

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.

SCHNEIDER, K. Das Vorkommen von Lepra im Kreise Memel und das deutsche Lepreheim bei Memel 1899 bis 1945. [Leprosy in the Memel District and the Memel leprosarium between 1899 and 1945.] *Offentl. Gesundheitsdienst.* (Stuttgart) **14** (1953) 465-469.

For centuries leprosy had been nonexistent in East Prussia until the first known case occurred in a Lithuanian peasant in 1848. In 1893, 13 cases were reported, 9 living and 4 that had died in recent years. This renewed occurrence in the Memel district was regarded as the last trace of the old center in the Baltic provinces. The last case was in 1934, a man who had become infected in Memel 12 years earlier. Between 1848 and 1944 there had been 94 known cases in the district, 42 males, 52 females. Of these, 3 were alive in the leprosarium in 1944, when the total there was 11. Two nursing-sisters were in attendance, of whom one had been there for nearly 40 years, the other for 17 years; neither had become infected. In 1943, five patients had been taken there, 4 men from Hamburg-Eppendorf and 1 from Magdeburg. The leprosarium was opened on July 20, 1899, for 16 patients and was enlarged for 22 ten years later. Up to 1944, 85 patients had been treated there, 45 from the Memel district and the rest from elsewhere, including 18 from Lithuania and 11 or 12 from South America; 43 were females, 42 were males; 56 were nodular, 21 anesthetic, and 8 mixed. Psychic disturbances have been common and difficult to deal with; they have included insomnia and nightmares, paranoia, delusions of poisoning, sense of helplessness, general depression and anxiety. In 1944 the inmates passed through a bad time owing to the war, and 10 of the 11 had died by 1945, 5 from dysentery and typhoid. The last one is under outpatient treatment in Hamburg. No spread of the disease had occurred during an observation period of more than 60 years.—[From abstracts supplied by E. Keil and in *Trop. Dis. Bull.* **50** (1953) 519.]

ROGERS, L. Leprosy incidence and control in East Africa, 1924-1952 and the outlook. *Lep. Rev.* **25** (1954) 41-59.

In a historical introduction the writer points out that in 1925, in a book written with Muir, he showed that child infections are of crucial importance. Most cases (95%) were due to close contact with lepromatous cases. Isolation of infectious persons was needed to reduce the incidence of new infections, but the failure of a century's compulsory segregation in South Africa showed that this was not enough. It was vitally important to trace and treat children already infected in their homes before they also became lepromatous or crippled. The new drugs greatly facilitated this end, as more patients were coming for treatment early. The success of this plan in Nauru Island and in Nigeria proved this. After a detailed survey of leprosy treatment in British East Africa, the prospects of controlling the disease in that area are considered. The enormous extent of the countries, the varying densities of population (5.5 per sq. mile in Northern Rhodesia to 55.5 in Nyasaland) and the varying incidence of the disease increase the administrative and financial difficulties. The disease is most prevalent in the hot humid areas, as pointed out in his book. He suggests annual surveys to trace early infective cases and further research to find the ideal drug. The relapse rate after sulfone treatment is still very high. He advocates combined use of sulfones and hydnocarpus oil.

—G. O. TEICHMANN

COCHRANE, R. G. A critical appraisal of modern trends in leprosy, with particular reference to advances in immunology, histopathology and treatment. Chapter 9 of *Modern Trends in Dermatology* (Series 2). London: Butterworth & Co. (Publishers) Ltd. (reprint, undated).

Khanolkar's work in Bombay, the writer says, has opened up the whole problem of the infectivity of leprosy, particularly the finding of bacilli in so-called closed cases and the fact that 20% of healthy contacts of leprosy persons were found to harbor *M. leprae* under the skin. However, it is admitted that the likelihood of infection is very slight in these cases. It is also said that Khanolkar's demonstration that *M. leprae* appears first in the nerves in the skin points to the possibility that the bacillus can become pathogenic in man only after passing through the skin nerves, and that this suggested "passage" through the nerve tissues opens up intriguing possibilities in relation to its cultivation. A positive lepromin reaction probably indicates that the person may be harboring *M. leprae*, dead or alive. [This statement is difficult to reconcile with the fact that many people living in countries where leprosy is absent give positive reactions.] The author believes that all persons who come into contact with leprosy, and every one who is infected, at first develop positive lepromin reactivity, which corresponds with Khanolkar's "silent phase." From this point one of three developments can take place: (1) the tissues may become sensitized and strongly reactive to lepromin; (2) they may become desensitized and nonreactive; or (3) they may remain in an unstable condition—neither fully sensitized or desensitized. Thus there are three primary groups or types of leprosy: tuberculoid (lepride), lepromatous, and dimorphous (borderline). Taking the lepromin reaction as a guide to grouping, the disease is considered in its clinical manifestations under the headings of macules, infiltrations and polyneuritic lesions. Under therapy, no mention is made of hydnicarpus oil. Of the sulfones the writer prefers the parenteral use of 50% aqueous solution of sulphetrone but he also gives details of the oral use of DDS (Dapsone). Great care in the use of sulfones in dimorphous cases is advised, as serious nerve damage is likely if they go into reaction. Treatment must be continued for a long time, as Khanolkar has shown that the nerves act as reservoirs of the granular forms of the bacilli from which the disease may recrudescence.

—G. O. TEICHMANN

AUSTIN, C. J. General survey of the local leprosy conditions in the British Solomon Islands Protectorate. South Pacific Commission Project H.7 Leprosy. Report No. 2, July 1952, mimeographed, 12 pp.

In 1937-38, Ross Innes carried out a 7-months leprosy survey of the British Solomon Islands Protectorate, examining about a quarter of the population of 90,000 and finding a leprosy prevalence of about 1%. The author visited the group in 1945 to advise on leprosy control, and the present report deals with a similar visit made in January-February 1952 under the auspices of the South Pacific Commission. The political situation and the antigovernment "Marching Rule" would have made it impossible to do a thorough survey if this had been intended or if time had permitted. It had unfortunately produced the situation Ross Innes had feared when he wrote, "The 'Bush' is the reservoir of leprosy on Malaita... Here then is the danger. If ever the bush folk come in great numbers to reside on the coast, and come to mix freely with each other and with salt-water folk, then there may be a great increase of leprosy." In spite of the prevalent attitude, however, the fact that 228 patients are now undergoing voluntary treatment—more than the total number of cases seen by Ross Innes and more than one-quarter of his estimate for the whole Protectorate—provide concrete evidence of postwar progress. All of these patients were seen during the tour, which included visits to leprosy stations on Guadalcanal, Malaita, Ysabel, Vella Lavella, and Kolobangara, as well as to the Island of Savo. Every opportunity was taken for discussion of the leprosy problem with those who might be interested, to try to

avoid a one-sided view of the situation. Of the roughly 2,500 people examined in cooperating villages, only 5 cases not already known were discovered. It is now obvious on political and economic grounds that the original intention of establishing a central leprosarium on Guadalcanal for all patients is impracticable, but the nucleus of such a hospital established at Tetera has already proved its value. It has at present 48 inpatients and 60 outpatients coming from a wide area on Guadalcanal, and it serves as a model and a training center for leprosy workers. The various missions—Anglican, Methodist, Seventh Day Adventist, and Roman Catholic—are already doing leprosy work within their means, and with the aid of the Lepers Trust Board of New Zealand are planning to do more. The latter board has offered the missions three "leprosy relief ships" at an estimated cost of £15,000 each, in addition to large building grants to individual missions, and has now at the instance of the author promised an additional £2,500 a year to provide for a "leprosy medical officer" to coordinate and expand the antileprosy campaign, mainly in the direction of the establishment of more local leprosy villages and to enlarge the scope of the work at Tetera.

—AUTHOR'S ABSTRACT

[CONGO BELGE] Rapport Annuel de la Direction Général des Services Médicaux, 1952 (unsigned), Mimeographed, 107 pp.

After mentioning the progress represented by sulfone treatment, with special reference to DDS, this report tells of the plan to create, as part of the general antileprosy program, one or two large "Communauté d'Isolement Organisé" (C. I. O.) in each province. These communities, with up to 1,500 patients each, will be for the lepromatous and other "multibacillary" cases, which represent 10-20% of the total, and are primarily to be centers of treatment; of necessity, however, they will be obliged also to take care of the bed-ridden, the invalids, and those with severe ulcerations, who need constant medical care. They are also to be centers for the study of leprosy. The first of them is being prepared at Mosango, in Leopoldville Province; the amount of 12 million francs has been put at the disposition of FOREAMI for the purpose. Two important leprosaria in Equateur will be changed into C.I.O.'s, and plans for other places are indicated. Four pages of statistics show the distribution of 26,948 cases (8,175 of them new) in 183 "agricultural villages of segregation" (evidently comprising all of the leprosaria of the country, of which 4 have more than 1,000 patients each). A total of 156,639 are under treatment by the various fixed medical units and itinerant services.

—H. W. W.

GRAY, J. A. C. Epidemiology of leprosy in American Samoa. U. S. Armed Forces Med. J. 4 (1953) 585-598.

American Samoa consists of 7 islands with a rapidly increasing population—18,602 in 1950—within sight of West Samoa, which is under New Zealand mandate. Three family groups are described which were infected from West Samoa, and were between them responsible for the infection of 41 out of the 45 recorded cases. The factors favoring the spread of leprosy are the warm, moist climate, the density of the population (244.7 per square mile, but actually much denser as many parts are uninhabited), and the changing social organizations as modern conditions infiltrate the old Samoan paternal system. Of the 45 recorded patients, 8 had died; 29 [were, at the time] at the Makogai hospital in the Fijis; 1 was at Carville; 3 were treated as outpatients, and 1 was unknown. Of the 45 cases, the type was unknown in 10. Of the remaining 35, 18 are given as lepromatous, 14 as tuberculoid, and 3 as uncharacteristic. The small white population has remained unaffected. Leprosy is considered a major public health problem, and steps are being taken to examine contacts of known cases, and school-children.—[From abstract in *Trop. Dis. Bull.* 50 (1953) 629.]

