

CURRENT LITERATURE

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

✓ LECHAT, M. F. James A. Doull (1889-1963). *Epidémiologie de la lepre. Maroc méd.* **42** (1963) 559-570.

It is impossible to indicate in a few words the great role that Dr. James A. Doull played in the field of leprology. Applying to the study of leprosy the new statistical methods, of which he was a master, he was able by the discussion of very many observations to put in evidence numerous factors of contagiousity, of diffusion, and of the evolution of leprosy in the midst of various populations. His studies further served as the basis of others, and thus have led to better knowledge of the possibilities of the antileprosy campaign—N. BOURCART.

BROWNE, S. G. Leprosy research; recent problems and achievements. *J. Nigeria Med. Assoc.* **1** (1964) 8-13.

56 This paper, which was presented at a conference of physicians of West Africa held in Accra in December 1963, summarizes for the benefit of general physicians not especially concerned with leprosy some of the recent achievements in leprosy research and the outstanding problems now confronting the research leprologist. It is shown that research in leprosy, particularly in the realms of bacteriology, immunology and therapeutics, has many points of contact with advances in related mycobacterioses.—AUTHOR'S ABSTRACT.

6 DUBOIS, A. Quelques cas de maladie de Hansen observés en Europe. [Some cases of leprosy observed in Europe.] *Bull. Acad. Roy. Méd. Belgique* **3** (1963) 173-184.

The author tells of 42 cases of leprosy studied at the Institut de Médecine Tropical at Antwerp, including 35 white patients most of whom were infected in the Congo. Noteworthy is the high proportion of lepromatous cases—15 of the 35, or about 40%, against hardly 10% in the Congo itself. This can be explained on the ground that, in the hygienic environment of the white people, only those who are highly susceptible are infected, and so they develop the malign form of the disease. The author points out the importance of prophylaxis in endemic countries.—N. BOURCART.

✓ MERKLEN, F.-P., COTTENOT, F. and BRISCHOUX, M. Multiples cas de lèpre chez des travailleurs noirs africains récemment transplantés en France métropolitaine [Multiple cases of leprosy in African workers recently transplanted to metropolitan France.] *Bull. Soc. française Dermat. Syph.* **70** (1963) 819-820.

The absence of any effective control at the place of embarkation or on arrival in France has resulted in bringing in workers with, among other things, leprosy. Brief details are given of 4 such cases, hospitalized in the Pavilion of Malte, Hospital St. Luis, in Paris, 1 from Senegal, 2 from Mauritius, and 1 from Mali. None was lepromatous.—H. W. WADE.

HIND KUSHT NIVARAN SANGH (Indian Leprosy Association). Annual Report for 1963. New Delhi.

The first part of this report was prepared by Dr. M. S. Chadha, Director General of Health Service, Government of India, who was appointed chairman of the Association by the President of India after the sudden death of Rajkumari Amrit Kaur, a picture of whom is the frontispiece of the report. That part, as usual, deals with the work of international agencies and other organizations working in the country, and of the Government of India. The first group comprises: WHO and UNICEF, the Mission to Lepers, the Swedish Red Cross (since 1962) and the Japan Leprosy Mission (started in 1963). Organizations in 10 other countries are also giving aid to leprosy institutions or activities

in India. The local organizations (apart from the Sangh itself) are the Gandhi Memorial Leprosy Foundation and the Central Leprosy Teaching and Research Institute. The National Leprosy Control Programme is about to embark on its IVth 5-year plan. The work of the Sangh is summarized in this section; details constitute the rest of the report.—H. W. WADE.

FERNANDEZ DE CASTRO, D. La unidad móvil en la campaña contra la lepra en México. [The mobile unit in the campaign against leprosy in Mexico.] *Dermatología (México)* **7** (1963) 245-259.

The author comments on the national picture of leprosy in Mexico before summarizing the work he is doing as head of one of the traveling brigades in the fight against leprosy. His working sector is located in the northern part of the state of Michoacan, where he controls 184 leprosy patients in the 7 townships he has covered up to the time of writing. The largest numbers of patients are discovered in the skin consultation service; in second place is the surveillance of contacts, of whom more than 80% of those known have been examined; the mass check-ups did not give good results. The logical future of the campaign is its integration with the general public health service. Practically all of the patients need help for rehabilitation, either physical, psychological, social or economic. The author concludes with a request for more ample supervision by the program authorities. [From author's summary.]

UTKU, E. La lèpre et la lutte anti-lépreuse en Turquie. [Leprosy and the antileprosy campaign in Turkey]. *Maroc méd.* **42** (1963) 642-645.

The number of persons with leprosy in Turkey is estimated to be 20,000. These can be assigned to endemic, endemo-sporadic, and sporadic zones, the first of which are nearly all in the eastern region. A four-year plan begun in 1962 permits setting up, by stages, the principal elements of the antileprosy campaign. Besides the administrative organization, there is in Ankara a Central Institute of Leprology, the purposes of which are training of personnel, organization of a dispensary and a center of rehabilitation and health education of the public, and research. The leprosarium of Elazig is to be transformed into a sanitarium, to serve as a center for rehabilitation and a hospital for indigents. The dispensaries and mobile equipment, which will be established as the plan progresses, will be responsible for the search for cases, their hospitalization, and treatment, and for prophylaxis. A regional pilot group for demonstration, after finishing its work in one sector, will transfer its entire organization to a new region. WHO is to supply technical information and scholarships, and will send a consultant for 2 months a year. UNICEF will provide medicines, laboratory and other supplies, and the vehicles. The Ministry of Public Health will meet all other expenses.—N. BOURCART.

LAI, S-H and FAN, K-Y. Statistical observation on leprosy patients of the leprosy clinic of the Taipei Public Health Teaching and Demonstration Center. *J. Formosan Med. Assn.* **62** (1963) 285. (In Chinese; summary in English.)

This is a report on 94 patients who attended the leprosy clinic of the Taipei Public Health Teaching and Demonstration Center, 1960-1962. Practically one-third of them (33%) were lepromatous, the others macular or neural, and most of them were early and mild cases. By age, the largest number was in the 20-24 years group; 1 patient was only 3 years old. Only 3 patients admitted family contact; 1 of them had 6 leprous persons among family members. More leprosy clinics should be set up in provincial hospitals and outpatient dispensaries.—[From author's summary.]

