LEPROSY REVIEW

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THE BRITISH LEPROSY RELIEF ASSOCIATION

VOL. XXVIII. No 4. OCTOBER 1957

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La Lepro, Official Organ of the Japanese Leprosy Association. Vol. 25, No. 5.
Ibid. Vol. 26, No. 1.
International Journal of Leprosy. Vol. 24, No. 3.
Ibid. Vol. 24, No. 4.
Book Review. BCG and Vole Vaccination. K. Neville Irvine.
The Rumanian Medical Review. Jan.-Mar., 1957.
Boletim do Serviço Nacional da Lepra. Vol. XV. Special Number, 1956. (Symposium on Erythema Nodosum Leprosum.)

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Rajah Sir Charles Brook Memorial Settlement, Kuching, Sarawak.
The Work of WHO, 1956.
International Digest of Health Legislation, WHO, 1957.
The Leprosy Centre at Paramibo, Surinam.
The Chronicle of the World Health Organization, 1957, Vol. 11, No. 3.
R.C.M. Leprosy Colony, Ndanda, Tanganyika, 1956 Report.
The Report of the Medical Services, Sudan, 1954-55.
The Report for 1956 of the Mission to Lepers, Hong Kong Auxiliary.
Annual Report, 1956, The Victoria Leprosy Hospital, Dichpali, India.
Report for 1956 of the Nigeria Leprosy Service Research Unit, Uzuakoli.
The Chronicle of the World Health Organization, 1957, Vol. 11, No. 6-7.
The Report for 1956 of the Medical Department of the Leonard Wood Memorial, Washington.

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EDITORIAL

Induced Leprotic Reaction

The subject of leprotic reaction is always of interest. We do not understand it fully, but we guess that much light will be thrown on the immunology of leprosy when we do come to understand the mechanism of reactional states. In this issue (page —) there is a useful example of the orderly and analytical approach to the subject,[1] and also in this issue (page —) a review of a symposium on the erythema nodosum leprosum section of the subject.[2] Clear-cut ideas on histopathology
and accepted, but at least there is general agreement on the beneficial nature of leprotic reactions, except for the danger of the enhancement of nerve damage if the nerves happen to be involved. In the long run the reactions are favourable in that the final victory of the patient over his disease is advanced by them. An increase in the incidence of such reactions is also generally reported and has been interpreted as due to the releasing action of sulphone therapy. Even in pre-sulphone days leprotic reaction was classified as being beneficial, and this led to essays in the artificial induction of leprotic reaction. The first method was the use of potassium iodide by oral administration. Danielssen [3] in 1886 used it quite extensively in the treatment and diagnosis of the disease, and it is clear that the activating or re-activating action of the iodide was the basis of the aid to diagnosis and the source of the post-reactional clinical improvement in the patient. Many other workers confirmed the action of iodide and by 1929 Muir [4] *et al.* again emphasized that iodide by mouth produce focal and general symptoms indistinguishable from lepra reaction, and that they have a specific effect in showing up concealed epromatous foci. On the whole, over the course of years, this method did not find general favour, as many considered it tricky to control and inclined to be dangerous. Yet it has not been forgotten, and in 1953 Schujman [5] reported on the question again. He reminded us that the lepra reaction can occur spontaneously in lepromatous patients, such as have a certain predisposition or special sensitivity, but some lepromatous cases never have it. It is prone to appear at puberty, menstrual periods, during and after childbirth, at times of emotion, and particularly in toxic and infectious intercurrent states. It may also be released by the administration of certain drugs, especially potassium iodide, hydnocarpus oil, and the sulphones. He used various provoking agents in his studies, including potassium iodide, tuberculin,

Stefansky leprolins, and smallpox vaccination intradermally, and found that potassium iodide and smallpox vaccination gave the surest and strongest reactions. Some lepromatous cases failed to react to any agent, even if the dose were high. Where there was a reaction to iodide or the vaccination, it was directly proportional in intensity to the dose of the iodide or the degree of positivity of the vaccination, and the clinical and bacteriological picture of the induced reaction was always identical with that typical of spontaneous reaction. More important still, he found that the immediate and remote effects were beneficial to the patient, and similar to those of spontaneous reaction.

The potassium iodide is made up as a solution of equal parts of the salt and distilled water, of which 20 drops contain approximately 1 gram of potassium iodide. The course begins with 10 drops by mouth daily, given 5 at lunch and 5 at supper, and 10 drops daily are added to reach 120 to 150 drops daily. When the patient does not show the least sign of reaction the medication is suspended, but sometimes signs of reaction appear the second day, and usually the full picture appears on the third day. The full picture includes fever, weakness, arthralgias, myalgias, and neuralgias, ocular reaction, and an exanthem which is nodose or polymorph erythema. If the reaction does not prejudice the general condition of the patient, the course of iodide and consequently the reaction are kept going for about 2 weeks, and in practice are suspended only when the pains are severe or the eye reaction too intense. The same patient can bear 3 or 4 induced reactions at intervals of 4 to 7 months. Smallpox vaccination by puncture or scarification gives very similar results, though the leprotic reaction is somewhat slower to appear and more often the symptoms have to be controlled by anti-reactive drugs.

The usual attitude of modern physicians to leprotic reactions is to consider them a nuisance and a danger, and to pounce on them with any or all of the anti-reactive medications, including latterly the corticosteroids, or even oral BCG. It is salutory, however, to consider this thread of wisdom coming down to us from the past, reminding us that it is possible and may even be advisable to induce lepra reaction artificially. Naturally we would recoil from any idea of using artificial induction in the non-lepromatous types, because of the real danger of nerve damage, but for the slow and anergic lepromatous types, even in these busy days of widespread sulphone therapy, perhaps Danielssen and Muir and Schujman and others have " got something."

REFERENCES

(1) SOUZA CAMPOS, N., and RATH DE SOUZA, P. Estados Reacionais na Lepra. (*Reactional States in Leprosy.*) Rev. Brasil de Leprologia, **25**, Jan.-Mar., 1957, 3-18.

(2) RAMOS E. SILVA, J., and many authors. *Symposium on Erythema Nodosum Leprosum.* Boletim do Serviço Nacional da Lepra, **15**, 1956. Special Number, 1-160. Rio de Janeiro.

(3) DANIELSSEN, D. C. Norsk. Mag. Laegevidensk, 1886.

(4) MUIR, WARDEMAN and LANDEMAN. Trans. Far East Assoc. Trop. Med. **2**, 1929, 362.

(5) SCHUJMAN, S. Reacción Leprosa Provocada (*Induced Leprotic Reaction*). Memoria de la III Conferencia Panamericana de Leprología, **1**, 1953, 162-166.

