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.

SMITH, D. T. Leprosy and tuberculosis. Cincinnati J. Med. **32** (1951) 163-164.

In a plea for the eradication of tuberculosis by the detection and isolation of all active open cases, the author describes leprosy as it existed in the 13th and 14th centuries. It, and not tuberculosis, was the common chronic disease during that period. He then discusses the type of isolation and care of leprous patients, holding that the program then practiced was effective and accounts for the disappearance of the disease at that time. It was not a sudden loss of virulence of the lepra bacillus or a sudden increase in the resistance of the population. A standard was set in the Middle Ages for the control of leprosy which has not been equaled for tuberculosis, even with our modern advantages, and a plea is made to practice what we have been preaching for the past 50 years. "Every individual with active tuberculosis must be detected, isolated, and treated until he is no longer infectious." —F. A. JOHANSEN

[TANGANYIKA] Annual Report of the Medical Department for the Year Ended 31st December 1949. Leprosy, p. 31. Govt. Printer, Dar es Salaam, 1951.

As a result of extensive surveys in the Southern Highlands Province and in the Lake Province, Ross Innes, the interterritorial leprologist, has estimated a leprosy incidence of 14.5 per 1,000 in the territory [See THE JOURNAL **18** (1950) 432]. Sulphetrone had been introduced for treatment during the year, and was being issued free of charge to all qualified medical practitioners, including mission doctors, who are prepared to provide the requisite personal control of the treatment of leprosy patients.

—H. W. W.

[QUEENSLAND] Annual Report on the Health and Medical Services of the State of Queensland for the Year 1950-51. Government Printer, Brisbane. Hansen's disease (leprosy), pp. 13-14.

(1) Regarding the white population, the number of patients remaining at the Peel Island leprosarium was down to 45, from 54 in the previous year; only 5 had been admitted (1 a readmission and 1 from South Australia), while 1 had died and 13 had been discharged thanks to the efficacy of the sulfones. During the past five years the majority of patients admitted have been relapses from previous treatment with chaulmoogra; it is still too early to say anything about relapses after sulfones. Doctors now graduating are all instructed in the diagnosis of leprosy, which has improved the chances of early diagnosis. Land has been acquired for the construction of a much improved leprosarium at Burpengary, 26 miles north of Brisbane, Peel Island to be abandoned. The matters of publicity for the education of the public, and of segregation of

bacteriologically positive cases are discussed, it being pointed out that recent regulations require a sufferer from active tuberculosis to be hospitalized if he is "flagrantly dangerous to other people—and in tuberculosis the method of spread of the disease is known." 2. Regarding the cases among the aboriginals, isolated in the Fantom Island leprosarium in Northern Queensland, there were 69 cases, down from 78; only 2 had been admitted, while 8 had been discharged and 3 had died. The disease in these people seems to run a more acute course than in white persons, but response to the sulfone drugs is even more gratifying. —H. W. W.

MALARET, P. S. Leprosy in Puerto Rico. Bol. Asoc. Mêd. Puerto Rico **43** (1951) 15-64.

The author presents a picture of leprosy as it occurs in Puerto Rico, based on a study of 195 cases which have been admitted to the Leper Colony in the last 24 years. This is an excellent epidemiological and statistical report which should be read by those interested. The following topics are dealt with: Historical outline; incidence; geographical distribution; age, sex and class; source of infection; marital status; age of onset and symptoms; type classification; clinical signs and symptoms; discharges; deaths; treatment. —F. A. JOHANSEN

ROMERO L., A. Epidemiología. I. Contagio familiar y extrafamiliar en lepra. II. Estudio de los convivientes que se encontraron enfermos de lepra en el periodo que va de 1946 a Agosto de 1950. [Epidemiology. I. Familial and extrafamilial infection in leprosy. II. Study of contacts who contracted leprosy during the period 1946 to August 1950.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 271-277.

A study of 272 patients of the Sanatorio de las Mercedes shows that in 179 cases (65%), the contagion was of the family type, the others having occurred outside the family. More cases occur in families of leprous persons, and the forms of the disease are more severe than in patients acquiring the disease outside their families. These facts point to the need of prolonged contact with the contagious patient for infection, and also to a family hereditary predisposition. The incidence among the patients' relatives was found to be 6%, a figure which may be increased with future control examinations. Only the bacteriologically positive lepromatous and undifferentiated cases were responsible for contagion. Contagion among relatives occurred in 70% when they lived in the same house and in 30% when they lived in different houses.—[From the author's summary.]

ROMERO L., A. Mortalidad entre los enfermos de lepra controlados. [Death rate in controled leprosy patients.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 278-280.

From 1946 to 1949, 19 leprosy patients died. Only one died of leprosy; 2 died of leprosy complications (nephritis and cirrhosis of the liver) and the rest from intercurrent diseases (4 of tuberculosis; 4 of cardiac insufficiency, etc.).—[From the author's summary.]

MELSOM, R. Tre nye tilfelle av lepra. [Three new cases of leprosy.] Tidsskr. norske laegefor. **72** (1952) 65-67.

Since 1930 there have been altogether 12 new cases of leprosy in Norway. Three of the patients are seamen who were infected while living in endemic areas in the tropics; the other nine are the remnants of the earlier

endemic in Norway, which has now died out completely. There are now altogether 11 leprous persons in the country, and the disease is just as rare there now as in the other Scandinavian countries. There are fewer cases per unit of population than in the United States, for example. Yet in less than a year three new cases have been discovered. The patients are siblings, two brothers and a sister, belonging to a small community just outside of Bergen. This family has suffered badly from leprosy for generations, and both the patients' mother and two maternal uncles were affected. The mother was admitted to the leprosy hospital in Bergen in 1931 and died in 1933. Of her ten offsprings, three died quite young; her husband and four of her surviving children are healthy; but three have leprosy. The course of the disease in these three cases has been remarkably uniform. The youngest son noticed in 1940 that his hands had become thin. The sister has had thin hands as long as she can remember. All three have for years been liable to develop sores from burns on the forearms, but these sores have not troubled them much. During 1950-1951, all three patients developed a maculo-nodular rash on the trunk and limbs. Biopsy of the nodules showed typical leproma in all of them. In all three, the disease seems to have made its appearance by involvement of the peripheral nerves after intervals of different lengths since the last possible exposure to infection. The latent period must have been long. In the course of one year all three developed an active, nodular eruption.

—AUTHOR'S ABSTRACT

MADSEN, A. A case of leprosy discovered in Oslo. Acta Derm. Vener. **31** (1951) 449.

A case report before the Norwegian Dermatological Society of a man 79 years of age who was born in Sweden but had moved to Norway in 1894 and had lived in Oslo since 1900. No history of leprosy in the patient's family could be elicited, and his wife and two adult sons living at home presented no evidence of it. Neural symptoms began to develop in 1930, and he was hospitalized several times and treated for infected and gangrenous plantar ulcers. Skin nodules developed in 1947. Acid-fast bacilli were numerous. To the author's knowledge no case of leprosy has occurred among the permanent inhabitants of Oslo in the past 35 years.

—H. W. W.

HASSELMAN, C. M. Über den Einfluss von Ernährungs- und Klimafaktoren auf die Epidemiologie der Lepra. [On the influence of nutritional and climatic factors on the epidemiology of leprosy.] Ztschr. f. Haut- u. Geschlechtskr. **6** (1949) 197-201.

Apart from the increased consumption of dried, salted and semi-fermented fish (the fish theory), it is not possible to determine an influence by any particular form of nutrition on the epidemiology of leprosy. In a population whose main diet is milk and milk products, as also raw nutrients, not restricted by any taboos, the incidence of leprosy is lower. The improvement in nutrition and living conditions is held to be responsible for the reduction in leprosy in Northern Europe. It is important that the individual nutrient components should be in correct proportion to each other. The objective of optimum nourishment should be a mixed diet, of the most expedient composition, in order to promote the development of the highest general powers of resistance.

—ERNST KEIL

ROMERO L., A. Contribución al estudio de la clasificación de los subtipos de lepra. [Contribution to the study of the classification of the subtypes of leprosy.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 234-243.

From a clinical study of 211 cases of leprosy (164 in the Sanatorio de las Mercedes and 47 dispensary cases) it is concluded that from the practical point of view the following subtypes of leprosy should be considered: (*a*) Lepromatous type: (1) diffuse, (2) infiltrative, (3) nodular, and (4) incipient. (*b*) Tuberculoid type: (1) reactional, (2) cutaneous, and (3) neurotrophic. (*c*) Undifferentiated type: (1) maculo-anesthetic (bacteriologically positive or bacteriologically negative), and (2) simple anesthetic (positive or negative.)—[From the author's summary.]

ROMERO L., A. Síntomas de principio de la lepra en enfermos menores de 15 años. [Early symptoms of leprosy in patients under 15 years of age.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 253-255.

The early symptoms of leprosy observed in patients under 15 years were: (*a*) Lepromatous type: (1) loss of eyebrows and eyelashes; (2) obstructive rhinitis; (3) purpuro-necrotic erythema. Nodules are very rare as an early sign; sepia-colored infiltrated plaques are also infrequent. (*b*) Tuberculoid type: (1) erythematous plaques with well-defined borders; (2) precocious trophic lesions of the hands. (*c*) Undifferentiated type: (1) achromic and anesthetic spots located, in order of frequency, on the gluteal region, lumbar region, thighs and back.—[From the author's summary.]

ROMERO L., A. Dermatosis entre los enfermos de lepra en tratamiento. [Dermatosis in patients under treatment.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 266-268.

In more than 200 leprosy patients observed in the Sanatorio de las Mercedes from 1949 to 1950 we found only 16 patients presenting dermatosis due to allergic manifestations in the course of treatment. Three cases of the generalized exudative eczematous type were due to promin. Thirteen cases, of the exudative eczematous, trichophytoid, and dry eczematous types, evolving toward lichenification, were due to injections of a crude liver extract.—[From the author's summary.]

ROMERO L., A. Anemia leprosa. [The anemia of leprosy.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 250-252.

Three cases of leprosy are presented which showed marked anemia. For two months they were given intensive antianemic treatment, without results. Later they were given diasone, and frank improvements of the anemia was noticed. This indicates that although sulfones are anemia-producing drugs, they can and should be used after investigating the cause of the anemia.—[From the author's summary.]

ROMERO L., A., CASTRO JENKINS, A. and ALVARADO, R. Complicaciones renales en los enfermos de lepra. [Renal complications in leprosy patients.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 244-249.

Renal lesions were observed clinically in 5.6% of the 214 leprosy patients studied in Costa Rica. It is probable that studies at autopsy and of the renal function in all leprosy cases would reveal a much higher in-

cidence of this class of lesions. Clinical study indicates that the renal lesions present, with special reference to the 9 cases of the diffuse lepromatous form, were of the degenerative type. The observed lesions were not modified by sulfone treatment.—[From the author's conclusions and summary.]

OSHIMA, S. On the refrigerated skin transplantation performed on leprous patients. La Lepro **20** (1951) 121-124 (in Japanese); English abstract, p. 121.

This paper presents the effects of 100 cases of refrigerated skin transplantation performed on 72 patients. This procedure produced striking results on the neuralgias and paresthesias due to leprosy, and was somewhat effective on asthma, but not at all on erythema nodosum leprosum, malum perforans pedis, or ulcer. There was no evident relationship between the effectiveness of the operation and the size of the transplanted skin, the time of refrigeration, the existence of hypoesthesia, sex, disease type, or velocity of blood sedimentation.—[From the abstract.]