ROLLIER, M. and ROLLIER, R. Réflexions sur la lèpre du nourrisson. A propos de tres cas personnels. [On leprosy of infants; three personal cases.] *Maroc méd.* **42** (1963) 546-555.

Leprosy of infants has until recently been regarded as exceptional, for it seems impossible that the disease can develop before the age of 3 years because of the slow incubation. Nevertheless, one must consider the great receptivity of the infantile organ-

ism, and the instances in which the contamination within the family is massive and the living conditions are bad. The authors discuss these conditions, and particularly the possibilities of infection *in utero* or by maternal feeding. They then report three infants with nodular tuberculoid leprosy, two of them at 1 year of age and the other at 2 years. All were born of lepromatous mothers, and in the case of some of them the father was also affected. DDS treatment for 3 to 8 months caused complete remission in the first case and arrested progress in the others. In the discussion the authors counsel preventive isolation of infants, family hygiene, and early vaccination with BCG.—N. BOURCART.

BURTON, G. J. Bedbugs in relation to transmission of human diseases. *Publ. Hlth. Rep.* **78** (1963) 513-524.

This is an extraordinary review of the literature of the past 55 years with reference to the relationship—known or suspected—of bedbugs to the transmission of human diseases. Among the 93 references listed, 6 concern leprosy; all but 1 of them date back to the 1911-1913 period, only 1 being recent (1961). In a tabulation of observations of survival times of various microorganisms in bedbugs, an item on leprosy (of 1911 publication) gives the location of the bacilli as the head, proboscis, and hemocoel, and 16 days as the survival time. In a summary of 93 studies in connection with all the diseases concerned, that part relating to leprosy is reproduced here, without reference numbers. This is not done because the subject is of special current interest, but because no such historical review is known to exist elsewhere.

Cimex lectularius. (1) Shaved skin of rat was stretched over a jar containing blood agar with many leprosy bacilli. In bedbugs which fed on this medium, leprosy bacilli were found in intestines and salivary glands. (2) Bedbugs were fed on leprosy lesions and dissected up to 100 hours after feeding; all bacilli were absorbed, with no multiplication. (3) Of 75 bugs fed on leprosy patients, 20 contained acid-resistant bacilli which 1 of them harbored for 16 days in head, proboscis, and hemocoel. Bugs could not transmit bacilli to animals or people by bite. (4) In Sainte Marie, Danish Antilles, 53 bedbugs were fed on leprosy lesions and dissected for different periods up to 34 days. All were negative except three, the results with which were doubtful.

Cimex hemipterus. Bacilli not taken up from skin of lepromatous patient during a blood meal; hence could not be transmitted to another person at a later meal.

—H. W. WADE.

HARGRAVES, J. Disabilities and deformities of leprosy in Northern Territory aborigines. *Med. J. Australia* **2** (1963) 225-227.

The disabilities and deformities found among 300 full-blooded aborigines, 187 males and 119 females, are classified according to the scheme recommended by the second meeting of the WHO Expert Committee. The examination involved 600 hands and 600 feet, and when more than one condition was found in an extremity (as anesthesia and claw-hand), that extremity was reckoned twice for that patient; the data so obtained are given in a table. Another table gives totals for the various types of the disease. The total of 239 with disabilities was practically 80% of the whole, and that percentage holds for both the lepromatous and tuberculoid groups (85 and 174 cases, respectively). Sex differences were evidently slight. (It may be noted that, under "miscellaneous," gynecomastia was recorded for 13 cases; there was involvement of the larynx in only 3.)

—H. W. WADE.

FASAL, P. Diffuse lepromatosis with erythema necroticans. *Arch. Dermat.* **98** (1963) 535.

This is a summary note of a case presentation. The patient was a Cuban woman resident in the continental United States since 1952, at which time numbness of the legs was noticed; skin lesions on the legs since 1955; diagnosed as leprosy in 1959. Examination showed sharply demarcated necrotic areas covered by crusts on the left leg and (ultimately) complete loss of eyebrows. A biopsy specimen from normal-appearing skin showed lepromatous changes, with many bacilli. The author felt that this case showed

that diffuse lepromatosis is more widespread than it was previously believed to be. (In discussion, Arnold remarked that the remarkable feature of the case was that there was no anesthesia to cold in her feet after she had had the disease for six years, which shows how little the nerves may participate in lepromatous leprosy. Referring to another case presented (a Filipino woman, an ordinary tuberculoid case with a single plaque on the forearm) Arnold pointed out an enlarged great auricular nerve, and remarked how useless that nerve is since excision of a piece of it causes no detectable damage to the patient.)—H. W. WADE.

BUCKING, E. P. [The classification of acute stages of leprosy.] *Vestnik. Derma. i Venerol. (Moscow)* **37** (1963) 46-53.

The following is from the English summary of the paper. The new scheme of classification of the acute stages of leprosy presented comprises three types of such manifestations: No. 1. Acute dissemination, (a) lepromatous (L), (b) tuberculoid (T), (c) neural, the last being acute progressive neuritis in all types of leprosy. No. 2. Acute transformations, (a) T into L (reactive tuberculoid), (b) T \div L (borderline phase of Wade), (c) L into T (acute infiltrations of Tajiri). No. 3. Acute paralepromatosis (erythema nodosum leprosum), which is a complex of acute inflammatory manifestations in the skin, nerves, eyes, liver and other tissues developing near lepromatous granulomas in the regressive stage. The "progressive" or "classical" lepra reaction is a combination of the No. 1a and No. 3 varieties of acute stages, their prevalence depending upon the effectiveness of antileprosy treatment. The study of 386 case histories recorded during 1948-1958 showed that after the beginning of sulfone therapy the occurrence of the No. 1a variety diminished quickly; the No. 3 type became more frequent during the first years of sulfone therapy, but later on also began to diminish.—[From *Trop. Dis. Bull.* **61** (64) 159-160.]

HARADA, N. Great auricular nerves and stiffness of shoulders. *Nagashima Arch. Leprosy* **6** (1964) 23-26 (in Japanese; English summary).