CHERRY, R. L. and CLARKE, W. M. ^{Mangan, C.W.} Technical assistance in public health. The six year program in Greece. *Publ. Hlth. Rep.* **69** (1954) 475-486.

This is a review of the major and multiple programs of the Public Health Advisory Group of the Mutual Security Agency Mission to Greece, which have subsequently served as a basis for programs in other regions. Among the many problems discussed is leprosy, and the following on "renewed interest in leprosy" is verbatim: "In the immediate post-war period, Greek treatment facilities for lepers were very unsatisfactory. Consultation on newer methods of intensive treatment with modern drugs was given, and local health officers were educated in the modern concepts of the social and epidemiological aspects of leprosy. The Ministry of Social Welfare arranged for foreign experts to visit leprosariums and to make recommendations. A bacteriological survey was also made on all leprosy patients, but some who were bacteriologically safe refused to leave the government-supported institutions where they had grown accustomed to a sedentary life. As a result of technical assistance in health, a new interest has developed in the improved treatment of lepers and control of leprosy."

—SR. HILARY ROSS

LOWE, J. The nature of maculo-anesthetic (tuberculoid) leprosy. The role of the tuberculoid case in the spread of leprosy. *Lep. India* **25** (1953) 46-49 (correspondence).

This letter is a vigorous criticism of a recent article by Khanolkar and Rajalakshmi [THE JOURNAL **22** (1954) 107]. The author first criticizes the claim to originality of the view of the spread of infection up the peripheral nerves, a view long held by most leprologists. But the nerves constitute only one of the routes of dissemination, and especially in lepromatous cases bacilli are also spread through the blood and lymph vessels. The strongest, however, is directed to Khanolkar's finding of bacilli in and on the skin of healthy contacts of both tuberculoid and lepromatous cases, and the interpretation of these findings. Many possible fallacies are connected with the ubiquitousness of acid-fast bacilli, as for example their presence in tap water. "Dr. Khanolkar views all cases of leprosy as infectious and apparently infectious. On the latter point his findings are at variance with those of dozens of research workers of international reputation. . . . An isolated report such as that of Khanolkar does not carry conviction. It must be confirmed by others."—[From abstract in *Trop. Dis. Bull.* **50** (1953) 720.]

QUAGLIATO, R. Incidência da lepra entre os comunicantes da Inspecção Regional de Campinas; 18 anos de observação (1934-1952). [Leprosy incidence among contacts in the Inspecção Regional of Campinas; 18 years of observation (1934-1952.) *Rev. brasileira Leprol.* **21** (1953) 133-142.]

This study is a survey of 6,000 of the 6,333 contacts recorded in the Inspecção Regional of Campinas (São Paulo) between 1934 and 1952, with follow-ups of from 6 months to 18 years. (During this period 1,448 patients were registered.) The 6,000 are divided into six chronological groups of 1,000 each, among whom in total 95 cases have appeared (15.8 per 1,000). Group 1 (15 to 18 years of observation) has produced 26 cases, of whom 13 had been removed from the source of infection for from 1 to 6 years, the rest for from 6 to 15 years. In Group 2 (13 to 15 years of observation) there were 19 old contacts who became patients, 11 of them in the first 6 years and the rest within 12 years. In Group 3 (10 to 13 years of observation) there were 25 cases, of whom 19 appeared before 6 years and the rest before 11 years. The remaining 3 groups are contacts with less than 10 years down to 6 months of observation, among whom 22 cases have appeared. The data for the first three groups show that the proportion of cases occurring later than 6 years after removal of the source of infection increases steadily, from only 6 out of 25 (24%) in Group 3, to 8 out of 19 (42%) in Group 2, and 13 out of 26 (50%) in Group 1.

It would be difficult to establish a practical time limit for the observation of contacts. Perhaps the Mitsuda reaction might serve for orientation in this respect.—[From author's summary.]

KOESLAN. Kupasan tjeramah H. Koperberg tentang soal lepra. [Outline of the talk given by H. Koperberg on some problems of leprosy.] *Madjalah Kedokteran Indonesia (J. Indonesian Med. Assoc.)* (1952) 230-237.

The author, who during 1936-1937 carried out epidemiological investigations in the district of Lamongan, Java, where 755 leprosy patients were examined, gave the following summary: From the bacteriological point of view, leprosy is little infectious (to most people) but it is extremely contagious (to some very susceptible people). This *principum contradictionis* should be considered as a paradox which needs another viewpoint. It may be interpreted as follows: Only a small proportion ($\pm 30\%$) of people are susceptible, and a still smaller part ($\pm 1\%$) are highly susceptible. Among the infectious diseases, leprosy is the only one of which the morbidity number is caused by the hosts only, and not by the infectious agent (relative or commensal infection). [Sic.] In leprosy we used to speak of conditional recovery, control and arrest, which means not to infect other people and not to be reinfected. The degree of arrest should be adapted to the susceptibility of the patient. In Lamongan 80% of the leprosy patients were of the greatest susceptibility. In order to determine if a patient is contagious or not, a "provocative method" is a *conditio sine qua non*, and also a test animal as susceptible as the most susceptible man. Probably true recovery from leprosy is possible only to persons of the household-contact classes (resistant against reinfection). To provide perspectives for leprosy research, the speculation is suggested that leprosy is more an allergic disease than an infectious one, and forms its own group in pathology. —R. BOENJAMIN

MITSUDA, K. On the etiology of erythema nodosum leprosum and the metabolism of leprosy bacilli. *La Lepro* 22 (1953) 111-112 (in Japanese; English abstract p. 111).

After treatment with promin or other drugs the numerous leprosy bacilli of the fresh nodule are destroyed and take on a granular form. Lepra cells are filled and swollen with phosphatid lipid granules through lysis of the bacilli. Certain products occur as the result of metabolism of the leprosy bacilli. These products will enter into the blood stream and cause ENL in the skin, iridocyclitis in eyes, and neuritis in nerves. The histopathological picture is chiefly composed of foamy lepra cells, leucocytes, lymphocytes and plasma cells. Pyogenic bacteria cannot be found, even when the lesion becomes abscessed.—[From abstract.]

BIRRELL, J. H. W. A note on leprosy as an etiological factor in the Weber-Christian syndrome. *Med. J. Australia* 2 (1953) 7.

The Weber-Christian syndrome, or relapsing febrile nonsuppurative nodular panniculitis, is a condition characterized by recurrent fever associated with the formation of single to multiple crops of inflammatory nodules, tender or painless, in the panniculus adiposus. In 1952 the author observed and reported the case of a 37-year-old man of Maltese origin who had lived in Australia for two years and who presented the typical symptoms of the Weber-Christian syndrome. Shortly afterward another person from Malta was seen at the Alfred Hospital, Melbourne, who presented a similar clinical and histological picture. Leprosy was suggested in this second case, and organisms typical of *M. Leprae* were found in biopsy material from one of the nodules. This immediately led to a reexamination of the biopsy material from the first case, and the discovery of similar organisms in it. These observations are thought to signify that the Weber-Christian syndrome is only a syndrome and not a specific disease, and that leprosy may well be one of the etiological agents. A

proportion of cases of the Weber-Christian syndrome may actually be cases of leprosy in a relatively early stage.—[From abstract in *J. American Med. Assoc.* **153** (1953) 1223.]

MONTEL, L. R. Lèpres nerveuses pures dermatologiquement asymptomatiques. Lèpres minimales, précession des lésions nerveuses sur les symptômes cutanés. [Pure neural leprosy without dermatological symptoms. Minimal leprosy, priority of the nerve lesions over the skin lesions.] *Bull. Soc. Path. exot.* **45** (1952) 749-757.

The author reports 4 observations of patients with neuritic lesions without skin manifestations, and 6 observations of patients with slightly disseminated skin lesions which appeared to have been preceded by neuritic lesions. In one case the latent period before the appearance of the skin manifestations was 24 years. Montel believes that these observations confirm the theory he has already set forth on this subject.

—M. VIETTE

KASLIWAL, R. M. and ANDLEIGH, H. S. An interesting case of leprosy. *Indian J. Med. Sci.* **7** (1953) 415-417.

The authors present a case of leprosy in which acute arthritis of the knees and elbows, associated with fever, was the initial symptom. Cutaneous and neural signs of leprosy subsequently appeared. It is believed that the association of arthritis with Hansen's disease may be due to an allergic reaction to the lepra bacillus.—[Abstract from *Excerpta Med.* **8** (1954) 161.]

COSSERMELLI, W. and PIMENTA DA SILVA, R. Ionização da acetil-beta-metil-colina (Mecholil) nas lesões tegumentares de lepra. [Ionization of acetyl-methylcholine (mecholyl) in skin lesions in leprosy.] *Rev. brasileira Leprol.* **21** (1953) 89-132.

The test is one of simple technique, and it is important where the specialist needs a supplementary test of good sensitivity, not traumatizing like other tests which involve pricking, and it is well tolerated by the patients. Furthermore, the reading of the results is done easily and quickly. Its value is most evident in colored persons and in those with erythematous lesions, in whom other commonly used tests such as those that depend on vasodilatation are obscured. With it one can demonstrate disturbances of sweating, evidencing a structural lesion, in the vicinity of a leprotic lesion, where morphologically there is no manifestation of the disease. It has advantages over ionization of pilocarpin, especially with reference to sensitivity and to the time and ease of reading. There is no relation between the degrees of sudoresis and erythema, or with formication. Certain changes of the nervous system may affect sudoresis, and the modifications of this phenomenon are sure indications of the severity and extent of the lesion, being in this connection of extraordinary importance for the neurologist.—[From authors' summary.]

