

## 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.*

FLOCH, H. Activités thérapeutique antiléprouses de la sulfone monoisopropylée et de la sulfone diisopropylée. [Effects of antileprosy therapy with monoisopropyl sulfone and diisopropyl sulfone.] Arch. Inst. Pasteur Guyane Française et Inini 17 (1956), Publ. No. 401 (July).

Three patients were treated with the diisopropyl sulfone (3460 CT), 200 mgm. per day, 5 days a week. Two of them, both tuberculoid, became markedly improved clinically in 5 months of treatment, and one showed histological improvement. The treatment of the third case, borderline, is yet too short to permit any conclusion. Another 8 patients were given the monoisopropyl sulfone (3461 CT), in the same dosage. Three of them, lepromatous, have been treated for too short a time to permit any conclusion except that the drug is very well tolerated. Another lepromatous patient was a very difficult case because of repeated reactions with any form of treatment yet given him; he abandoned the treatment with the monoisopropyl sulfone on his own. The other 4 patients (2 lepromatous, 1 tuberculoid and 1 borderline) were clinically, bacteriologically and even histologically improved in 4 to 7-1/2 months of treatment, the borderline case becoming bacteriologically negative, which is remarkable. With the diisopropyl sulfone there was significant improvement in 2 tuberculoid cases, but the possibility of spontaneous improvement is not to be forgotten. The observations with the monoisopropyl sulfone are indisputably of interest, it being active in tuberculoid as well as in lepromatous cases. Both of these propylated derivatives are remarkably well tolerated in all cases, so much so that a patient has only to be on the 100 mgm. dose for a month before passing to the standard 200 mgm. daily dose.

—AUTHOR'S ABSTRACT

YOSHINAGA, T. Studies on the absorption of promin through the skin. La Lepro 25 (1956) 138-142 (in Japanese; English abstract p. 138).

Promin mixed with strichnine nitrate was used to determine the absorption time of the drug through the skin of mice by estimation of the time of death. The results indicate that promin is the superior drug as an ointment. Investigating the absorption of promin through the skin of rabbits, it was found that the drug in the urine was at its highest concentration at the 6th hour. Also in rabbits was studied the influence of promin absorbed through the skin on the quantity of Ca in the blood and urine, and Fe in the blood, it being found that their quantities increased slightly. —[From abstract.]

YOSHINAGA, T. Studies on the application of promin through the mouth. La Lepro 25 (1956) 143-146 (in Japanese; English abstract p. 143).

Studying the decomposition of promin, it was found not to decompose in the incubator at 37° C. HCl in artificial gastric juice causes almost complete decomposition in 40 minutes, and Na<sub>2</sub>CO<sub>3</sub> in artificial enteric juice did so in 60 minutes. When promin was poured into the stomach, the highest concentration in the urine occurred at the 3rd-4th hour. Comparing oral and intravenous medication, the former is 23 to 51% of the latter. Promin given through the stomach of rabbits caused slight increase in the quantities of Ca in the blood and urine, and Fe in the blood.—[From abstract.]

GIROLAMI, M. Ulteriori osservazioni sulla terapia della lepra con l'idrazide dell'acido isonicotinico. [Further observations on the treatment of leprosy with isonicotinic acid hydrazide.] *Arch. italiano Sci. med. trop.* **35** (1954) 567-606.

Treatment by isonicotinic acid hydrazide (6 tablets daily), or by one of its derivatives, the calcium-sulfone-methane of isonicotinic hydrazide (8 tablets daily), was given to 27 leprosy patients who were observed for from 77 to 365 days. The treatment was given for periods of 40 days, with 15 days of rest; tolerance was good. There was improvement of the general condition, appetite and sensitivity. The skin lesions subsided. The bacteriological examination, before treatment positive in the nasal mucus in 9 cases and in the inguinal lymph nodes in 26 cases, became negative in the nasal mucus in all cases and in the inguinal lymph nodes in 22.—[From abstract in *Bull. Inst. Pasteur* **54** (1956) 2736.]

SINHA, S. C. P. Observation on the treatment of leprosy with Streptopas (Lepetit) from 1952-1954. *Indian J. Med. Sci.* **9** (1955) 124-125.

The author reports the results of outpatient treatment of 700 leprosy patients with Streptopas, vitamin B, thiosemicarbazone, and iron preparations. The cases were classified as nodular, 25%; neural, 15%; and mixed, 60%. Smears were positive in 60%, while 30% were diagnosed on clinical findings only. Resolution in nodular lesions was found to commence after the 10th injection of Streptopas, and the improvement continued in varying degree in most patients. Some required a second course of Streptopas after a rest of one month. The improvement in patients with the neural type was very satisfactory, but in those with the mixed type the clinical response was variable. Perforating ulcers were the quickest to respond to this treatment. Keratitis and iridocyclitis showed a better response than to other drugs. Nasal ulcers responded quickly and completely. If smears could be made, reduction of the bacilli in the skin smears from 200-300 organisms per field to 2-10 per field was observed within 130 days. Nasal smears became negative after the third injection. Toxic reactions were not common. More recently it has been found that Streptotibine gives better results.—[From a report in *J. A. M. A.* **158** (1955) 1048 (foreign letters), which does not state the nature of the drug used (streptomycin with PAS?) or the dosage.]

MAJUMDAR, T. D. Clinical experiences with phenylmethyl-amine-p-aminobenzene sulphonate on lepra reaction. *J. Indian Med. Assoc.* **26** (1956) 314-315.

The author used a new compound of benzylamine to treat a series of leprosy patients. Because benzylamine had been found to have a bacteriostatic action on tubercle bacilli, its hydrochloride was tried on patients with neural leprosy and lepra reaction. The rate of improvement was slow, and the results did not compare well with those obtained with sulfone treatment. The sulfones, however, are less effective against neural than against other forms of leprosy, and they are even dangerous in patients with lepra reaction. A stable combination of benzylamine with sulfonilic acid was given a clinical trial. It was given intramuscularly on alternate days in doses of 50 mgm., and was found to have a beneficial action in reactions. Usually its effect starts with the third or fourth injection and the reaction is controlled by 18 injections.—[From a report in *J.A.M.A.* **161** (1956) 993 (foreign letters).]