Thickening or hardening of great auricular nerves was found in many of the leprosy patients suffering from stiffness of the shoulders. Under treatment by excision of the great auricular nerves (with perineural injection of xylocaine) the shoulder stiffness was cured in almost all cases. It is therefore thought that leprosy lesions in the great auricular nerves may be the cause of the stiffness of the shoulders. The morphologic changes in the great auricular nerves are not commensurate with the degree of stiffness.—[From author's summary.]

HIBI, H. On the corneal findings of lepromatous leprosy patients showing positive lepromin reaction. *Nagashima Arch. Leprosy* **6** (1961) 14-19 (in Japanese; English summary).

The cornea was observed by the slit-lamp microscope in 24 patients with lepromatous leprosy (14 males, 10 females) who gave positive lepromin reactions. The results are summarized as follows: 1) Neovascularization in limbus corneae and leprosy infiltration were seen in all cases. 2) Pannus cornea leprae was seen in 10 cases, and parenchymatous keratitis in 8 cases; these changes combined were manifested in 4 cases, while in the remaining 2 cases neither change was observed. 3) Beaded corneal effects were found in 8 of 19 cases (except for 5 cases of severe parenchymatous keratitis and pthisis bulbi). In conclusion, slit-lamp microscopic changes of the leprosy cornea remain for a long time, even in lepromatous cases in which the skin is clinically recovered and, the lepromin reaction has become positive.—[From author's summary.]

WATERS, M. F. R. Chemotherapeutic trials in leprosy. 1. Comparative trial of macrocyclic plus dapsone and dapsone alone in the treatment of lepromatous leprosy. *Leprosy Rev.* **34** (1963) 173-192.

The author reports on a carefully designed and controlled clinical trial of macrocyclic and dapsone in combination, in comparison with dapsone alone, in the treatment of pure lepromatous and near-lepromatous leprosy, in which study the author had the

active cooperation of the designers of the trial and other experts. The final analysis was made on 16 matched pairs and a total of 44 patients in the Sungei Buloh Settlement in Malaya. Of the total, 21 received dapsone alone and 23 the combined therapy. During the trial the dose of dapsone given was large, 200 mgm. twice weekly by injection, and the full dose was maintained despite the occurrence of erythema nodosum leprosum. All 44 patients showed improvement. However, the addition of macrocyclon to the dapsone treatment failed to increase the rate of clinical, histologic, or bacteriologic improvement, although there may have been some reduction in the percentage of solid-staining organisms in skin smears. All patients showed a marked fall, so that after 9 months an average of 96% of the bacilli examined were irregularly stained. [An appendix of 10 tables is given. There is a special significance in this work in that a carefully controlled clinical trial has been shown to be feasible for any potentially active antileprosy drug, and that in a relatively short time. The original paper well repays meticulous study.]—[From abstract by J. Ross Innes in *Trop. Dis. Bull.*, **61** (1964) 161-162.]

RAM, J. A. Preliminary study of the therapeutic effect of 'Vadrine' in leprosy. *Leprosy Rev.* **34** (1963) 209-211.

Vadrine [2-pyridyl-(4)-1,3,4-oxdiazalone-(5),p-amino-salicylate] is a new anti-leprosy drug already reported on by Brodhage and Smith, Jopling and Ridley, and Allan. The present report is of a 3-month clinical trial in the Punjab, India, on 11 lepromatous patients, distressed with nasal, ocular, and laryngeal complications, who had been steadily getting worse in spite of full dosage of DDS for 6 months. Vadrine, 30 mgm./kgm. per day orally, with 600 mgm. weekly of DDS, was given. Very little effect was seen on the ocular and laryngeal lesions, but there was marked improvement in the bacillus index, and in most cases the bacilli appeared in broken or granular forms. In a few patients the nose became free of leprosy bacilli. A severe reaction was noted in only 1 of the patients. The author thinks that Vadrine in combination with DDS has an accelerating effect.—[From abstract by J. Ross Innes in *Trop. Dis. Bull.* **61** (1964) 164-165.]

FIOL, H., JONQUIERES, E. D. L., CAPURRO, E. T. and SANCHEZ CABALLERO, H. J. Tratamiento de la lepra con Methimazole. [Treatment of leprosy with Methimazole.] *Leprológia* **8** (1963) 96-101.

A trial of Methimazole was made in 9 cases (4 lepromatous, 2 dimorphous [borderline], 3 tuberculoid) in a dosage of 30-40 mgm. daily. Tolerance was excellent, of 7 patients who reached one year of treatment, all were improved; 2 lepromatous cases were changed to sulfones after 4 months because of progressive worsening; an L3 patient was improved in 60% of clinical lesions. After two years a dimorphous case, formerly improved, became lepromatous, after which all lepromatous and dimorphous cases were changed to sulfones. Tuberculoid patients were improved. Two of them continued treatment until today (June 1964) and are apparently cured.

—[AUTHORS ABSTRACT, supplied by E.D.L.J.]

LOGINOV, V. K., LETICHEVSKAYA, A. M., AKSANOVA, R. and KHRICOV, G. A. Experiments in the treatment of leprosy with Etoxid (preliminary information). *Leprosy Rev.* **34** (1963) 212-218; translated from *Ucheniye Zapiski (Astrakan)* 1962, 3 (8).

Etoxid is a diethoxythiocarbamide, derived from diphenylthiourea, synthesized by Shukin in 1953; in the Russian literature there are many reports on its high bactericidal activity in tuberculosis. At the Astrakhan Institute for the Study of Leprosy the authors used Etoxid in the treatment of 24 lepromatous, 11 tuberculoid, and 11 indeterminate cases. The dosage was 0.1 gm. t.d.s. increasing weekly up to 0.3 gm. t.d.s. until the 21st week, when it was increased to 1.5 gm. The treatment was carried on for 40 weeks, followed by 1 month of rest. The general impression of the authors is of significant clinical, bacteriologic, and immunologic improvement in a relatively short period of time, in some cases as short as 15 to 20 weeks.—[From abstract by J. Ross Innes in *Trop. Dis. Bull.* **61** (1964) 164.]

BARCLAY, C. A. and WILKINSON, F. F. Ensayo clínico del preparado Ro 4-4393, a dosis única semanal, en el tratamiento de la lepra. [Clinical trial of Ro 4-4393, in a single weekly dose, in the treatment of leprosy.] *Leprológia* **8** (1963) 71-82.