LEPROSY IN MALTA

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Malta is the largest of a group of small islands situated in the middle of the Mediterranean. The aggregate area of the whole group is 121.8 square miles and the population is 314,369, with a density of 2,624 per square mile, one of the highest, if not the highest, in the world. The latitude is 35° N. and the longitude 14° E. The group of islands lies 60 miles south of Sicily and about 180 miles north of Africa and forms part of Europe. They enjoy temperate climate with an average annual rainfall of 21.5 inches.

Malta is the largest and most important of the islands. It is 17 miles long, 9 miles wide, with an area of 96 square miles. In its capital, Valetta, is the seat of the Government, and there is also the centre of the social, economic and industrial life of the Maltese archipelago.

Gozo, which is the second largest island, is 9 miles long, 4½ miles wide, and covers an area of 26 square miles.

Comino, the smallest island of the group, is 1½ miles long and 1¼ miles wide.

Almost half of the population live around the harbour, in urban areas where there are naval docks and some industries. The rest of the inhabitants are mostly engaged in agricultural pursuits.

The standard of living is of European pattern, the social services are advancing and the medical services have reached a high level. The general health is well maintained, no major infectious diseases have occurred for many years, and the only endemic disease is undulant fever.

Leprosy is one of the oldest diseases known on the face of the earth. The prejudice against the disease is such as to sever the victims from the sympathy and the society of other men. Both the Bible and the Koran contain references to the repugnance with which the disease was looked upon in olden times. The extraordinary horror of leprosy haunted ancient and modern men and engendered that sense of leprophobia which has been the bane of the wretched victims of the disease throughout the span of the ages.

Very little material is available on the history of leprosy in Malta; its origin is unknown, but it certainly existed in the island

since remote times. It was suggested that the first cases were imported by the Phoenicians. Those sea-faring people, traders and colonizers, who came from the Near East, were the first historically recorded inhabitants of these islands. Malta was in the centre of their other possessions in the Mediterranean, owing to which position it became an emporium of a flourishing trade.

It is more probable, however, that the first cases of leprosy were introduced into these islands, in common with other countries on the Mediterranean littoral, during the Saracen domination between 870 and 1090 A.D., through the influx of leprosy-infected Arabs. In support of this contention is the fact that the only Maltese word meaning leprosy is " gdiem," pronounced " djem," the origin of which is from "judâm " or " djudhãm," the Arabic word for leprosy. The expansion of commerce and the migration of troops and mercenaries in the Middle Ages, an epoch in which war constituted one of the principal human activities, probably also played a part in the further diffusion of leprosy in these islands.

The early incidence of leprosy in Malta is obscure, but as far back as the year 1659 the disease must have been prevalent because on the 29th October on that year the Grand Master of the Order of Malta who ruled over the island, appointed a commission to provide for the care of sufferers from leprosy. On the 30th December, 1704, regulations were issued by the Chief Medical Officer of that time warning barbers against the dangers of accepting victims of leprosy as clients in their shops. From then onwards references to the disease were made from time to time in writings of medical men. By the second half of the nineteenth century the disease began to cause some anxiety among the population because in 1883 a committee composed of seven medical practitioners was appointed by the Governor " to investigate and study the incidence of the disease and to suggest means to check its spread."

Factors that no doubt had largely contributed to such an increase in the incidence of the disease were (i) the return of emigrants from countries in North Africa, where leprosy is known to be endemic, to which countries the Maltese had emigrated in large numbers during the economic depression that hit Malta between 1865 and 1872, and (ii) the stationing in Malta in 1878 of a strong contingent of Indian troops numbering over 6,000 men, in connection with the Russo-Turkish War. That this latter event had contributed largely to the increased incidence of leprosy in Malta can be seen from the earliest statistics which show that leprosy cases were most numerous in the villages lying near the place where the Indian troops had camped, the locality known as Imriehel.

In common with the policy then generally adopted in European countries, the Committee appointed in 1883 recommended that persons infected with leprosy should be compulsorily segregated. Other alternatives had been considered by the Committee before recommending segregation, but each had to be discarded. This accounts for the fact that it was only in 1893, that is after the lapse of 10 years from the appointment of such a Committee, that the first Leprosy Ordinance entitled ' An Ordinance for Checking the Spread of the Disease Commonly Known as Leprosy ' was enacted by the Local Government.

The Ordinance contained three main provisions, namely: (i) Compulsory notification of every case of leprosy immediately it became recognized by medical men and by certain other persons, namely, police officers, hotel keepers, etc.; (ii) Compulsory examination of each notified case by a Board of five experienced medical men (styled the Leprosy Board); (iii) Segregation of confirmed leprosy cases in a leprosarium so long as such cases were deemed to be a danger to the public health.

Segregation of confirmed cases in a leprosarium could not, however, be implemented immediately, as no special institution was as yet available for the housing of leprosy patients. A small number of patients in an advanced stage of the disease who had voluntarily applied for admission into an institution, were accommodated in a separate ward of the Asylum for the Aged and Incurables formerly known as the Poor House and now known as the St. Vincent de Paul Hospital.

Meanwhile the erection of a leprosarium was commenced in the locality known as Mgieret, an elevated site about 200 yards behind the St. Vincent de Paul Hospital. The male division was completed in 1900 and male patients were admitted and segregated therein. The female division, however, was not opened until 1912, when female patients were admitted and compulsory segregation was made general.

The Leprosy Hospital, known to-day as the St. Bartholomew Hospital, is a large and spacious building, having accommodation for the housing of 118 patients, i.e. 68 men and 50 women and about 40 staff. It is constructed on a plan of two lateral wings emerging at right angles from each side of a central block. The right wing is the male division, the left, the female division, while the central block, separating these two divisions, consists of the administration block, concert hall, dispensary kitchen and waiting rooms. With few exceptions, the patients are accommodated in the various wards in groups of from 4 to 10, according to the size of the ward.

Adjoining the hospital, stretching to the east and west of it and enclosed within high boundary walls, are plots of land, part of which is distributed into allotments for cultivation by the patients.

Following the repeal of compulsory segregation, the staff of the hospital at present consists of a resident medical superintendent who performs professional and administrative duties, three Sisters of Charity, a chaplain, a ward master, an assistant apothecary and clerk, 15 male and 9 female hospital attendants and 14 male and female domestic staff.

Concurrently with the opening of the leprosarium, special regulations were issued. Under these rules complete isolation from all contacts with society was enforced. Patients were permitted to see only their nearest relatives on certain days and in a special room. Only dangerously ill patients could be visited in the ward at any time. Such rules had undergone extensive alterations in the course of time.

As it may well be expected, this segregation of leprosy patients and the severe regime to which they were subjected, were the cause of discontent among the inmates and ugly incidents were of frequent occurrence. The hospital came to be regarded as a prison, with the result that patients suffering from leprosy were driven to secrecy and concealment.