MELAMED, J. A. and JONQUIERES, E. D. Butazolidina-Irgapyrin en el tratamiento de la lepra y especialmente de la reacción leprosa; comunicación previa. [Butazolidin and Irgapyrin in the treatment of leprosy, especially of lepra reaction.] *Día Méd.* **27** (1955) 795-811.

The pharmacological properties of Butazolidin and Irgapyrin were found useful by the authors in the treatment of various manifestations of leprosy, especially the states of lepra reaction. Their effects are considered as of three categories: (1) Antiexudative, analgesic, and antipyretic, which activities were evident in 13 cases in reaction (12 lepromatous and 1 tuberculoid). (2) Antigranulomatous, cytostatic or

cytolytic, with respect to which the authors suggest the hypothesis that the exuberance of the granuloma, whether lepromatous or tuberculoid, does not imply greater organic defense; on the contrary, it may interfere with the effectiveness of the sulfones. The combined medication, Butazolidin-Irgapyrin, seemed to be effective in a dimorphous case. (3) Sustained action. In view of the fact that Butazolidin serves to prolong the action of certain drugs (PAS, analgesics, etc.), the authors have initiated studies to determine if there is such an effect with the sulfones. —G. BASOMBRIO

MELAMED, A. and JONQUIERES, E. D. L. Butazolidina e Irgapyrin en el tratamiento de la lepra y especialmente en la reacción leprosa. [Butazolidin and Irgapyrin in the treatment of leprosy and especially in lepra reaction.] Arch. argentinos Dermat. 6 (1956) 413-421.

This further report tells of the observed effects of Butazolidin and Irgapyrin on various manifestations of leprosy which are theoretically susceptible to some of their pharmacologic properties. Irgapyrin was often effective in acute lepromatous reactions, checking the exacerbation during the first week of treatment. In chronic reactions the outcome was favorable after almost uninterrupted long-term treatment with Butazolidin. Both drugs were also found to be good in painful conditions, although they did not prevent the necessity of neurolysis in paralyzing neuritis. In tuberculoid reactions the results were somewhat doubtful, and rather on the negative side. On exuberant leprosy granulomas the medication did not show a frank inhibitive action. The clinical data, and experimental findings in dogs, do not suggest that these medicaments have any delaying action on the excretion of the sulfones used in the treatment of leprosy. Although the tolerance in general was good, attention is called to the possibility of different complications, especially the so-called "paradox phenomena."—[From the authors' summary, supplied by G. Basombrio.]

Bosq, P. Linfogránuloma maligno (Hodgkin) y lepra, concomitantes en una misma enferma; tratamiento con mostaza nitrogenada. [Malignant lymphogranuloma (Hodgkin's disease) and leprosy coexisting in the same patient; treatment with nitrogen mustard.] Día Méd. 27 (1955) 3195-3198.

The case of a woman with lepromatous leprosy of 13 years duration, whose condition had been progressively worsening for some time, is reported. On admission to the sanatorium because of leprosy, in September 1954, she was found to have an early form of the malignant granuloma called Hodgkin's granuloma. Treatment with nitrogen mustard (Dichlorén) was well tolerated, in spite of her generally poor condition, with notable improvement: gain in weight, and return to normal of the temperature and also of the red-cell sedimentation rate. Although it is difficult to evaluate accurately the influence of nitrogen mustard on the leprosy itself, it can be stated that there were favorable effects in that the skin lesions clearly improved and the bacilli became much reduced in numbers. A Carville [sic] done in August 1955 gave 4 positive and 7 negative. Since the nitrogen mustard was tolerated, despite the advanced state of the disease, it is hoped that this treatment may also be beneficial to other patients. It is added that small doses of nitrogen mustard, without phlebotomy, had greatly benefited the few patients treated.—[From the author's summary, supplied by G. Basombrio.]

BERGEL, M. Consideraciones sobre quimioterapia de la lepra. [Notes on the chemotherapy of leprosy.] Semana Méd. 107 (1955) 196-198.

A review is made of what the author considers to be the most important features of leprosy infection and of the biology of *M. leprae*, with respect to chemotherapeutic significance. Elements which he believes may serve as the basis of the search for new antileprosy chemotherapeutics are discussed, among them the antioxygens and the metallic prooxygens inactivators.—[From the author's summary, supplied by G. Basombrio.]

GIL ESPASA, D. Cirugía plástica de cejas en la enfermedad de Hansen. [Plastic surgery of the eyebrows in Hansen's disease.] Fontilles 3 (1955) 517-518.

After pointing out the considerable frequency of alopecia of the eyebrows and its indubitable psychological effects the author holds that surgical treatment is advisable, it being the only procedure that makes possible the repair of the majority of the cases. He recommends the technique of Monks and Esser, with certain modifications by Sánchez Galindo. These techniques are described; and three photographs show the good results obtained.

—F. CONTRERAS

TERENCIO, J. Injertos laminares en la lepra. [Sheet grafting in leprosy.] Fontilles 3 (1955) 528-531.

In Fontilles, as in probably many other leprosaria, there has been a decrease in the number of patients with ulcers of the foot, from 63% in 1943 progressively down to 14% in 1954. Many of these ulcers heal with medication, without or with the aid of topical treatment, although sometimes bed rest is necessary. For the more stubborn cases other procedures are used, among which micrografts have given good results. This has the advantage of easy application, being done without elaborate surgical procedures. There are, however, a few patients who have been bacteriologically negative for years but still have extensive, persistent ulcers which do not improve under specific treatment. With four of these patients cure was obtained by resorting to sheet grafting, the results of which greatly excelled those obtained with micrografts.

—F. CONTRERAS

[FONTILLES] Notas clínicas I. Terapéutica placentaria en las úlceras hansenianas.

[Clinical notes I. Placental therapy in leprosy ulcers.] Fontilles 3 (1955) 532.

This is a report of an experimental treatment, in 8 lepromatous cases, of large stationary ulcers which did not respond to other treatments even after medication had succeeded in improving the other specific manifestations of the disease. The ulcers were treated by applying over them fine strips of placental tissue which had been obtained aseptically, stored in a refrigerator, and exposed to the sun for 30 minutes before application. The results were very promising in almost all the cases, and especially the rapid healing of one of the ulcers which had been caused by a burn.

