have three advantages over the sulfones. (1)

Bacteriological improvement occurs rapidly whereas with the sulfones more than a year elapses before any significant bacterial change is noted. (2) Thiacetazone treatment seems to be completely free from mental depression and the slowing of cerebration that are noticed in patients who do intellectual work and who are under sulfone treatment and; (3) It is also relatively free from toxicity. There has been no tendency towards anemia or lepra fever so common under sulfone treatment. —G. O. TEICHMANN

- 6 ZIELER, K. Über die Behandlung des Aussatzes (Lepra) mittels JK-Einspritzungen in die Blutbahn. [Treatment of leprosy by intravenous injection of potassium iodide.] *Dermat. Wchnschr.* **120** (1949) 273-280.

The iodine therapy of leprosy as recommended by Olpp in 1929, as well as the diagnostic iodine provocation test, are both rejected as being too dangerous.—[Abstract from *Excerpta Med.* **4** (1950) 400.]

- 6 HASHIMOTO, T., ADACHI, S., SATO, M. and HASEGAWA, S. The cepharanthin treatment of leprosy. *Japanese J. Exper. Med.* **20** (1950) 461-472.

Because they had found cepharanthin, an alkaloid of the biscolaurin type, useful in the treatment of dermatological and urological forms of tuberculosis, they began in 1942 a trial of it in leprosy. Finding it superior to chaulmoogra drugs, they extended and have continued the work with it. In the meantime Mitsuda, Furumin, Ohta and Hayata have separately used it and reported on it favorably. It is used in minute dosage, and may be administered intravenously (0.1-0.3 mgm. 3 times a week) or orally (0.1 mgm. once daily). It has been used for 2 months or more in 64 cases at the Niigata Medical College, and in 380 cases at the Kusatsu leprosarium, with very good results especially in macular (i. e., tuberculoid) cases.

—H. W. W.

- 6 GUADAGNINI, M. El mal perforante plantar y la gangliectomia simpático lumbar. [Perforating plantar ulcer and sympathetic lumbar ganglionectomy.] *Semana Méd.* **57** (1950) 235-244.

Sympathetic lumbar ganglionectomy is indicated in perforating plantar ulcer in leprosy patients when it is accompanied with continuous pain, and when it does not respond to local treatment or absolute rest. Total healing occurs in 70% of cases, and that proportion may be increased by selection of cases, eliminating patients with degenerative neuritis of marked degree as indicated by advanced muscular atrophy and paresis. Relapse of healing occurs in 50% in the first, second or third year, and is more frequent when neurotic lesions predominate over cutaneous ones. Antialgic effect is found in all cases operated upon, a situation which is liable to be changed should new local infections occur.—[From author's summary, supplied by G. Basombrio.]

- 6 BOENJAMIN, R. Over de behandeling van het primair effect bij lepra. [Treatment of the primary lesion of leprosy.] *Med. Maanblad.* **2** (1949) 360-368.

[This article is essentially the same as the one which appeared in *THE JOURNAL* **17** (1949) 217-228.]

- 505 6 NEMIR, R. L., SCHULMAN, I. and CLEMONS, H. Promizole: Factors determining adequate dosage. *American Rev. Tuberc.* **62** (1950) 618-631. Promizole, less toxic for humans than promin and diasone but with