The authors give the results of the determination of blood levels of free sulfonamide after administration of Ro 4-4393 in 20 patients with lepromatous leprosy. These patients were divided in three groups, receiving between 1 and 1.5 gm. in single weekly doses for 3 months. With the dose administered the blood levels were uniform for a week, after which they gradually rose because of the slow elimination of the drug. Comparing the clinical and the bacteriologic changes, the authors conclude that, in spite of the short period of treatment, the effects of the drug are favorable. This conclusion is based on the excellent tolerance to it, on the effectivity of the blood levels, and the sustained bacteriologic improvement in the nasal mucosa.

—[Authors' summary, supplied by E. D. L. Jonquieres.]

MERCAU, A. R., CARBONI, E. A., DEPAOLI, E. A. J., SERIAL, A., FERNANDEZ PODESTA, T. A. Tratamiento de la lepra con sulfas de acción lenta (dimetoxi-sulfanilamida-diazina). [Treatment of leprosy with a long-acting sulfonamide (sulfadimethoxine).] *Leprológia* **8** (1963) 83-87.

Sulfadimethoxine was used in the treatment of 13 patients (12 lepromatous and 1 indeterminate). It was administered orally, the dosage 1 gm. daily, for periods ranging from 3 to 10 months. Improvement was seen in 6 of the cases, 1 remained stationary, and 3 became worse.—E. D. L. JONQUIERES

MERCAU, A. R., CARBONI, E. A., DEPAOLI, E. A. J., SERIAL, A., FERNANDEZ PODESTA, T. A. Tratamiento de la lepra con sulfas de acción lenta (sulfametoxipiridazina). Año y medio de tratamiento. [Treatment of leprosy with a long-acting sulfonamide (sulfamethoxy pyridazine); a year and a half of treatment.] *Leprológia* **8** (1963) 88-95.

Sulfamethoxy pyridazine was used for the treatment of 14 patients (12 lepromatous, 2 indeterminate), the dosage 1 gm. daily by the oral route, the treatment period a year and one-half. All cases were improved. Therapeutic action seems to be slower than with other antileprosy drugs. Leprosy reaction was noted with the same frequency as with other such drugs, which is in disagreement with Schneider's findings.—E. D. L. JONQUIERES

HIRAKO, T. and SAKURAI, H. Chemotherapy of leprosy chiefly with sulfamethoxy pyridazine. *Leprosy Rev.* **34** (1963) 193-202.

The authors have studied the problem of the treatment of relapsing cases of leprosy, of which there are about 30 cases each year among about 1,200 patients in Tama Zensho-en leprosarium. Promin therapy had apparently failed, and a change to DDS resulted in only temporary improvement. Sulfamethoxy pyridazine by mouth was then tried on 100 lepromatous cases. The dosage for 55 patients was 0.75 gm. on alternate days, and for the other 45 patients 0.5 gm. daily. The drug was found effective in both new and relapsed cases. No particular side effect was noted over the 24 months period of observation. The authors believe that improvement, primary or secondary, is due to an epithelioid-cell reaction based on a strong activation of the reticuloendothelial system. Sulfone drugs cause it, thiourea drugs not so well or not at all, and sulfamethoxy pyridazine best of all because it can remain effective for a long time in the blood. It causes what they call a "biological action," which augments its true specific action.—[From abstract by J. Ross Innes in *Trop. Dis. Bull.* **61** (1964) 163-164.]

CONSIGLI, C. A., BIAGINI, R. and VAZQUEZ, C. Tratamiento de la lepra con Ciba 1906 inyectable. [The treatment of leprosy with injectable Ciba 1906.] *Leprológia* **8** (1963) 102-107.

Two types of suspensions (watery and oily) were used in 5 patients (4 lepromatous and 1 dimorphous), in a dosage of about 1 gm. (5 cc.) once a week, for from 7 to 21 months. Only in 1 case was local pain registered in the gluteal region. Good results were

seen in the 2 cases which reached 21 months of treatment; the rest were benefited in low degree.—E. D. L. JONQUIERES

SCHVARTSMAN, S. and MARCONDES, E. Intoxicação accidental por sulfonas em pediatria. Apresentação de 12 casos. [Accidental poisoning by sulfones in childhood; presentation of 12 cases.] *Rev. Hosp. Clin. Fac. Med. São Paulo* **18** (1963) 345-350.

From São Paulo the authors report on 12 cases of accidental poisoning of children by sulfones in the year June 1962-May 1963, although only 3 cases had been reported in the period from 1953 to 1957. The reasons for this increase are said to be: (a) the progress which permits many more cases to be given domiciliary treatment; and (b) the fact that, because the sulfones are given orally, they are supplied in dragées which have a pleasant appearance and an agreeable taste. The drug being absorbed very rapidly, the symptoms may appear within a few minutes, or with a delay up to 24 hours. They consist of nausea, vomiting, agitation, and hyperexcitability, and in grave cases there is considerable disturbance of electrolyte balance. The excited phase is followed by depression, sometimes with torpor, incoordinated movements of the limbs, and tonic-clonic convulsions. The most marked sign is cyanosis due to methemoglobinemia, apparent chiefly on the face and the extremities. In moderate cases the amount of dyspnoea is not proportional to the cyanosis. Diagnosis is based on the history and the detection of methemoglobin and of sulfonamides in the urine. The methemoglobinemia can be dealt with by slow intravenous injections of a solution of methylene blue, 1-2 mgm./kgm. body weight, sometimes combined with slow infusions of ascorbic acid, 1-2 gm. Total blood transfusion or peritoneal dialysis may be necessary. Other treatment is symptomatic. The 12 cases were in children 2-7 years old, one-half of whom were boys. It was extremely difficult to ascertain accurately the amount of the drug which had been ingested, or the length of time since the onset of symptoms. The longest stay in the hospital was 30 days, but 4 patients were hospitalized for only 1 day. Two children required peritoneal dialysis for acute renal insufficiency, and 2 needed total blood transfusion (although 1 of these was in the hospital for only 2 days). All recovered.—[From abstract by W. K. Duncombe in *Trop. Dis. Bull.* **61** (1964) 162-163.]

MECADANTE, F. F. and JONQUIERES, E. D. L. Valoración de las altas definitivas concedidas en el Dispensario Central de Leprología. [Evaluation of the definitive discharges given in the Central Leprosy Dispensary.] *Leprología* **8** (1963) 115-118.