PENNEK, J. La thérapeutique sulfonée à la léproserie de la Désirade (résultats d'ensemble). [Sulfone therapy in the Désirade leprosarium (aggregate results).] *Bull. Soc. Path. exot.* **46** (1953) 65-75.

Diasone, Cimedone and Disulone (DDS) were used successively (doses not indicated) in treating 58 lepromatous and 27 tuberculoid or indeterminate cases, for 1-1/2 to 2 years. Some of the patients also received, in addition, 20 cc. of chaulmoogra weekly by intramuscular injection. Dermatologically, 37 lepromatous patients improved, 15 of them markedly; 22 patients remained stationary; and 3, who could not tolerate the sulfones, have become worse. Of the 17 tuberculoid or indeterminate patients with cutaneous lesions, only 5 showed improvement. Anesthesia improved in a few cases (6 lepromatous and 4 others), as did contractures of the hands (in 2). On the contrary, the polyneuritic disturbances were aggravated in 6 lepromatous cases. Bacteriological improvement was less notable; there was no negativization of skin lesions. Ocular

lesions did not subside, but they generally remained stationary. Subconjunctival injection of placenta extract in 5 lepromatous cases brought about the cessation of pains and increase in visual acuity. The sulfones were generally well tolerated, Diasone least, Disulone most. One or several lepra reactions, generally arrested by decreasing the doses, occurred in 33 patients. The use of DDS is recommended.

—M. VIETTE

6 MONTOYA, R. and PESCE, H. Psicosis sintomáticas por tratamiento sulfónico en leprosos. [Symptoms of psychosis caused by sulfone treatment in leprosy.] *Rev. brasileira Leprol.* **20** (1952) 141-155.

The authors give details of 9 out of 377 patients treated with sulfones in the Colonia de San Pablo, Loreto, Peru, in whom there developed mental complications caused by the treatment when DDS was administered in the dosage of 300 mgm. daily by mouth [a dose usually considered excessive, the reviewer comments]. The symptoms included macropsia, hallucinations, ideas of persecution and of catastrophe, dulling, depression, suicidal tendency, fugitive convulsions and irritability. Almost all of the 9 patients showed symptoms of asthenia and anorexia from the beginning of the sulfone treatment, but they were free from other localized clinical organic complications. These mental complications, along with other general signs of intolerance, called for a smaller daily dose of DDS, a more gradual increase in dosage at the beginning of treatment, and the administration of vitamin B components when necessary.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 723.]

8 MELAMED, A. J. Reacción leprosa: acción profiláctica de la isoniazida. [Lepra reaction; prophylactic action of isoniazid.] *Día Méd.* **26** (1954) 866-868.

Isoniazid seems to prevent the occurrence of lepra reaction, or to decrease its frequency and intensity. This effect indicates the usefulness of the drug in the treatment of leprosy cases which have frequent reactions, whether spontaneous or due to the effects of sulfones. The slight effect of the drug on the lesions and on the bacilli in them makes it desirable to combine it with recognized antileprosy drugs (sulfones), once the liability of the patient to reaction is overcome.—[From author's summary, supplied by G. Basombrio.]

8 DORENLOT, H. Huit cas de réaction lépreuses traités par l'ACTH. [Eight cases of lepra reaction treated with ACTH.] *Bull. Soc. Path. exot.* **46** (1953) 56-65.

Eight sulfone-treated patients with lepromatous leprosy were given ACTH during lepra reactions. The ACTH was injected intramuscularly for 4 days in daily doses ranging from 12.5 to 60 mgm. The effect of the treatment was always definite and rapid on the fever, pains, and edema of the face, almost always on the nodules or infiltrates, and slower on the edema of the extremities and iritis when these existed. In 7 of the cases, however, the reaction symptoms reappeared, necessitating a second course of ACTH treatment in 6 of them, and a third course in the seventh. The relapses appeared 1 to 10 days after the end of the first treatment, the more slowly the higher the dose given. The 60 mgm. daily dose, whether administered in the first course or during the relapses after the lesser dosages, brought about complete arrest of the reaction. There was no serious complication during the treatment, or in the evolution of the disease during the succeeding months. Antihistamin drugs, although inactive at the onset of the reaction, seemed to be beneficial in relapses appearing after an ACTH treatment. The author believes ACTH to be a useful drug for lepra reaction.

—M. VIETTE

8 WILKINSON, F. La acción de la vitamina B₁₂ en altas dosis en el estado de reacción de la enfermedad de Hansen. [The action of vitamin B₁₂ in massive doses on the reactional state in Hansen's disease.] *Día Méd.* **26** (1954) 1293-1295.

Injections of 1000 micrograms of vitamin B₁₂, given daily in series of 5 injections,

proved to be innocuous, to make possible continuation of the specific treatment, and to have a triple effect: on the skin and eye involvements due to the reaction, relief of pain, and recovery of the general condition.—[From author's conclusions, supplied by G. Basombrio.]

SIGALL, M. O. Tratamiento de las amiotrofias de origen hanseniano con vitamina E (Ephynal 'Roche'). [Treatment of leprotic amyotrophies with vitamin E.] *Fontilles* 3 (1953) 245-247.

Eight cases of thenar and hypothenar leprosy amyotrophy were treated for 18 weeks with local and very deep injections of vitamin E. All these cases showed marked and in some cases almost complete muscular recovery.—[Abstract from *Excerpta Med.* 8 (1954) 75.]

LEPROSY REVIEW. *Physiotherapy* Number. 25 (1954) No. 1.

This issue of this periodical is devoted primarily to articles on conservation and rehabilitation work being done at the Rehabilitation Centre, Christian Medical College, at Vellore, in India by Dr. Paul Brand and Nursing Sister Ruth Thomas. The matter is introduced by a guest editorial by Mr. J. I. P. James, a surgeon of the Royal National Orthopaedic Hospital, who apparently does similar work for leprosy patients in England. He draws a parallel between the problems faced by the orthopedic surgeon with such patients and those presented by poliomyelitis patients before the development of such deformities was prevented—before it was learned that in motor paralysis deformity is caused by disuse and muscle imbalance. Some amelioration of disabilities that have developed in leprosy can be offered by the surgeon, but the important point is that "*deformity is preventable and unnecessary.*" This note is followed by a brief unsigned one (obviously by Cochrane) in which this number of the *Review* is spoken of as "a landmark in leprosy history." The two items immediately below do little more than indicate the scope of the articles, which should be read in the original by everyone interested in this important matter.

—H. W. W.

BRAND, P. W. The place of physical medicine and orthopaedic surgery in leprosy. *Lep. Rev.* 25 (1954) 5-10.

It is pointed out that in leprosy the surgeon and physical therapist have three important objectives: the prevention of deformity, its correction when present, and the rehabilitation of the crippled patient. The causes of deformity are summarized as constituting three main groups: (1) those associated with paralysis of motor nerves, (2) those associated with paralysis of sensory nerves and (3) those associated with the direct effect of leprosy on the tissues of the hand. The two important deformities of the hand—limitations of movement and stiffness of the joints, and destruction of the fingers through absorption—are discussed with respect to the causative factors. Anesthesia removes the safeguard of pain and temperature sensation, and thus permits many injuries that aggravate absorption. With preventive care regarding the secondary changes that follow anesthesia and paralysis, it should be possible for the great majority of patients to keep their hands intact and active, even without surgery. As for surgical reconstruction of the hands, discussed summarily, 15 different operations are in regular use at the Centre. Reconstruction of the hand demands—and should permit—the total rehabilitation of the patient, which is the ultimate objective. The rehabilitation program of the Centre is discussed and tribute is paid to R. G. Cochrane, "who saw the possibilities and importance of these aspects of the treatment of leprosy long before he was able to get an Orthopaedic Surgeon or Physiotherapist to co-operate with him and work them out."

—H. W. W.

THOMAS, R. E. An investigation into paralysis patterns in the forearm and hand in leprosy. *Lep. Rev.* **25** (1954) 11-15.

———. Physiotherapy and neural involvement in leprosy. *Ibid.* 16-36.

———. Suggestions for treatment by physical methods in neural leprosy. *Ibid.* 37-41.

(1) Although paralysis in leprosy appears to be haphazard in some respects, in one important respect it conforms to a certain pattern—it affects only certain nerves, and these nerves only at certain anatomical levels. For the purpose of discovering this pattern 50 patients with significant or severe paralysis of the forearm and hand were tested with a Ritchie-Sneath electric stimulator to diagnose the presence and degree of muscle denervation. (A preliminary survey of 20 patients with various degrees of disturbance had shown that the muscles of the upper arm were normal in every case, so these were not included in the detailed survey.) Muscles supplied by the ulnar, median and posterior interosseous nerves were tested separately. The paralysis patterns in these 50 patients showed a certain uniformity in that the muscles supplied by one nerve were usually all paralyzed at the same time and to about the same degree. Muscles supplied by the ulnar nerve in the forearm and hand, and muscles below the wrist supplied by the median and posterior interosseous were rarely or only slightly paralyzed. Paralysis is often not continuous but may show periods of improvement and regression.

(2) The second paper deals with the methods used to increase the functional activity of the hands of leprosy patients. It is pointed out that the loss of even a part of the 20 small muscles of the hand may cause serious imbalance and greatly reduce the usefulness of the member. The importance of dealing with the mental state, of overcoming the loss of will to work so often found in these patients, and the winning of their confidence and cooperation, is stressed. Massage with groundnut oil, paraffin wax packs and electric stimulation are explained as all having their place in rendering the tissues supple and in maintaining the tone of the paralyzed muscles, but the main stress is laid on exercises, assisted passive, assisted active and free active. Details are given of a number of different and useful exercises, and these are illustrated by 15 photographs. Any exercise which tends to hyperextend the metacarpophalangeal joints should be discouraged, as these joints tend to hyperextend too easily. Courses of exercises should extend over several months to be of real benefit, and should be linked up with some rehabilitation program aiming at enabling the patient to earn his living after leaving the institution.