—F. CONTRERAS

[FONTILLES] Notas clínicas II. Globulina gamma en el tratamiento de la lepra. [Clinical notes II. Gamma globulin in the treatment of leprosy.] Fontilles 3 (1955) 533.

Other articles cited have reported the importance which serum globulins may have in the treatment of lepra reactions, and particularly the gamma globulin—which, however, is not used because of its high cost. There has become available, however, a gamma globulin of placental origin which has a concentration of 325 mgm. per 5 cc. ampule. This has been used in the dose of 1 cc. per 5 kgm. of body weight, the injections being repeated every 5-6 days. In the first experiment good results were noted, the fever subsiding as well as the cutaneous manifestations. As usual, however, after several days the fever and other symptoms reappeared, and they stubbornly defied further use of this therapy.

—F. CONTRERAS

DE OLIVEIRA, S. and MAGARÃO, M. F. Tratamento da reação leprótica com anti-alérgicos. [Treatment of lepra reaction with antiallergics.] Rev. brasileira Med. 12 (1955) 380-383.

The authors employed cortisone per os in 16 cases of lepra reaction in lepromatous patients with satisfactory results, but on discontinuing the treatment after 8 days the reactions relapsed. The Velez test, which was positive in all 16, remained positive in 15. Repeated series of the same treatment ended with the same result: amelioration and relapse. Using Théophorine Roche per os in 15 reaction cases of the erythema nodosum



and erythema multiforme type, tolerance was found to be satisfactory and 10 of the cases were cured, without relapses during 12 months. The Velez test became negative in 9 of the 15 cases. All of the patients resumed their sulfone treatment. Comparing the final results of treatment of reactions by various methods, the authors conclude that Théophorine is the best medicament.

—H. C. DE SOUZA-ARAUJO

LECHAT, M. La chlorpromazine (Largactil) dans le traitement de 44 réactions leprotiques écloses après vaccination antivariolique chez les lépreux. [Chlorpromazine (Largactil) in the treatment of 44 lepra reactions following smallpox vaccination in leprosy patients.] *Ann. Soc. belge Med. trop.* **35** (1955) 343-356.

Chlorpromazine (Largactil) seems to cause marked improvement in lepra reaction following smallpox vaccination. Among 332 lepromatous patients 44 had such reactions, and in most of them they were severe. With small doses of Largactil 35 patients recovered quickly and completely, 6 improved less completely and 3 showed no improvement. All reactive and active lesions had disappeared by the 10th day of the treatment in 28 of the patients. After suspension of the treatment the reaction reappeared in 11 of the cases.

—A. DUBOIS

BORGES DE MACEDO, O. and BERTI, F. A hidrazida do ácido iso-nicotínico na reação leprótica. [Isonicotinic acid hydrazide in lepra reaction.] *Rev. brasileira Leprol.* **23** (1955) 41-52.

Isonicotinic acid hydrazide given orally to cases with lepra reaction caused subsidence of nodules which had existed for several months and had been resistant to other medications used. In some cases the response was rapid, occurring in a matter of days; in other cases with deeper nodules favorable results were observed only after 1 or 2 months of treatment. Acute cases with fever generally resisted the medicament. There was a surprising effect on cubital nerve pain, superior to that obtained with any other remedy employed. The impression gained was that this drug is the best one in cases of subacute lepra reaction. The authors then observed the effects of the drug in 28 patients with the erythema nodosum type of reaction. Of the 21 patients who remained after 7 had abandoned the treatment, most (81%) showed good results, the rest (19%) exhibiting no effect. The drug was given by mouth in daily doses varying from 100 to 200 mgm. It is concluded that the drug, given orally, is the best means of combating subacute lepra reaction.—[From the authors' conclusions and summary.]

TAKEDA, K. Hyaluronidase spreading reaction in the normal people. (Part 3.) Investigation of cutaneous disposition with employment of hyaluronidase. *La Lepro* **25** (1956) 93-101 (in Japanese; English abstract p. 93).

The early (1 hour) and terminal (24 hours) reactions of intracutaneously injected hyaluronidase in healthy people were observed, having the local reactional area and intensity as the objects of measurement. The results obtained are as follows: There are moderate individual variations of spreading, especially marked in those in whom the tuberculin reaction is changing to positive. The spread is weaker in the male than in the female, in whom it is strongest before and after menstruation and weak in other periods. As for age, it is strongest in the juvenile period, decreasing during puberty and youth, not changing thereafter. Spread is affected by the season, being generally lowest in the autumn, increasing from winter to spring, and again decreasing from summer to autumn.—[From abstract.]

TAKEDA, K. On hyaluronidase spreading reaction in various skin diseases. (4th report.) Investigation for skin constitution by means of hyaluronidase. *La Lepro* **25** (1956) 129-137 (in Japanese; English abstract p. 129).

Studies of the hyaluronidase spreading reaction (HSR) were carried out, concerning hyaluronidase and hyaluronidase with trypan blue added, in normal persons and patients with various dermatoses, leprosy, and other diseases. In the normals and

in the dermatosis cases the trypan blue-HSR and HSR showed a similar tendency and the average values were the same. The reactional areas of HSR alone were larger than those of trypan blue-HSR. A sex difference was observed; male > female. In the dermatology patients there was no direct relation between HSR and the decrease of eosinophiles. The reaction was influenced by the kind and stage of the disease, being increased in acute diseases. In the urologic diseases the HSR was similar to that of the normals, while it was decreased in anuria, cancer and diabetes. In leprosy, HSR was specifically negative in 13.3% of lepromatous cases, 6.1% of neural cases, and 21.4% of macular (tuberculoid) cases.—[From abstract.]

✓ WAALER, E. Benforandringer i os maxillare ved lepra. [Changes in the maxillary bone in leprosy.] *Nordisk Med.* **53** (1955) 823-824.

This paper deals with the appearance of the nasal spine and the maxilla in autopsy material from leprous individuals. The previous findings of Möller-Christensen, and of Möller-Christensen, Melsom, Bakke and Waaler, are confirmed. Five cases showed almost complete atrophy of the anterior nasal spine, whereas in two cases the nasal spine was not significantly altered. No bone destruction or active changes in the bone could be demonstrated. Hence the disappearance of the nasal spine is either neurotrophic in nature or due to a long-standing chronic inflammation in this region which is followed by pressure atrophy of the bone. —AUTHOR'S ABSTRACT

✓ HARADA, K. Histochemical studies on leprosy. (The 2nd report.) The mode of formation of acute infiltration. *La Lepro* **24** (1955) 384-391 (in Japanese; English abstract p. 384).