Of the patients with tuberculoid leprosy treated with sulfones in the central dispensary in Buenos Aires, 65.7% were definitively discharged after 5 years of treatment. Of the patients with dimorphous [borderline] leprosy, 24% were discharged after 5-8 years of treatment, and after a definite change to positivity of the lepromin reaction. Only 2 lepromatous cases were definitively discharged after more than 10 years of treatment, and 1 of them relapsed. Since then, no other lepromatous cases were discharged, even those few in which the lepromin test turned to positive.—AUTHORS' ABSTRACT.

CONTRERAS, F. Guérison et récupération de l'hansénien. [Cure and recuperation of the leprosy patient.] *Maroc méd.* **42** (1963) 963-966.

The greatest difficulty in connection with the social recovery of old cases lies in the fear of contagiousity, and the long-held belief that leprosy is incurable. It is for this reason that, in Spain, one should be most cautious about talking about cure, and should make repeated bacteriologic examinations to make sure of the negativity of the patients. To make the campaign against leprosy efficacious, it is necessary to efface the unjustified differences between leprosy and other infections.—N. BOURCART.

OLIETE, J. and TERCENIO, J. Alopecia total de cejas tratadas mediante injerto pediculado. [Total alopecia of the eyebrows treated by means of pedunculated grafts.] *Rev. Leprol. Fontilles* **5** (1963) 719-722.

The authors comment on the different surgical methods for the correction of

madarosis, recommending the Esser method of arteriovenous flaps. A case with excellent results is described.—F. CONTRERAS

SAKURAI, H., KAWAGUCHI, M. and MAKUDA, E. Histopathological findings on 115 corpses of leprosy. *Nagashima Arch. Leprosy* **6** (1964) 17-22 (in Japanese; English summary).

Histopathologic findings in a total of 115 autopsies performed up to July 1963 are reported (75 of which were dealt with in an earlier (1962) issue of the *Archives*). By type, there were 77 lepromatous and 38 neural cases; by sex, 80 males and 35 females. Sections of all visceral organs were examined for bacilli, with positive findings in 63.8% of the lepromatous type and 5.3% of the neural one; bacilli were found almost twice as often in the nerves as in the skin. Histologically, nerves with numerous bacilli showed proliferation of connective tissue and an abundant cellular infiltrate. In some old nerve lesions of neural cases there was calcification in some degree. Lepromatous infiltrates were frequently found in the skin, without bacilli but with lepra cells and infiltrates in which lymphocytes and epithelioid cells predominated. In the testes of lepromatous cases bacilli were always found, in the younger cases almost all of the seminiferous tubules had undergone hyaline degeneration; on the other hand, no leprous changes were found in neural cases, even in aged ones. Erythema nodosum leprosum lesions of the skin were frequently encountered, and also (microscopically) in the nerves and testicles. Amyloid was occasionally recognized in lepromatous cases. The main causes of death, on the basis of histopathology, were contracted kidney and pneumonia; many of the autopsies were on old persons and persons who had long been bed-ridden. Tuberculosis was the cause of death in only 6 cases; even by microscopic examination, tuberculosis was found in only 12% of the autopsies. Cancer was found as a complication in 14.2% of the bodies, almost always adeno-carcinoma. In the few specimens in which both leprosy and cancer were encountered together, the leprosy bacillus had not invaded the cancer cells. There were some instances of tuberculosis or of cancer in which *M. leprae* had spread greatly in the skin and nerves just before death. This abrupt spread was presumably due to the general prostration of the patients who suffered from these complications.

—[From authors' summary.]

CONTRERAS RUBIO, F. La histopatología de la amiloidosis en la enfermedad de Hansen. [Histopathology of amyloidosis in leprosy.] *Rev. Leprol. Fontilles* **5** (1963) 679-718. (From doctorate thesis.)

After discussing the general pathology of leprosy, the author goes on to a study of amyloidosis. The chemical composition of amyloid is considered, and the histochemical aspect of the substance. The different theories on the formation of its deposits are discussed, and also the form of reabsorption by the liver and spleen. The methods and techniques employed in Fontilles for the study of amyloidosis are given in detail. Anyone interested in the subject should consult the original publication. (The work was distinguished by the Faculty of Medicine of Madrid with the Extraordinary Prize for the doctorate degree.)—F. CONTRERAS

NYKA, W. Studies on *Mycobacterium tuberculosis* in lesions of the human lung. A new method of staining tubercle bacilli in tissue sections. *American Rev. Resp. Dis.* **88** (1963) 670-679.

The author relates the history of the staining of the tubercle bacillus in tissue sections, pointing out that the inadequacies of the Ziehl-Neelsen stain for that demonstration have led to about 100 other procedures—none of which represents any real improvement. He himself demonstrates tubercle bacilli in lung tissue, especially near the lesion foci which show none after the usual procedure. For fixation he uses either of two solutions of corrosive sublimate and formaldehyde, neither of which is stable, to which is added either H_2O_2 or periodic acid. The staining procedure used is a slight modification of Gomori's methenamine-silver nitrate method as applied to fungi. [For details of the method, which is far from simple, the original article should be consulted.]—H. W. WADE

HIBI, H. Effect of Promin and other sulfones on eye leprosy; histological findings. Nagashima Arch. Leprosy **6** (1961) 57-58 (in Japanese; English summary).

The histopathology of the eyeball was investigated in 14 cases (12 lepromatous and 2 neural) that had been treated with Promin and other sulfone drugs. The 15 balls examined, the clinical findings in which were known, were enucleated from 4 to 21 hours after death. (1) Leprosy bacilli in the eyeball were degenerated and markedly reduced, although in a few cases the bacilli were latent in the cornea and sclera for a long time in spite of continual treatment. (2) Lepra cells were reduced in number, in parallel with the absorption of skin lesions; in the iris, ciliary body, chorioid and retina, there was marked vacuolar degeneration. (3) The leprosy infiltrations around the vessels of the subconjunctiva, iris and ciliary body were atrophic; in a few cases there was a considerable amount of lymphocytic infiltration in the episclera, iris and ciliary body. (4) These changes were not specific to sulfone treatment, but were seen after natural healing or healing due to chaulmoogra treatment, and there may be no essential difference between them. (5) The condition of the bacilli and the lepra cells of the eyeball is in general similar to that in the peripheral nerves and skin of the same individual.