(3) This paper gives details for the use of faradic current to stimulate the muscles of the forearm and hand. —G. O. TEICHMANN

TOUZIN, R. and MERLAND, R. Elimination de la "Sulfone Mère" par le lait de femme. Conduite à tenir vis-à-vis de l'enfant issu de lépreux. [The elimination of the "parent sulfone" in the milk of women. Method to employ with children born of leprosy patients.] *Méd. Trop. (Marseilles)* **12** (1952) 536-541.

At a leprosarium in Tananarive, Madagascar, only 7 out of 160 children isolated from parents at birth during a period of 18 years contracted the disease. The number of births is increasing, however, and to prevent overcrowding other arrangements had to be considered. Consequently, 9 lepromatous and 7 tuberculoid mothers, who had improved greatly on 200 mgm. of DDS per day, were allowed to keep their infants and nurse them. On determining the concentration of DDS in the blood and the milk of 6 of these women, it was found that in the milk it was on an average about 45% of the blood concentration. It is believed that this concentration would not be sufficient to prevent the children from contracting leprosy from their mothers, but as yet the children show no signs of the disease.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 316.]

ARCURI, F. and FERRINI, O. Jodoprotidemia nella lebbra. [Iodoprotein blood levels in leprosy.] *Acta Med. italica Mal. Infett. e parass.* **7** (1952) 253-255.

The authors, of the University of Genoa, determined the iodoprotein levels in 30 cases of leprosy. The patients were aged 15-76 years, and about one-half were lepromatous. The levels found were from 2 to 6.6 gamma per cent, with an average of 4.1, which is below the normal average of 5.2 gamma per cent quoted by a number of other workers. The results are related to the clinical and pathological changes, from which the authors conclude that a state of hypothyroidism occurs in leprosy.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 315.]

MAUZE, J. and ARNAUD, G. Quelques valeur des dosages des sérum albumine, sérum globuline, cholestérol et calcium chez les lépreux. [Serum albumin, globulin, cholesterol and calcium levels in leprosy patients.] *Bull. Soc. Path. exot.* **46** (1953) 495.

It is concluded from studies in 23 cases of leprosy that only the inversion of the albumin/globulin ratio is a more or less constant finding. Serum calcium and cholesterol show levels too variable to be of any significance with regard to the disease.—[Abstract from *Excerpta Med.* **8** (1954) 120.]

KASOLAPKINA, L. I. and ALAMDAROFF, I. N. Sostoianie nervnykh volokon v eskperimental' nykh lepromakh. [Condition of the nerve fibers in experimental lepromas.] *Vestnik Vener. Derm. (Moscow)* (1953) No. 3, pp. 14-17.

Subcutaneous injections into rabbits of a dry antigen containing lepra bacilli produced nodules similar to those in human pathology. They contained cells that had undergone a lipid and vascular degeneration and groups of lepra bacilli. Nerve fibers in these experimental nodules undergo disintegration and even fragmentation. Examination of a subcutaneous nodule appearing 9 months after intravenous infection of a rabbit revealed fibroblasts, histiocytes, no bacilli or lipid degeneration, while fragmentation of the nerve fibers was even greater than in nodules appearing after subcutaneous infection.—[Abstract from *Excerpta Med.* **8** (1954) 69.]

MARIE-SUZANNE (SR.), NOEL, R. and SOHIER, R. Comparaison des lésions histologiques provoquées chez le rat blanc par inoculation du bacille de Hansen et de divers autres bacilles acido-résistants. [Comparison of the histological lesions induced in white rats by inoculation of the Hansen bacillus and various other acid-fast.] *Ann. Inst. Pasteur* **82** (1952) 50-54.

White rats were inoculated subcutaneously and intramuscularly with Hansen bacilli of a leproma suspension, bacilli obtained in cultures of leprous tissue ("Chauviré" strain), and 3 strains of nonleprosy acid-fast bacilli. Histological examinations of the resulting lesions were made with specimens taken every 30 days for 10 months. In the first two months there was observed, with the Hansen bacillus, the "Chauviré" strain, and with one of the other acid-fasts, rapid dissemination of free histiocytes containing numerous bacilli without nodular epithelioid structure. Of the two other strains of acid-fasts, one induced epithelioid nodules with diffuse lymphocyte reaction, and the other a banal reactional granuloma. In the tenth month the lesions induced by the Hansen bacillus and by the "Chauviré" strain were of either the tuberculoid or the lepromatous type, with the presence of typical globi. The first strain of the other acid-fasts provoked a necrotic lesion surrounded by a lymphocyte zone with some histiocytes. Of the other two acid-fasts, one produced no lesion and the other only simple cicatrices. The Hansen bacillus and the "Chauviré" bacillus, then, provoked in the white rat identical lesions, tuberculoid and lepromatous, which were not produced by the paratubercle bacilli used.

—M. VIETTE

GUPTA, N. P. MEHROTRA, T. N., MANGALIK, V. S. and CHANDY, P. J. Serological test for syphilis. False positive reactions in leprosy. *Indian J. Med. Sci.* **7** (1953) 23-32.

These authors carried out several tests—Wassermann (MRC method No. 4, using sheep heart antigen), Kahn Standard, Meinicke slide, and VDRL slide—on specimens from 263 leprosy patients, 151 lepromatous and 112 tuberculoid. All 4 tests were positive in 14 (5.4%), 3 tests were positive in 25 (9.5%), 2 were positive in 64 (24.3%); 1 only was positive in 92 (35%), and all were negative in 68 (25.8%). The positives include all weak and doubtful positives. The percentages of false positive reactions were: WR 56.5, VDRL 36.5, Kahn 25 and Meinicke 14. Heating of test sera to 65°C. for 4 minutes tended to reduce the number of false positives with the WR from 50 to 2 and with VDRL from 50 to 5; 6 positive syphilitic control sera were not reversed by heating. The duration of leprosy or of treatment had no effect. In general, sera from lepromatous patients gave a higher percentage of positive reactions from those from tuberculoid cases.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 629.]

HONDA, H., HOSHINO, K., OSHIMA, T., MASUDA, T. and SAKAMOTO, K. On sero-reaction of leprosy with cardiolipin-cephalin antigen. *La Lepro* **22** (1953) 128-130 (in Japanese; English abstract p. 128).

The authors present a serological antigen with improved proportions of its components. These are [verbatim]: 0.2% cardiolipin (1), 1% cholesterolin (15) and 1% cephalin (20), and 1% kaolin is added to this. With this antigen more positive reactions were obtained in lepromatous sera than with Ogata's method (complement-binding reaction), and nonspecific reactions were fewer than with any other method. They think that the complement-binding reaction with this ratio of antigen components may be a useful method for the serodiagnosis of leprosy.—[From abstract.]

DE ALMEIDA, J. O., DE FREITAS, J. D. M. and BRANDO, H. Complement fixation test with a triple antigen for syphilis, tuberculosis, leprosy, or Chagas disease in blood banks. *American J. Trop. Med. & Hyg.* **3** (1954) 490-494.

Serological tests used in blood banks for ruling out syphilitic donors are not applicable in South American countries where Chagas disease and leprosy are endemic and the prevalence of tuberculosis is high. The authors devised a screening test using a triple antigen: (a) cardiolipin, (b) antigen from tubercle bacilli, and (c) trypanosome extract. Complement fixation tests were made on 786 sera from blood donors using this triple antigen and with each of the antigens separately. The results indicate that this test can be used for screening purposes. There were no false negatives. Leprous sera did not react to the *T. cruzi* antigen.—SR. HILARY ROSS

SCHMID, E. E. and THILLAINATHAN, P. O. On the specificity of Luotest in leprosy. *Ceylon J. Med. Sci. (Sect. D)* **8** (1953) 171-176.

Luotest is a preparation made from syphilitic rabbit testes, which Rottmann and others claim to give specific results in the diagnosis of syphilis when it is used in a skin test—0.2 cc. intradermally, read after 24 or 48 hours. The authors tried the test in 175 leprosy patients, of whom 144 were without clinical signs or history of syphilis or yaws (69 lepromatous, 69 neural, and 6 mixed). There were many more positive reactions (13 as compared with 5), among the neural than among the lepromatous cases, which latter type has the greater influence on the seroreactions for syphilis. After the Luotest there were more reversals from serum positivity to serum negativity than in the opposite direction, and there were more of these reversals in the lepromatous cases than in the neural.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 818.]

YOKOTA, T. The histopathological study of the Mitsuda reaction. (Part I.) *La Lepro* **22** (1953) 113-120 (in Japanese; English abstract p. 113).

———. The histopathological study of the Mitsuda reaction in the case of the tuberculoid leprosy. (Part II.) *Ibid.* **22** (1953) 121-124 (abstract p. 121).

———. The histopathological study of Mitsuda reaction in the case of subsided lepromatous leprosy. III. *Ibid.* **22** (1953) 228-231 (abstract p. 228).

———. The histopathological study of Mitsuda reaction in the case of lepromatous leprosy. IV. *Ibid.* **22** (1953) 232-235 (abstract p. 232).

———. The histopathological study of Mitsuda reaction. V. *Ibid.* **22** (1953) 292-297 (abstract p. 292).