Hence, it was only natural that, with few exceptions, only those leprosy patients in an advanced stage of the disease, who were hopeless and helpless, gave themselves up or were reported by their relatives, while those in whom the disease was in the initial stages, especially those who were able-bodied and in the prime of life, went into hiding in the countryside. Moreover, once leprosy patients were compulsorily segregated in hospital, it was difficult to obtain their co-operation with regard to treatment.

In the light of increasing knowledge, an amended Leprosy Ordinance was published in 1919. Compulsory segregation still remained the law, but patients in whom the disease had been arrested could, under this new amendment, be discharged from hospital. Patients so discharged were bound to present themselves every six months for examination by the Leprosy Board, and were precluded from taking certain trades and occupations.

In order to break the monotony of their stay in the institution and render life more bearable, provisions were made for each patient to be kept fully occupied in accordance with his inclination and capacity. Thus, patients who were able to assist in the domestic service of the hospital or to perform agricultural, tailoring, or other work, were so employed in return for a small monthly gratuity.

Govenment also afforded m netary relief to the families of leprosy patients in the form of monthly subsidies. Amusements were also organised to while away the time for the inmates in the long evenings.

A further amendment to the Leprosy Ordinance of 1919 was enacted in 1929 with a view to bringing the law into line with current trends then obtaining in Europe and in other parts of the world. Under the new bill, leprosy patients presenting no contagious manifestations of the disease were permitted to receive treatment as out-patients. By this new amendment it was hoped to induce the hitherto hidden early amenable cases of leprosy to come forward for treatment. The fear of compulsory segregation, however, still loomed in the minds of the majority of the sufferers from this disease, who were terrified by the thought that should the disease become infective at some later stage, they would lose their liberty.

The final blow to segregation was dealt in 1953 when the Leprosy Ordinance was again amended, abolishing the compulsory segregation of patients affected with leprosy and this method of prevention which in Malta had proved ineffective, came to an end.

The chief aim in abolishing segregation has been to attract early cases to come forward voluntarily for treatment. Previous experience has shrown that unless fear of compulsory segregation is dispelled from the minds of persons affected, the disease will remain difficult to control, as it will continue to be driven underground. As in tuberculosis, so in leprosy, the earlier in the course of the disease the treatment is instituted, the more hopeful will be the outlook for the patient; this is especially so nowadays when encouraging results have been obtained from sulphone therapy.

Under the new Leprosy Ordinance various sections of the principal law have been repealed, but cases of leprosy still have to be notified to the sanitary authorities by the medical practitioners, and certain precautionary measures have been retained. In exceptional cases segregation may still be enforced by the competent authorities under a different enactment, i.e. the Prevention of Disease Bill, when such a course is imperative, such as for example, in the case of a patient who persistently refuses regular treatment and does not avoid spreading the infection to other persons.

The new legislation was enacted with the object of attracting early cases to come forward for treatment, but at the same time it had the effect of diminishing the number of patients undergoing treatment in hospital. In fact many of the patients availed themselves of the liberty conceded by law and left the hospital. Other

patients, however, were not in a position to ask for their discharge. Disfigurement, indifferent relatives, the absence of proper accommodation at home and above all straitened financial circumstances, will always keep a number of patients inside the hospital.

To alleviate the lot of these patients and to render their life in the hospital as pleasant as possible, immediate steps were taken to provide them with comfort and amenities. A new hospital coach has been provided and outings are being organized more frequently; facilities for regular home visits have been arranged; the tobacco allowance has been increased, and the remuneration for services rendered in the hospital has also been increased. Rediffusion sets have been provided both in the male and female divisions, and television sets are being installed. Cinema shows take place weekly and performances by local theatrical companies are given regularly. In addition generous cash allowances are granted monthly to families or dependents of leprosy patients undergoing treatment at the hospital.

Incidence and Anti-Leprosy Campaign

In 1913 when segregation was compulsory the incidence index for leprosy was 0.54 per thousand; the estimated civil population for that year being 216,617.

In 1930, the rate was 0.34 on an estimated civil population of 234,454.

In both instances the rate was based on the number of patients segregated in relation to the estimated population of the islands at that time. In the latter instance it took into account neither the number of patients who had been paroled under the amended Leprosy Ordinance of 1919, after having undergone treatment at the hospital, nor the number of leprosy cases on the official records of the Leprosy Board, who were suffering from leprosy in a non-infective stage and consequently not recommended for segregation, following the amended Leprosy Ordinance of 1929. Naturally no account could be taken of the number of patients in hiding.

The total number of registered cases of leprosy in Malta and Gozo as on December, 1956, was 144. This figure, on an estimated civil population of 314,369 gives a rate of 0.45 per thousand. In the absence of a detailed survey it is not possible to give an accurate figure of the number of cases of leprosy in these islands, but it is calculated that their number does not exceed 200, the rate per thousand being therefore approximately 0.64. All attempts to carry out a complete examination of contacts and other close relatives have in the past proved unsuccessful. The lepromatous rate is 66%

of all known cases, and the child rate in the 534 cases notified since 1920 is 3% (children under 15 years of age numbered 21).

As already stated, in order to induce patients and their contacts to come forward for treatment, generous grants have been instituted to the households of patients suffering from leprosy. Such generous grants will also help contact-families to raise their own resistance to infection by better feeding and housing.

Social assistance is given in some measure to all patients suffering from leprosy and also their dependents. However, those patients who are not undergoing treatment in the hospital must attend at regular intervals for examination and treatment at the Out-patients' Clinic to qualify for the assistance. Should they fail to attend regularly for treatment their allowance will be temporarily discontinued.

The health authorities spare no effort to encourage patients to come forward for treatment and to persuade contacts to report for periodical examination at the Clinic.

BCG vaccination is freely offered to all contacts of leprosy patients, particularly children.

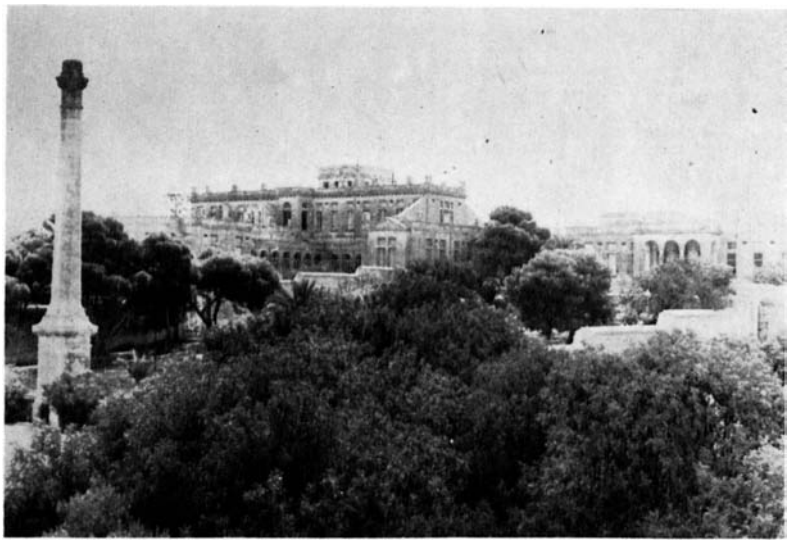
Sanitary inspectors pay frequent visits to the homes of patients living outside the hospital and give instructions and advice as to the precautions to be taken in order to prevent or minimise the danger of spreading the infection. On the suggestion of the Medical and Health Department, the Housing Department has on occasions provided suitable accommodation for families in which leprosy has occurred.