FISHER, A. A. A case for diagnosis: sarcoid of the lip? A. M. A. Arch. Derm. & Syph. **63** (1951) 539.

This is a brief report of a case presented for diagnosis before the Bronx Dermatological Society, New York, which has certain points of interest, although no conclusion was reached. The patient was a woman aged 54, born in Spain, who had lived in the United States for 30 years. The lesion, which had appeared on the upper lip some two months previously, was a light brown waxy nodule extending into the left nostril. A first biopsy specimen had been reported as xanthofibroma, but that had been ruled out; a second one was diagnosed as sarcoid. The slides showed epithelioid-cell grouping with small round cells in the characteristic distribution observed in sarcoid, but the "atypical appearance and high degree of vacuolation is little known." Sections stained for acid-fast bacilli were negative, as were nasal smears for lepra bacilli. The tuberculin reaction was positive (normergic reactivity). LEIDER had made the Kveim and lepromin tests, finding the former negative and the latter positive. He remarked that the histopathologists made the diagnosis of sarcoid but with reservations, and that the clinicians leaned toward sarcoid but considered other possibilities. Sarcoid may be correct, he said, but from the skin tests the condition must be tuberculoid leprosy. SACHS thought that the presence of giant cells favored sarcoid rather than leprosy. NEXMAND (of Copenhagen) regarded the histological picture as typical of sarcoid, but was not convinced that the condition was of that nature. —H. W. W.

FLOCH, H. Le 1087 MM, sulfone monosubstituée, en thérapeutique antilépreuse. [The monosubstituted sulfone 1087 MM in antileprosy therapy.] Arch. Inst. Pasteur Guyane et Terr. Inini, Publ. No. 235, August 1951, 4 pp.

In 10 patients treated with aminohydroxyethylaminodiphenyl sulfone the results were entirely analogous to those obtained with other sulfones, particularly with 1500F, another monosubstituted sulfone, which is a very effective and interesting sulfone. The hydroxyethyl derivative is perhaps the better tolerated, or at least more regularly supported, than is the succinyl drivative, perhaps because of the fact that the former is not

transformed into DDS in the organism. It provokes, however, like the other sulfones, numerous lepra reactions in the first months of treatment. The monosubstituted sulfones, 1087 MM and 1500F, which are active in leprosy, are considered together with DDS to present particularly interesting properties.—[From the authors' summary.]

FLOCH, H. and HORTH, R. L'association sulfones-thiosemicarbazone dans la thérapeutique anti-lépreuse. [The sulfone-thiosemicarbazone combination in antileprosy therapy.] Arch. Inst. Pasteur Guyane et Terr. Inini, Publ. No. 232, June 1951, 6 pp.

It seems indisputable that thiosemicarbazone is active in leprosy. Its effect is evidently much superior to that of chaulmoogra and its derivatives, and quite analogous to those of the sulfones with respect to the cutaneous manifestations of the lepromatous form, at least in the first months of treatment, but inferior to DDS and 1500F especially with respect to the bacteriological condition. The lesions of the mucous membranes are less susceptible to the action of TB-1 than to the sulfones; the neural lesions are often resistant to both. TB-1 does, however, merit inclusion in antileprosy therapy. Its principal value seems to be in combination with the sulfones, when the latter are not well tolerated, in patients in whom the lepra-reaction threshold is low, and in those in whom the usual progress toward clinical and bacteriological clearing under the sulfones has slowed down.—[From authors' summary.]

FLOCH, H. and LECUILLER, A. Peut-on considérer une posologie-retard de la diamino-diphényl-sulfone administrée par la voie buccale dans le traitement de la lèpre? [Could a retarded schedule of DDS by oral route be taken into consideration in the treatment of leprosy?] Inst. Pasteur Guyane et Inini, Publ. No. 237, August, 1951.

The mother substance, DDS, possesses numerous advantages over the compound sulfones. The methods of choice for its administration are the usual one of 3 doses per day, or deposit injections of 1.2 gm. in 10 cc. suspension of 0.02% agar in saline. When these cannot be used it is still possible to employ this drug by the administration of massive weekly doses of 800 mgm. by mouth. Doses of 400 mgm. or even 600 mgm. weekly are insufficient, judging from the blood levels encountered, but 600 mgm. may be administered 2 times per week. Tolerance is, on the whole, satisfactory, at least as regards immediate tolerance. This increases rapidly, and it is greatly improved by the concomittant administration of vitamin PP. It is more difficult to say what the tolerance of these patients—or, more exactly, of their liver—would be after many months of treatment; the widespread use of such a dosage in the terrain which one may, *a priori*, consider as the terrain of choice, and where it might be of most service, Black Africa would answer this question. It should be said that our patients had for the most part already been under DDS therapy in the usual dosage. It is evident that the beginning of treatment by massive doses should be gradual and if possible accompanied by the administration of protoxalate of iron to ensure avoidance of the anemia of the first months of treatment. It would be well, for example, to start with a weekly dose of 50 mgm., then increase to 100, 200, 400 and up to 600 at the end of 6 weeks. It would always be possible, if need be, to alternate series of intramuscular injections of deposit DDS and series of massive weekly doses by

mouth, which is highly practicable in the less developed regions where strict medical surveillance is difficult. —AUTHOR'S ABSTRACT

FLOCH, H. and LECUILLER, A. Administration massive hebdomadaire de la sulfone-mère par voie buccale dans le traitement de la lèpre. [Weekly oral massive doses of DDS in the treatment of leprosy.] Therapie (Rev. Thérap. et Pharmacodyn.) **6** (1951) 342-348.

[This article is evidently identical with the one dealt with in the preceding abstract.]

FLOCH, H. and LECUILLER, A. L'administration-retard de la succinyl-sulfone (1500F) par la voie intramusculaire. [Repository (spaced) administration of succinyl-sulfone (1500F) by the intramuscular route.] Therapie (Rev. Thérap. et Pharmacodyn.) **6** (1951) 349-353.

The authors have used succinyldiaminodiphenyl sulfone (1500F) by the intramuscular, intravenous and oral routes, with a view to spacing the intramuscular injections more widely and maintain a sufficient blood concentration. They have used the following repository solution: the diethanolamine salt of 4-succinylamino-4'-aminodiphenyl sulfone, 5 gm. (diethanolamine, 1.16 gm. and the sulfone 3.84 gm.) polyvinyl-pyrolidone, 2.5 gm., and distilled water to make 20 cc. The findings with respect to the blood levels and urinary elimination show that this preparation can be injected twice a week in 10 cc. doses. Doses of 20 cc. may also be injected every 5 days, but besides the real inconvenience in that the injections are not given on a fixed day, this dose is not always well tolerated locally. The use of vitamin PP may also, in this case, prevent certain reactions of intolerance. —AUTHOR'S ABSTRACT

FLOCH, H. and LECUILLER, A. Mode d'action des sulfones dans la lèpre (V). Comment agit l'aminohydroxyéthylaminodiphényl sulfone (sulfone monosubstituée) administrée par la voie buccale. [Mode of action of sulfones in leprosy. How aminohydroxyethylaminodiphenyl sulfone acts when administered by mouth?] Arch. Inst. Pasteur Guyane et Terr. Inini, Publ. No. 233, July 1951, 4 pp.

This drug (1087 MM) introduced by M. I. Smith as hydroxyethyl, is recovered unchanged in the blood of patients treated orally. It is eliminated in the urine either unmodified, or as a transformation product (perhaps due to oxidation of the substituent ethyl), or as a mixture of the two, but not in the form of DDS. The proportion of 1087 eliminated unchanged seems to be in direct relation to the quantity of the product to be excreted; in low concentrations (8 to 9 mgm. per cent of sulfone expressed as 1087) only the hydroxyethyl was found; in high concentrations (100 mgm. per cent) only a derivative of the 1087; in medium concentrations the H/SH values are intermediate, and the urine contains 1087 and derivative in variable proportions. It seems beyond doubt that, in the present case, the modifications of the sulfone molecule are due to the action of the kidneys. This seems noteworthy because, with the other sulfones (promin, DDS, 1500F), it is the liver which plays the most important role in the transformations which these products undergo in the organism.—[From authors' summary.]

BOLGERT, M., MONTEL, L. R. and MOLINEDO, R. Lèpre et acide para-amino-salicylique. [Leprosy and PAS.] Bull. Soc. Path. exot. **44** (1951) 521-522.

The authors have recently treated 3 patients with PAS. Because the improvement obtained was not marked, they conclude that PAS has only a minor value in the treatment of leprosy, the sulfones remaining the most effective. —R. CHAUSSINAND

MONTESTRUC, E. Lèpre ler Memoire de l'Institut Pasteur de la Martinique, 1950, pp. 33-43; *also*, Arch. Inst. Pasteur Martinique **4** (1951) No. 1-2.

In 1949-1950, 243 patients (150 lepromatous, 22 tuberculoid and 71 indeterminate) were treated by cimedone and disulone, with results entirely comparable with those obtained previously with promin and diasone. Confirming the views of certain other workers, the author holds that the mother sulfone gives results comparable with those obtained with its derivatives, is practically nontoxic in the effective doses employed, requires much smaller doses than the other sulfones, offers the possibility of the intramuscular route (2 or 3 times per week), and is relatively low in cost. These features, he holds, are of great importance in the selection of the drug to be used in the sulfone treatment of leprosy. —H. FLOCH

MONTESTRUC, E. and BLACHE, R. Résultats obtenus dans le traitement de la lèpre par les sulfones françaises: cimédone (sulphetrone) et disulone (sulfonemère). [Results obtained in the treatment of leprosy by French sulfones: cimédone (sulphetrone) and disulone (DDS).] Rev. coloniale Méd. et Chir. **23** (1951) 50-52.

[From an abstract supplied by R. Chaussinand, it would seem that this article is the same as the one dealt with in the preceding abstract. It appears that 218 of the cases had been treated since 1947 with the American-made sulfones, the other 25 being previously untreated patients. Particular mention is made of one patient whose lesions had for many years resisted treatment with chaulmoogra oil and diasone, but who had shown amelioration from the third series of DDS. It is also stated that lepra reactions occurred in 25% of the cases under diasone, 20% under cimedone, and 45% under DDS, and that the authors believe that these reactions are indications of the activity of the sulfones against the Hansen bacillus.]

MUIR, E. Treatment of leprosy with diaminodiphenyl sulphone (DDS). Trans. Roy. Soc. Trop. Med. & Hyg. **46** (1952) 113-122.

After remarking on the profound change in the prognosis of leprosy since the introduction of sulfone therapy, this article gives the results the author has had with DDS in Purulia since 1949 [see THE JOURNAL **18** (1950) 299-308]. As complications are likely to occur most frequently within the first three months, induction of the drug was slow, commencing with the minimal effective dose of 100 mgm. twice weekly and gradually increasing to a maximum of 400 mgm. twice weekly. All except a few advanced and sensitive patients could tolerate this dosage indefinitely. Sulfone-produced reactions, even in the bad cases, usually left the patients better than before. Vitamin B_{12} was found useful in making intolerant cases tolerant to DDS, and he had had good reports of ACTH. Finally, the control of leprosy in a community by means of DDS is discussed.

—G. O. TEICHMANN

COCHRANE, R. G. The action of sulphones in leprosy, with particular reference to histopathology. Trans. Roy. Soc. Trop. Med. & Hyg. **46** (1952) 122-126.