similar therapeutic effects in experimental tuberculosis in animals, has been used in the Children's Medical Service of Bellevue Hospital in New York since 1944, first alone and later in combination with streptomycin. Marked inconsistencies between doses administered and resulting blood levels led to the pharmacological investigation here reported, which will be of interest to anyone employing this drug. Absorption of single doses was found to be fairly complete, evidently occurring in the upper gastrointestinal tract since there was no absorption after administration by enema. In general the peak of blood concentration occurred after 2 to 4 hours, but there was no correlation between dose and peak level. For example, a graph shows about the same low curve after a dose of 0.05 gm./kgm. as after one of 0.03 gm./kgm., and equally high curves resulting from 0.04 gm./kgm. and 0.07 gm./kgm. The differences with the same dose (0.08 gm./kgm.) in different individuals were great. Of 4 individuals—who previously had had long treatment—one had less than 1 mgm.% of blood while another had nearly 6 mgm.%, and two had a higher level after 24 hours than did the other two at the peak. Similar differences were seen in children receiving continuous dosage. The concentration in the cerebrospinal fluid (patients with tuberculous meningitis) ranged from 18 to 24% of the blood levels, and seldom were in what is considered a therapeutically effective concentration. As a rule the amount of conjugated drug in the blood was relatively small. Excretion in the urine in patients under continuous treatment ranged from 42 to 86% of the daily intake, but there was no correlation between intake and recovery in the urine. Only a little of the drug as excreted in the urine was in the acetylated conjugate form, but the fact that the concentrations in the urine were far above the known solubility of the drug in water indicates that some conjugate is formed which involves some structure other than the diazotizable amine. It is concluded that because therapeutically effective blood levels should be maintained, and because the dosage necessary for that effect varies so greatly from patient to patient—a fact not due to differences in absorption and not satisfactorily explained by differences in urinary excretion, tissue storage, or capacity for drug destruction—the dosage must be ascertained for each individual patient on the basis of determinations of blood concentrations.

—H. W. W.

- BERTI, F. A., RIECKMANN, B., PEREGO, C. and RZEPPA, H. W. The production of 4,4'-diamino-diphenylsulfone and derivatives on a large scale for the anti-leprotic campaign in the State of São Paulo, Brazil. *Men. Inst. Butantan* **21** (1948) 107-109 (English version, pp. 111-115).

This paper, which deals with the preparation of sulfones cheaply on a large scale, is mainly of technical nature. Five methods of preparing 4,4'-diaminodiphenyl sulfone are described, the one found to be of most practical value being as follows: The amination of 4,4'-dichlorodiphenyl sulphone satisfied the required conditions, giving 4,4'-diaminodiphenyl sulfone in a 70% yield. Various methods of obtaining this starting material have been tried, such as sulfonation of chlorobenzene with sulfur trioxide or fuming sulfuric acid, condensation of 4-chlorobenzenesulfonic acid with chlorobenzene, the action of sulfonyl chloride upon chlorobenzene in the presence of aluminum chloride, and the condensation of 4-chlorobenzenesulfonylchloride with chlorobenzene using ferric chloride or aluminum

chloride as the condensing agent. This last method with aluminum chloride proved to be the best, practically as well as economically. The advantages of this method are simplicity of the installation and equipment required, reduction of the number of intermediate reactions, absence of by-products and isomeres, availability of raw material, high purity of intermediate and final products, and very low production costs.—[From abstract in *Trop. Dis. Bull.* **47** (1950) 372.]

153. ✓ BAKER, B. R., KADISH, A. F. and QUERRY, M. V. Sulfones. I. X,X' diaminodiphenylsulfones isomeres. *J. Organ. Chem.* **15** (1950) 400.

To determine the relationship between the therapeutic action of 4,4'-diaminodiphenyl sulfone and its chemical constitution, the authors have studied the influence of the position of the amine radical on the activity of the sulfone. There are 6 possible isomeres of this substance having an amine radical on each phenyl nucleus. Three have already been described: 2,4'-diaminodiphenyl sulfone, 3,3'-diaminodiphenyl sulfone, and 4,4'-diaminodiphenyl sulfone. By nitration of the nitro-4 and 2-diphenyl sulfones and reduction, the authors have prepared the 2,3' and 3,4' isomeres. The 2,2' isomere has been obtained by reduction and hydrolysis of 2-acetamino-2-nitrodiphenyl sulfone. Only the 4,4' isomere has therapeutic activity.—[From abstract in *Bull. Inst. Pasteur* **48** (1950) 969.]

593 ✓ SMITH, M. [Technique of sulfone determination in skin tissue.] *Lep. Rev.* **20** (1949) 134-136 (correspondence).