—[From author's summary.]

MONTAGNA, W. Phylogenetic significance of the skin of man. Arch. Dermat. **88** (1963) 1-19.

Note is made of this article, a guest lecture by a biologist who describes himself as a "zealot about skin," because it may be of interest to those who are concerned with leprosy, especially those who are dermatologists. First man's place in the animal kingdom: a primate (difficult to define satisfactorily), and a member of the Hominoidea, along with the anthropoid apes—the chimpanzee, the gorilla, and the orang-utan. In man, the skin is becoming progressively archaic. The "strange tussocks" of hair that occur here and there over the body are, it is suggested, ornamental rather than useful, as, e.g., the mane of the lion; as Aristotle observed, many are connected with sexual maturity. The principal deeper peculiarities of the human skin are the very complex sculpturing of ridges and furrows, mounds and craters, which differ greatly on different parts of the body, as shown by line-pictures obtained by plastic impressions of the surface (shown are the forehead, elbow, chest and back), and the very different (and strange) pictures of the under surface of the epidermis of different areas. (The ridges are erroneously called "rete pegs" by the histologist, as if they were single pillars of cells.) Many other features are discussed and pictured. "In conclusion," the author says, "the skin of man is a remarkable and unique organ. Far from being a generalized assemblance of all the known cutaneous appendages, it has modified the structure and function of each of these in such a way that each has become idiosyncratic. The advancing nakedness, the most significant specialization that is occurring, has forced the skin to adopt new mechanisms for protection. Of these, none is more unique than the cutaneous vascular system, which subserves the general circulatory system, and the attainment of eccrine sweat glands which are learning the new function of responding to thermal stimulation. "This is the framework of our ignorance. Those of us for whom the study of skin is the first love should be happy that much remains to be learned."—H. W. WADE

ABE, M. and HIJIOKA, H. Studies on the preparation, standardization and preservation of lepromin. IV. Fundamental studies on potency test in guinea-pigs sensitized with defatted leprosy bacillus. La Lepro **33** (1964) 21-27 (in Japanese; English summary).

To determine the biologic potency value of the Dharmendra antigen, guinea-pigs were sensitized with defatted leprosy bacilli suspended in liquid paraffin, and various conditions necessary for the optimal sensitization as well as the specificity of cutaneous reactions were investigated. Animals sensitized by heat-killed tubercle bacilli were used for controls. Sensitization of the guinea-pigs with the defatted leprosy bacilli took about 10 times the amount of bacilli as sensitization with dead tubercle bacilli, and a longer

period of incubation. The cutaneous reaction in guinea-pigs sensitized with the former was relatively specific to the Dharmendra antigen. Testing the adjuvant effect of the lipid fractions extracted from leprosy nodules on the sensitization by, as well as the cutaneous reactivity to, the defatted leprosy bacilli, it was found that the alcohol-insoluble fraction has an intensifying effect on the potency of the Dharmendra antigen, in contrast with an inhibitory action shown by the alcohol-soluble one. The skin-sensitizing activity of defatted leprosy bacilli was not influenced by the addition of the acetone-insoluble lipid, which was composed of these two fractions, because of their contradictory effects.

—[From authors' summary.]

BARUA, D., GHOSH, S., BOSE, R., GANGULI, S. and DAS, B. M. Vole bacillus antigen as a substitute for lepromin. *Bull. Calcutta Sch. Trop. Med.* **11** (1963) 157-158.

This report is of another attempt to find a satisfactory substitute for the leprosy bacillus for making lepromin; actually, however it is Dharmendra's antigen that is referred to, since the readings were made after 24 hours. The vole bacillus from a culture on Loewenstein-Jensen medium was treated as usual for that antigen and tested in parallel with it on 404 leprosy patients. Because 32.4% of the 111 lepromatous cases gave positive reactions, it was considered unsatisfactory. (Incidentally, there were 11 positives with the Dharmendra antigen.) Of 293 tuberculoid cases, 246 (80%) were positive with the vole antigen (and 217,—or 73%,—with the Dharmendra antigen). With a preparation of vole bacilli grown on Dubos' medium without bovine albumin, 79% of tuberculoid cases and 5.7% of lepromatous cases were positive, which result was regarded as encouraging.

—H. W. WADE

NISHIMURA, S., KOSAKA, K., TAKAHASHI, T. and SAKURAI, H. Influence on the lepromin reaction of mouse skin tissue components. *La Lepro* **33** (1964) 1-6 (in Japanese; English summary).

The lepromin reaction in lepromatous-type patients is useful in differentiating the leprosy bacillus from other acid-fasts. A problem is the influence of the tissue components, apart from that of the bacterial cells, on the skin reaction. To clarify this, antigens were prepared by the Mitsuda method from the skin of healthy men, and that of healthy mice, and also of the lepromas of men and mice; and, finally, a suspension of *M. ulcerans*. In total, 71 leprosy cases (56 lepromatous and 15 tuberculoid) were injected with the various antigens, and the reactions were examined comparatively. Similar experiments were carried out twice. With the mouse skin antigen the early-stage reactions (average 3.6-5.3 mm) and the late-stage reactions (average 2.3-3.2 mm) were larger than with the human skin antigen (1.2-2 mm and 0.4-2.1 mm, respectively). In conclusion, the lepromin test, when comparing it with antigens made with the murine leprosy material should be done with the antigen prepared by Dharmendra's method, rather than with Mitsuda's lepromin. Otherwise the antigen should be diluted as much as possible and when determining it, it is important to consider the reddening difference. [What leads to this conclusion is not evident. H.W.W.]—[From authors' summary.]

MAEDA, M., ABE, M., KOBAYASHI, S., TAKEDA, M., ARAKAWA, I., OKAMURA, K., YOKOTA, T., KASUGA, T., TSUCHIYA, M., NAKAMURA, K., NAGAI, T. and IDE, J. Skin reaction caused by tissue suspension. *La Lepro* **33** (1964) 7-15 (in Japanese; English summary).