Fragmentation of the acid-fast rods of *M. leprae* has been noted in both untreated cases and cases treated with hydnocarpus oil. Under the sulfones, however, this change is noticed to a marked degree sometimes within 3 weeks on a fairly small dose. In some sensitive patients this is accompanied by a period of reaction which is different from the erythema nodosum leprosum form. Accompanied by high fever, numerous subcutaneous nodules appear and frequently seem to coalesce, and the skin, particularly of the forearms and thighs, has a leathery feel. The nodules in the dermis become fixed and suppurate, and in the small bead of pus which is extruded there are enormous numbers of bacilli, many in globus formation. This phenomenon is regarded as an unfavorable one; unlike erythema nodosum, it is a reactivation of the disease, and sulfone therapy should be suspended or continued very carefully. In some way sulfones interfere with the metabolism of *M. leprae* and then fragmented and granular forms are noted. Bacilli seem to disappear from inside the large masses leaving clear spaces with granular forms clinging around the periphery of the globus or macrophage cell. Gradually the granulomatous infiltration disappears and the histopathology returns to the preleprom-atous or uncharacteristic [*sic*] stage. Bacillary granules frequently remain in the nerves, which may act as reservoirs from which the disease may recrudesce. As long as maintenance doses of sulfones are continued there has as yet been no evidence of relapse in patients who have become bacteriologically negative. Particular care has to be taken in treating reactional tuberculoid and uncharacteristic cases with sulfones to prevent severe reactions. —G. O. TEICHMANN

LOWE, J. Studies in sulphone therapy. Lep. Rev. **23** (1952) 4-29.

The writer attempts to answer the question, Do the complex disubstituted sulfones act by liberation of DDS in the body, or have they additional advantages of their own? Until recently it has been difficult to estimate how much of the complex compounds is degraded into DDS in the body, but it has been found that DDS is readily soluble in organic solvents such as benzene and ethyl acetate but practically insoluble in water, whereas the reverse holds for the disubstituted sulfones. This fact has been used for estimating the DDS content in the blood and urine. Sulphetrone is unstable in solution, especially in high dilution, at high temperatures, and if acid. Diasone is the most stable, and promin the least stable of these three disubstituted sulfones *in vitro*. They undergo more degradation into DDS when given orally than when administered parenterally. Their tolerated doses vary inversely with the degree to which DDS is produced in the body. The author holds that, when given by mouth, they produce enough DDS to explain their therapeutic action without postulating a separate action of the undegraded substances. When given parenterally, very little free DDS is found in the blood, and it is suggested as possible that there may be produced monosubstituted sulfones which are therapeutically active. In therapy with DDS, 200 mgm. daily is the maximum dose tolerated by most patients, although many have taken 300 mgm. daily for 2 years; 500 mgm. twice weekly is well tolerated; as little as 30 mgm. daily may induce slow clinical improve-

ment. The optimum dosage is one rising slowly to 400 mgm. twice a week. DDS can be given to pregnant women and nursing mothers. Patients receiving sulfones rarely develop secondary infections due to gram-positive organisms. DDS also appears to delay streptomycin resistance in cases of tuberculosis. —G. O. TEICHMANN

LOWE, J. Para-acetamidobenzaldehyde thiosemicarbazone in the treatment of leprosy. Lancet **262** (1952) 436-439.

Trial of TB-1 was started in September 1951, and about 100 patients were being treated with it. This report deals with 71 patients who had received it for 5 to 13 months. There were three groups: (*a*) lepromatous cases which had had no previous treatment, (*b*) tuberculoid cases, and (*c*) lepromatous cases which had not been able to stand DDS because of complications. Except in one case the drug was well tolerated, and toxic effects were much less than have been reported in tuberculosis. The exceptional case was that of a young man who developed agranulocytosis; he recovered under penicillin and was transferred to DDS and did well. The dosage used was one 50 mgm. tablet daily for 3-4 days, 2 tablets for 3-4 days and thereafter 3 tablets daily. Comparing TB-1 with DDS, the results were very similar. With TB-1 allergic symptoms such as drug fever and dermatitis were rarer and milder. Complications, including "reaction," eye inflammation and neuritis, were also fewer and milder. The clinical and bacteriological response was satisfactory. TB-1 is, however, much more expensive and less simple to give than DDS.

—G. O. TEICHMANN

SCHUJMAN, S. Nuestro primeros resultados con el empleo del derivado adhehídico de la Tiosemicarbazona (T.B.1) en el tratamiento de la lepra. [Our first results with the aldehyde derivative of thiosemicarbazone (TB-1) in the treatment of leprosy.] Arch. argentina Dermat. **2** (1952) 68-69.

This is a report of one year's experience with 14 patients, 2 tuberculoid type and 12 lepromatous, which shows the efficacy of TB-1 in both clinical forms because of the clinical and bacteriological regression observed. The excellent tolerance of this drug makes it an additional weapon in the therapeutic arsenal of leprosy. —G. BASOMBRIO

LOWE, J. A.C.T.H. and cortisone in leprosy. British Med. J. **1** (1952) 601 (correspondence).

Trials of ACTH and cortisone in acute and subacute complications of leprosy have been made in 38 such cases during a period of 4 months. In all cases the immediate response to treatment had been excellent. Severe "reactions," acute neuritis, and severe eye inflammation were relieved within a day or two. The cessation of treatment had, however, far too often been followed by a recurrence of the symptoms and also by development of other complications. Further treatment had given only temporary relief, and the complications had become more severe and frequent, definitely indicating an aggravation of the leprosy. All attempts to prevent this deterioration by modification of dosage had failed, and the conclusion is that in general the use of these hormones is contraindicated in leprosy. A short three-day course may be of value in severe sulfone sensitization involving danger to life, or in severe eye inflammation threatening blindness. —G. O. TEICHMANN

WALTER, P. Über die Behandlung der leprösen Schleimhauterkrankung mit TB 1/698. [On the treatment of leprous mucosa infection with TB-1.] Ztschr. f. Hals-, Nasen- u. Ohrenheilkd. **2** (1950) 218-219.

Laryngological findings in the case of lepromatous leprosy were described by Grosch and Kaliebe [see THE JOURNAL **19** (1951) 506]. Pain on swallowing (dysphagia), sensation of dryness in the throat, coughing and hoarseness were pronounced. The purulent secretion from the nose and throat was loaded with Hansen bacilli. The nasal septum was perforated; the mucous membrane of the palate was inflamed and showed cicatrization; the uvula was swollen and inflamed; the epiglottis showed nodules and ulcerations; the vocal cords were reddened and swollen; and there was tracheitis. After two weeks of treatment with TB-1 there was considerable retrogression of these lesions, and some had healed completely. The secretion from the nose was now only slight, and repeated smears revealed no more bacilli. The rapid and thorough effect in this case was surprising, and the drug is considered the sovereign remedy for the treatment of leprous infections of the mucous membranes.

—ERNST KEIL

TANIMURA, T., SHIMIZU, Y., NISHIMURA, S. and KONO, M. Treatment results of tibione against leprosy. La Lepro **20** (1951) 203-206 (in Japanese); English abstract, p. 203.

Tb-1, beginning with 30-50 mgm. daily and increasing to 200-300 mgm., total dosage 5-50 gm., was administered to 12 leprosy patients, including 4 with lepra nodosa, 6 with lepra maculosa, and 2 with lepra nervosa. Toxic symptoms seen were slight anorexia and liver damage, not requiring discontinuance of the drug. Marked improvement occurred in 2 cases, moderate in 3, and slight in 6; in 3 cases there was no distinct effect. Resorption of the leprous lesions and transformation of the bacilli were observed on histopathological examination. Larger doses of this drug can be recommended in leprosy cases than in tuberculosis. If these beneficial effects are confirmed, this drug should be regarded as one as promising as are the sulfones for the treatment of leprosy.—[From the abstract.]

KEIL, E. and MUDROW-REICHENOW, L. Die chemotherapie der Lepra. [The chemotherapy of leprosy.] Aerztl. Praxis **4** (1952) No. 8 (Feb. 23).

This is a summary survey of the development of the chemotherapy of leprosy. Mention is made of chaulmoogra oil; iodine and gold preparations; sulfone compounds, particularly DDS; thiosemicarbazones, particularly Conteben; also PAS, penicillin and streptomycin. The only two groups which are today generally applied in practice are the sulfones and the thiosemicarbazones. Although the former are cheap and effective, they are so toxic that they can only be applied under medical supervision. The thiosemicarbazone compounds, particularly Conteben, have a greater efficacy and are so well tolerated that they can also be used in ambulant therapy.

—AUTHORS' ABSTRACT

TANIOKU, K. Co-studies on the treatment of leprosy with promin and other sulfones. Part (a). The pharmacologic studies. La Lepro **20** (1951) 174-184 (in Japanese); English abstract, p. 173.

As regards the pharmacologic actions of promin and related preparations, the author's experimentation has led to the following conclusions:

(1) Antibacterial effects of promin, promizole, diasone and methyl-promizole: *In vitro*, the bacteriostatic action of promin upon tubercle bacilli (Human, H 37RV) was a little inferior to that of the others, which were much alike. No difference was seen between promin and diasone in their bactericidal action. Promin seemed to be more effective than the others in rat leprosy. (2) Absorption and excretion: When given intravenously or by mouth in man, all of these preparations are absorbed and excreted in urine rapidly, although the excretion rate of diasone is somewhat the lowest. Promizole is a little more acetylated in the human body than the others. (3) Concentrations in organ tissues: The concentrations of all in nerve tissues are lower than in skin tissues. Promin accumulates somewhat more slowly in organic tissues than the others, and to a lesser degree. (4) Influences on blood: All caused anemia, promin somewhat less than the others. The resistance of erythrocytes decreases after continuous treatment for 1 to 2 weeks. (5) Influences on the circulatory organs: No change was seen in blood pressure. The capillary permeability in the skin has a tendency to increase although microscopic findings of the skin capillaries and the skin temperature showed no change. (6) Influences on the reticuloendothelial system: In animals, promin activates this system slightly; no definite results were obtained with the others. (7) Influences on metabolism: No change was seen in the basal metabolism, while protein, carbohydrate, calcium and cholesterin metabolism are all disturbed temporarily. (8) Influences on vitamin metabolism: Decrease of blood level of vitamin B_1 was observed after administration of all of these drugs. (9) Influences on the liver: No remarkable changes in the several tests applied. (10) Influences on skin reactions: Q.R.Z. and Mitsuda's reaction are not influenced. (11) Influences on acid-base balance: The CO_2 combining power of the blood sometimes decreases and it may lead to acidosis. (12) Influences on phagocytosis of leucocytes and electric mobility of erythrocytes: A temporary increase of the phagocytic function was seen, with no remarkable change with respect to the latter. (13) The results of slide-cell-cultures show that the antibacterial effect of serum on tubercle bacilli is not proportional to the blood level of each drug. (14) The serum of patients treated with promin inhibits the oxygen consumption of the liver of the rat. (15) Diamino-diphenylsulfone and its derivatives seemed to be generally antagonistic to PABA. (16) Diamino-diphenylsulfone inhibits the oxygen consumption of emulsions of leproma.—[From the abstract.]

MITSUDA, K., YOKOTA, T. and SAIKAWA, K. Co-studies on the treatment of leprosy with promin and other sulfones. Part (b). The histopathological studies. La Lepro **20** (1951) 185-191 (in Japanese); English abstract, p. 185.