In this letter, published without a title, the writer warns of fallacious results of determinations made when procaine or any similar local anesthetic with a diazotizable amino group has been used; cocaine hydrochloride is recommended. The method he employs, given in detail, involves grinding the tissue with acid-washed sand in N/1 HCl, of which a total of 10 cc. per gram of tissue is used in three separate grindings, one-third of the total fluid being used each time.

—H. W. W.

✓ PARAS, E. M. Blood chemistry studies in leprosy. III. Total calcium diffusible and non-diffusible calcium, albumin and globulin. *Philippine J. Sci.* **78** (1949) 73-83.

It is shown that the presence of lepra reaction, and the advancement of the disease itself, have no appreciable influence upon the normal level of the diffusible calcium. A great majority of the lepra reaction cases showed a general abnormal lowering in the total calcium, nondiffusible calcium and albumin, and an abnormal shift above normal of the globulin. The nonreacting cases failed to show appreciable alterations in these constituents. It is concluded that in leprosy there is no deficiency in the physiologic serum calcium, i. e., the diffusible serum calcium. The abnormal rise in the level of the globulin in lepra reaction cases is believed to be at the expense of the albumin, causing its fall to below normal which in turn causes the lowering of the nondiffusible calcium and the total calcium. The author suggests that protein therapy be given a trial in patients suffering from lepra reaction, especially in those manifesting low serum albumin.

—J. O. NOLASCO

✓ CHIYUTO, S. A comparative study between boiled (Mitsuda-Hayashi technique) and formalinized lepromin. *Bull. Bur. Hlth.* **26** (1950) 157-169.

Boiled and formalinized lots of lepromin were tested simultaneously

in children of leprosy parents, the ages ranging from 5 months to 24 years, all with clinical signs of leprosy, all but 6 of which are recorded as having reacted positively to both antigens. Favorable results are claimed for the formalinized preparation as compared with the boiled one, although the total number of positives were the same; only 6 cases are recorded as negative to each of the lepromins. This favorable effect consists of a larger number of local reactions measuring 3 to 5 mm. in diameter, of which there were 66 with the formalinized preparations against only 36 with the boiled one. Between 6 and 14 mm. the frequencies are decidedly in favor of the boiled preparation, it is stated, the totals being 136 against 101. The author briefly reviews the prevailing interpretation of the lepromin reaction as one of allergy, and adds that the knowledge on the allergic phenomena in tuberculosis seems not applicable in explaining its different aspects.

—J. O. NOLASCO

ISRAEL, H. L., SONES, M., STEIN, S. C. and ARONSON, J. D. BCG vaccination in sarcoidosis. *American Rev. Tuberc.* **62** (1950) 408-417.

Vaccination of sarcoid cases with BCG was regarded as offering possibilities of elucidating the cause of the tuberculin anergy which is so common in that disease, if not also its etiology. Reports of such vaccinations in the literature, from six sources, comprise a total of 24 cases so treated, of which only 6 developed tuberculin sensitivity. The authors report the results obtained by them in 20 cases which met the diagnostic criteria imposed, including negative response to tuberculin, and which were subjected to serial tuberculin testing after vaccination; 6 of them were revaccinated once, 2 of them twice, and 1 three times. The local reactions to the primary inoculations did not, as a rule, differ from those in the controls, and no acute effect (Koch phenomenon) was seen after revaccination. In 7 of the patients tuberculin sensitivity did not develop at all, and in the 13 in which it was induced it was much weaker and much less well maintained than in control volunteers. The depression of immunological response in sarcoid is held not to be specific with respect to tuberculin, for pertussis vaccine [and, apparently, other antigens not specified] failed to produce normal sensitization. Hence it is indicated that the abnormal response to BCG vaccination is due to interference with general immunological mechanisms, although it is not implied that sarcoid cases are anergic to all agents. BCG vaccination, it is concluded, is not helpful with regard to either diagnosis or prognosis, nor do its effects establish sarcoidosis as an anergic form of tuberculosis.

—H. W. W.

SOUZA-ARAUJO, H. C. Four strains of cultures (two chromogenic and two non-chromogenic) of acid-fast bacilli isolated from rats and mice inoculated with emulsion of Stefansky's lepromin from Pasteur Institute of Paris. *Fifth Internat. Congr. Microbiol.*, Rio de Janeiro, Aug. 1950.