Treatment

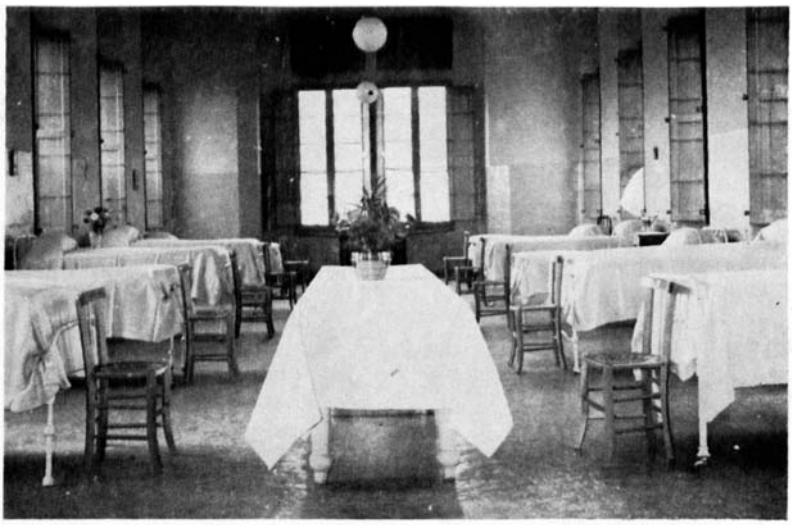
The use of chaulmoogra oil and its derivatives has long been abandoned in our hospital. Our experience is that patients did not derive much benefit from the use of these drugs, which frequently aggravated the condition of those patients suffering from the lepromatous type.

Although many different forms of treatment have been tried in our hospital, sulphone treatment in various forms has remained the standard treatment of leprosy. It is now nine years since sulphone treatment of leprosy was first introduced in our hospital, and since that time marked improvements have been noted, especially in the general health and clinical appearance of patients, the majority of whom are of the lepromatous type. Bacteriological improvement is, however, slow.

As we do not know whether the infection is ever eradicated from the patient, we continue to administer sulphone treatment



General view of St. Bartholomew's Leprosy Hospital



One of the larger wards

indefinitely, at reduced doses, even to those patients in whom the disease has been arrested.

On the whole, sulphones are well tolerated. Reactions from their use, such as erythema nodosum leproticum, mild mental derangement, etc., are occasionally met with. Such reactions subside after reduction of the dose or temporary withdrawal of the drug. Iron and yeast preparations are administered concurrently with sulphone treatment.

In common with all leprosy subjects of European descent, our patients in the past suffered extensively from eye and throat complications. Good results have been achieved from the local use of cortisone in leprotic eye complications. Leprotic blindness is now rare. Lepromatous laryngeal involvement, once so common among advanced lepromatous cases, is now extremely rare in patients undergoing treatment with sulphones. The death rate from leprosy has fallen also in recent times.

The government ophthalmologist visits the hospital at regular intervals to examine and treat the eye complications of the patients. The dermatologist pays frequent visits to the hospital in his capacity as senior leprologist. Leprosy patients who in the course of their disease develop some acute medical or surgical condition are admitted temporarily at St. Luke's General Hospital for the required treatment, and they are kept in separate wards. School medical officers are also instructed to look for the disease during their routine inspections of school children. No efforts are being spared in the teaching of young doctors how to diagnose the disease in its various phases.

Conclusion

The present trend in dealing with leprosy patients does not seem to favour compulsory segregation; this method is becoming obsolete; it has its utility as a check on the spread of disease, but it has also many drawbacks, social, ethical and administrative, and it certainly does not seem to agree with the modern outlook of thought and life. It has been ascertained that the ancient system of compulsory segregation may do more harm than good in causing the early cases to be hidden for fear of life-long imprisonment, until it is too late for effective treatment, and they have already infected members of the household. With the modern drugs and modern methods of treatment the course of the disease may be favourably modified, especially if patients seek medical advice early. Improved standards of living, better hygienic conditions, health education and adequate social services have also their beneficial effects.

BIBLIOGRAPHY

" International Congress for the Defence and Rehabilitation of the Leprous." Rome, April, 1956—Edizione Mediche e Scientifiche, Rome.

' Round the World of Leprosy," by R. V. Wardekar. Gandhi Memorial Leprosy Foundation, Wardha, N.P. India.

" Leprosy in the United States," by L. F. Badger. Trop. Dis. Bull., Vol. 53, No. 5, May, 1956. Abstract, p. 601.

" The Incidence and Epidemiology of Leprosy in Uganda," by J. A. K. Brown. Trop. Dis. Bull., Vol. 52, No. 9, Sept., 1955. Abstract, p. 903.

" Report of the Health Conditions of the Maltese Islands for the Year 19 Govt. Printing Office—Malta, 1954.

INJECTABLE SULPHONE

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We have now concluded a two-year study of injectable sulphone and have reached the following conclusions:—

Twenty lepromatous and ten tuberculoid cases were selected. Two lepromatous patients died of intercurrent infections and one absconded.

Drug: The drug used was Avlosulfon soluble.

Dosage: (Each c.c. of Avlosulfon is equivalent to 200 mgm. of DDS.) First month, ½ c.c. twice weekly. Second month, 1 c.c. twice weekly. Third and subsequent months 1½ c.c. twice weekly.

The maximum dose reached therefore equalled 600 mgm. DDS weekly. Our oral doses usually amount to 1,200 mgm. weekly, but the smaller dose by injection was decided on (1) because it was considered that all of the drug injected would be absorbed, and (2) larger doses would be more painful, as the drug is given intramuscularly.

Duration. The project was planned to last two years and the results were assessed at the end of the second year.

Presulphonisation. Most of the lepromatous cases had previously been treated with sulphones, four for a period of five years and the rest for periods not exceeding three months. The tuberculoid cases had received very little previous treatment as they were recent admissions.

Toxicity. One patient developed exfoliative dermatitis but responded to cortisone and treatment was resumed within three months. There was no evidence of renal or liver damage. Adjuvant iron or vitamin B therapy was not found necessary.

Reactions. With the exception of Erythema Nodosum Leprosum (ENL), which we regard as a normal reaction in lepromatous cases receiving sulphones, and which occurred in nine of the 17 lepromatous cases, no reactions occurred.