In order to determine the influence of the tissue components contained in the Mitsuda suspension upon the lepromin reaction, the skin reactions caused by two different preparations were compared with the Mitsuda reaction. The tissue suspensions were prepared from (a) the skin of a leprosy patient free from leprosy bacilli, and (b) the skin of a healthy person, both by the Mitsuda method. There were no significant differences in the sizes of reactions to these tissue suspensions, which denies the possibility that some tissue components might be involved in the Mitsuda reaction. Therefore, the reaction caused by tissue components can be considered a nonspecific one, unrelated to the essential lepromin reaction provoked by the Mitsuda antigen. The more the tissue components in

the antigen [i.e., lepromin?], the larger were the 15-day reactions. This indicates the need of eliminating as much as possible of the tissue components in the Mitsuda antigen. Comparison of the sizes of the skin reactions caused by the tissue suspensions with those provoked by the Mitsuda antigen indicated that the reactions read at 48 hours (9-13 mm), and after 15 days (3-10 mm) were a mixture of the specific reaction to leprosy bacilli and the nonspecific one due to the tissue components. Concerning the mode of appearance of the skin reaction caused by the tissue suspensions, there was no difference between the two clinical types of leprosy at 48 hours, but at 15 days the tissue suspensions of higher concentrations than the Mitsuda antigen induced larger skin reactions in cases of the nonlepromatous type than in those of the lepromatous type. On the basis of these results the criteria for reading the positive Mitsuda reaction at 15 days are discussed.— [From authors summary.]

✓ CURBAN, G. V. Contribuição para o estudo da reação de Rubino. [A study of the Rubino reaction.] *Rev. brasileira Leprol.* **30** (1962) 179-216.

In 1926 Rubino, using sheep cells fixed with formalin in the complement-fixation reaction, found that with sera from leprosy patients the formalin-treated red cells sedimented in a few minutes. This reaction, seen most often in severe cases, proved too inconstant to be specific for leprosy, and interest in the Rubino reaction dwindled. The author believed its further study worthwhile because of a possible relationship between the immune reaction which causes the phenomenon and the different states of body resistance in leprosy, and he applied it in 231 leprosy cases of diverse types, along with 40 controls. In all of the controls the reaction was negative. In leprosy there was a positive association with tuberculoid and indeterminate leprosy. Statistically there was insignificant association with sex, age, race, duration or stage of development of the disease, and with erythema nodosum leprosum. There was significant association in the lepromatous type with cases which had had treatment with sulfones, with advanced stages of the disease, with the Mitsuda reaction. The author comments that the association between a positive Rubino and a negative Mitsuda, or between a negative Rubino and a positive Mitsuda, shows immunologic antagonism. It was not possible to determine the immunologic factor responsible for a positive Rubino reaction. The author thinks it depends on an original predisposition, and that the reaction of Rubino constitutes a research instrument for the study of the states of resistance in leprosy.— [From abstract by J. Ross Innes in *Trop. Dis. Bull.* **61** (1964) 158-159.]

✓ MUNOZ DA ROCHA, J. M. Reação de imunoaderência na lepra (Novo subsídio para classificação e prognóstico da lepra.) [Immune-adherence test in leprosy, (A new contribution to its classification and prognosis)] (summaries in English and French). *Publ. Cent. Estud. Leprol. (Parana)* **3** (1963) 8-17.

The author prepared a suspension of leprosy bacilli by the chloroform extraction method used by Dharmendra, and performed the immune-adherence test (method of Nelson) with Type O human erythrocytes, applying it to sera of leprosy cases (indeterminate, tuberculoid, and lepromatous) and of healthy individuals. The reaction was negative in all lepromatous sera, but positive in 88% of those from tuberculoid cases; indeterminates were 68% positive. It is said that in indeterminate cases it can serve the same role as the Mitsuda test, to predict the future clinical form of the disease if the case progresses, and generally in determining the organic resistance to the bacillus. It has no diagnostic value in leprosy.— [From author's summary.]

✓ LIM, S. D. and FUSARO, R. M. Leprosy. I. β_{2A} and β_{2M} immunoglobulins in leprosy sera. *Arch. Dermat.* **89** (1964) 86-88.

Various techniques used by other investigators have demonstrated that certain measurable components are present in lepromatous sera, but present with less certainty in the sera of tuberculoid patients. The authors have evaluated the β_{2A} and β_{2M} microimmunoelectrophoretically, because these two globulins were elevated in lepromatous sera but

not in tuberculoid sera. This test, it is suggested, may prove useful in differentiating these two types of leprosy. [The two pictures given are quite unintelligible to one not familiar with the technic.]—H. W. WADE.

MERKLEN, F. P., COTTENOT, F. and GALISTIN, P. Anticorps mis en évidence par immunofluorescence dans des sérums de lèpre humaine. [Antibodies revealed by immunofluorescence in the sera of human leprosy.] *Comp. rend. Acad. Sci. (Paris)* **257** (1963) 2212-2213.

By means of the direct and indirect technics of immunofluorescence, the authors have been able to detect, in the sera of both lepromatous and tuberculoid leprosy cases, a specific antibacillary antibody that fixes to the Hansen bacillus. The Stefansky bacillus is also capable of fixing this antibody of leprosy sera. The same technics show, in the sera of progressive tuberculosis cases, the presence of an antibody equally capable of fixing the Hansen and Stefansky bacilli, but that can be removed by absorption with a BCG culture. These experiments indicate an antigenic relationship among the three mycobacteria employed.—N. BOURCART.

MORI, T., KOSAKA, K. and DŌMAE, K. Antigenic analysis of leprosy and murine leprosy bacilli by the Ouchterlony method. *Nagashima Arch. Leprosy* **6** (1964) 1-5 (in Japanese; English summary).

The antigenic structure of the leprosy bacillus, the murine bacillus, and an unidentified bacillus isolated from a leprosy bacillus-inoculated mouse was studied by the Ouchterlony method. The immune sera used were those against these three bacilli, and also Nojima's strain (isolated from a human leproma), BCG, the Johne bacillus; also the extracts of ground-up cells of many acidfasts. Those extracts contain numerous antigenic components, and the precipitation curve of the antigen-antibody reaction is very complex. The concentration of the antigenic components varies so much that, if the antigen is diluted so that one antigen is of suitable concentration, others may be too weak to elicit the precipitation curve. Consequently, it was possible only to ascertain a general trend regarding the antigenic structure of the acid-fast organisms studied. The results suggest that the antigen or antibody should be a single entity, to be used for antigenic analysis by the Ouchterlony method.—[From authors' summary.]