The following were the findings in the histopathological study of the skin lesions of 54 lepromatous cases, 3 of lepra maculosa, and 1 of lepra nervosa, which had been treated with promin and other sulfone drugs in the period of four years since 1947: (1) Promin, promizole and diasone prevent the bacilli from multiplying, causing degeneration and reduction of their vital force. (2) Simultaneously with the prevention of the multiplication of the bacilli, there is proliferation of the connective tissues and cicatrization of the lesions. (3) Lepra cells which, before treatment had been round, oval or polymorphous with projections, became flatter and

spindle-formed and were reduced in number. Their position against the epidermis changed from perpendicular to parallel, corresponding to the absorption of the lesion, and lipoid bodies and vacuolar degeneration were seen. (4) The leprous infiltrations extending through the cutis became atrophic and separated from each other, around vessels, sweat glands and nerves. The bacilli, however, persisted in nerves for a long time. (5) These changes are not specific to sulfone-treated cases, but are seen in those showing natural healing or improving under chaulmoogra oil, and there may be no essential difference between them.—[From the abstract.]

HAYASHI, Y. and BABA, S. Co-works on treatment of leprosy with sulfone drugs. Part (c). The clinical studies. La Lepro **20** (1951) 193-200 (in Japanese); English abstract, p. 192.

Promin was used in the treatment of 714 leprosy patients—552 of lepra tuberosa, 112 of lepra nervosa, and 50 of lepra maculosa—for from 4 months to 4 years, with the following results: (1) Resorption of nodules or infiltrations; 396 (72%) were improved, 149 (27%) were unchanged, and 7 (1.3%) became worse. (2) Leprous ulcers: 264 (69%) of 382 were healed or improved, 102 (27%) were unchanged, and 16 (4.2%) were aggravated. (3) Leprous macula: 42 (84%) of 50 were improved, 7 (14%) were unchanged, and 1 (2%) were aggravated. (4) Neuralgia in lepra tuberosa: 70 (15%) of 456 were improved, 266 (58%) were unchanged, and 120 (26%) were aggravated. (5) Neuralgia in lepra nervomaculosa: 11 (9.8%) of 112 were improved, 75 (67%) were unchanged, and 26 (23%) aggravated. (6) Anesthesia in lepra tuberosa: 49 (9.2%) of 433 were improved, 302 (57%) were unchanged, and 182 (34%) were worse. (7) Anesthesia in lepra nervosa: 6 (5.4%) of 112 were improved, 80 (71%) were unchanged, and 26 (23.2%) were more marked. (8) Anesthesia in lepra maculosa: 4 (11%) of 36 were improved, 19 (53%) were unchanged, and 13 (36%) were aggravated. (9) Motor paralysis in lepra tuberosa: 54 (10%) of 525 were improved, 232 (44%) were unchanged, and 239 (45%) were aggravated. (10) Motor paralysis in lepra nervosa: 10 (9%) of 112 were improved, 66 (59%) were unchanged, and 39 (32%) were aggravated. (11) Erythema nodosum appeared in 403 cases (73%) of the lepra tuberosa cases. (12) Bacilli disappeared from the nasal smears of 79 (76%) after periods varying from 6 months to 3 years. (13) Bacilli are not easily extinguished from the tissues. (14) The toxic manifestations were general weakness, anorexia, anemia and urticaria, of light degree. (15) In rare cases the Mitsuda reaction changed to positive: in one it became moderately positive, and in three weakly positive. (16) The results of promizole treatment on 74 cases were favorable, and its toxic manifestations were less than those of promin.—[From abstract.]

COTTINI, G. B. and MUSUMECI, V. Ulteriori osservazioni sul valore dei sulfoni e della streptomicina nella terapia del morbo di Hansen; contributo personale. [New observations on the value of the sulfones and of streptomycin in the therapy of leprosy.] Minerva Méd. (Torino) **42** (1951) Suppl. Jan. pp. 174-177.

Fifteen patients were treated with streptomycin in doses of 0.5 to 1.0 gm. per day for from 3 to 6 months, with 1 to 2 weeks of rest every 30 days, and with sulfones by mouth in doses of 3.0 gm. per day and by the

intravenous route in doses of 18.0 gm. per day. Italian sulfones were used, but neither the names nor their chemical compositions are mentioned. It is concluded that the sulfones constitute the basic treatment of leprosy, streptomycin having no value except in the course of the septicemic febrile outbreaks or in the evolutive forms. It may also be used as the *traitement d'attaque*, whereas cure is pursued with the sulfones.

—R. CHAUSSINAND

ROMERO L., A. Uso de la vitamina "E" en las atrofías musculares que presentan los enfermos de lepra. [Use of vitamin E for muscular atrophies in leprosy patients.] Rev. méd. Costa Rica **17** (1950) Leprosy issue, pp. 260-263.

The author has treated 29 cases of muscular atrophy of the hands of leprosy patients with vitamin E, with clinical improvement in 18 cases. Atrophies in cases of diffuse lepromatous are the most difficult to modify, which is the opposite of what was observed in the undifferentiated form. It is supposed that atrophies of the diffuse lepromatous form are more resistant because many of these cases are the resultant of an undifferentiated form of prolonged evolution. The duration of the disease has a great influence on the reversibility of the atrophy, improvement being the greater as the disease is the more recent.—[From the author's summary.]

ROMERO L., A. Tratamiento de la iridociclitis en enfermos de lepra. [Treatment of iridocyclitis in leprosy patients.] Rev. méd. Costa Rica **17** (1950), Leprosy issue, pp. 264-265.

The iriodocyclitis which frequently appears during lepra reactions improves rapidly, within 3 days, with the daily intravenous administration of 1 gm. of streptomycin in one liter of glucose solution. Neither the streptomycin nor the glucose solution when given alone gives satisfactory results.—[From the author's summary.]

YANAI, S. Experimental studies on chemotherapy of leprosy. III. The correlation between observable signs of healing. La Lepro **20** (1951) 80-84 (in Japanese); English abstract, p. 80.

Regarding the area of a leproma and the weight of the spleen, there are the following relations: r 0.50, Fo F (1%). In cases where the area and weight of a leproma, indicate the degree of the postmortem leprous lesion in the rat, the increase in the weight of the spleen stands in inverse correlation to the degree of the lesion. It is in clear contrast with the cases of experiment tuberculosis. [The abstract, verbatim.]

ROLLIER, R. Notes préliminaire sur un nouveau traitement de la lèpra. [Preliminary notes on a new treatment of leprosy.] Maroc Méd. **29** (1950) 238.

Ten lepromatous patients were treated for 10 months with plants used in native therapy: a Moroccan Sapotacea, a sarsaparilla of Oriental origin. The patients are given, morning and afternoon, a decoction of 15 gm. of these plants for a period of from 15 days to 1 month. They follow a diet deficient in salt, in fatty substances and meat, and they should preferably remain sheltered from sunlight. No ill-effect has been observed. Improvement was noted in 9 of the treated patients between the 15th and the 75th day after the termination of treatment, with subsidence of the lepromas and sclerosis of the subcutaneous cellular tissue. Biopsies of the

nasal mucosa and of the skin showed a diminution in the numbers of bacilli, with partial loss of acid-fastness and granular change. Histologically the infiltrate in the lepromas was vacuolated. In 3 cases the bacilli were completely absent in the third month of treatment.—R. CHAUSSINAND

ROLLIER, R., NOURY, WEISGERBER and MAURY. Essai de traitement de la lèpre par une variété de salsepareille. [Trial of the treatment of leprosy by a variety of sarsaparilla.] Maroc Méd. **30** (1951) 776-780.

The authors were led to this form of treatment on learning of the custom of the Arabs of South Morocco of treating their syphilis cases with "hachba," which is the local name for sarsaparilla (*Smilax ornata*), and on noticing by chance that a lepromatous patient who had undergone this treatment had got rid of all signs of the disease. They treated 25 cases, 18 lepromatous and 7 tuberculoid, some for 2½ years, with a decoction obtained by boiling 30 gm. of the powdered root in 200 to 300 cc. of water for 15 to 30 minutes, or with an 8.2% soft aqueous extract. The former product was given daily, in two doses; of the latter from 4 to 8 30-gm. tablets were given daily, also divided morning and evening. The treatment was given for periods of from 20 to 40 days, or for 3 months with 1 month of rest, or continuously with 1 day of rest for every week. Clinical improvement of the cutaneous and nerve lesions was noticeable after 2 or 3 months in the lepromatous cases, with the exception of a single one in which a 3-month treatment with the parent sulfone had no effect. In the tuberculoid cases the anesthetic lesions had regressed, and in 2 cases had even disappeared completely. Claw hands, even irreducible ones, had improved to a point that with 2 patients permitted grasping (*préhension*), previously impossible. From the bacteriological point of view, the bacilli had decreased in number and showed a granular aspect in the nasal mucus. In 1 case they disappeared completely. The bacilli had also decreased in number in the histological sections of the cutaneous lesions, in 5 cases disappearing in 6 months, while there had appeared a process of vacuolization and sclerosis. Side-effects were mild anemia, moderate gastric and articular pains, and congestive phenomena in the pulmonary tract with acute edema in 1 case. Interruption of treatment for several months led to a reappearance of the lesions, but they subsided again upon resumption of the treatment. Lastly, lepra reactions have appeared after the resumption of the interrupted treatment, but they responded to antihistamin and B_{12} treatment. —R. CHAUSSINAND

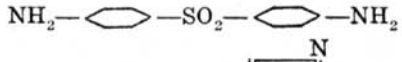
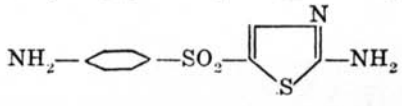
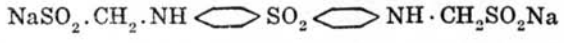
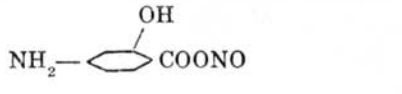
KONO, M. and KAGEYAMA, R. Studies on chemical treatment of leprosy on the distribution of promin. La Lepro **20** (1951) 89-91 (in Japanese); English abstract, p. 89.

The distribution of promin in the blood and other organs of men and rabbits was determined after intravenous injections by which the promin level in blood was kept at the same level after one hour. In the internal organs the promin level was highest after two hours, the order being: kidney, skin, blood, heart and lung. Only a very small quantity of it was found in the peripheral nerves and the brain.—[From the abstract.]

IMAKITA, T., KONO, M. and KAGEYAMA, R. Spectral analysis of chemotherapeutic agents for lepra and tuberculosis. La Lepro **20** (1951) 114-117 (in Japanese); English abstract, p. 113.

In general, chemotherapeutic agents show marked absorption of ultra

violet region. This absorption is known as the result of resonance produced in the intermolecular vibration. We studied the chemotherapeutic agents for leprosy and tuberculosis to compare with ordinary sulfonamide preparation with respect to the pH of the medium. The results were as follows:

Chemical structure of agents	Wave length of maximum absorption, $m\mu$		
	257		290
	263		300
	260		319
	224	260	319
	255		320
Dihydrostreptomycin sulfate	257		280

It is noted that these agents show two marked absorption maxima at 260 $m\mu$ and between 280-300 $m\mu$. The absorption at 260 $m\mu$ is ascribed to the intermolecular vibration of the basic animo radical which is contained in almost all chemotherapeutic agents, and this absorption holds in the acidified medium, while in preparations of ordinary sulfonamide agents this absorption is notably reduced. It may be said that chemotherapeutic agents for the acid-fast bacteria offer strong resistance to the change of medium from neutral to acid. This resistance is believed due to the free amino radical in those agents.—[From the abstract.]