(1) Observations were made on 34 biopsy specimens from 8 cases of neural leprosy, these specimens taken from the sites of Mitsuda tests at various times after injection of the antigen. Control tests were made with suspensions of other killed organisms, such as *M. leprae murium*, *M. Phlei* (Timothy), and BCG. Within the first 3 days after injection, an inflammation of the nonspecific acute exudative type was observed, but a tuberculosis-like granulomatous development began approximately 8 days after injection and was fully established after 2 weeks. Only very rarely has this granulation been seen to display caseous degeneration. This tuberculosis-like granuloma was found to differ very slightly from the histological changes found after the injections with the other mycobacteria mentioned. The sojourn of the inoculated organisms within the epithelioid or giant cells was long. In the case of neural leprosy the Mitsuda reaction may be regarded as a normal reaction rather than one of allergic nature. The histological picture in the Mitsuda reaction was the same regardless of the outcome of the tuberculin test.

(2) Fifteen biopsy specimens from 5 cases of tuberculoid leprosy were studied. The same early, nonspecific, acute exudative inflammation was observed as before, and after 8-14 days there appeared the same tuberculoid granuloma, which is caused by the destruction products of the injected lepra bacilli. The bacilli were destroyed in the tissue earlier than in the neural cases. The allergic nature of the early reaction, described by Büngeler and Fernandez, could not be confirmed from the histopathological standpoint. There are no essential differences between neural and tuberculoid leprosy as regards the histopathology of the Mitsuda reaction.

(3) Fourteen specimens of the Mitsuda reaction were obtained from 7 lepromatous cases which had become positive under chaulmoogra oil treatment. These specimens were removed from 3 hours to 82 days after the injection. The nonspecific acute exudative inflammation, with marked infiltration of neurotrophile leucocytes and histiocytes, was observed until 48 hours after injection, but it disappeared gradually thereafter. The tuberculoid granuloma, regarded as the histological manifestation of the positive Mitsuda reaction, appeared after 8-14 days. Caseation was found only exceptionally in the tuberculoid granuloma. The injected bacilli were found even after 82 days. The fact that these subsided lepromatous cases, formerly negative, gave positive Mitsuda reactions is regarded as evidence of acquired resistance to lepra bacilli.

(4) Sixteen biopsy specimens of the sites of the Mitsuda test were removed from 6 lepromatous cases, and also specimens where either heat-killed *M. leprae murium* or BCG had been injected. The usual acute inflammation was observed after 48 hours, but of less degree than in Mitsuda-positive cases. This inflammatory process disappeared quickly, and left only slight cell infiltration around small vessels, sweat glands and hair follicles; no tuberculoid granuloma was found. On the other hand, the tuberculoid granuloma developed where the other mycobacteria had been injected. This fact shows the specificity of Mitsuda reactions. The injected lepra bacilli disappeared sooner than they did in the neural and tuberculoid case. The negative reaction in the lepromatous case is the evidence of lack of resistance against lepra bacilli.

(5) The formation of the tuberculoid granuloma would be caused by the phosphatid fraction of the lepra bacilli. There is no relation between the Mitsuda and the tuberculin reactions. The histopathological picture of the Mitsuda reaction in nonleprous persons does not differ from that of neural and tuberculoid cases. [These are the only statements with elements that are new in this summarization of the preceding reports.]—[From summaries.]

SCHUJMAN, S. El valor del estudio inmunológico en la lepra. [The value of the immunological study in leprosy.] *Semana Méd.* **105** (1954) 146-154.

The author begins with general considerations of the value of the lepromin reaction in prognosis and classification. With regard to the nature of the reaction from the immunological point of view, he regards the early (Fernandez) and late (Mitsuda) reactions to be of different nature, the former one of allergy and the latter one of relative immunity or resistance. This resistance is a form of normal reaction in the majority of the adults, for which previous contact with *M. leprae* is not necessary, or cosensitization with other acid-fast bacilli. Inability to react to the presence of *M. leprae* is the abnormal thing; it is a specific incapacity of lepromatous cases and a small proportion of healthy persons, since both react against other acid-fast bacilli with nodules of tuberculoid structure. The condition of immunity or resistance is independent of allergy because it can exist alone as is seen in healthy adults and some contacts who show positive late but negative early reactions. Immunity is a previous and indispensable condition for the occurrence of later sensitization; only persons who give the late reaction can be sensitized [for the early one] by repeated injections of the Mitsuda antigen; on the other hand, sensitization has never been attained with this antigen in lepromatous cases, because of their lack of previous immunity or resistance. The allergic condition depends on immunity; the author does not remember having seen any case with a positive early reaction in which the late one was negative. In lepromatous patients, who habitually react with a late nodule to other acid-fast bacilli, the author has been able to obtain sensitization (early reactivity) to such antigens by repeated intradermal injections of them. He considers these facts about immunity and allergy in leprosy to be very important because of their possible relation to or application in other diseases caused by acid-fast bacilli.—[From an abstract by J. C. GATTI, and a translation of the original summary and conclusions supplied by the author.]

ROSEMBERG, J., SOUZA CAMPOS, N. and AUN, J. N. Reação de Mitsuda induzida por efeito de diversos esquemas de vacinação BCG oral e pela técnica de multipuncturas de Rosenthal. [The Mitsuda reaction induced by the effects of diverse schemes of BCG vaccination, oral and Rosenthal's multiple puncture technique.] *Rev. brasileira Leprol.* **20** (1952) 183-196.

The authors divided into 5 groups 121 children who had been isolated from both leprosy and tuberculosis since birth and were all tuberculin-and lepromin-negative. (1) To 20 of them single doses of 100 mgm. of BCG were given orally; (2) to 20 others, 2 doses of the same amount were given at an interval of a week; and (3) 30 others received 3 doses at weekly intervals. A fourth group of 21 was vaccinated with BCG intracutaneously by the multiple puncture method on one occasion. The remaining 30 children were not vaccinated and remained as controls. Lepromin was injected in all groups on the day of the beginning of vaccination. Positive reactions appeared between the 15th and 65th days in all the children of the vaccinated groups except 1 in Group 2 and 1 in Group 4. All of the control group remained negative. Eight months after vaccination the lepromin test was repeated, and this time only the 1 case in Group 4 remained negative. Among the several conclusions from this experience is that the prophylactic routine of oral administration of BCG to newborns with the 100 mgm. single dose of BCG as is being done in Brazil, is

the easiest method and suffices to convert the Mitsuda reaction with the same regularity as does the multiple-puncture technique.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 722.]

ROSEMBERG, N., SOUZA CAMPOS, N., AUN, J. N. and BRANDI, R. Contribuição ao estudo sobre a vitalidade do B.C.G. (Nota prévia.) [Contribution to the study of the potency of BCG; preliminary note.] *Rev. Brasileira Leprol.* **21** (1935) 11-35.

In addition to the standard tuberculin tests, Mitsuda's lepromin test is of value in checking the potency of BCG and its absorption in the body. Lepromin is injected on the same day that BCG is given. When onset of the reaction is observed, tuberculin tests are made. Young children, preferably newborn and infants who have been isolated from birth, should be used. With this method, BCG was found to be potent after ten days in the refrigerator at 4°C. When given orally, it caused a positive lepromin reaction within sixty days. Results were similar with Rosenthal's multi-puncture technique. After BCG had been in the refrigerator for 45 days, the lepromin test seldom became positive and tuberculin allergy was absent. With heat-killed BCG, results were even more disappointing. The use of tetrazole reduction to test the potency of BCG is still questionable. There is an unexplained interval between the time when tetrazole is no longer reduced and the time when the bacilli die. The tuberculin and lepromin tests demonstrated that the usual dosage of 0.1 gm. of 10-to-15-day-old BCG is usually sufficient. However, when only 25-day-old BCG is available, the amount should be 0.2 gm.—[From abstract in *American Rev. Tuberc.* **68** (1953) 116.]

URQUIJO, C. A. Sobre una nueva aplicación de la vacuna B.C.G. [A new application of the BCG vaccine.] *Rev. Asoc. Méd. Argentina* **68** (1954) 769-770.

The author reports the first results of the experiments carried out by a group headed by Dr. G. Basombrio. Tuberculin tests (Mantoux, 1:1000) were performed on 87 leprosy patients of whom 84 were lepromatous, 2 incharacteristic and 1 tuberculoid. Repeated lepromin tests of all of them had given negative results, in spite of prolonged sulfone treatment. BCG vaccine (0.15 mgm.) was injected intradermally in 16 patients, and after 31 days tuberculin and lepromin tests were performed. The latter gave positive early (Fernandez) reactions in 5 cases, and positive late (Mitsuda) reactions in 7 cases. In 3 of them the Mitsuda reaction was positive but the Fernandez reaction was negative, and the reverse situation was seen in 1 case. Another 27 patients were tested with tuberculin (Mantoux, this time 1:10), and all of them gave positive results. They were all given BCG by mouth, 1, 2 or 3 doses of 100 mgm. at weekly intervals. After from 25 to 40 days they were lepromin-tested; 9 gave positive Fernandez reactions and 12 showed the Mitsuda reaction in some degree. The Mitsuda reaction seemed to be the more influenced, the larger the total dose of BCG ingested. This was not so with the Fernandez reaction. It seems an extraordinary fact that a relatively small amount of avirulent BCG, received either intradermally or by mouth, can influence the results of the lepromin test in persons heavily impregnated with the Hansen-bacillus infection.—[From author's summary, supplied by G. Basombrio.]

OHARA, T. NAKAGAWA, S. and IKEHATA, T. Studies on desensitization in tuberculosis, with special reference to the relation between allergy and immunity in tuberculosis. *Japanese J. Tuberc.* **2** (1954) 116-127.

When tuberculous rabbits are desensitized by repeated injections of small doses of tuberculin or heat-killed tubercle bacilli, the serum antibody titer of the animals increases remarkably, while the tuberculin skin reaction weakens gradually and disappears finally. On the other hand, the increase of the antibody titer runs parallel with the increase of resistance against tuberculosis, thus prolonging the survival time of the animals. Consequently, "desensitization-anergy" should be considered as a state

of immunity. Further, from point of view of "desensitization-nergy" the relation between allergy and immunity in tuberculosis was discussed.—[Author's summary.]