Adjuvant Treatment. As is our practice, the macules occurring in tuberculoid cases were treated with intradermal injections of ethyl esters of hydnocarpus oil.

Results: Tuberculoid. Nine of the ten tuberculoid cases have been discharged. Six were discharged after three months' treatment, two after 10 months' treatment, and one after 13 months. One patient is still positive. He entered the project with positive

skin smears and is probably a borderline type. One patient had a reaction in his macules prior to starting the project and smears were 3+. The lesions subsided rapidly and showed no more bacilli.

Lepromatous. Three of the lepromatous cases previously treated with sulphones for a period of five years became negative and were discharged. One is still positive though there is no evidence of clinical activity. All the cases which had little previous treatment are still positive, but the average bacteriological index has dropped from 12.5 to 5.8.

These figures may be compared with a previous project when the following results were obtained after two years.

Group 1. Oral Sulphone. Bacteriological index dropped from 12.6 to 8.8.

Group 2. Oral Sulphone plus INH. Bacteriological index dropped from 14.9 to 9.5.

Group 3. INH plus Streptomycin. Bacteriological index dropped from 12.8 to 8.7.

Group 4. Streptohydrazid. Bacteriological index dropped from 12 to 9.

The injectable sulphone therefore showed the best results.

So far as clinical changes are concerned there were:—

Marked improvement	7
Slight improvement	8
Stationary	2

Comment. So far as the results are concerned we are satisfied that Avlosulfon Soluble is as good as, if not better than, oral diaminodiphenyl-sulphone (DDS). It has the disadvantage that it has to be injected and, because of this, patients became very "needle shy" before the end of two years and begged to be taken off injections. For routine use I therefore recommend oral DDS.

I have to thank Imperial Chemical (Pharmaceuticals) Ltd. for supplies of the Avlosulfon Soluble and the Secretary for Health, Union of South Africa, for authority to submit this article for publication.

EXPERIENCE WITH ANTIGEN MARIANUM IN THE TREATMENT OF LEPROSY

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Antigen Marianum has been prepared in the ' Laboratoire de Recherche sur la Lepre '' at Lyons. It is a dilution of a culture of *Mycobacterium marianum* isolated in that laboratory from a leproma. Blanc (1953) has experimented with intradermal injections of this into healthy subjects and into patients with leprosy. He observed after three monthly injections a change from negative to positive Mitsuda reaction in 20 out of 29 lepromin negative '' controls,'' 57 out of 90 patients with '' indeterminate '' type of leprosy and 11 out of 29 patients suffering from lepromatous leprosy. He has achieved even better results when he gave two series of injections. As many as 51 lepromin negative lepromatous patients out of 55 (90%) became lepromin positive although curiously enough only 101 out of 132 (76%) '' indeterminate '' ones.

From these results Blanc derived the idea of a treatment of leprosy based on immunotherapy instead of chemotherapy. In the beginning he combined the injections of the antigen with sulphones but later the sulphones were omitted. Moreover he has applied this treatment not only to lepromin negative cases but to lepromin positive tuberculoid ones as well. According to him the improvement on this treatment was faster, more stable, and accompanied by fewer reactions than with sulphones.

In 1954 Sister Marie Suzanne, the Director of the Lyons laboratory, offered me a supply of the antigen for a clinical trial on my patients at Ossiomo settlement in Western Nigeria. The trial started in February, 1955, on 49 patients admitted since the previous September. They were divided into two groups. One group was put on the antigen treatment, the other was kept as a control. All patients admitted to the Settlement subsequently until August, 1955, were added to the trial, in all 63 in the treatment group and 63 as controls. As to the type of the disease among the treated patients, 33 were lepromatous, 27 tuberculoid and 3 dimorphous (indeterminate). Among the controls there were 26 lepromatous cases, 33 tuberculoid and 4 dimorphous.

In spite of the favourable results reported by Blanc, I was not prepared to go so far as to give the antigen as the only form of treatment to the patients. All patients continued their routine treatment with sulphones.

Method

0.1 ml. of the antigen was injected once a month into the skin of the frontal aspect of each forearm alternatively for six months. Then followed a rest of 2 months, after which the injections were resumed.

The bacteriological examination was performed in the first instance by taking only one smear from the apparently most affected portion of the skin. The results of the test were classified into four categories: +1 for less than 10 bacilli in the field of vision under an immersion lens, +2 for 10-20 bacilli, +3 for 20-30 bacilli and +4 for more than 30 bacilli in the field. Later I decided to introduce a more exact evaluation by the use of a bacteriological index. The difference was that instead of taking one smear I took six and added the figures; so for instance if the classification based on the old system was +3 the expected index would be around 18. I used this index method in my first evaluation test in September, 1955, and intended to use it in further periodical examinations.

At the end of September, 1955, I proceeded on a long leave and the trial was stopped two months later. Consequently I can report here only on the results found by me in September, 1955, after the patients had received between 1-6 months of the treatment, and the position in March, 1957, when I saw them again 16 months after the trial was stopped.

Immediate Reaction to the Injection

General

All patients had a rise in the temperature on the day following the injection. In about 25% of them the temperature rose above 100° F. In the majority of patients the general reaction lasted only one day but in some it went on longer, up to one week. Following each injection one or two patients went into the erythema nodosum type of lepra reaction. The general reaction has been stronger in the lepromatous patients than in the tuberculoid. On the whole, the degree of the general reaction has been constant in individual patients after each injection.

Local

A few hours after the injection an inflammatory swelling about an inch in diameter developed at the site. By the next day a papule formed which changed into a nodule. Four or five days after the injection the nodule started to ulcerate. The ulceration remained for a few days and began healing about a week to ten days after the injection. The scar was still very obvious several months after

the injection but after a year it was hardly visible. No tolerance to the injection was developed. Every consecutive injection brought the same general and local reaction.

Change in the Sensitivity to Lepromin

I performed the Mitsuda test with crude lepromin in 19 lepromin negative patients a month after the end of the first series of injections. I found that 4 patients had converted to a positive reaction, 2 to a weak positive reaction and 13 remained lepromin negative. Therefore my results were not as favourable as those of Blanc who had a conversion in 90% of his lepromatous patients after six injections of the antigen.

Clinical and Bacteriological Findings

The patients have been reviewed twice, in September, 1955, and in March, 1957. By the time of the first review one lepromatous patient æt. 8 years had died of acute nephritis of unknown origin. Between the first and the second review 2 lepromatous and 5 tuberculoid patients of the treated ones, and 3 lepromatous and 1 tuberculoid among controls left the settlement. Therefore at my second review I was able to evaluate 30 lepromatous, 22 tuberculoid and 3 dimorphous treated cases, and 23 lepromatous, 32 tuberculoid and 4 dimorphous controls. These patients had received between four and eight injections of the antigen.