BOYER, F., TROESTLER, J., RIST, N. and TABONE. Recherches sur le mode d'activité des sulfones. II. Étude analytique. [Investigations on the mode of action of the sulfones. II. Analytical study.] Ann. Inst. Pasteur **78** (1950) 140-143.

In a preceding study it was demonstrated that the bacteriostatic activity of the aminodiphenyl sulfones, mono- and disubstituted, increases under the influence of aging in the incubator or heating in the autoclave, and that the increase of this activity seems to be related to the liberation of the parent sulfone. To demonstrate this the Marshall technique is not applicable because it provokes hydrolysis of the substituted sulfones; consequently, chromatography as proposed by Consden and collaborators was employed for the analysis of the amino acids. The study by this method of 4-amino-4′-succinyl-amino diphenyl-sulfone (1500F), phenyl-glycin-sulfone, diasone, promin and cimedone has shown that all these products contain the parent sulfone in variable proportion. Heating in the autoclave increases the amount of this substance. The parent sulfone itself, studied by the same method, is stable and may be considered as a pure body. The same method has permitted the recovery of the parent sulfone in the urine of rabbits treated by mouth, either by this sulfone or by cimedone.

—R. CHAUSSINAND

YOSHINAGA, T. On the factors which intensify the complement binding reaction with kephalin antigen. La Lepro **20** (1951) 63-67 (in Japanese); English abstract, p. 63.

Factors which help the antigenic power of the kephalin colloid chemically and intensify the reaction have been investigated. Tinctures of aurantium, digitalis and valerian increased slightly the complement-binding reaction of leprous serum. Phenol-alcohol and hydrochloric-acid-phenol-alcohol increased it, especially the latter remarkably. In a group of cyclopentanoperhydrophenanthren compounds (chol acid, chol acid sodium, glycocol acid, cholesterin, and ergosterin) cholesterin and ergosterin intensified the reaction. Vitellin also strengthened the reaction, but it showed nonspecific reactions. Egg albumin, egg globulin and casein did not increase the reaction.—[From the abstract.]

YOSHINAGA, T. The 0° C method of complement binding reaction with antigen of lecithin, kephalin and emulsion of leprous tissue. La Lepro **20** (1951) 68-70 (in Japanese); English abstract, p. 68.

The antigens of kephalin from bovine brain and lecithin from egg yolk decreased or extinguished the reaction more remarkably at 0°C. than at 37°C., but with syphilitic serum it caused no decrease. The same fact was observed when emulsions of human or murine leproma with salt solution, or its alcohol or ether abstract was used, instead of the antigens above mentioned.—[From the abstract.]

KITAMI, Y. Measurement of the concentration of hydrogenic ion in saliva of leprous patients. La Lepro **20** (1951) 125-127 (in Japanese); English abstract, p. 125.

The saliva was collected from the parotid glands and the glandula sublingualis and submaxillaris of 339 patients with lepra nodosa, 85 with lepra nervosa, and 14 with lepra maculosa, and the pH measured with the paper method. Parotid saliva was always acidic, the sublingual-submaxillar saliva weakly acidic and nearer to neutral. Male saliva was higher in acidity than female. As for the disease types, acidity was highest in lepra nodosa, and lowest (nearly neutral) in lepra maculosa.—[From the abstract.]

CHAKRAVARTI, H. Studies on plasma protein. IV. Leprosy. Indian Med. Gaz. **66** (1951) 196-199.

A study has been made of the plasma protein patterns in 47 untreated cases of leprosy, 29 neural and 18 lepromatous. Of the neural cases, changes were least marked in those of the tuberculoid variety. In the simple neuromacular group changes like hyperproteinemia due to rise in the globulin fraction were found in many cases, the degree of this change varying directly with the extent of the lesion. In the lepromatous group considerable rises in total proteins and globulin were found in almost all cases; albumin was normal or only slightly depressed. The hyperglobulinemia found in these cases is similar to what has been observed in kala-azar, but unlike kala-azar the albumin fraction is least affected and from the power of albumin fabrication it is presumed that the liver function is least affected in this disease.—[From the author's summary.]

RABILLOUD, B. and MARIE-SUZANNE. Technique de coloration combinée du bacilli de Hansen sur les coupes histologiques. [Technique of combined staining of the Hansen bacillus in histological sections.] Bull. Histol. appl. **27** (1950) 39.

The technique described shows, besides the bacilli, the disposition of the connective tissue structures and permits study of the reactional tissues. Fix in Holland's fluid; paraffin sections. After deparaffinizing and prolonged washing, stain in carbol-fuchsin with heat, differentiate in 25% sulfuric acid, and wash carefully. Stain the nuclei with hemalum, avoiding overstaining; wash. Stain with fuchsin-ponceau (Masson: 1 part of acid fuchsin, 1%, and 2 parts of ponceau, 1%). Differentiate in phosphomolybdic acid, 2%. Stain the background with light green, 1%, and wash in water with 0.5% acetic acid.—[From abstract in *Bull. Inst. Pasteur* **49** (1951) 799.]

MARTI, W. J. and JOHNSON, B. H. Acid-fast staining technic for histologic studies. American Soc. Clin. Path., Tech. Bull. **21** (1951) 45.

This technique for paraffin sections, given only in briefest form, is: (1) xylene, 2 changes, 10 dips each; absolute ethyl alcohol, 2 changes, 10 dips each; 95% alcohol, 10 dips; tap water, 10 dips; stain 30 minutes at room temperature in Kinyoun's carbol-fuchsin (basic fuchsin 4 gm., phenol crystals 8 gm., 95% alcohol 2.0 gm., distilled water 100 ml.) to which Tergitol 7 is added, 1 drop to 30 ml.; wash; decolorize for 3 minutes in nitric acid-alcohol (to 95 ml. 95% alcohol add 0.5 ml. NOH_3, sp. gr. 1.42; the mixture should not be yellow); wash; 95% alcohol, 1 minute; wash; 1% aqueous malachite green, ½ minute; wash; 95% alcohol, 10 dips; absolute alcohol, 2 changes, 10 dips each; xylene, 2 changes, 10 dips each; mount in balsam. —H. W. W.

PUTT, F. A. A modified Ziehl-Neelsen method for demonstration of leprosy bacilli and other acid-fast organisms. American Soc. Clin. Path., Tech. Bull. **21** (1951) 92-95.

The difficulty of demonstrating leprosy bacilli in tissue sections is ascribed to their weak resistance to acid decolorization, factors involved being the method of fixation, the basic fuchsin employed, and the method of differentiation. The author recommends formalin for fixation, Magenta-3 ("new fuchsin") for the dye, and an acetic-alcohol decolorizer. Deparaffinize and wash as usual; stain 3 minutes at room temperature in carbol-fuchsin (Magenta-3, 1 gm.; phenol, 5 gm.; absolute ethyl or methyl alcohol, 10 ml.; dissolve completely, gradually adding, with shaking, distilled water to 100 ml.); transfer directly to sat. aq. lithium carbonate, 1 minute, (discarding the solution when it becomes blue); differentiate in 5% glacial acetic acid in absolute ethyl alcohol, 3-5 minutes; absolute alcohol, 2 changes, 1-2 minutes each; ½% methylene blue in absolute alcohol, 1-2 minutes; absolute alcohol, 2 changes, ½ minute each; toluene, 2 changes; mount with permount. It is stated that excellent results have been obtained with leprosy bacilli in previously stained sections, 40 years old, after removing the coverslips and destaining in 10% HNO_3 followed by 3% NH_4OH. —H. W. W.

WADE, H. W. Demonstration of acid-fast bacilli in tissue sections. American J. Path. **28** (1952) 157-170.

I. Procedures for paraffin sections. On the basis of previous work,

when there was developed a technique which was employed for many years but not previously published, and further recent work which resulted in the technique here recorded, an explanation is given of the basic conditions which make for difficulty in demonstrating acid-fast bacilli in tissue sections, particularly leprosy bacilli. That condition is the instability, the liability to extraction, of the waxy lipidic component of the bacillary cytoplasm upon which acid-fastness depends. The first application of a lipid solvent or other reagent which may affect that component does not of itself extract it (so the bacilli are still acid-fast in the paraffin block despite the treatment received during embedding), but it does "condition" it so that the less invulnerable bacilli—usually in the majority—are extracted when another lipid solvent is applied, as when paraffin sections are treated with xylene and alcohol. The technique described is an improvement of Fite's latest method, which is a new and revolutionary one in which the paraffin is removed from the sections by a solvent which contains an oil which prevents extraction of the bacilli (a "protective" method). The mixture recommended is either aviation gasoline and liquid petrolatum, 2:1, or rectified turpentine, the latter preferred when the former leaves the Virchow cells too retentive of the fuchsin. The xylene-olive oil mixture of Fite extracts much more of the fuchsin-retaining element. As in Fite's method the deparaffinized sections are blotted and passed directly to water. Staining is done with ordinary carbol-fuchsin, 20 minutes at room temperature. For decolorizing, 20% aqueous sulfuric acid for routine use, but when the lepra cells are too red a more drastic agent such as acid alcohol may be used for a duplicate slide. Counterstaining by dilute (¼th or ⅛th) Loeffler's methylene gives excellent results. After the final wash the slides are dried in the air, the trace of oil retained in the sections being sufficient to prevent shrinkage; this is an important feature of Fite's technique. Coverslips are mounted with a synthetic medium, not Canada balsam. With the same materials employed in other ways, bacilli which have been rendered unstainable can to some extent be made acid-fast again ("restorative" method, of which type is that of Faraco). [These procedures are based on Zenker-fixation and embedding through thin cedar oil. If chloroform, xylene or benzene is used in embedding, the same results cannot be obtained since these substances tend actively to remove the fuchsin-retentive element from the cytoplasm of the bacillus-bearing cells.]

II. Application of the carbowax technique. In this method the tissues are embedded for sectioning in a mixture of solid "carbowax" compounds, which are water-soluble polyethylene glycols. They are passed to the melted wax directly from 70% or 80% alcohol, or even water, and the sections are cleared of the wax with water; hence no active lipid solvent is applied at any stage. The processing with this peculiar embedding medium cannot be described adequately in an abstract but it is described in summary fashion in this report, and the subject is dealt with more fully in another article [see the following abstract]. As with the paraffin method, a restorative effect can often be achieved, when needed, by treatment of the sections with liquid petrolatum either by using the gasoline-oil mixture as the flotant for mounting them on the slide, or by treating them later with that mixture for 2-3 hours or longer. The numbers of bacilli that can be demonstrated in old lesions after such treatment are often amazing. The carbowax method is said to be admirably suited to the study of intra-

cellular lipids, and it should be tried out for the demonstration of such elements in leprosy lesions. —AUTHOR'S ABSTRACT

WADE, H. W. Notes on the carbowax method of making tissue sections. Stain Tech. **27** (1952) 71-79.