Acute infiltration [see Tajiri, *THE JOURNAL* **23** (1955) 370-384] is a temporary exanthema which appears in the course of lepromatous leprosy, and may also occur in indeterminate or polyneuritic cases. The Mitsuda reaction changes from negative to positive. That which appears in indeterminate cases can be easily mistaken for borderline. In such cases it occurs from the place of newer lepra cells (stainable with Sudan black); in polyneuritic cases it takes place upon the part of old lepra cells (stainable by Sudan III). Histologically it consists of every zone of epithelioid cells, lymphocytes, lepra cells and giant cells in the center, and is distinguishable from "acute aggravation" by the presence of lepra cells. The change in such a case is nearer to fatty necrosis rather than tuberculoid. The changes seen in giant and epithelioid cells are shown histochemically to originate in the absorption of decomposed products of fatty acids.—[From abstract.]

[The foregoing being somewhat obscure in places, Prof. Kanehiko Kitamura, our Contributing Editor for Japan, was asked to elucidate. He retranslated the original Japanese summary and inserted relevant portions from the text, with the following result.]

One cannot differentiate the skin lesions of acute infiltration from those of acute aggravation on the basis of the quantity of bacilli in the tissues. In the lesions of acute infiltration there are lepra cells, for whose demonstration the Sudan black stain is available. These lesions consist histologically of concentric zones—from the inner to the outer side—of epithelioid cells, lymphocytes and lepra cells surrounding the central portion which shows giant cells. The lipids contained in the lesions of cases of acute infiltration in the polyneuritic form are stainable with Sudan III, while in those of cases that occur in the indeterminate form they are stainable only with Sudan black. Such histologic changes in the skin lesions of acute infiltration are regarded as showing a reducing process of neutral fat into glycerol and fatty acid. However, these products are not due to the bacilli themselves (which, according to Mitsuda, have hitherto been hidden in the depth of the body, and having newly entered the circulating blood have reached the skin), but probably due to fat necrosis of cells on the basis of some changes in the immunological condition of the body.

✓ DASTUR, D. K. The motor unit in leprous neuritis; a clinico-pathological study. *Neurology (Bombay)* 4 (1956) 1-27.

The author states that leprous neuritis is the most common single cause of myopathy in India. Biopsy specimens of muscle tissue were obtained from (64?) outpatients attending the clinic of Acworth Leprosy Home, Bombay, the cases of 1 to more than 15 years duration. The ulnar and lateral popliteal nerves were almost always affected. In most patients there was some correlation between sensory and motor impairment. The motor power and function in the upper extremity were unaffected in 17 patients, moderately affected in another 17, and severely affected in 30, with atrophy of the muscles of the hand and impairment of movements. In the lower extremity, weakness of adduction and abduction of the toes was the first sign, followed by dangle foot and trophic lesions. Atrophy of the toes was more common than atrophy of the fingers. Contracture of fingers was related to some type of trauma and not to paralysis alone. Muscle biopsy revealed a reduction in the density or even loss of innervation of the affected muscle and beading or fragmentation of nerve fibers, atrophy of end-plates, and prominence of Schwann's nuclei, with proliferation of endoneurium and perineurium. Rarely, there were concurrent regenerative changes, such as collateral branching and formation of growth cones and immature end-plates. Various stages of muscular atrophy due to the neuritis, comparable to those produced in nerve trauma and muscular dystrophy, were seen in hematoxylin-eosin sections. Acid-fast organisms rarely were detected in the intramuscular nerve twigs or connective tissue. The intrafusal fibers were always spared. Histological changes in the muscle fibers precede those in the motor nerve fibers and endings. The neuritic process progresses slowly, and gives adequate time for diagnosis and treatment. As a routine diagnostic procedure, examination of a single hematoxylin-eosin section of muscle is recommended.—[From a report in *J.A.M.A.* 161 (1956) 993 (foreign letters).]

X SUGAI, K. and FUKUSKI, K. Histopathological studies on human leprosy. (The 1st report.) Findings of lymphatic system. *La Lepro* 25 (1956) 159-171 (in Japanese; English abstract p. 159).

All of the lymph nodes and lymphoid tissues were collected at 15 autopsies on leprosy patients, and 603 specimens were examined histologically. The tissue reactions were divided into 4 types: (1) The large-cell type occurred chiefly in the reticulum, which contained simple large migrating cells. (2) In the foamy-cell type there were foamy cells which stained with Sudan III, and in advanced cases diffuse fatty infiltration. (3) The fat-accumulating type shows fatty infiltration, giant vacuoles suggestive of fatty masses, and giant cells of the foreign-body type. (4) The necrosed type exhibits necrosis. In macular [tuberculoid] and neural leprosy the findings were similar to those of simple lymphadenitis. In nodular [lepromatous] leprosy fatty infiltration is a chief histological change. This fatty infiltration of lepromatous leprosy is constituted by the so-called foamy cells, derived from the reticulum system. In the lesions with giant vacuoles and foreign-body giant cells, fatty tissue debris from the filter activity of the lymph nodes, the reticuloendothelial system, and the foreign-body giant cells with strong phagocytic ability accumulate fatty substances. Fatty infiltration is most marked in the superficial lymph nodes, especially the inguinals; there is no sign of it in the visceral nodes except the portal liver and pylorus nodes. In a case after ENL there was marked necrosis in these nodes. Foamy cells were found in the lymph follicles of the spleen in nodular leprosy, but other tissues presented no change. Bacilli (fluorescence microscope) were extremely few. In general, bacilli were recognized in a small number of cases as brilliant granules in cells with dull fluorescence (a kind of foamy cell).—[From abstract.]

SWERTS, L. Tests à la tuberculine et à la lépromine dans la Chefferie Makoda. [Tuberculin and lepromin tests in the Makoda Chiefdom.] *Ann. Soc. belge Med. trop.* 35 (1955) 801-804.