Tuberculoid and Dimorphous Cases

It is difficult to estimate improvement in bacteriologically negative cases of leprosy where one had to depend on findings which are to a certain extent subjective. Certainly there has been no significant difference in the progress between the patients who had been receiving the injections of the antigen and those receiving no antigen. Five tuberculoid patients who received the antigen were fit for discharge before my second review, but so were 6 tuberculoid and 2 dimorphous controls.

Lepromatous Cases

Here one can base the evaluation of the progress not only on clinical but also on objective bacteriological findings.

The first batch of patients, who have had eight injections of the antigen, are shown in Table I and their controls in Table II. I have tried to compare the results in these two groups by the following computation: I have multiplied the figures in the first column by six to obtain an approximate index comparable with the indices in the other two columns and then added the indices

in each column. In this way I obtained the figures 216, 170 and 77 for the treated patients and 138, 100 and 37 for the controls, showing actually slightly better results for the controls than for the treated patients (75% improvement in the controls against 65% in the treated). However, due to rather imperfect matching of patients in the two groups, there was a lesser number of severe cases among the controls than among the treated. This might have affected the results.

The findings for the second batch of patients, who have had seven injections, and their controls are shown in Tables III and IV. Here the computation gives figures 126, 91 and 41 for treated patients and 36, 29 and 6 for the controls, again more favourable to the controls, but subject to the same criticism as the first batch.

The findings for the third, fourth and fifth batch, all of whom have had six injections of the antigen, and their controls, are presented in Tables V and VI. The additions give the figures 168, 152 and 81 for treated cases and 102, 93, and 52 for controls showing the same degree of improvement (about 50%).

The sixth batch of patients, who have had five injections, and their controls are presented in Tables VII and VIII. The figures are 24, 27 and 22, and 25, 36 and 12, again showing better results in the case of the controls.

Finally the seventh batch of patients with four injections and their controls are shown in Tables IX and X. The figures are 64, 60 and 40, and 42, 36 and 22 respectively. Here as in the sixth batch the patients were well matched but still the results are better for the controls.

Patient's number.	Feb. 1955	Sept. 1955	March 1957
3500	+ 4	19	13
3504	+ 3	16	2
3510	+ 4	21	12
3514	+ 4	15	5
3520	+ 3	9	2
3531	+ 4	22	14
3558	+ 4	23	14
3560	+ 4	24	12
3568	+ 3	16	3
3572	+ 1	—	—
3580	+ 2	5	—

Table I

Results of bacteriological tests in the first batch of treated patients.

Patient's number.	Feb. 1955	Sept. 1955	March 1957
3517	+ 3	17	12
3532	+ 2	7	—
3543	+ 3	19	5
3551	+ 1	4	—
3559	+ 3	9	—
3567	+ 2	—	—
3571	+ 1	1	—
3573	+ 4	19	11
3583	+ 4	23	9

Table II

Results of bacteriological tests in the first batch of controls.

Patient's number.	March 1955	Sept. 1955	March 1957
3509	+ 4	17	9
3566	+ 3	4	—
3587	+ 3	17	6
3591	+ 4	23	16
3597	+ 4	19	10
3601	+ 3	11	—

Table III

Results of bacteriological tests in the second batch of treated patients.

Patient's number.	March 1955	Sept. 1955	March 1957
	+ 3	17	6
3611	+ 3	12	—

Table IV

Results of bacteriological tests in the second batch of controls.

Patient's number.	April 1955	Sept. 1955	March 1957
3613	+ 4	18	9
3623	+ 4	22	12
3630	+ 4	16	9
3634	+ 4	23	16
	May 1955		
3644	+ 3	18	8
3646	+ 4	24	18
	June 1955		
3659	+ 2	13	—
3664	+ 3	18	9

Table V

Results of bacteriological tests in the third, fourth and fifth batch of treated patients.

Patient's number.	April 1955	Sept. 1955	March 1957
3625	+ 4	20	12
3627	+ 2	14	
3629	+ 4	24	21
3631	+ 2	10	—
	May 1955		
3643	+ 1	2	—
3666	+ 4	23	19
	June 1955		
3677	+ 1	14	2
3680	+ 4	22	10

Table VI

Results of bacteriological tests in the third, fourth and fifth batch of controls.

Patient's number.	July 1955	Sept. 1955	March 1957
3674	+ 3	21	22
3679	+ 1	6	—

Table VII

Results of bacteriological tests in the sixth batch of treated patients.

Patient's number.	July 1955	Sept. 1955	March 1957
3677	+ 1	14	2
3680	+ 4	22	10

Table VIII

Results of bacteriological tests in the sixth batch of controls.

Patient's number.	August 1955	Sept. 1955	March 1957
3686	+ 4	21	18
3688	+ 3	20	6
3691	+ 4	19	16

Table IX

Results of bacteriological tests in the seventh batch of treated patients.

Patient's number.	August 1955	Sept. 1955	March 1957
3685	+ 3	12	4
3689	+ 4	24	18

Table X

Results of bacteriological tests in the seventh batch of controls.

As for the clinincal improvement there is again the difficulty of objective evaluation based on clinical descriptions. I have certainly not observed any marked difference between the treated patients and the controls. It is, however, interesting and perhaps should be put on record that several of the better educated patients who have had long experience of the Settlement have formed the opinion that lepromatous patients who have had the injections of the antigen have definitely improved faster than the general run of patients on sulphones. How far this opinion was influenced by the common belief in greater efficacy of injections compared with drugs taken by mouth I am unable to say.

Conclusions

The general idea of a treatment of leprosy through the stimulation of a positive allergic response to the bacillus is a tempting one. The question is whether it is really possible artificially to induce such response in a lepromatous patient the essence of whose disease is the inability to create it naturally in spite of the presence of the bacilli in his body. It is known that sulphones only rarely convert the lepromin test in lepromatous patients. Schujman (1956) in his experiments with the BCG vaccine and the Stefansky antigen has found that although it was possible to convert the lepromin reaction in 50% of his lepromatous subjects such conversion was very short lived. He concluded that induced lepromin reaction in lepromatous cases has no practical value. Blanc claims that he has achieved such conversion by means of the Antigen Marianum in 90% of his lepromatous patients. I have been unable to confirm it since I have achieved it only in 30% of my cases. Blanc does not state how permanent the conversion has been. I have not been able to perform the lepromin test in my patients at the second review.

So while on theoretical grounds the idea behind the use of the antigen for the treatment of lepromatous leprosy seems to be sound, on further investigation it does not appear to work so well in practice. On the other hand I do not see any theoretical basis for the use of the antigen in tuberculoid leprosy. The essence of this type of the disease is a strong immunological response. Even if it were possible to make it still stronger it is questionable whether this would be desirable considering the possible damage to the peripheral nerves through an excessive formation of fibrous tissues. We know that a great many of the signs and symptoms in this type of leprosy are caused by this excessive response of the tissues to the bacillus.