On undertaking to employ this new and unique method of making tissue sections, by means of solid water-soluble waxes called "carbowax" compounds, it was found that the few published reports on the subject dealt but inadequately with basic considerations, and the study reported here was carried out. The principal subjects dealt with are the physical characteristics of the different grades of these compounds, each of which is designated by a number which—with one exception—represents the average molecular weight of its component polymers; the grades which are best suited for histological work, it being found that a 15:85 mixture of the 1540 and 4000 grades is usually satisfactory at the room temperature in the Philippines; certain special problems involved in the embedding procedure and in making and handling sections; the peculiar problem of floating the sections for mounting on slides, resulting from the high solubility of these waxes in watery and most other flotants, for which purpose distilled water with 10% carbowax 1540 and 0.005% of Turgitol 7, a wetting agent is recommended; and that of satisfactory affixation of the sections to the slide, found to be best accomplished by using slides upon which a thin layer of Mayer's egg albumin has previously been dried. The mounted sections can be stained by any ordinary method with no preliminary treatment other than passing them through water if any of the wax remains from the flotant, and the usual treatment to remove mercury deposits in Zenker-fixed material—although that is not at all necessary if the sections are to be stained for acid-fast bacilli. For that purpose this method has proved highly satisfactory, and it has certain advantages for routine histological purposes, one of them being speed and another the preservation of most lipidic elements. —AUTHOR'S ABSTRACT

TERADA, M. The electron microscopic studies on bacterial viruses and acid-fast bacillus. II. On acid-fast bacillus. La Lepro **20** (1951) 137-146 (in Japanese); English abstract, pp. 136-137.

Eighteen types of acid-fast bacilli were studied by electron microscope. The most interesting results were seen in *M. leprae*. (1) Study showed that the tip of the nerve fibers extend into the bacilli. These minute neuro-fibrillae are about 60 $m\mu$ in width, with the granules or lateral stripes arranged in a regular line. This fact that the end of the nerve fibers extend into the bacillus is surprising and would indicate that the affinity between the leprosy bacillus and the nerve fibers must be explained. Further study in cooperation with the clinician is planned. (2) Ramification of nerve fibers; what was considered the tip of the nerve fiber under the ordinary microscope is now shown to be composed of a bundle of so-called ultra-neurofibrillae each about 60 $m\mu$ in width and arranged in regular stripes or granules. These again form larger bundles when the lepra bacilli are caught in the midst of the neurofibrillae. (3) We believe that *M. leprae* in the human is covered with a halo or capsule. About ten years ago I succeeded in staining this covering substance calling it a bacillus-halo, but this time I could definitely see it with the electron microscope. (4) In addition we demonstrated the various structures in

the acid-fast bacillus—granulas or vacuoles—and discussed these structures, the method of the multiplication of the lepra organism including its possible filterable stage. [From the abstract.]

[The illustrations of this article, the legends of which are in Japanese, including several electron micrographs evidently of leprosy bacilli, three of them showing bacilli in association with long, fine strands corresponding in appearance to the description of the "ultraneuro-fibrillae."]

SAIKAWA, K. The histopathological studies of the peripheral nerves in the various clinical phases of leprosy II. La Lepro **20** (1951) 71-75 (in Japanese); English abstract, p. 71.

Histopathological examinations of the great auricular nerve were undertaken in 14 cases of obsolete lepra nervosa, by biopsy or autopsy. In 9 cases of 10 in which there were thickened nerves, lepra bacilli were found in the medullary sheath, axis cylinder and neurilema nucleus of the nerve fibers. Various changes of the nerve fibers were found. One petrified nerve was encountered. Resorption of the leprous changes is slower in the nerve than in the skin.—[From the abstract.]

SAIKAWA, K. The histopathological studies of the peripheral nerves in the various phases of leprosy. III. Nodular leprosy. The case of erythema nodosum leprosum. The case of acute infiltration. La Lepro **20** (1951) 76-79 (in Japanese); English abstract, p. 76.

Histopathological examination of the great auricular nerve was undertaken by biopsy in five cases of erythema nodosum leprosum type of reaction and one case of acute infiltration type. In the former condition the foam-cell infiltration in the interstitial tissue was found, together with many polymorphonuclear neutrophilic leucocytes, lymphocytes and granulated bacilli, although the bacilli in the nerve fibers were generally rod-formed. The foam tissue and tuberculoid change were both found in the interstitial tissue of the acute infiltration case.—[From the abstract.]

SAIKAWA, K. The histopathological studies of the peripheral nerve in the various clinical phases of leprosy. IV. Summary and discussion. La. Lepro **20** (1951) 99-105 (in Japanese); English abstract, p. 99.

The peripheral nerve and skin in the various clinical phases of leprosy, examined by Mitsuda's reaction, were studied by means of biopsy. The conditions were: the early stage of nodular, neural and macular leprosy; the erythema nodosum leprosum, acute infiltration, and acute exacerbation reactions; the transitional stage from neural to nodular leprosy; obsolete neural leprosy; and nodular leprosy with positive Mitsuda reactions. The important findings were as follows: (1) There is an intense affinity between nerve fibers and the lepra bacillus, and in the extremely early stage of the disease the bacillus exists in the nerves. It also remains latent there for a long time in spite of continual treatment. (2) The histopathological changes on the peripheral nerve and skin are generally of the same character. (3) The changes found in nodular and neuromacular leprosy are essentially different. With regard to the degeneration of the nerve fiber, no differences could be found in the different types. (5) Two cases of nerve abscess in macular leprosy, and one case of calcification in neural leprosy, were encountered in this study.—[From the abstract.]

KIRSCH, E. Beitrag zur Pathologie der Lepra auf der Grundlage der heute für sie geltenden Einteilungsprinzipien. [Contribution to the pathology of leprosy on the basis of the principles of present-day classification.] Virchow's Arch. Path. Anat. **317** (1950) 602-610.

After a review of the schemes for the classification of leprosy laid down at the International Congress in Cairo in 1938, the Pan-American Conference in Rio de Janeiro in 1947, and the 5th International Leprosy Congress in Havana in 1948, the author reports on two cases of lepromatous leprosy. A 39-year-old patient with advanced lepromatous leprosy and pulmonary tuberculosis, Mitsuda negative, showed extensive formation of infiltrates and lepromas, with large numbers of Hansen bacilli in the nasal smear and the ulcer secretion. Chaulmoogra oil, antileprol, cortenil, vitamin preparations, sulphetrone and TB-1 proved ineffective, and the patient died from anemia and cachexia. Histological examination revealed with particular clarity the perivascular arrangement of the histiocytic proliferations of the skin, spleen and liver. The proliferating, fatty-degenerating leprosy cells are regarded as originating from the reticulo-endothelial system. In the second case, the patient 59 years of age, there was a similarly advanced lepromatous condition with extensive formation of infiltrates and lepromas; also ulcerations of the skin and mucous membranes, especially in the throat. Histologically typical lepromas were found, containing histiocytes, round cells, leuco- and lymphocytes, vacuoles and masses of acid-fast bacilli. —ERNST KEIL

FERNANDEZ, J. M. M. El empleo del B.C.G. en la profilaxis de la lepra. [The use of BCG in the prophylaxis of leprosy.] Día Méd. **1** (1952) 286-292.

The author describes the immunoallergic tests employed in leprosy and tuberculosis, and emphasizes the prognostic value of the Mitsuda reaction. Considering the correlation between the immunoallergic phenomenon of leprosy and of tuberculosis, he holds that both the spontaneous tuberculous infection and the provoked tuberculosis inoculation may convert a negative Mitsuda reactor into a positive one. He describes the experiments he has made along this line with BCG, in which he succeeded in provoking positivity to the Mitsuda test in 92% of 123 children by means of BCG given intradermally. He concludes by recommending the use of BCG (orally or intradermally) in all contacts with a leprosy focus whose lepromin reactions are negative.—[From author's summary, supplied by G. Basombrio.]

SCHUJMAN, S. Study of the evolution of the immunological state of lepromatous cases benefited by various antileprotic medications (sulfones and chaulmoogra). Paper presented at the III Pan-American Leprosy Conference, Buenos Aires, December 1951.

From a study of the immunologic evolution of 150 lepromatous cases treated over a period of several years and definitely benefited by the antileprotic medications used (100 cases with sulfones and 50 with chaulmoogra), the author has arrived at the following conclusions: (*a*) That modification of the immunological condition does not follow with improvement, whether that be moderate or marked, because the patients usually remain lepromin negative. (*b*) Only in cases made totally negative, both clinically and bacteriologically (12 with chaulmoogra and 8 with sulfones),

was any such change observed; in 2 the lepromin reaction changed from negative to positive (1+), and in 3 from negative to weakly positive (±). (*c*) It cannot be said whether this favorable change of the immunology was caused by the modification or was due to the spontaneous increase of reactivity that can be seen in old lepromatous released cases.—[From the author's summary.]

SCHUJMAN, S. Provoked lepra reaction. Paper presented at the III Pan-American Leprosy Conference, Buenos Aires, December 1951.

The author, convinced of the favorable influence of lepra reaction in the ultimate evolution of lepromatous cases, provoked reactions artificially by means of KI in one group of patients and smallpox vaccination in another group. Reactions cannot be induced in all lepromatous cases, but when they are obtained the condition is exactly the same as spontaneous reaction. With KI he has provoked 3 reactions in the same patient at intervals of several months, and with smallpox vaccination 2 reactions with an interval of one year, without any ill effects. In the cases with provoked reactions the same beneficial effects have been observed as in spontaneous reactions. This study is being continued.—[From the author's summary.]

TERNI, M. and SIGNORINI, L. F. Intradermo-reazioni in leprosi con un antigene acido-resistente. [Intradermal reactions with an acid-fast antigen in leprosy.] Boll. Ist. Sieroter. milanese **30** (1951) 76-78.

Intradermal injections in leprosy subjects have been made with the Mitsuda antigen and with a killed suspension of an acid-fast organism whose characters were previously reported [see THE JOURNAL **18** (1950) 161-167]. This was done in order to determine whether the culture bacillus would exhibit the properties of the Hansen bacilli or those of saprophytic acid-fasts. The culture suspension was tested in 38 leprous subjects, of whom 24 had the lepromatous form of the disease, and in 15 controls; 19 of the leprosy patients were also subjected to the Mitsuda test. Although 29% of the lepromatous cases gave positive reactions to the suspension, this result was not as frequent as published reports indicate is the case with saprophytic acid-fast bacteria. It is believed that the cultivated organism possesses some antigenic properties resembling those of the Hansen bacillus. —AUTHORS' ABSTRACT

CASTRO JENKINS, A. Reacciones de Eagle, VDRL y Kahn en lepra. [Eagle, VDRL and Kahn tests in leprosy.] Rev. méd. Costa Rica **17** (1950) 189-196.

A high percentage of positive seroreactions for syphilis has been found, although in a lesser degree than reported by others. The Eagle test has always given the greatest number of positive reactions, followed by the VDRL and then the Kahn tests. This suggests greater specificity of the last two, due to the high degree of sensitivity of the first of these antigens. These findings are observed not only in leprosy but also in all the routine reactions. Although the number of tuberculoid cases was small, it was surprising to find 100% negative VDRL reactions in this clinical type. A relation between the results of the tests and the duration of treatment with sulfones and the duration of segregation is suggested. There was a relationship between the seriousness of the disease and a high incidence of positive results in the lepromatous form, followed by the incharacteristic

and then the tuberculoid forms. Cases with nodular lepromatous leprosy gave the highest number of positive reactions, a fact which is ascribed to the greater difficulty of making them negative for Hansen bacilli. There was a marked correlation between the results of the tests and the bacteriological findings.—[From the author's summary and conclusions.]

HONDA, H. and YOSHINO, K. The seroreaction of leprous serum with antigen of cardiolipin. La Lepro **20** (1951) 128-132 (in Japanese); English abstract, p. 128.