When planning BCG vaccination of the population of the Chefferie Makoda in the Nepoko region, tuberculin and Mitsuda tests were made of all the population. The former test was the Mantoux, with OT 1/1000. The latter was with a product containing 0.4 gm. of desiccated lepromas per 100 cc.; nodules larger than 4 mm. were read as positive (3-4 mm,  $\pm$ ). The number of persons tested is not stated, but the results are shown in a graph by 5-year age groups and by sex. The tuberculin positives remained relatively few in the earlier age groups (about 5% in the 5-10-years group), rising abruptly in the 16-20 group to stabilize at around 50-60% at 36-40 years, after which males gave somewhat more positives than females. The lepromin curves are very different, with much higher percentages from the outset ("absence of a latent period"), the sexes equal until about 16-20 years, after which males gave somewhat more reactions than females. However, the curves leveled off at that time ("platform"), at 65-75% positives—much sooner, and considerably higher, than with tuberculin. These results indicate that in this population "impregnation by the Hansen bacillus precedes that of the Koch bacillus"; and they do not agree with the idea that the development of lepromin positivity is due to the Koch bacillus. —H. W. W.

TISSEUIL, J. Au sujet de l'article de Hervé Floch: "La réaction de Mitsuda rendue positive par une primo-infection tuberculeuse est-elle accompagnée d'une immunité relative anti-lépreuse?" [On an article by Hervé Floch: Is the Mitsuda reaction, rendered positive by a primary tuberculous infection, accompanied by relative immunity to leprosy?] *Bull. Soc. Path. exot.* **48** (1955) 376-377.

The author criticizes the cited article by Floch [see *THE JOURNAL* **23** (1955) 481], questioning the validity of conclusions as to relative resistance to leprosy among the Creole and European patients, founded on the proportions of lepromatous cases—very slight—and on comparative tuberculin skin test in these two communities. He argues that negative tuberculin reactions may be caused by massive leprosy infection in the skin which may hinder diffusion, and asserts that a negative von Pirquet should be supplemented by a Mantoux test, and a negative Mantoux by test vaccine.—[From abstract in *Trop. Dis. Bull.* **53** (1956) 65.]

JONQUIERES, E. L. Positivación de la reacción de Mitsuda mediante la aplicación de BCG. [Positive conversion of the Mitsuda reaction by means of BCG.] *Medicina* **15** (1955) 116-130.

In an attempt to improve the prognosis of Mitsuda-negative "arrested" patients at the Sommer Sanatorium, BCG vaccination was performed in 57 such cases with different forms of leprosy in regressive or residual stages; and 23 changed to Mitsuda positive, representing 46% of successful attempts. The percentage increased with repeated BCG vaccination. On the other hand, none of 5 active cases that were vaccinated became positive. Of the total of 62 vaccinated patients, many of whom had previously been found tuberculin positive, only 3 showed a distinct but transient intolerance, with short-lasting cutaneous and neural reactivations. From these observations over periods of from 6 months to 2 years it is concluded that the method is innocuous with regard to possible activation of latent tuberculous or leprosy foci. One-plus positive Mitsuda skin reactions showed histologically a tuberculoid structure; no two-plus reaction was biopsied. Doubtfully positive reactions were not taken into account in this study. The observations of Convit and associates are therefore confirmed, and their method is recommended for residual and unstable cases in order to hasten the discharge of inpatients.—[From the author's summary, supplied by G. Basombrio.]

MONTESTRUC, E. Comportement différent au cours d'une réaction lépreuse du B.C.G.-test et de l'I.D.R. avec une suspension de "Myc. Bact. marianum." [Different behavior of the BCG and the *M. marianum* intradermal tests during lepra reaction.] *Arch. Inst. Pasteur Martinique* **9** (1956) 52-53.

During a lepra reaction of a lepromatous patient the author observed that



the reaction to a BCG test (by scarification) made 15 days before the onset of the lepra reaction was strongly positive, contrary to an intradermal test with the marianum antigen made 21 days before the lepra reaction. The author regards this as evidence of antigenic relationships between the Hansen bacillus and the Koch bacillus, and as a confirmation of the view that the use of the *M. marianum* vaccine in antileprosy prophylaxis is not justified.

—H. FLOCH

PEREIRA FILHO, M. J. and NERY-GUIMARAES, F. Mitsuda's reaction induced by BCG in the normal rhesus ("Macacca mulatta"). *Mem. Inst. Oswaldo Cruz* **53** (1955) 609-619.

Living BCG vaccine was administered by various routes to 12 rhesus monkeys which had been proved negative to tuberculin and lepromin. In the monkeys which were given the vaccine intraperitoneally and intratesticularly the Mitsuda reaction became 3+ positive after 8 months and continued until 12 months. In those vaccinated orally, intradermally, by scarification and by multipuncture the conversion was only 1+. In 5 other monkeys vaccinated orally or intradermally with killed BCG vaccine, conversions were slower and less marked. The tuberculin conversions were most marked (3+) in the peritoneum and testicle monkeys; in the others the conversions were slower and more transient.—[From abstract in *Trop. Dis. Bull.* **54** (1957) 51.]

✓ ARONSON, J. D. and TAYLOR, H. C. The relative sensitivity of the skin of the forearm and shoulder to tuberculin. *American Rev. Tuberc. & Pulm. Dis.* **72** (1955) 245 (notes).

The tuberculin reaction following BCG vaccination is likely to differ quantitatively and qualitatively from that occurring after natural tuberculosis infection. The tendency is to become less marked and more diffuse with the passage of time, although the Koch phenomenon is usually seen if BCG is reinjected. Tuberculin and other tests are usually made on the volar surface of the forearm, but the authors have observed that reactions are more localized if made in the thicker skin of the deltoid region of the shoulder. Double tuberculin tests of 139 BCG-vaccinated persons, made on the forearm and in the deltoid area, gave the following results: Forearm, 92 (66%) positive, 43 doubtful, and 4 negative. Deltoid, 136 (98%) positive, 2 doubtful, and 1 negative. With few exceptions the edema and redness on the shoulder were the more sharply defined and more marked. It is concluded that the deltoid area is better for the tuberculin test after BCG vaccination. [The authors limit this brief report to the immediate observation, and do not suggest that the deltoid region would be preferable for tuberculin testing of unvaccinated persons or for other tests, but the report is abstracted here for the attention of those who use the lepromin test. The reviewer has often observed in dogs that reactions to lepromin injections in the thicker, firmer skin of the chest are morphologically different—firmer and more discrete—from those resulting from injections into the thinner, softer skin of the belly. Some workers have applied that test to the skin of the back instead of the usual forearm area, and a Letter to the Editor from Fernandez in reply to an inquiry about the matter appeared in the last issue of THE JOURNAL, p. 475.]