A strain of rat leprosy material obtained from the Institut Pasteur proved less pathogenic in white rats than one previously worked with, but a variety of mice obtained from the United States (*Mus musculus*, black race C-57, Rockland Farms) proved highly susceptible to it, sometimes showing large musculo-cutaneous lepromata in 48 days. From lesions in this and another breed of mice four cultures were grown, 2 chromogenic and 2 nonchromogenic. All were pathogenic, the nonchromogens more than the others, and all were recoverable from the inoculated animals. The

chromogens were found (by Andrade) to be negative to the cyto-chemical virulence test of Dubois, while the nonchromogens were positive.—[From the author's pre-congress summary.]

145-6 SOUZA-ARAÚJO, H. C. Non-chromogenic culture of an acid-fast bacillus isolated from a leper, pathogenic for murine, *Macacus rhesus* and man; strain "Hecke." Fifth Internat. Congr. Microbiol., Rio de Janeiro, August 17-24, 1950.

This culture, the author's "Hecke" strain, which appeared after 50 days in 1 of 10 Loewenstein tubes inoculated with leproma material from a patient, grew out in 2 weeks in subcultures on the same medium and on glycerine agar and broth. Black mice inoculated subcutaneously showed nodules in less than 10 days (white mice and white rats were less susceptible). One mouse which died had subcutaneous abscesses from which the culture was recovered, and bacilli were demonstrable in smears from the viscera. Inoculated guinea-pigs did not develop tuberculous lesions. Subcutaneous inoculation of a monkey caused olive-sized granulomatous, leproma-like nodules with acid-fast bacilli within and outside of cells. Two volunteer leprosy patients were inoculated intradermally in the thigh, with strong local and slight general reactions. A second inoculation induced nodules which ulcerated, and from which the culture was recovered. A third inoculation caused the same response, regarded as the Koch phenomenon.—[From the author's pre-congress summary.]

SOUZA-ARAÚJO, H. C. Bacteriology of human leprosy: Two new chromogenic cultures of acid-fast bacilli isolated from two patients, pathogenic for laboratory animals and for man; fulfillment of Koch's postulates. Fifth Internat. Congr. Microbiol., Rio de Janeiro, August 17-24, 1950.

One of these cultures, the "Chaves" strain, which appeared as a single colony in a mixed culture and which could be recovered from experimental lesions in animals, was inoculated intradermally on the thighs of the source patient and his wife—the same patients who had been inoculated with the "Hecke" strain. Both reacted more strongly (Koch phenomenon) than they did to the latter culture, and the culture was recovered from the resulting lesions. Three monkeys were inoculated with various lots of the materials involved and all developed leproma-like lesions. These facts signify fulfillment of Koch's postulates. The other culture, the "Emilia" strain, obtained from 1 of 6 Loewenstein tubes, was inoculated into the cheeks and forehead of a monkey which, within 8 days, developed the appearance of a lepromatous woman. Smears from a nodule and the feces were positive for acid-fast bacilli, and the culture was recovered.—[From the author's pre-congress abstract.]

SOUZA-ARAÚJO, H. C. Bacteriology of leprosy; a review. Fifth Internat. Congr. Microbiol., Rio de Janeiro, August 17-24, 1950.

Researches done with twenty-five classical cultures of so-called *Bacillus leprae*, during ten years.—[Author's pre-congress summary.]

8 TISSEUIL, J. Tension superficielle et orientation des bacilles de Hansen et de Stefansky. [Surface tension and orientation of the Hansen and Stefansky bacilli.] Bull. Soc. Path. exot. **42** (1949) 144-146.

The bacilli of Hansen and of Stefansky are both intracellular, the former occurring in cigar-like packets and the latter in needle-like bundles,

but it is not possible to distinguish them from each other. The Hansen bacillus appears to be embedded in a homogeneous gelatinous material, while the other is free in a heterogeneous medium. The organisms of human leprosy seem to be submitted to a surface tension effect which enables them to retain their grouping in tissue sections and in nasal mucous except in young forms, and their parallel distribution is dependent on surface tension. On the other hand those of Stefansky, being free, are able to group themselves by chance.—[From abstract in *Trop. Dis. Bull.* **47** (1950) 367.]