NISHIHARA, H., LAWRENCE, C. A., TAPLIN, G. V. and CARPENTER, C. M. Immunogenicity of gamma-irradiated *Mycobacterium tuberculosis* H37Rv (GIV) in mice. *American Rev. Resp. Dis.* **88** (1963) 827-832.

It had previously been shown by certain of the authors that virulent tubercle bacilli, when lyophilized and exposed to gamma irradiation (from a Cobalt-60 source), are rendered noninfectious and noncultivable but are not actually killed; such bacilli continue to respire on suitable substrates. It is now reported that bacilli so treated, unlike vaccines of bacilli killed by heat and/or chemicals, can give protection more or less equivalent to that given by BCG. It (GIV) gave significant protection to mice against challenge doses sufficient to kill all control animals in less than thirty days. The use of an adjuvant significantly increased the immunogenic activity of GIV. Four doses of 0.1 mgm., or a single 1.6 mgm. dose with adjuvant gave protection equivalent to that resulting from vaccination with living BCG.—H. W. WADE.

SEN GUPTA, P. C. Attempt at transmission of *Myc. leprae* to the rhesus monkey; further observations. *Bull. Calcutta Sch. Trop. Med.* **11** (1963) 94-96.

The experiment included (a) 4 monkeys inoculated with an almost cell-free suspension of leprosy bacilli and treated with prednisone; (b) subsequent reinoculation of these monkeys under the same conditions; (c) 1 inoculated with Kedrowski's bacillus, and (d) 1 control injected with heat-killed bacilli. The injections were made on the forehead, superficially or subcutaneously. Results: (a) nodular lesions about 12 mm. in diameter appeared in about 3 weeks; the histology at about 6 weeks was varied, the bacilli generally numerous; 8 weeks later there was a tendency to tuberculoid granulomas, and bacilli

were absent. (b) Reinoculation (at about the time of the second biopsy) caused larger nodules (up to ± 25 mm.) in all of the animals; acid-fasts numerous (4+). No nodules formed in the other animals (c) and (d). Most of the animals became positive (Dharmendra antigen, early hypersensitivity?) The only conclusion offered is that the production of granulomas is an indication that the bacilli were in a living state.

—H. W. WADE.

HART, P. D'A. and VALENTINE, R. C. Growth (without multiplication) of *Mycobacterium lepraemurium* in cell-free medium. *J. Gen. Microbiol.* **32** (1963) 43-53.

This report is of a medium in which the murine leprosy bacillus consistently elongated, of the optimal conditions for their elongation, and of the technic employed in determining that change. The electron microscope was generally used in making measurements. The mean length of the bacilli doubled in about 4-17 days, which is about the generation time in host cells, and quadrupled before they became degenerate after about 2 months. These changes occurred in media at about pH 6.0-6.4; bacilli incubated at pH 7.2 or more, or 5.0 or less, did not lengthen. Since the presence of isoniazid in the medium prevents elongation of the bacilli, it is suggested that this might be made a preliminary *in vitro* test of drugs to be used for the treatment of leprosy in man. [In large part from author's summary.]

UENO, Y., MITSUFUJI, Y., OSHIMA, F., HIGUCHI, M. and NAKAMURA, M. A simple method of isolation and purification of *Myc. lepraemurium* from infected tissues. *Kurume Med. J. (Osaka)* **10** (1963) 12-20.

A simple method is described for the isolation and purification of *M. lepraemurium* from infected tissues by treatment with trypsin followed by sodium desoxycholate. This procedure is harmless for the infectivity of the bacilli, the tissue can be almost completely removed from the starting homogenate, and it can be performed under sterile conditions.

—[From authors' summary.]

MATSUO, Y., MITO, A. and HAIZUKA, M. Studies of phosphorous metabolism of leproma in murine leprosy. *La Lepro* **33** (1964) 16-20 (in Japanese; English summary).

After intravenous injection of P³²-orthophosphate, rats with murine leprosy were killed at serial intervals and the subcutaneous lepromas were resected. The rate of incorporation of P³² into the lepromas was rapid, and increased consistently for the first hour; relatively high levels of P³² were maintained during the following 24 hours. The bacilli were then collected. There was some delay in the taking up of the P³² by the bacilli, compared with leproma, but there was a parallel relationship between them. The phosphorus fractions of the lepromas resected at hourly intervals were obtained by the method of Schneider. The P³² was rapidly taken up in the acid-soluble fraction, and the specific activity increased consistently for one hour. The incorporation of P³² into the acid-soluble fraction was significantly high in the phospholipoid fraction, in contrast to the low levels in the nucleic acid and phosphoprotein fractions. The turnover rate of the phosphorus, however, was more active in the nucleic acid fraction than in others.

—[From authors' summary.]

CLARK, H. F. and SHEPARD, C. C. Effect of environmental temperatures on infection with *Mycobacterium marinum* (Balnei) of mice and a number of poikilothermic species. *J. Bact.* **86** (1963) 1057-1069.

M. marinum, which (like *M. leprae* and *M. ulcerans*) grows preferentially in the mouse footpads, presumably because of its relatively low temperature, was studied in broth cultures for its temperature requirements. It was found to grow best between 25°-35°C, more slowly at 37°C and little at 15°C or below. In mice, footpad temperatures were within a few degrees of the environmental temperatures; the deep-body temperatures were 36.5°-37.3°C. For footpad infections with this microorganism, the optimal environmental temperature was 20°C. Inoculated intravenously, mice developed peripheral infections of the nose, feet, and tail at environmental temperatures of 4°-30°C,

with severe pulmonary involvement, and at the lower temperatures the mice tended to succumb most rapidly to systemic infections; on the other hand, at 34°C, intravenously-infected mice did not develop either peripheral infections or pulmonary involvement. Young opossums, with slightly lower deep body temperatures (34°-36°C), developed footpad infections after local injection, but no systemic involvement after intravenous infection. Cold-blooded animals (reptiles, amphibians, and fish), whose deep-body temperatures were nearly identical with environment temperatures, when injected intraperitoneally showed susceptibility (most at 30°C environmental temperature), but there was no tendency to peripheral involvement. Transmission studies revealed instances in which *M. marinum* was shed into water in which the animals were kept, and also instances of infection of animals from infected water.—[From authors' abstract.]