—H. W. W.

RAMOS E. SILVA, J. Sobre a alegada influência da inervação periférica em alergia dermatológica. Sensibilização de leprosos anestésicos ao dinitroclorobenzeno. [The supposed influence of the peripheral innervation on cutaneous allergy. Sensitization of anesthetic leprosy patients to dinitrochlorobenzol.] *O Hospital* **48** (1955) 679-787.

Charpy and others of the Marseille school believe that the sensory nerve endings in the skin and the vegetative nerve fibers play the chief part in the sensitization which occurs in allergic contact eczema. The author therefore tried, on six patients with anesthetic leprosy, the application of a 10% solution of dinitrochlorobenzol in acetone to both anesthetic and normal patches of the skin. In both cases sensitization

occurred in exactly the same way. Furthermore, tests made after the sensitization of the anesthetic and the normal patches of skin gave equally positive results. These findings constitute an argument against any considerable participation of the nervous system in the process of sensitization.—[From author's summary, supplied by H. C. de Souza-Araujo.]

AQUINO, U. M. DE. Intradermorreação no framboésia. II. Natureza da reação e sua especificidade. [Intradermal test in yaws. II. Nature of the reaction and its specificity.] Hospital (Rio de Janeiro) **45** (1954) 451-462 (English summary.)

The author employs a suspension of tissue from an early, infectious, proliferative yaws lesion to prepare an antigen for intradermal tests. Early reactions are read after 24, 48 and 72 hours, and later reactions after 8, 15, 21 and 30 days. The subjects tested included 65 persons with yaws, 29 with tuberculosis, and 158 normal controls (105 young adults, 53 schoolboys). Positive reactions [this apparently referring to early reactions] were 91% in yaws, 73% in tuberculosis, 75% in the schoolboys, and 53% in the young adults. Late reactions were most pronounced in late secondary and early tertiary yaws. They also occurred in healthy young adults, but not in the presence of tuberculosis. The author suggests that a positive late result indicates some degree of resistance and immunity to the treponemata, but that tuberculosis prevents the occurrence of the reaction.—[From abstract in *Trop. Dis. Bull.* **54** (1957) 575.]

[The abstractor remarked that this test must be regarded primarily as the basis of an investigation into immune reactions and not as an aid to diagnosis. To be noted is the similarity of the antigen to lepromin, and the fact that the late reactions—of which details are lacking—may be of interest in that connection.]

FLOCH, H. Antigènes de *M. leprae* et *M. tuberculosis*. Modifications apportées aux propriétés antigéniques du B.C.G. par l'action de divers solvants. [*M. leprae* and *M. tuberculosis* antigens. Changes in the antigenic properties of BCG caused by different solvents.] Arch. Inst. Pasteur Guyane Française et Inini **17** (1956), Publ. No. 398 (June).

Considering that the Koch bacillus is richer in the various antigenic elements than is the Hansen bacillus, the author believes that one could attempt theoretically to remove by extraction from BCG at least certain of the antigenic fractions which distinguish it most greatly from the Hansen bacillus while leaving in it most of the fractions that give the latter its microbial specificity. The results obtained varied considerably with the different BCG antigens employed; the action of the solvents was not always the same. The percentage of positive reactions to each of the BCG antigens studied on the total of the corresponding negative lepromin reactions is particularly interesting. In decreasing order the following rates have been obtained: BCG-isobutyl alcohol, 100%; BCG-methyl alcohol, 91%; BCG-acetic acid, 82%; BCG-acetone, 75%; BCG-ether, 66%; BCG-benzene, 60%; BCG-ethyl acetate, 50%; BCG-ethyl alcohol, 40%; BCG-petroleum ether, 25%; and BCG-chloroform, 14%. Petroleum ether and chloroform therefore appear to have the most effect on the mosaic of antigens of BCG, tending to resemble that of the Hansen bacillus. The action of other solvents were much less interesting.

—AUTHOR'S ABSTRACT

CONTRERAS, F. TERENCIO, J. GUILLEN, J. and VAZQUEZ CONTRERAS, J. Las reacciones de Hanger, Gross, cadmio y formolgelificación en sueros de enfermos de Hansen. [The Hanger, Gross, cadmium and formol-gel tests with sera of leprosy patients.] Fontilles **3** (1955) 519-526.

The tests listed were applied to the sera of 100 patients, 66 lepromatous, 22 indeterminate, and 12 tuberculoid. The techniques followed are described, and the results obtained are tabulated. The conclusions may be summarized as follows: All of these tests give more strongly positive results in lepromatous than in indeterminate

cases, and they are almost always negative in tuberculoids. In the lepromatous forms the positivity increases as the clinical condition of the patients worsens; the tests are strongly positive when there is evident visceral involvement, and when the patients have lepra reactions. Especially the Hanger and the cadmium reactions are strongly positive in those cases which show a marked increase of gamma globulin. All these reactions, if positive, constitute further proof of the dysproteinic state in leprosy.

—AUTHORS' ABSTRACT

OLITZKI, A. L. and SAGHER, F. Kahn's universal reaction in leprosy. *J. Invest. Dermat.* **27** (1956) 35-42.

The authors applied Kahn's universal serological reaction at repeated intervals to 27 patients with leprosy under sulfone treatment for a period of three years, and conclude that changes in the curves occurred with clinical improvement. Three main patterns of response are described. The characteristic nonsymmetrical curve observed by Kahn in lepromatous leprosy appears to occur in the earliest stages of improvement. Among the 27 patients examined this pattern appeared at least once in each of 13 patients during the course of treatment. [Studies made at Carville in 1947-1951 on 130 cases indicate that, although there is no indication of any distinctive serological pattern in lepromatous leprosy, treatment can alter the type of the universal serological reaction. See *THE JOURNAL* **21** (1953) 27-34.]

—SR. HILARY ROSS

FUKUDA, M. Hemagglutination test of Middlebrook and Dubos in leprosy. *Sci. Rep. Res. Inst. Tohoku Univ. Series C*, **6** (1955) 41-52.