WILKINSON, F., DUPONT, J. and BOSQ, F. J. P. Esquema práctico para interpretar las baciloscopias practicadas en los enfermos de lepra. [A practical scheme for the interpretation of bacteriological findings in leprosy patients.] *Día Méd.* **26** (1954) 850-860.

The proposed scheme, called "Sommer," with which, in a form quick and easy of interpretation, one can give the correct impression of bacteriological findings. It employs a table in which the number, morphological aspect and staining affinity of the bacilli are used to form a "standard" scheme which permits one to record and interpret the bacteriological findings, and to compare these with other findings to ascertain the improvement or the advancement of the course of the disease. It is also useful for the graphic interpretation of the action of drugs.—[From author's summary, supplied by G. Basombrio.]

WILKINSON, F. F. Resultados de la inoculación al cobayo con material obtenido de enfermos de lepra. Comunicación previa. [Results of the inoculation of guinea-pigs with material obtained from leprosy patients; preliminary report.] *Día Méd.* **26** (1954) 189-192.

Undertaking to investigate whether the Hansen bacillus itself is alone the causative agent of leprosy or if other factors intervene in its introduction and growth in the organism, the author carried out experiments with the diffusion factor. For this purpose he inoculated leproma suspensions mixed with hyaluronidase by different routes into 54 guinea-pigs, using as controls suspensions of tuberculoid and indeterminate lesions. In one group he used the testicular route, with and without hyaluronidase. In some of these animals he obtained testicular lesions, histologically histiolympocytic infiltrates. In 14 or nearly one-third, of the intratesticular group, there appeared a tubercle in the umbilical region; the mechanism of the production of these lesions is not understood. One of them was removed, ground up, mixed with hyaluronidase and inoculated intratesticularly in 4 guinea-pigs. In one of these there was produced, in 14 days, a testicular vaginitis with seropurulent secretion, and there were whitish miliary nodules in the interstitial tissue. Histologically these lesions corresponded to the lepromatous structure but Hansen bacilli could not be demonstrated. Another observation was that in the first of the guinea-pigs inoculated intratesticularly with hyaluronidase-leproma suspension there appeared in 10 months, in the skin of the scrotus, a soft nodule with caseous content. Smears showed some acid-fast bacilli and a typical globus full of them. The nodule healed in 27 days. In an area of normal aspect adjacent to the scar there were found acid-fast bacilli resembling *M. leprae*. One guinea-pig, 6 months after the inoculation, gave a positive lepromin reaction with the ordinary human antigen. The author concludes that *M. leprae* alone is the causative agent of leprosy infection, that in order to obtain positive inoculations an adequate route and large numbers of bacilli are necessary, and that hyaluronidase, either that which is present in the testicle tissue or mixed with the inoculum, favors the experimental infection in the guinea-pig.—G. BASOMBRIO

NOEL, R. MARIE-SUZANNE (SR.), BORDET, P., PARIS, R. A., CHEPAS, G. and RICHARD, R. Sur la formation de cristaux provoquée par l'inoculation de divers bacilles acido-résistants sur la membrane chorioallantoïdienne de le l'embryon de poulet. [Crystal formation induced by inoculation of different acid-fast bacilli into the chorioallantoic membrane of a chick embryo.] *Compt. rend. Acad. Sci.* **236** (1953) 538-539.

Eight days after the inoculation of Stefansky bacilli, crystals were observed appearing in the chorioallantoic membrane of the chick embryo. Smears and histo-

logical sections of the membrane gave nearly the same results with the Hansen bacillus and the so-called "Chauviré" bacilli. This refers to whitish masses, isolated or confluent, studding the entire surface of the membrane. These crystals are insoluble in the usual fixatives. Planting on egg white at 2°, then 37°, then at room temperature resulted in the propagation of crystals throughout the medium. These formations were observed, in inoculated eggs, in 32.4% with the Stefansky bacillus, 37.4% with the Hansen bacillus, and 34% with Chauviré bacillus. Examined with the polarizing microscope, these crystals were optically negative; the angle of the optic axis is about 60°; the indices are between 1,515 and 1,560. Chemical analysis has given: C, 30.87%; H, 3.83%; N, 24.08%. The ash represents 11.7% of the weight of the crystals. Spectrum examination showed the presence of calcium. The crystals, observed microscopically on platinum heated to 350°, remained unaffected up to 250°, above that they became slightly tarnished but without deformation or fusion. —M. VIETTE

NOEL, R. and MARIE-SUZANNE (SR.). A propos de la formation de cristaux sur la membrane de poulet inoculée avec des bacilles de Stefansky. [On the formation of crystals in the chick membrane inoculated with Stefansky bacilli.] *Compt. rend. Acad. Sci.* **236** (1953) 753-754.

Rounded masses, incrusted on the inner surface, formed by crystals of varied forms and shapes, were observed in the chorioallantoic membrane of 32.4% of the chick embryos inoculated with Stefansky bacilli. These crystals were not affected by alcohol, toluene, paraffin, ether, chloroform, or nitric, sulphuric or hydrochloric acids. In sections they are sometimes isolated, sometimes mixed with the bacilli. They seem to be stearic tuberculin acids. It was not possible to obtain these crystals elsewhere than in the egg, several methods having been tried. —M. VIETTE

WILLIS, H. S., VANDIVIERE, H. M. and GENTRY, W. H. Tetrazolium as an aid to the study of tubercle bacilli. *American J. Med. Sci.* **225** (1953) 410-415.

The dye tetrazolium (2,3,5, triphenyltetrazolium chloride) undergoes reduction in the presence of living cells to form an easily detectable red compound (formazin). Agriculturists have used it commercially to determine the percentage of viability in seed. The purpose of the authors was to determine the viability of suspensions of BCG. The bacilli were harvested, washed and treated with tetrazolium in an incubator for 2 hours, during which time the living cells reduce the dye to red formazin. This is extracted with acetone and centrifuged and the colorimetric transmission of the supernatant fluid is then read to obtain the percentage of viable bacilli present. To determine the value of the viability test, 20 mgm. per cc. of 8-day cultures of tubercle bacilli (BCG and R₁) grown in Dubos' Tween 80 medium with bovine albumin were used, made into vaccines with Dubos' basal medium as a diluent. One half of the resulting suspension was killed by flowing steam and the other half was maintained as "live" vaccine. Dilutions were made containing "live" vaccine in concentrations of 20 mgm. to 0 mgm., together with reciprocal numbers of dead bacilli to give a concentration of 20 mgm. per cc. in each suspension. For reduction studies the suspensions were washed to remove residual enzymes which may be retained after the death of the bacilli and may reduce the tetrazolium. To each tube was added 1 cc. of 0.25% solution of tetrazolium contained in Dubos' basal medium with 0.5% glucose and 0.02% Tween 80, adjusted to pH 7.2. Tubes were incubated at 37.5°C for 2 hours. When slides are prepared and stained by the Ziehl-Neelsen method, using a counterstain of 1% malachite green, reduction of the tetrazolium is indicated by red bacilli with "blue" dots present at areas of presumed greatest metabolic activity. A footnote states: "At once someone will say 'Much granules.' It is true that these areas which reduce the tetrazolium to blue formazin within the bacilli are blue and resemble to some extent the blue or black Much granules. However, bacilli from the

same source fail to reveal such dots when stained conventionally. Furthermore, Much's granules tend to be present at any point in the bacillary body, while the blue formazin areas tend to be polar. So it seems logical and proper to associate the blue discoloration with metabolic phenomena." Results of the work indicate that, with proper technique, the tetrazolium salts have the capacity to indicate viability of bacterial suspensions by undergoing reduction to either red or blue formazin, as the case may be, in the presence of living cells. These substances can be used to standardize inocula so as to insure comparable doses of bacterial suspensions in inoculating animals. When incorporated in media or added to cultures and incubated briefly, neotetrazolium is reduced at points of growth and this greatly facilitates colony counting and enhances the photogenicity of cultures. Neotetrazolium may be of aid in determining whether nongrowing tubercle bacilli recovered from tissue after chemotherapy and excision are viable or not.

—SR. HILARY ROSS

Y MACKANESS, G. B., SMITH, N. and WELLS, A. Q. The growth of intracellular tubercle bacilli in relation to their virulence. *American Rev. Tuberc.* **69** (1954) 479-494.

In a previous study [THE JOURNAL 22 (1954) 117] it was observed that only virulent strains of tubercle bacilli regularly and rapidly multiplied in and destroyed the host cells (rabbit monocytes), the capacity of a strain to multiply intracellularly seeming to reflect the characteristic *in vivo* virulence of the strain. The present study is an extension of that work, with several strains differing widely as to virulence, down to BCG. Quantitative measurements were made with the monocyte cultures and with the livers and spleens of mice. The growth rates of different strains varied greatly, and in both situations a correlation was found between the relative rates of increase and virulence. It is suggested that the virulence of tubercle bacilli may be a function of capacity to survive and multiply in an intracellular environment. It is noted that Suter [THE JOURNAL 22 (1954) 1, 118] concluded that virulent and attenuated strains grow equally well in monocytes *in vitro*, although apparently avirulent strains would not grow, but the authors regard certain aspects of Suter's technique as open to criticism. They also found that the physiologic state of the bacilli affects their rate of adaptation in the intracellular situation. Aged bacilli have a longer lag period than young bacilli, and the effect of age on the intracellular growth pattern increases markedly with the degree of attenuation. Thus, aged bacilli of a virulent bovine type show only a small increase in lag period whereas in an inoculum of BCG of equivalent age most of the bacilli are virtually incapable of growth and are largely digested intracellularly *in vitro*. —H. W. W.