- ✓ SATO, S. and MAYAMA, A. Study of the so-called boil-fastness (resistance of staining against boiling) of leprosy bacilli. *Sci. Rep. Res. Inst. Tohoku Univ., Series C*, **2** (1950) 21-24.

This report concerns a phenomenon (*Kochfestigkeit*) studied by Preis, but with respect to the leprosy bacillus apparently by no other workers than certain Japanese and not extensively by them. Fifteen thin, air-dried smears are stained in carbolfuchsin for 15 minutes at 37°C, washed, and placed in boiling water (98°C), after which 1 is removed every 30 seconds and examined without counterstain to determine the time at which decolorization occurred. Regarding the influence of the pH of the water used for boiling, it was found that the city water of Sendai (pH 6-6.2) was best for the purpose. Among other things it was found that in smears of the skin lesions of 82 lepromatous cases the range (minutes of resistance) was from 1 in 2 cases to as much as 8 in 1 case, but the largest numbers lie in the 1.5, 2 and 2.5 minutes groups. Practically no smears from other sources in lepromatous cases (nasal secretion, blood, bone marrow and peripheral nerve) showed more than 4 minutes resistance, and that was the limit with materials from neuromacular cases. Resistance in lepromatous cases was greater in advanced than in moderate and slight ones, and in reactive than in inactive ones. When nodules were ground and suspended in 2 changes of saline to remove the tissue juice, the bacilli decolorized somewhat sooner than did those in control smears made directly from the same nodules. —H. W. W.

- ✓ HANKS, J. H. and WALLACE, R. E. Sterilization of the skin. *Proc. Soc. Exper. Biol. & Med.* **71** (1949) 200-201.

A technical problem in leprosy research is how to obtain uncontaminated viable material for tissue cultures. The authors have used various skin disinfectants immediately before removal of specimens of rat skin. They observed the tissue cultures of the uppermost or papillary layer at intervals up to 14 days, and expressed the results in terms of (1) the proportion of explants free of bacterial contamination, and (2) the proportion of positive for epithelial cells. In a controlled trial, the antiseptics were applied for 2 minutes. With a 3.5% concentration of tincture of iodine 1:2 in 70 per cent alcohol by weight, 40% of the cultures showed no epithelial migration. With 0.1% zephiran or 2% aqueous mercurochrome, at least 17% showed bacterial contamination and at least 33% showed final failure of epithelial migration, partly due to contamination. In contrast to the effect on the upper layer of epithelial cells, the disinfectants had no inhibitory action on the tissue culture of fibroblasts or of epithelial cells from the deeper or reticular layers of the skin. Without presenting data, the authors express satisfaction with 1:4 tincture of iodine applied

for 5 minutes, followed by its removal with alcohol.—[From abstract in *Trop. Dis. Bull.* 47 (1950) 368.]

- 6 DUBOIS, A. and FESTER, A. A propos de la culture du bacille de Stefansky. [On the cultivation of the Stefansky bacillus.] *Ann. Inst. Pasteur* 79 (1950) 567-570.

The cultivation of the germ of murine leprosy is so difficult that the publication of anything suggestive of success is justified. Previously the senior author, with W. Gavrilov [*THE JOURNAL* 6 (1938) 519], reported seemingly favorable results but it proved impossible to maintain subcultures indefinitely. Recently, with a strain of English origin, serial passages in animals have been obtained more easily than in previous work, probably in part because inoculations have been made into the crural muscles rather than subcutaneously. Some of the resulting local lesions have been preserved in equal parts of glycerine and distilled water in the refrigerator at about 4°C. On the surface of one such nodule, removed nearly 6 months after inoculation, there were seen after a full year neat, white, somewhat spheric "colonies" which could be photographed. (The photograph is poorly reproduced in the article, but numerous minute white points and several larger ones are nevertheless to be seen.) These colonies were composed of acid-fast bacilli which were neither tubercle bacilli nor saprophytes. It is believed that they probably were the Stefansky bacillus. However, no growth could be obtained in cultures, and as yet—after nearly a year—the phenomenon has not been repeated.