The hemagglutination test of Middlebrook and Dubos, as modified by Scott and Smith, was applied in 149 leprosy cases, and 86% of the lepromatous cases and 53% of the neuromacular cases gave positive reactions with titers ranging from 8 to 2048. The titers in lepromatous cases were higher than those in neuromacular cases, but there was no significant relationship between the titer and the clinical condition of the patients except for those suffering from erythema nodosum leprosum. The carbohydrate fraction of tubercle bacilli has a better sensitizing effect on erythrocytes than the protein fraction. Water-soluble extract or carbohydrate or protein extracts of lepromas, and urine of leprosy or tuberculosis patients, did not serve as sensitizing antigens, nor did a typhoid bacillus antigen (polysaccharide). The fact that erythrocytes sensitized with tuberculin or components of tubercle bacilli are rendered agglutinable by leprosy sera indicates a close similarity in structure of the leprosy and tubercle bacilli. Consequently the test is not useful for diagnosing leprosy, or for determining the form of leprosy or in clinical use.—[From the author's conclusions.]

ROY, A. T. and BANERJEE, G. Some preliminary observations on the haemagglutination test for leprosy. *Ann. Biochem. & Exper. Med. (Calcutta)* **15** (1955) 55-58.

The method followed was Scott and Smith's modification of that of Middlebrook and Dubos, with further modification by the authors. In each case 8 serum dilutions were employed: 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256. With sera from 23 cases of the lepromatous type the percentages of positive reactions relating to each dilution of serum, respectively, were as follows: 100, 91, 91, 82, 73, 34, 17, 4. Sera from 30 neural cases (Nm<sub>1</sub> and Nm<sub>2</sub>) gave the following percentages of positive reactions with respect to the successive serum dilutions: 83, 76, 60, 43, 20, 3, 0, 0. Sera from 33 healthy individuals with no history of contact gave the following results: 30 were negative, 2 gave nonspecific positive reactions, and 1 had a true positive reaction up to the 1:4 dilution. The authors believe that there is indication for study along this line, for arriving at an early diagnosis of leprosy.

—N. MUKERJEE

FLOCH, H. Hémagglutination dans la lèpre. Essai à l'aide d'une "lépromine" ultra-sonnée. [Hemagglutination in leprosy. Trials with an ultrasonic-treated lepro-

min.] Arch. Inst. Pasteur Guyane Française et Inini **17** (1956), Publ. No. 399 (July).

The author concludes regarding the question of agglutination, by leprosy sera, of human red blood cells of the O group sensitized by an ultrasonic-treated lepromin, as had previously been done with the same lepromin but before ultrasonic treatment, that he has not been able to detect any antigen-antibody reaction. There seems to be no justification for the claim that hemagglutination can corroborate in any way whatsoever, any more than any other serological reaction known so far, the so-called South American (now international) classification, the application of which has marked, for the author, a great progress.

—AUTHOR'S ABSTRACT

TAKAYAMA, Y. Studies on the inoculation to different animals of leprosy bacilli. (The 3rd report.) On the susceptibility of cats and nutrias with *M. leprae murium*. La Lepro **25** (1956) No. 3 pp. 147-158 (in Japanese; English abstract p. 147).

After intraperitoneal inoculation of cats and nutrias with the murine leprosy bacillus, the peritoneal fluid was collected for the study of the cells and extracellular acid-fast bacilli. The distribution of bacilli was also determined by autopsy. The intraperitoneal inoculation of cats caused no infection that was evident in 2 months, although in some cases there was multiplication of bacilli in the testes. After 2 months in cats the bacilli were still infectious for white rats. The nutrias also showed no murine leprosy. Multiplication of bacilli in the migrating cells of the peritoneal cavity could not be observed in these animals, nor in white rats. These cells in cats, or nutrias, or white rats were not different in their properties, but the migrating stage of monocytes and neutrophilic leucocytes were different in cats and nutrias and in white rats. —[From abstract.]

HANKS, J. H. Retention and differentiation of carbolfuchsin-stained mycobacteria in diagnostic films. American Rev. Tuberc. & Pulm. Dis. **74** (1956) 597-607.

This study was made to determine how the numbers of acid-fast bacilli in smears are affected by different reagents, and how their loss can be minimized. Unprotected smears, e.g., of bacilli taken directly from cultures, are particularly subject to loss. This can be greatly reduced by (a) making the smears on a dried film of dilute protein, as 5% serum, or by (b) mixing the bacilli with the dilute protein before spreading; and especially by (c) over-coating the latter kind of smear with dilute gelatin and hardening that in formaldehyde vapor (admittedly too laborious for routine use). Counts showing 100 bacilli after method (c), showed 80 after (b) and 60 after (a). [Since smears from leprosy lesions contain more or less tissue juice, they would be of the second category.] The results, however, depend greatly on whether or not the reagents used are disruptive of protective films, and also to some extent on lessening the number of manipulations required. Carbol-fuchsin—itsself a fixative, so that heat-fixation of films is unnecessary—is protective, as are also acidified sulfates, whereas acid alcohol is particularly disruptive. The best differentiator for smears is dilute sulfuric acid (5%), which gives both active hydrogen and protective sulfate ions; it is not destructive to cells and filming proteins, whereas the other mineral acids are. Methylene blue (0.05-0.2%) is added to it for simultaneous counterstaining. This decolorizer is selective in discharging the stain from the tissue components while preserving it in mycobacteria. Mention is made of finding by Badger that, comparing results with the acid-alcohol method and the original Gabbett's solution (25% aqueous sulfuric acid with 2% methylene blue), there was a ratio of 40:100 in favor of the latter in the numbers of leprosy bacilli found in smears from Carville patients. In this process the sequence to which the smears are subjected is: fixative (carbol-fuchsin), water, fixative (sulfuric acid with methylene blue) and water. The obvious advantages are superior retention of bacilli and saving of time and work.

—H. W. W.



HANKS, J. H. Retention and differentiation of mycobacteria in tissue sections. *American Rev. Tuberc. & Pulm. Dis.* **74** (1956) 608-615.