X MACKANESS, G. B. The growth of tubercle bacilli in monocytes from normal and vaccinated rabbits. *American Rev. Tuberc.* **69** (1954) 495-504.

The work dealt with above was extended to a study of tubercle bacilli in monocytes from normal and vaccinated ("immunized") rabbits to determine if in the latter the growth characteristics of ingested bacilli are altered. Streptomycin was used to restrain the growth of extracellular bacilli, in a concentration that does not affect the growth of intracellular bacilli [THE JOURNAL 22 (1954) 118]. In an experiment with virulent bacilli the lag period in the two types of monocytes seemed to be identical, and there was no significant difference in the bacillus counts after 3 days incubation. Similar results were obtained with attenuated bacilli. Regarding the survival time of normal and "immune" monocytes infected with virulent bacilli, it was found that at all levels of infection the "immune" cultures always died sooner than those of normal cells if the two had been infected with equivalent numbers of bacilli. The results, it is held, "do not encourage the belief that the monocytes of vaccinated rabbits have any specific capacity to suppress the growth of tubercle bacilli resident within them." This is not in agreement with a conclusion reached by Lurie, in an experiment with infected cells implanted in the anterior chamber of rabbits'

eyes (see below). The author suggests that the bacteriostasis observed in that case might have been due to the transfer of allergy to the chamber implanted with the "immune" cells; also that the difference in cytology may have been due to this transfer to the host animal's own cells. It is also contrary to the findings of Suter, whose method of work is criticised (see above). The author recognizes that his results may perhaps be attributable to the fact that the rabbit, in contrast with the guinea-pig, develops only a mild degree of tuberculin hypersensitivity, but even so he holds that present evidence of "antiblastic immunity" in the mononuclears of vaccinated or tuberculous animals is not conclusive. —H. W. W.

LURIE, M. B. Growth of tubercle bacilli in monocytes from normal and vaccinated rabbits. *American Rev. Tuberc.* 69 (1954) 1059-1060 (correspondence).

This is a discussion of Mackaness' views about certain of the writer's findings (see above). Certain points beyond the controversy are of interest. One is the question of what is meant by "allergic sensitivity." In that connection it is pointed out that Raffel has shown that true allergic sensitivity can be induced by treating animals with the combined "wax" and protein of the tubercle bacillus, but this allergy does not inhibit the multiplication of the bacilli. Another point is the significance of the epithelioid character of cells in the anterior chamber of the eye which has been implanted with "immune" cells. The writer asserts that "...as the 'immune' cells destroy the tubercle bacilli, epithelioid cell formation is a direct consequence," for he has shown amply in previous work that "epithelioid cell transformation of mononuclears is always associated with the intracellular destruction of tubercle bacilli." [No better demonstration of this could be desired than the differences between the lesions of lepromatous and tuberculoid leprosy.] —H. W. W.

SUTER, E. Growth of tubercle bacilli in monocytes from normal and vaccinated rabbits. *American Rev. Tuberc.* 69 (1954) 1060-1062 (correspondence).

This note, like the preceding one, comments—at some length—on reports by Mackaness (see above), of findings which differed from those reported by the writer of a study of intracellular multiplication of tubercle bacilli in macrophages from experimental animals. The differences concern (a) the rate of multiplication of strains of varying degrees of virulence within macrophages from the same species, and (b) the inhibitory power on intracellular bacilli exhibited by macrophages from BCG-vaccinated animals. Regarding (a), Mackaness found the rate of multiplication in cells from rabbits to correspond to the degree of virulence or attenuation of the strain of bacillus, whereas Suter had found virulent as well as attenuated strains multiplied at a similar rate in macrophages from guinea-pigs. Suter says that he has made no direct comparative experiments with rabbit and guinea-pig macrophages, but upholds the validity of his observations and conclusions. Regarding (b), Mackaness did not confirm Suter's findings of the growth-inhibitory property of macrophages from BCG-vaccinated animals. Recent observations indicate that there are several factors which might possibly explain the differences: the number of bacilli present in the cells at the beginning of the experiment, inhibition being almost negligible if there are large numbers present; the degree of hypersensitivity of the animals from which the macrophages are obtained, a matter under investigation; and, finally, a difference of technique that may be important, Mackaness having used paraffin oil, *vs* Suter's glycogen—to obtain the peritoneal exudates. [The notes dealt with by this abstract and the preceding one cover more ground than is shown in these abstracts, especially the one by Suter, and they should be read in the original by anyone interested in this subject.] —H. W. W.

8 LURIE, M. B. Studies on the mechanism of immunity in tuberculosis. The fate of tubercle bacilli ingested by mononuclear phagocytes derived from normal and immunized animals. *J. Exper. Med.* **75** (1942) 247-268.

This is a study of the mechanism of increased resistance to reinfection in tuberculosis. The author had previously shown that in the body of an infected (immune) animal the bacilli are destroyed at once if in small numbers, or are inhibited from multiplication if in larger numbers, whereas in the normal animal the bacilli—whether few or many—at first grow unhindered; but this failure of growth within the “immune” phagocytes was unexplained. The experiments here reported were designed primarily to determine whether phagocytic mononuclears of immunized animals, when removed from their normal environment, would still inhibit bacilli in their cytoplasm more than similar cells from normal animals. Briefly, they involved the preparation of suspensions of normal and immune phagocytes with ingested bacilli, which were then injected into the anterior chambers of new rabbits, the preparation from a normal source-animal on one side, the one from an immunized animal on the other side. It was found that the cells of the immunized animals in the new environment retained their increased capacity to inhibit the growth of the bacilli in their cytoplasm. This bacteriostatic effect depended upon the cells themselves and not on any fluid element, although “immune” serum increased the degree of inhibition when the preparation was made *in vitro*. (It had been shown previously that bacilli situated extracellularly *in vivo* are definitely inhibited in their growth by continual exposure to the body fluids.) As for the changes of the implanted cells themselves in the anterior chambers, the normal cells multiplied more than the immune cells did, while the latter tended to change to the epithelioid type, but little is said of that. This article should be examined in the original, for itself and for the references to previous studies. —H. W. W.

8 MACKANESS, G. B. Artificial cellular immunity against tubercle bacilli; an effect of polyoxyethylene ethers (Triton). *American Rev. Tuberc.* **69** (1954) 690-704.

The polyoxyethylene esters which compose the nonionic surface-acting substance known as Triton have a strongly antituberculosis effect in the mouse which cannot be explained on the ground of bacteriostatic action. Virulent bacilli will grow in liquid media containing it, and it has even been recommended as a substitute for Tween 80 in media for promoting dispersed growth. On the other hand, avirulent strains are inhibited by it. In monocyte cultures, the author has found 0.1% Triton to be without effect on the intracellular growth of virulent bacilli. Because of these facts, and because therapeutically active polyoxyethylene esters depress tuberculin sensitivity in tuberculous or vaccinated animals, the author has suggested that they must in some way modify the host in its response to tubercle bacilli. In the experiments here reported a comparison was made between monocytes from control animals and those from animals treated by injections of Triton, both rabbits and guinea-pigs being used. In the cells from the treated animals the tubercle bacilli grew slowly or not at all, and sometimes they were even destroyed, whereas they grew freely in the cells from untreated animals. This effect was not due to any bodies developed in the serum, and Triton itself when added to cultures of monocytes from untreated animals in concentrations that were tolerated by the cells was not inhibitory. It is believed therefore that its action is indirect. No light has been thrown on the mechanism of the suppressive action of these esters *in vivo*, but a site at which the inhibitory action could take effect has been revealed. Since it is improbable that such a surface-active agent enters the cell and acts directly on the intracellular organism, it is probable that the monocyte itself becomes modified in some way. Triton possibly enters it *in vivo*, but not in monocyte cultures *in vitro*. —H. W. W.

- BERMANN, R. Essais de coloration du bacille de Stefansky et du bacille de Hansen par le noir Soudan B.N. [Staining the Stefansky and Hansen bacilli with Sudan Black B.N.] Bull. Acad. Nat. Méd. **137** (1953) 295-298.

It was found that the bacilli of about 80% of cultures of tubercle bacilli were stained with Sudan Black B.N. if, before making smears, the bacilli were suspended in 100% alcohol. Differentiation was done by applying acetone, the stain still persisting in the bacilli for as long as 6 hours treatment with this reagent. When the same technique was used with the Stefansky bacillus, it was found necessary to apply the stain 2 to 4 times in order to get staining. The same was found to be the case with cultures of other acid-fast bacilli. In contrast with this, all attempts to stain the leprosy bacillus proved negative. The author takes these results as evidence confirming the opinion of Chaussinand [THE JOURNAL **17** (1949) 170] that the Stefansky bacillus has more affinity with the tubercle than with the leprosy bacillus.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 946.]

- BERG, J. W. Chemistry of acid-fastness. Proc. Soc. Exper. Biol. & Med. **84** (1953) 196-198.

A study was made of the chemical reaction between crystal violet and lipids of the mycolic acid type, considering this to be a prototype of the more general reaction between basic dyes and the acid-fast lipids. The reaction went to completion in chloroform; and at the end, one mole of dye had combined with one mole of mycolic or leprosinic acid. The complex so formed was soluble in xylene as well as chloroform, although the dye had originally been soluble only in the latter solvent. The complex exhibited an intense absorption band in the near ultra violet (3500A) which was not present with either the pure dye or the pure acid. Other acids were tested, and while they might react with the dye, the specific absorption peak was not produced. If either the carboxyl or the hydroxyl group of the leprosinic acid was blocked, the characteristic reaction did not occur.—[Abstract from *Stain Tech.* **29** (1954) 223.]