—AUTHOR'S ABSTRACT

6 SYMPOSIUM ON THE TUBERCLE BACILLUS

A series of lectures on the tubercle bacillus by authorities from various countries was organized at the Institut d'Hygiene et de Bactériologie of the University of Lausanne by Prof. Paul Hauduray, from April 22 to 25, 1949, and extensive summaries appeared in the *Bulletin of the World Health Organization* [2 (1949) 299-331]. It was stated that the lectures were to be published in full in English and French, but the firm which was said to be dealing with the English version has reported that they know nothing of the matter. The following abstracts comprise the main points of the summaries referred to.

JENSEN, K. A. (*Copenhagen*). Human and bovine types of tubercle bacillus.

Both types of bacilli are involved in human tuberculosis, a fact of epidemiological importance. Their cultures are differentiated on the basis of morphology of the colonies and their pathogenicity in animals. The human type is characteristically eugonic, developing more easily and abundantly than the dysgonic bovine strain, although occasional aberrant stains are encountered. With both types there occur strains of attenuated virulence, usually obtained from lupus cases, and labile strains are also encountered. In the human organism the bovine type may undergo transformation to the human, and mixed infections may result in that way; but cross infection may also occur. There is evidence that the bovine type has a type-specific protein antigen (absent, however, in avirulent BCG) whereas the human type appears not to have a specific fraction, and it is speculated that it may perhaps be a variant of the bovine type which has lost its specific element.

WELLS, A. Q. (*Oxford*). Murine type of tubercle bacillus.

This organism, discovered in voles (field-mice) in England in 1937, was found to affect the lymph nodes and lungs of 20% of 4,309 animals examined. It is the most pleomorphic of the tubercle bacilli, exhibiting among other curved and S-shaped forms. Tuberculin prepared from its cultures causes positive reactions in animals infected with the human, bovine and murine types, and, conversely, human tuberculin is reactive in the murine infection. The three types cannot be distinguished by serological methods. The murine type is highly pathogenic for voles—although very atoxic in them—but only potentially so for guinea-pigs, requiring massive doses injected subcutaneously to produce lesions. Consequently, it is regarded as probably useful for immunizing purposes, and it has been injected intracutaneously in man, with local reactions like those induced by BCG and with the induction of tuberculin positivity, which persists for several years, and apparent resistance to tuberculosis.

PENSO, G. (*Rome*). The paratubercle bacilli.

The term "paratubercle bacilli" is applied to all mycobacteria—widespread in nature—other than the pathogens (i. e., the 4 tubercle bacilli, those of human and murine leprosy, and that of hypertrophic enteritis of cattle). The view that they can be distinguished on the grounds of ready cultivation and nonpathogenicity for laboratory animals is erroneous. The author has found that there are four positive criteria for classifying the mycobacteria. First is the inhibitory effect of PAS on the pathogens in cultures, which serves for the initial distinction between tubercle and paratubercle bacilli; the others are growth temperature, metabolism with respect especially to utilization of carbohydrates, and the action of phages, of which five kinds have proved of value. Pathogenicity and immunological reactions are not useful criteria. On this basis seven groups of the mycobacteria [referring, apparently to the "paratuberculosis" group] have been distinguished.

HAUDURAY, P. (*Lausanne*). Acid-alcohol resistance of tubercle and paratubercle bacilli.

Various studies of the nature of acid-alcohol resistance are reviewed. The validity of those based on chemical fractionation are questioned, while emphasis is laid on the biological approach, i. e., the study of colonies and the effects of different culture media. Mycobacteria can be both resistant and nonresistant, the latter forms being either very young or very old, although some of the cyanophilic elements seen may not be bacillary in nature. The existence of nonresistant forms of the tubercle bacillus in pathological products is accepted. Alexander-Jackson's "differential triple stain" has been found of value, and an improved modification of it has been devised by Hauduray and Tanner. Various attempts to suppress acid-alcohol-resistance of tubercle bacilli and to induce it in other microorganisms are reviewed, the latter phenomenon including treatment with a fatty substance before staining—an effect seen only in the botanically related genera *Mycobacterium*, *Corynebacterium*, and *Actinomyces*.