Browning's Wassermann reaction and complement-binding reaction of leprous and syphilitic serum with antigen of many ratios of cardiolipin (NISSIN), kephalin and cholesterin gave us the following results: the antigen of cardiolipin (1), kephalin (30), and cholesterin (15), produced positive reaction with 57% of leprous serum (lepra tuberosa 75%, l. nervosa 25%, and l. maculosa 67%), but with only 10% with syphilitic serum. —[The abstract, verbatim.]

CHAUSSINAND, R. Modifications morphologiques du bacille de Hansen observées au course des traitements antilépreux. [Morphological modifications of the Hansen bacillus observed in the course of antileprosy treatments.] Rev. brasileira Leprol. **19** (1951) 1-3.

In certain untreated lepromatous cases the cutaneous lesions regress spontaneously and the bacilli degenerate. In lepromatous cases treated with chaulmoogra ethyl esters the process of degeneration of the bacilli appear identical. It therefore seems that chaulmoogra acts to strengthen the natural functions of the defense of the organism. In the course of treatment with the sulfones one may observe the same process of degeneration, but the appearance of the germs is characterized by an irregular swelling and weak Ziehl staining. From this it seems that chaulmoogra and the sulfones have different effects upon the bacillus of Hansen.

—AUTHOR'S ABSTRACT

MALFATTI, M. and JONQUIERES, E. Investigaciones a través de la óptica electrónica de la acción del tratamiento médico sobre la morfología del *Mycobacterium leprae.* [Investigations by means of the electron microscope of the effect of medical treatment on the morphology of the *Mycobacterium leprae.*] Semana Méd. (Buenos Aires) **101** (1952) 408-423.

Examination of the bacilli with the electron microscope gives evidence of morphological changes resulting from sulfone therapy. The dense bacillary forms are those of most virulence, and those with condensations in beads (en barra) are not abnormal but represent an evolutive stage of the germ. The irregular, granular forms indicate disturbances of the bacilli, and they present irregularity of outline and changes of the cell membrane. The presence of vacuoles is the most marked indication of disintegration. The microgranules which persist in the globi correspond to the L forms of Klieneberger, which, dependent on their size, are filterable, and are capable of resisting the action of drugs and of regenerating new bacillus forms. The isolated forms are the most susceptible to the effects of therapy. The globi are the last to disappear due to their relative impenetrability to the drug, the number of bacilli in them, and their tendency to persist in the L form, as elements insensitive to treatment and

capable of regenerating bacillary forms, which explains the new outbreaks in cases repeatedly found negative for bacilli. The action of sulfone therapy is evident in the bacillary stage, but it is uncertain and doubtful with respect to the microgranular forms which correspond to the L phase. Except for the modifications caused by the natural termination of the vital cycle of the bacillus, or its natural death, it is beyond doubt that the direct intervention of the organism in the physico-chemical reactions—improperly called reactions of defense—renders observation difficult since it makes it impossible to ascertain which of the morphological changes of the germ are due to this action and which are due to the chemotherapy, although from the comparison of the appearance of the bacilli in untreated patients one may deduce that it is the sulfones which are responsible for most of the changes described in this study.—[From the authors' summary, supplied by G. Basombrio.]

MONTESTRUC, E. and BLACHÉ, R. Considérations sur les modifications bacteriologiques apportées par les sulfones dans la lèpre à type lépromateux. [Considerations on the bacteriological alterations brought about by sulfones in lepromatous type leprosy.] Rev. colon. Méd. et Chir. **22** (1950) 110-112.

Of 209 patients treated with sulfones, 115 were lepromatous, of which 70 had received treatment for 2 years and the rest in accordance with their admittance. Diasone was used principally, in 2-month courses with a total of 50 to 55 gm. for an adult, followed by a rest period of 15 days, or 5 courses per year. Promin—little used because of the necessity of daily intravenous injections—was given in 2½ month courses with a total of 270 gm., followed by 15-day rest periods, or 4 courses per year. Cimedone was used only after 1949, in 1-month courses of 72 gm. followed by 1 week of rest, or 10 courses per year. For children the doses were reduced according to age, weight, and tolerance. The different products have given good results, particularly in lepromatous leprosy: improvement of the lesions of the mucosa, and decrease of the infiltrations and resorption of nodules. Histological improvement (decrease of infiltrates and appearance of sclerosis) and bacteriological improvement (diminution of the bacilli and appearance of granular forms, then isolated granulations) have been likewise observed. Two cases improved to the point of negativity of the nasal mucosa and of the dermal serosity during the first year, and others during the second year. The more recent the disease the more marked is the improvement. —R. CHAUSSINAND

NISHIMURA, S. and HONDA, H. Studies on cultivation of leprosy bacilli. La Lepro **20** (1951) 92-95 (in Japanese); English abstract, p. 92.

The medium of Nakamura and Endo containing mucin from bovine submaxillary gland provided no multiplication of either human or murine leprosy bacilli at the first, second and third generations after many cultivations. Nor has the mucin in Nakamura's medium any power to accelerate the growth of tubercle bacilli, although we found that the serum in it helped their multiplication.—[From the abstract.]

CHAUSSINAND, R. and BESSE, P. Inoculation du bacille de Hansen et du bacille de Stefansky à la perche Arc-en-ciel ("Eupomotis Gibbosus"). Note preliminaire. [Inoculation of Hansen and of Stefansky

bacilli in the rainbow perch *Eupomotis gibbosus*. Preliminary note.] Rev. brasileira Leprol. **19** (1951) 4-7.

The numerous attempts at inoculation of the Hansen bacillus in different animals seem always to have failed. The best results obtained by leproma grafts caused only localized, regressive infections. Inoculations into cold-blooded animals having been attempted only exceptionally, the authors have inoculated 4 rainbow perch (*Eupomotis gibbosus*) with a suspension rich in bacilli from an advanced lepromatous case, four others being kept for a control. Three of the inoculated fish died 3, 3½ and 4 months after the inoculation. On autopsy no macroscopic lesions were found, but there were numerous acid-fast bacilli in the viscera. The fourth fish died 20½ months after the inoculation, and minute granulations containing numerous acid-fast bacilli, generally homogenous, were found in the mesentery. Microscopic examination of the liver revealed dilation of the capillaries and veins, some of which contained masses of acid-fast bacilli, free or agglomerated, without involution forms. It seems that the Hansen bacilli had survived and multiplied in the organism of this fish. No acid-fast bacilli could be detected on autopsy of the controls. An identical experiment was carried out on 3 perch with Stefansky bacilli. These fish died 10½, 11 and 20 months after the inoculation. The autopsy findings are comparable with those observed with the Hansen bacillus. A portion of the liver of the perch which died after 20 months was ground up and injected into a white rat, which died 3 months later. The lymph node in relation to the point of inoculation, which contained quite numerous acid-fast bacilli, was ground and injected into 2 other rats. One of them shows, after 4 months, hypertrophy of the related lymph node. The death of the perch is ascribed to bacillary emboli. The absence of infection in the controls, and the absence in the inoculated animals of the usual signs of infection by paratuberculosis bacilli, point to the presence of Hansen and Stefansky bacilli which have survived and multiplied.

—AUTHOR'S ABSTRACT

HANKS, J. H. Metabolic inhibition of *Mycobacterium leprae murium* by serum components which modify the hemagglutination or infectiousness of certain viruses. Bact. Proc., Soc. American Bacteriologists, 1952, p. 99.

M. leprae murium resembles viruses in its dependence on host cells and its failure to respond to exogenous substrates *in vitro*. Since its endogenous metabolism is modified by the classical virus inhibitors of serum, the data it affords may throw light on certain problems of virus synthesis *in vitro*. Although the stimulatory components in animal serums occur in preponderance over the inhibitors, washed suspensions of *M. leprae murium* incubated for 24 hours in serum retain but 5-10% of the hydrogen transfer capacity possessed by control suspensions in balanced salt solution. Among the beneficial components of serum are: human and bovine albumin, redissolved Cohn fractions II and III of human serum, the crude globulins which are precipitable from rat and human serum by dilution in water and acidification with CO_2, and the crude lipids extractable with alcohol-ether. Purified representatives of the inhibitors are: the B_1-lipoprotein of Oncley, the mucoproteins of the Cohn fraction IV-4, the influenza virus hemagglutination inhibitors of Stulberg, and the PP1 growth factor of Smith and Morton. In native serum the beneficial and

inhibitory materials apparently occur as complexes. Methods for neutralization or removal of inhibitors are discussed. Although serum is of primary importance for synthesis of cell materials, it does not in general increase the yield of viruses *in vitro*. It would be of interest to know to what extent its potential virtue is diminished by the presence of virus-inhibitory materials. —F. A. JOHANSEN

WATANABE, Y. On the cultivation of murine leprosy bacilli. La Lepro **20** (1951) 97-98 (in Japanese); English abstract, p. 97.

The cultivation of Stefansky's bacillus on the media devised by myself and by Nakamura presented many bacilli in the first generation, but they decreased and disappeared in the second and third generations. The inoculation of these bacilli to rats to determine whether they were living proved that those which had been observed in large numbers in the first generation were dead after 60 days on [my?] medium. On the mucin medium they were not found dead till 80 days. It follows that the mucin medium may keep these bacilli alive longer than any other one, but does not allow them to proliferate.—[From the abstract.]

NAKAMURA, M. and SHINGU, M. Proliferation of murine leprosy bacilli in rats. (Part I.) La Lepro **20** (1951) 118-120 (in Japanese); English abstract, p. 118.

After intraperitoneal inoculation of murine bacilli, they appear and proliferate in the liver, spleen and kidney after a week, and in the course of time are disseminated into every lymphatic gland and other organs, but they proliferate most markedly in the spleen and great omentum. They could not be found in the brain. Their proliferated type are general acid-fast bacilli.—[From the abstract.]

NAKAMURA, M. and SHINGU, M. Effects of subcutaneously and intravenously injected protomin on murine leprosy. La Lepro **20** (1951) 109-112 (in Japanese); English abstract, p. 109.

Three groups of 6 rats were used. The first group was injected with protomin subcutaneously, the second intravenously, and the third was the control. Injections were administered 48 times, and the observation was for 4 months. Both subcutaneous and intravenous injections could not suppress the disease and produced no difference in the size of the lepromata. It was interesting, however, that the intravenous group showed no or very slight lesions of the skin In short, protomin has not as marked an effect on murine leprosy as on human leprosy.—[From the abstract.]

DOUNCE, A. L. and SHANEWISE, R. P. Liver catalase of tumor-bearing and leprous rats. Cancer Res. **10** (1950) 103-107.

Twelve rats of the Wistar Strain, one-year-old males and females, had been inoculated ten months earlier in the inguinal region with suspensions of *M. leprae murium*. When the livers were removed for determination of catalase activity, 11 of the rats were found to have the disease in an advanced stage. The liver catalase was determined by a manometric method which is briefly described. An average decrease of 29% in the catalase activity occurred in 10 of the 12 rats. The authors could not evaluate this significance without pathological examinations of the liver, which they were not able to carry out. They suggest that the mechanisms to be ruled out are, (*a*) fatty liver, and (*b*) a replacement of infiltration

of liver parenchymal cells with tissue or material of low catalase activity such as connective tissue or amyloid. —F. A. JOHANSEN

YASUMOTO, K. Effects of PAS and tibione on murine leprosy and on murine leprosy bacilli in vitro. La Lepro **20** (1951) 106-108 (in Japanese); English abstract, p. 106.

Of 3 groups of 4 rats each, first group was given 25 mgm. of PAS, the second 0.3 mgm. of tibione, daily for 60 days by mouth, and the third was used as the control. Both drugs caused considerable toxic manifestations, but they suppressed the murine disease. No effect on the morphological appearances of the bacilli *in vitro* could be seen.—[From the abstract.]