- HUMMEL, K. Zur "Kaltfärbung" von Tuberkelbakterien unter Zuhilfenahme von Oberflächen-aktiven Stoffen. ["Cold staining" of tubercle bacilli with the aid of surface-active substances.] Klin. Wchnschr. **31** (1953) 862.

Aubert found that tubercle bacilli can be stained "cold" if a wetting agent is added to the staining solution; he found propylene glycol and Tween 80 to be the most effective for this purpose. The author examined a number of other stain-promoting wetting agents, particularly Cremophor AP carbolfuchsin solution (Bad. Anilin-u. Sodafabrik, Ludwigshafen, Rhine). Basic fuchsin, 10 gm., is dissolved in 25 gm. of pure crystalline phenol at 80°C. on a water bath. After cooling, 50 cc. of 95% ethyl alcohol is added with stirring, then distilled water to 300 cc. Cremophor AP, 30 drops (1 cc.), which has been liquefied in a hot water bath or incubator, is then added with constant stirring. Decolorization is effected with 1% HCl-alcohol and a further bleaching with sodium sulphite (10%) for 3-5 minutes. A nonspecific staining of nonacid-fast rods has never been observed. This method is said to be superior to the Ziehl-Neelsen method. —E. KEIL

- TANIMURA, T., NISHIMURA, S. and NAKAMURA, T. On the vole bacillus. Med. J. Osaka Univ. **3** (1952) 373-381.

The vole bacillus is the only acid-fast besides the Stefansky bacillus to be found in the rat family. In 1937, the same year that Wells observed it in England, one of the authors (Nishimura) reported the recovery from voles in Japan of an acid-fast organism which he finally concluded "appertained to the human tubercle bacillus." The present article summarizes the studies made after that time, using seven essentially similar strains which were obtained from voles caught in Osaka during some two years, 1942-1943. The usual features of such microorganisms are described summarily,

with comparisons with tubercle bacilli, but most of the article deals with animal experimentation. For various reasons, one of them being their failure to transfer the infection serially in white rats, the authors concluded that this germ is a human tubercle bacillus, without specificity to the rat family but with affinity to it.

—H. W. W.

TANIMURA, T. and NISHIMURA, S. Experimental study on the chemotherapy of leprosy. I. Efficacies of the drugs upon murine leprosy. *Med. J. Osaka Univ.* **3** (1953) 675-684.

Reporting experiments on young rats inoculated with suspensions of murine leproma diluted 2,000 times, and treated with various drugs, including chaulmoogra oil, promin, thiosemicarbazone, and cepharanthin. The only one of these which had any effect on the infection was chaulmoogra oil; with that, the onset of the disease was retarded, and the weight of the nodules produced was much less than that of the nodules of the rats which received no chaulmoogra. The promin was given in two experiments. In the second of these it was first given subcutaneously in daily doses of 0.3 cc. of a 30% solution, 6 days a week, for 20 days. The animals could not stand this dosage, so it was reduced to 0.1 cc. three days a week. These rats had been inoculated 115 to 268 days before the treatment was begun. Only 7 of the 17 rats used survived the last injection, the rest dying of cachexia, pneumonia and other diseases.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 820.]

TANIMURA, T., NISHIMURA, S. and KONO, M. Experimental study on the chemotherapy of leprosy. II. Study on chemical agents and the conditions which may influence their efficacies. *Med. J. Osaka Univ.* **3** (1953) 685-694.

The results obtained in the treatment of leprosy with sulfones and with thiosemicarbazone are compared. The concentrations obtained of promin and promizole in blood, urine and various organs are given. Euglobulin in blood plasma absorbs neither promin nor promizole, but albumin combines with both. In the discussion the authors point out that drugs like chaulmoogra oil or cepharanthin, which stimulate the resistance of animals and produce favorable effects in the treatment, react in the same manner in both human and murine leprosy, either positively or negatively. On the other hand chemical agents such as the sulfones and tibione, which seem to act directly upon the pathogenic organisms, behave differently against human or murine leprosy.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 820.]

TAKAYAMA, Y. Studies on the inoculation to different animals of rat leprosy bacilli. Report 1. On the susceptibility to rat leprosy bacilli of hamster. *La Lepro* **22** (1953) 131-134 (in Japanese; English abstract p. 131).

The hamster was found to be susceptible to rat leprosy infection, apparently in slightly greater degree than the rat. The methods of experimentation with rat leprosy in the hamster are essentially the same as with the rat.—[From abstract.]

KANDA, Y., NAKAGAWA, Y. and NAKAMURA, M. On the susceptibility of infant and adult mice to rat leprosy. *La Lepro* **22** (1953) 135-137 (in Japanese; English abstract p. 135).

The susceptibility of suckling, infant and adult mice to rat leprosy was observed after intracerebral, subcutaneous and intraperitoneal inoculations of *M. leprae murium*. Suckling and infant mice were found not more susceptible to rat leprosy than adult mice. The inoculum induced an inapparent infection in the brain of the mouse.—[From abstract.]

GOULDING, R., ROBSON, J. M. and REES, R. J. W. Intracorneal murine leprosy and its response to isoniazid. *Lancet* **1** (1953) 423-424.

Forty mice were inoculated intracorneally with a suspension of rat leprosy bacilli.

The mice were divided into 4 groups, 3 of which were given, with their food, thiosemicarbazone, sulphetrone, and isoniazid, respectively. There was practically no difference in the development of lesions between the first 2 of these groups and the controls, the lesions advancing clinically and showing histologically large cells full of bacilli and extracellular bacilli. But in the isoniazid group the lesions retrogressed till only corneal opacities remained, while histologically there were no extracellular bacilli and intracellularly only ill-defined acid-fast material and granules. The authors acknowledge that this does not necessarily mean that isoniazid should be of value in human leprosy.—[From abstract in *Trop. Dis. Bull.* **50** (1953) 524.]

- 8 BARNETT, M. and BUSHBY, S. R. M. Isoniazid in murine leprosy. *Lancet* (1953) 494 (Mar. 7) (correspondence).

Observations of the writers in mice infected intravenously support the findings of Goulding, Robson and Rees in their single experiment. The authors note that a report of their work had been submitted to the *Lancet* but had been turned down as "too experimental," so it was published elsewhere [*THE JOURNAL* **21** (1953) 422]. The rest of this brief note has to do with the forecasting of the usefulness of drugs for human leprosy by such experiments, and observations with the sulfones and other drugs.
—H. W. W.

- 8 CRUICKSHANK, J. C. A trial of isoniazid in rat leprosy. *Lancet* (1953) 624 (Mar. 28).

Four groups of 10 white rats each were inoculated intraperitoneally with murine leprosy and treated as follows, the isoniazid being given in the food (20 mgm./kgm. daily): A, untreated controls; B, isoniazid for 4 weeks, starting on the day of infection; C, isoniazid 20 weeks, also starting immediately; and D, isoniazid 4 weeks, starting 4 weeks after infection. Within 46 weeks all of the controls had died, while those treated for 20 weeks were alive and in good health. The results in the other two groups were disturbed by deaths from an intercurrent infection, but there was more or less suppression of the rat leprosy. Because drug-resistant organisms appear in human tuberculosis, the surviving rats were to be observed for many more months. [If there has been any further report from this source, we have not yet learned of it.]
—H. W. W.

- 8 LEVADITI, C., VAISMAN, A. and CHAIGNEAU-ERHARD, H. Activité thérapeutique de l'isonicotinhydrazide (INH) dans la lèpre murine. [Therapeutic action of isoniazid in murine leprosy.] *Compt. rend. Acad. Sci.* **236** (1953) 549-551.

A rich suspension of Stefansky bacilli was inoculated into 15 rats intramuscularly, and 10 of them were treated daily by subcutaneous injections of 25 mgm./kgm. of INH. One rat died on the 81st day; the other 9 and also the controls were sacrificed on the 127th day. The animals had increased in weight. At autopsy all the controls presented lesions at the point of inoculation and in the corresponding lymph nodes; no visceral lesions were noted. In the treated rats no bacillus-yielding lesions were seen at the point of inoculation except in one case. The rat that died on the 81st day showed lesions in the lungs, without bacilli. The authors conclude that INH in the dose used radically suppresses the infection provoked in rats by the inoculation of Stefansky bacilli.
—M. VIETTE

- 8 MACHICAO, N. and LA PLACA, E. Lepra-like granulomas in frogs. *Lab. Invest.* **3** (1954) 219-227.

The authors report a study of leprosy-like granulomatous lesions observed in two species of frogs (*Pleurodema cinerea* and *P. marmoratus*) collected near La Paz, Bolivia, caused by a cytophilic acid-fast bacillus which they were unable to cultivate. Of 663 frogs of these species examined, 129 (19.6%) were found infected,

while the condition was found in only a few toads (*Bufo spinulosum-spinulosum*) and in none of several other kinds of frogs. The liver was the organ constantly involved, and it was often greatly enlarged and studded with great numbers of elevated, rounded nodules. Lesions were also found in various parts of the digestive tract, and skin lesions, essentially subcutaneous [evidently of relatively slight degree] were an important characteristic. Nerve involvement is suggested [and rather insisted upon, on inadequate grounds]. Occasionally a mucopurulent secretion in the nose and pharynx contained many bacilli. Histologically the granulomas were focal infiltrates of histiocytic cells, with lymphocytic areolas, the cells with granular or finely vacuolated cytoplasm—also called foamy, suggesting Virchow cells—with abundant intracellular bacilli giving pictures identical with the globi of leprosy lesions. The lack of evidence of injury of the host cells is commented on. Repeated attempts to cultivate the bacilli were unsuccessful. Lesions were reproduced by injection of saline suspensions into the susceptible species, but not in other species. Injection of warm-blooded animals was not attempted. It is suggested that the infection may have come from certain insects ingested by the frogs. The condition is believed not to be tuberculous; "the possibility of batrachian leprosy is suggested." —H. W. W.