However, my aim has been to test Blanc's results in practice. Unfortunately my trial has been cut short and its value is there-

fore limited. Nevertheless if the results of the injection of antigen were going to be spectacular even 8 months should have been sufficient to indicate them. This is not the case as far as an objective bacteriological test is concerned. As for clinical improvement compared with the controls, the results seem to have been negative as well. Yet I cannot ignore completely the impression gained of certain favourable results reported by the patients, for whatever it is worth.

I have to point out that I was not prepared to go as far as Blanc and deprive my patients of the tried routine treatment with sulphones. In my experience the antigen has been only added to the sulphones. Possibly my patients on the antigen would have improved just as much if they had not taken the sulphones at the same time. With regard to the question as to which treatment is preferable, each injection of the antigen gives a certain amount of general and local reaction, which however harmless is certainly very unpleasant to the patient. Because of that, oral treatment with sulphone seems preferable.

I wish to emphasize again that my trial was rather abortive. For the final evaluation of the treatment with Antigen Marianum one has to wait for the results of other trials like the one being conducted at the present time by Wolcott at Carville.

Summary

1. A treatment trial with Antigen Marianum was conducted on 55 leprosy patients with 59 controls; all cases received the sulphones.
2. The trial was cut short so that only 5-8 monthly injections of the antigen was given to the patients.
3. No definite difference was observed in the rate of improvement of patients who received the antigen and sulphones compared with the patients on sulphones alone.

Acknowledgements

My thanks are due to the patients and members of the staff of the Ossiomo Settlement for their co-operation, to Sister Marie Suzanne for the supply of the antigen, to Dr. S. J. Healy, Area Superintendent Ossiomo Settlement, for permission to review the patients in March, 1957, and to the Director of Medical Services, Western Nigeria, for permission to publish.

REFERENCES

BLANC, M., *et al.* (1953). J. des. Sc. Med. de Lille, p. 584.
BLANC, M., and PROST, M. (1955). Int. J. Leprosy, **23**, 23.
SCHUJMAN, S. (1956). Int. J. Leprosy, **24**, 51.

LACK OF EFFECT OF CORTISONE ON THE NEGATIVE LEPROMIN TEST

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In sarcoidosis, a disease which has certain resemblances to leprosy, the tuberculin test is negative in a majority of patients tested with 100 T.U. Yet two-thirds of such Mantoux-negative patients give a positive reaction to as little as 5 T.U. if the tuberculin is incorporated in an oily vehicle (James and Pepys, 1956).

Citron and Scadding (1957) mixed cortisone with tuberculin and found that although the tuberculin reaction was inhibited in hypersensitive subjects, a positive reaction was induced in 14 out of 28 patients with sarcoidosis who were tuberculin negative.

In both these experiments the production of a positive skin reaction was attributed to retention of the tuberculin, either by oil or by cortisone, at the site of injection. The conclusion was that in sarcoidosis there might be a residuum of sensitivity to tuberculin which could not be detected by ordinary tuberculin tests.

These experiments led us to consider if any latent sensitivity to lepromin in lepromatous leprosy would be revealed by the addition of cortisone to the lepromin, or whether the lack of sensitivity would prove to be absolute.

Method. Double strength lepromin was diluted with cortisone acetate suspension in such a way that 0.1 ml. of the mixture contained a normal test dose of lepromin plus 1.25 mg. of cortisone acetate. The mixture was used to test six lepromin negative patients with lepromatous leprosy, the injections being given intracutaneously in the usual way.

Results. The reactions were negative in all six patients, both at 48 hours and between 2 and 5 weeks.

REFERENCES

CITRON, K. M., and SCADDING, J. G. (1957). Quart. J. Med., 26, 277.
JAMES, D. G., and PEPYS, J. (1956). Lancet, 1, 602.

THE PREPARATION OF COMPOST IN THE HAY LING CHAU LEPROSARIUM, HONG KONG

N. D. FRASER, M.B., CH.B.

[NOTE:—No originality is claimed for the methods described here; suggestions and ideas from many friends and a variety of sources have been tried and used or rejected; the process now described is the result of some years of experiment.]

When the development of Hay Ling Chau as an island leprosarium began in 1951, I was determined that there would be no avoidable waste and that everything that could be used should be composted and returned to the ground; all waste paper was to be burned; all broken glass and tins (if not needed for the planting out of tree seedlings) were to be buried or dumped in the deep sea; and the rest was to go on to the compost heaps.

In spite of repeated urging, however, I found nothing was being done to carry out my instructions and finally I was told "The patients who are doing the vegetable gardening say that they will grow all the vegetables needed; they will grow them in the way they have been grown by the Chinese people for centuries; they will not use compost." It seemed clear that in China, the home of compost making, there were many systems of nourishing the soil and this group of Cantonese vegetable gardeners preferred to all others the objectionable and unhygienic liquid contents of open cess pits.

It looked as if an impasse had been reached; but as more patients were transferred more labour became available, and a former ship's steward, badly crippled though he was, offered to carry out any instructions connected with the composting. So for a start a simple pile of vegetable refuse was built up, and from time to time turned over. The resulting rich humus so appealed to the gardeners that their ideas began to change, though they still preferred their liquid manure; the soil being sandy and very soft needed the humus to help it retain moisture, but the repeated watering with liquid manure certainly grew plenty good vegetables—which were well cooked before being eaten!

But when our pig-breeding was successfully established a more scientific approach was needed and much valuable inspiration and help was found in Sir Albert Howard's "Farming and Gardening for Health and Disease," and especially in the notes on the Trengganu Household Composting Plan as used in Malaya.

The site—it is an advantage if the composting can be done on

a hill slope with access at the top to bring in the material to be used, and access below to take away the finished product. Water should be easily available. Such a site was available adjacent to our sties, with a stream flowing nearby. Briefly four pits were cut into the bank with access for filling at pit-top level; at ground level a concrete bed was laid, divided into sections by gutters, 4 in. deep by 6 in. wide; 3 ft. below the concrete bed another road made it easy to load the compost into our trailer.

The Pits

The pits are roughly 6 ft. from front to back, 4 ft. deep and 3 ft. wide, with an open front. They are faced with brick or stone walls with a cement mortar finish to prevent any possibility of fly larvae crawling from the contents into the surrounding soil. Inside the pit a few inches above the base of each wall a ridge was made on which to rest bamboo sections to allow free drainage and ventilation; a drain down the centre of the pit connects with the drains in the concrete bed; the walls are slotted to allow boards to be dropped in, to close the front as the pit is filled.

Gutters surround the pits at pit-top level; gutters also divide the concrete bed into four sections just outside the pits and four sections adjacent to the lower road. These gutters are kept filled with water by blocking the outlet with a sod, and are drained daily into sump-pits, the contents of which can be used for watering flowers and vegetables. Flies are inevitably attracted by the pits and their contents, and lay eggs there; the larvae hatch out and try to get into surrounding soil to develop into the pupal stage; they fall into the gutters and are drowned.