In this extension of the study (see preceding abstract), in which the leprosy tissues used had been fixed in formalin, the first problem was deparaffinization. For that, four methods were compared: a rapid one and two slow ones, in all of which xylene was used [one of them a radical variant of the xylene-oil method of Fite and Wade's turpentine-oil modification of that], and removal of the paraffin by a hot fluid before or while staining. After the last one, which served as a control, myriads of brilliantly-stained bacilli could be demonstrated; the slow methods also gave myriads of bright red bacilli; the rapid, all-xylene method revealed much smaller numbers. Emphasis is placed on the "insecure anchorage" of the bacilli in the sections and consequent loss because of violent disturbances occurring in deparaffinizing and during interactions between alcohol and solvents or water, acid alcohol being particularly injurious. The best results in decolorizing were with 4% sulfuric acid containing 0.2% methylene blue. Acid alcohol tends to destain bacilli with impaired resistance due to influences such as age, or chemotherapy, or reagents. Violent action can be avoided during deparaffinization by use of solvent-oil mixtures, and later by not using alcoholic reagents. [These are the principal and doubtless valid points of this article, which is open to comment on several counts. For one thing it virtually ignores the factor (i.e., *sequential* treatment by harmful reagents) that in the reviewer's long-held opinion is the primary one involved in the difficulty of adequately demonstrating acid-fast bacilli in paraffin sections. See *THE JOURNAL* **20** (1952) 413. However, the article does not purport to prescribe a particular technique for that work.] The author recommends in the diagnosis of mycobacterial disease the use of impression films made directly from the cut surfaces of specimens. They directly and readily reveal the presence of bacilli and their relationships to the host cells, and for many purposes can replace histological examinations. —H. W. W.

NERURKAR, R. V. and KHANOLKAR, V. R. Use of fluorescence microscopy in the diagnosis of leprosy. *Indian J. Med. Res.* **44** (1956) 397-402.

It is difficult to find acid-fast bacilli in smears from tuberculoid patients, and still more difficult to demonstrate them in contacts of leprosy patients or in smears from patients after treatment with sulfones. In 1952 a concentration technique was made available, and the authors have now used fluorescence microscopy on 20 subjects (18 tuberculoid patients and 2 contacts without symptoms). Acid-fasts were found in all, without difficulty. For control, skin specimens were obtained from persons who attended the hospital for minor injuries; none of these showed acid-fast bacilli. The advantages of the method are that (1) the pressure mincer, being hand operated, can be used anywhere even when electricity is not available; (2) crushing of the tissue is thorough and easy; and (3) the fluorescing organisms are more easily seen against a partially dark background than with the Ziehl-Neelsen staining method, and there are therefore fewer chances of missing isolated organisms.—[From a report in *J.A.M.A.* **162** (1956) 999 (foreign letters).]

CARDAMA, J. E. Estudio bacilosópico de la capa descamativa de enfermos lepromatosos. [Bacteriological study of the desquamative layer of the skin of lepromatous patients.] *An. Científicos* **3** (1954) 61.

The method of Khanolkar and Hajalaksmi for the demonstration of *M. leprae* in skin biopsies was used in the search for bacilli in the desquamations of 70 lepromatous patients in different degrees of advancement of the disease. Bacilli were found in 26 cases (37%), but never in large numbers; in only 5 cases were several seen, in 11 only one was found, and in 10 there were only acid-fast granules. However, the search was made of only 1 sq. cm. of the affected skin. The elimination of bacilli seemed to have a relation with the degree of the advancement of the disease, for they were ob-

tained in only about 31% of the  $L_1$  and  $L_2$  cases, but 78% of those of  $L_3$  grade.—[From the author's summary, supplied by G. Basombrio.]

NAGUIB, M., REES, R. F. W. and ROBSON, J. M. Production of leprous lesions by *Mycobacterium lepraemurium* exposed to heat or to an antiseptic. J. Path. & Bact. **71** (1956) 409-420.

Suspensions of *M. leprae murium* from rat lepromas were heated at 60°C. for 15 minutes, 1 hour, and 2 hours, respectively, or were subjected to the action of Merthiolate 1/10,000 for 15 minutes. They were then inoculated intracorneally into mice. Untreated suspensions were employed as controls. Lesions were first noted in the control mice in approximately three weeks; they developed gradually and spread both locally and systemically. In mice inoculated with either heat-treated or merthiolate-treated bacilli, lesions developed after a much longer latent period (up to eight months after inoculation), these then spreading systemically. The administration of isoniazid to animals inoculated with heat-treated bacilli still further delayed the appearance of lesions, and also reduced the number of mice in which they developed.—[In part from abstract in *American Rev. Tuberc. & Pulm. Dis.* **75** (1957) 32, supplied by Sr. Hilary Ross.]

HADLER, W. A. and ZITI, L. M. Estudo da reação da lepromina no rato previamente inoculado com *M. lepraemurium* e com *M. tuberculosis* (BCG). [Study of the lepromin reaction in the rat previously inoculated with *M. leprae murium* and *M. tuberculosis* (BCG).] Rev. brasileira Leprol. **23** (1955) 53-75.

In the normal rat the lepromin reaction is always negative, macroscopically and histologically. In this study adult rats that had been injected intraperitoneally with 5 mgm. of *M. leprae murium* or 5.5 mgm. of *M. tuberculosis* (BCG strain) were later injected intracutaneously with suspensions of *M. leprae* or of the rat leprosy bacillus (about 0.074 or 0.35 mgm. of bacilli) and were observed for 120 days in comparison with normal controls similarly skin-tested. The previous inoculations changed reactivity of the rats' tissue, so that (a) the macroscopic lesion was larger, remained longer, and showed two peaks (initial and final) during its evolution; and (b) the histological changes were intense, showing necrotic areas, abscesses and fibrosis. Nevertheless, the cytology of the lesions was the same in the controls as in the previously inoculated rats, namely, rat-leprosy cells which store the bacilli without lysing them. In both groups, changes in the bacilli appeared slowly and apparently without active participation of the lepra cells. The regressive pictures are the same in appearance and rate of development in both groups, in contrast with the behavior of the guinea-pig. Previous inoculation of BCG or the rat leprosy bacillus induces some degree of hypersensitivity to lepromin in the rat, but without modifying the histological structure of the reaction lesion, which is always that of a negative reaction. This means absence of a positivizing effect.—[From the authors' summary.]