CHAIN, E. B. (*Oxford*). The biological activity of substances extracted from the tubercle bacillus.

This paper deals with the various substances extracted from tubercle bacilli: the lipids (specifically the phosphatides, precipitated from either

solution by acetone; the glycerides, soluble in acetone; and the cerides, a waxy material obtained by chloroform after exhaustive extraction with alcohol-ether), the carbohydrates (polysaccharides), and the proteins. From the summary it would appear that the title is somewhat misleading in that the presentation deals more with the chemistry of the extractives than with their biological activity. Some mention is made of the serological characteristics of the carbohydrates—which with many bacteria constitute haptens which determine the specificity of the reactions—but more is said of the chemical characteristics of the two kinds found in the tubercle bacillus, somatic and lipid-bound. Two main protein fractions (A and B) of tuberculin nature are considered, one with low electrophoretic mobility (mol. wt. 16,000) and one with high mobility (mol. wt. 32,000), and more briefly a third one (C) which exhibits less biological activity than do the others in their undenatured state. It is noted that, although the tuberculin proteins are antigenic as test substances, they cannot alone induce the allergic state (i. e., tuberculin sensitivity) but can do so when injected together with the chloroform-soluble wax fraction, which also serves to establish allergic sensitization with substances such as picryl chloride and egg albumin. This fraction, therefore, has acquired a new significance for the understanding of the allergy of tuberculosis.

FLOREY, H. W. (*Oxford*). Antibiotics active against the tubercle bacillus.

Attempts to treat tuberculosis with antagonistic microorganisms are traced back to 1885, and historical value is ascribed to the idea of Schiller (1927) that an organism may be "trained" to produce a substance antagonistic to another organism. The difficulties faced in present-day work in the field of tuberculosis are mentioned, with emphasis on the essential differences between human and experimental tuberculosis. A detailed consideration of streptomycin is followed by a list of other substances derived from fungi and actinomyces, none of which has as yet shown much promise in tuberculosis. The same is said of various polypeptides derived from certain bacteria which have bacteriostatic action *in vitro*, some of them active against Gram-positive microorganisms and others (the polymyxins) against Gram-negative bacteria.

TRÉFONÉL, J. (*Paris*). Chemotherapeutic agents active against tubercle bacilli.

The author, who first showed that sulfanilamide is the active principle of Domagk's "prontosil," says that work in the field of tuberculosis began with the demonstration by Rich and Falle (1938) of the action of certain sulfonamides against the experimental infection, but that none of the substances of that group has given the hoped-for clinical results. The sulfones, however, have been found to be valuable adjuncts to streptomycin and are therefore worthy of investigation. The element sulfur probably plays a fundamental role, and the activity of the derivatives increases with the degree of oxidation. If the hydrogen of phenylmercaptan is replaced by an aromatic radical, activity again increases with the degree of oxidation, the final product being the "parent substance," di(*p*-aminophenyl)sulfone (sulfone 1358F). [Otherwise designated diaminodiphenyl sulfone, or DDS.] The formulae of this substance and certain derivatives are given. Discussing the study of chemotherapeutic products in experimental tuberculosis and their use in the clinical disease it is pointed out, among other things, that a substance may be inactive *in vitro* but active

in vivo, or conversely. Mention is made of thiosemicarbazone, a sulfur-bearing compound not of the sulfonamide [i. e., sulfa] group, and more is said of the recently-introduced *p*-aminosalicylic acid, whose mode of action, it is concluded, is analogous to that of the sulfones. It is stated that sulfathiodiazole has been used with some success against leprosy, and that the sulfones have been shown to be the best drug for that disease although of limited value in tuberculosis.

—H. W. W.