SHIGEMATSU, S. and NAKAMURA, M. Relations between the onset of murine leprosy and serum fractions. La Lepro **20** (1951) 201-202 Japanese text; English abstract, p. 201.

Observing the serum fractions by electrophoresis after the onset of murine leprosy, there was found a tendency of the γ-globulin to decrease, instead of to increase as is thought specific in lepra tuberosa.—[From the abstract.]

SEEBERG, G. Increase of sensitivity to organic luetin on repeated testing. Acta Derm.-Vener. **31** (1951) 442-445.

Tests with "organic luetin," extracted from rabbit syphilomas, were made on 28 children with congenital syphilis. The tests were repeated at intervals of 6 days, 22 of the children receiving three tests. Two did not respond at all. Two responded only on the third test. The remaining 24 showed increased response on the second test (change from negative to positive, or increase of the reaction), and in 14 of the 22 given the third test there was further increase. In the majority, therefore, there was increasing sensitivity with repetition of the test. This is held to be comparable with the intensification of reactions observed in repeated tuberculin tests. [Information regarding the basis of this last statement would be desirable in view of the usual experience that, at least in practical work, repetition of tuberculin testing does not induce or increase sensitivity. It is of course well-known that raw tuberculoproteins, undenatured by heat, are antigenic, but they induce the anaphylactic type of reactivity, not the delayed "bacterial" or tuberculin type. That luetin, with its whole organisms and their products, should increase reactivity is in keeping with what frequently occurs on repetition of injection of lepromin.] —H. W. W.

SEEBERG, G. Tuberculin sensitivity in lymphogranulomatosis benigna. Acta Derm. Vener. **31** (1951) 426-434.

This is a study of the effects of depot tuberculin (DT) in this disease (sarcoid), many cases of which are relatively insensitive to tuberculin. The DT preparation is tuberculin (OT, mixed human and bovine used), emulsified 1:100 and 1:1000 in a vehicle composed of liquid paraffin 8 parts, anhydrous lanolin 1 part, and saline 1 part. This had been found by the author to cause intensified and prolonged reactions in cases of lupus vulgaris, because of the concentration and persistence of the antigen at the site of injection; and this has now been found to be true also in Mantoux-positive sarcoid cases. Of 8 cases negative to 1 mgm. of tuberculin (OT, diluted 1:100 in saline), 6 gave relatively strong, long lasting

reactions to DT; individual graphs show persistence at the end of observation periods ranging from 20 to 91 days. This result is ascribed to retardation of absorption of the antigen, giving time for the cell-transported antibodies, present in low concentrations, to accumulate in sufficient amounts to give positive responses. —H. W. W.

POLLAK, A. and BUHLER, V. B. Fatal atypical acid-fast infection. Proc. American Assoc. Path. & Bact., April 1951, *in* American J. Path. **27** (1951) 753 (abstract).

The authors have recently observed two fatal cases of infection by an atypical acid-fast organism, with distinctive morphologic and bacteriologic features, and several other cases apparently belong to this group. One patient, a 21-year-old white male, became ill with gradual onset of fever, weakness and increased fatiguability 14 months before death. Pancytopenia appeared and the temperature reached 103°F. The tuberculin reaction was negative. The course was steadily downhill despite all medication. Necropsy revealed scattered large mesenteric nodes whose normal structure was replaced by partially calcified caseous and purulent masses; similar caseous masses were seen in the spleen, and smaller miliary nodules in the lungs. Microscopically the lesions were poorly outlined, with some necrosis, few giant cells, and large acid-fast bacilli. The second patient was a 4-week-old infant born 2 months prematurely who, at 2 weeks of age developed cyanosis and dyspnea and died 11 days later with diffuse bronchopneumonic consolidation of both bases. At autopsy the other organs were grossly normal. Microscopically, the lungs presented inflammatory foci containing enormous numbers of large, elongated acid-fast organisms. Similar lesions were found in a hilar node, in the liver, and in the malphigian bodies of the spleen. Numerous acid-fast organisms were also found free in the splenic pulp. The organism recovered from the first case and observed in the second one is a large, beaded, strongly acid-fast bacillus that tends to occur in packets and clumps. Its appearance in tissues is very similar to that of *M. tuberculosis*, although the organisms are much larger. It grows with relative ease on Petragnani's medium, but the colony is yellow. It produces a mild, self-limited disease in guinea-pigs, and is also mildly pathogenic for mice. A similar organism has been recovered from several patients who are under observation. —[From the abstract.]

KILE, R. L., ROCKWELL, E. M. and SCHWARZ, J. Use of neomycin in dermatology. J. American Med. Assoc. **148** (1952) 339-343.

The authors' summary and conclusions are as follows: (1) Neomycin is a valuable antibiotic for topical therapy. (2) In a series of 675 patients with skin infections, neomycin was more effective for most skin infections than other topical agents we have used. (3) Some patients with hemolytic streptoccic and pyocyanie infections did not respond satisfactorily to neomycin. (4) The sensitizing index of neomycin is very low, so that it may be used generally without fear of reactions. —H. W. W.

CROSS, J. B. Diasone and promin as therapeutic agents in experimental toxoplasmosis. Proc. Soc. Exper. Biol. & Med. **76** (1951) 548.

On the assumption that toxoplasmosis is essentially a disease of the reticuloendothelial system, a therapeutic trial with sulfoxone (diasone) sodium and with glucosulfone (promin) sodium seemed justified because

these sulfones had proved beneficial in leprosy, also a reticuloendothelial disease. Sulfoxone was given subcutaneously, and glucosulfone (0.5%) was put in the food. Both drugs not only suppressed the symptoms but repeatedly eliminated the carrier state. Mice treated with glucosulfone survived over a year, but sulfoxone appears to be less toxic and more potent, since it protected mice when therapy was delayed for one-third of the survival time of untreated mice.—[Abstract from *J. American Med. Assoc.* **146** (1951) 1350.]

WAREMBOURG, H. and NIQUET, G. L'association huile de chaulmoogra-streptomycine en tuberculose pulmonaire. [Combined use of chaulmoogra oil and streptomycin in treatment of pulmonary tuberculosis.] Presse Méd. **59** (1951) 1387-1388.

Combined treatment with chaulmoogra oil and streptomycin or *p*-amino-salicylic acid was given to 20 patients with advanced pulmonary tuberculosis. The treatment with chaulmoogra oil was instituted when the other drugs had been used previously and seemed no longer effective. Injections of 2 cc. of the entire oil, with 800 units per gram of vitamin A added, were given daily for seven days, and then 5 cc. for 23 days. Good results were seen in 14 of the patients, with persistent improvement of the pulmonary lesions and of the general condition; 2 patients improved temporarily, and 4 were therapeutic failures. In 2 patients with good results from two months of the treatment, the former resistance of the Koch bacillus obtained from sputum to 50 units of streptomycin decreased to a sensitivity to 1 unit. The chaulmoogra oil was well tolerated, with no untoward reactions. Chaulmoogra oil therefore deserves a place in the therapeutic armamentarium of pulmonary tuberculosis.—[From abstract in *J. American Med. Assoc.* **148** (1952) 683.]

CORNBLEET, T. Sulfoxone (diasone) sodium for dermatitis herpetiformis. A. M. A. Arch. Derm. & Syph. **64** (1951) 684-687.

It is reported that 13 patients with dermatitis herpetiformis, some of whom were refractory to other treatment, including sulfapyridine, improved decidedly or had complete remissions while taking sulfoxone sodium. None had any major untoward results, although decrease of hemoglobin and red cells was observed during the first weeks of the treatment. A statement of interest is that sulfoxone tablets currently available and in use in leprosy did not produce consistent effects in this disease, but reproducible clinical results were obtained with specially coated tablets prepared for this study by the Abbott Laboratories. This matter is being investigated further, and the new-type tablets will not be generally available until the investigations are completed. —H. W. W.

SMITH, L. W., WUERTHELE-CASPE, V. and ALEXANDER-JACKSON, E. Pathologic changes induced experimentally in laboratory animals by microorganisms recovered from the blood and tumor tissues of human cases of malignant disease. Proc. American Assoc. Path. & Bact., April 1951, *in* American J. Path. **27** (1951) 736-738 (abstract).

An organism which has tentatively been classified as probably a mycobacterium because of its acid-fast character and pleomorphism, has been obtained uniformly from all cases of malignant disease, including the standard experimental animal tumors, but not from the blood of any

normal control case. Inoculation of experimental animals with small amounts of filtrates from a special broth medium, intraperitoneally or subcutaneously, results in varying pathologic pictures; the lesions may be restricted to the site of inoculation or may show widespread metastases, perhaps dependent in part on the size of the dose and individual differences in susceptibility or resistance. With intraperitoneal inoculation there occurs either a widespread diffuse autolysis of all organs without demonstrable focal lesions, or a widespread systemic chronic granulomatous process with innumerable foci in the lungs, liver, spleen, and other organs. The characteristic lesion is a pseudocaseous chronic granuloma, usually yellowish-gray, quite firm, and showing little or no liquefaction necrosis; they frequently coalesce or extend to regional structures. Grossly it is impossible to tell whether they are inflammatory or neoplastic. Repeated transfer to successive animals results very frequently in the development of large, progressive focal lesions with hematogenous metastatic distribution. Histologically, these lesions are for the most part of a chronic proliferative nature more suggestive of a chronic granulomatous infection than of a true neoplasm, but occasional cases present morphological evidence of a transition to actual neoplasia.—[From the abstract.]

[In response to questions in the discussion, the senior author stated that they had obtained about 3 to 4% of rather frankly malignant tumors following 7 to 10 transfers in their animals; that the induced tumors were not necessarily the same as those from which the cultures had been obtained; that most of the induced malignant tumors had been of the lymphoid series, which are most readily stimulated to neoplasia; and that there had been three instances in which the induced experimental tumor was found to be a carcinoma, not identical with the carcinoma of origin. He personally believed that we cannot have cancer without an infectious agent—and that the organism described is the responsible one—but that we can have the organism without cancer, just as we can have immune carriers with any other low-grade infection.—EDITOR]

DE SOUZA-ARAUJO, H. C. Acid-fast bacilli isolated from a tick parasite of Cobre "Limpa Campo." Bact. Proc., Soc. American Bacteriologists, 1951, p. 101 (abstract).

The isolation of acid-fast bacilli from an ectoparasite (*Amblyoma rotundatum*) of toads (*Bufo marinus* and *B. crucifer*) and a water snake (*Constrictor constrictor*) has been reported. In this study ticks from two nonvenomous snakes (*Drimachon bifossatus*) were triturated separately, treated with 10% NaOH, washed repeatedly, and inoculated each onto five tubes of Loewenstein medium. Between 22 to 60 days of incubation growths appeared in 2 tubes from snake No. 1 and 1 tube from No. 2. The former cultures were thick, pearly-white, of humid and dull aspect; the latter culture was of granular appearance, pale-rose and dry. All were acid-fast, gram-positive, and fluorescent; the pink one was also Dubos-positive. Growths in plain broth or agar were poor; those in glycerine media were good. Subcutaneous inoculations of the chromogenic strain in guinea-pigs produced small nodules within 2 weeks, and larger nodules in white rats. One rat that died after 12 days showed a tumor, the size of a large olive, with central caseation. Smears of the pus or tissue showed only acid-fast organisms. The study is being continued.—[From the abstract.]