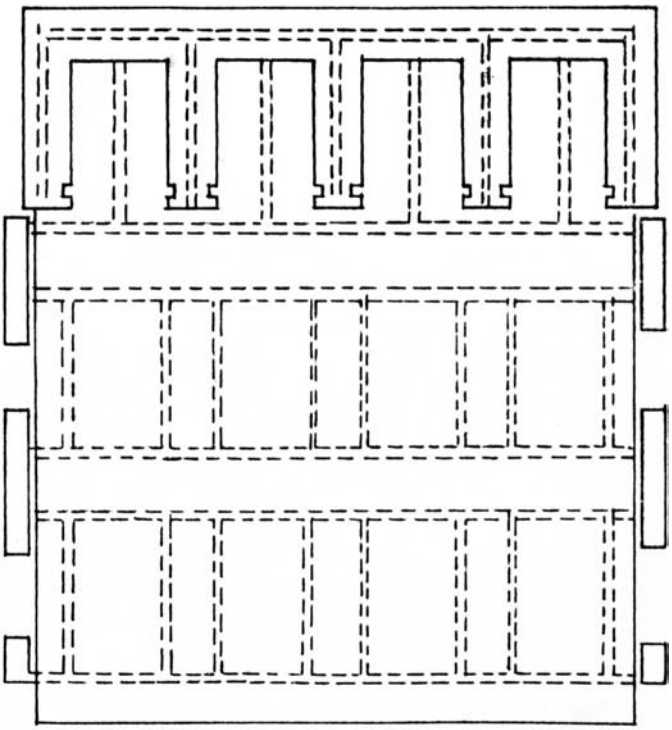
Use

Each pit is fillled in the course of one week.

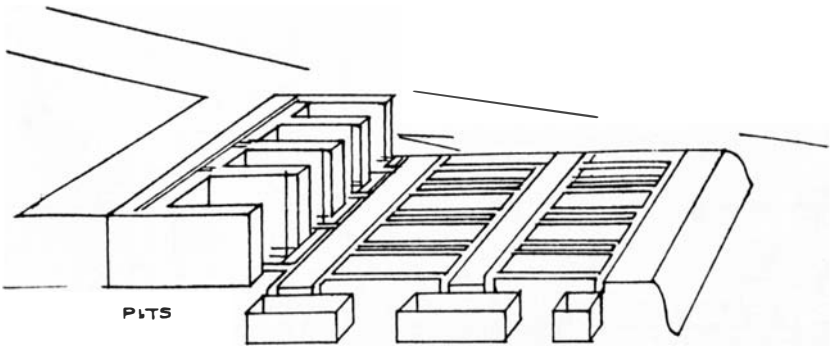
Bamboos are laid across the bottom resting on the ledges and on loose bricks alongside the drain. A layer of bedding from the sties, or of grass cut from the hillside, is spread over them. To this is added a layer of pig manure from the sties nearby; another layer of grass, bedding or vegetable waste; and then a thin layer of garden soil. Each day the pit should be filled to the depth of one foot; its own weight compresses and settles the mass so that seven days' filling goes into a four-foot pit. The temperature within the pit should rise to 120° to 130° F.

At the end of four weeks the four pits are filled. The first pit is then dug out, and the contents are built up again on the concrete bed, surrounded by gutters kept filled with water (a wooden

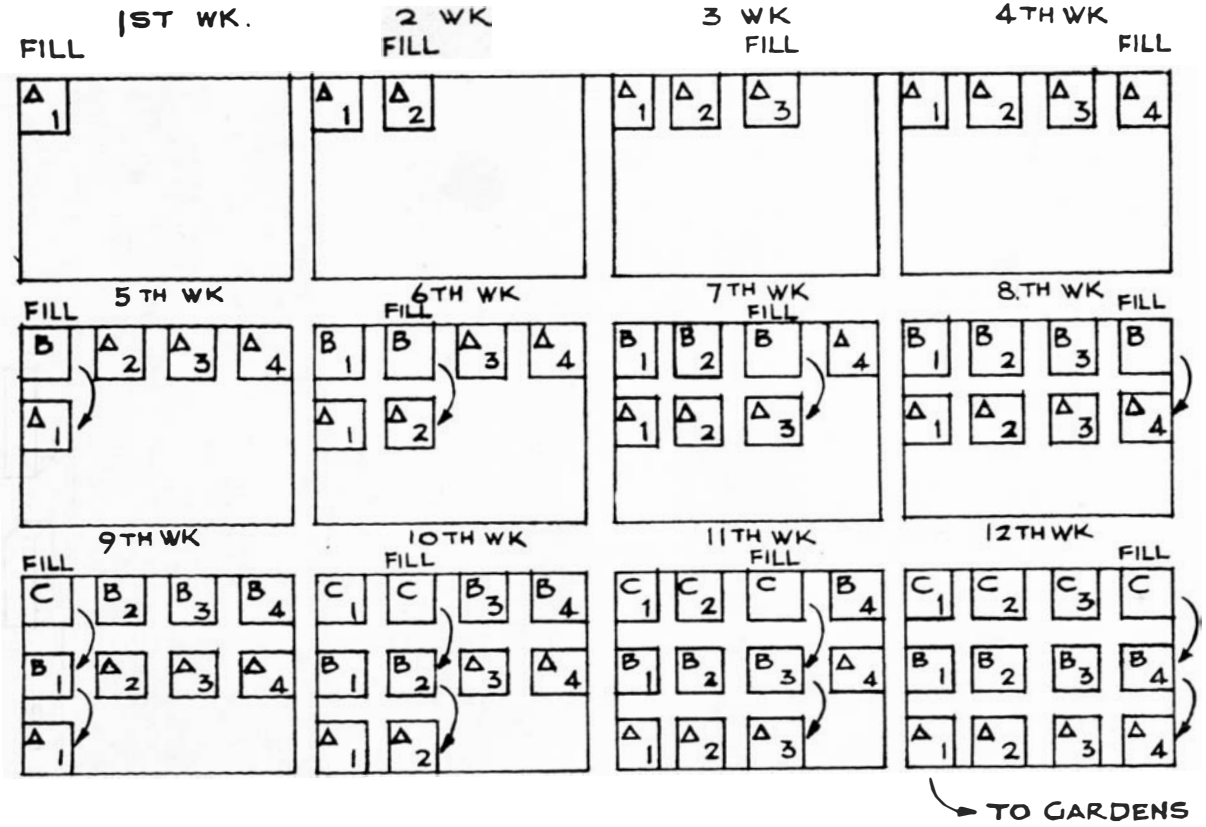
PITS WITH GUTTERS



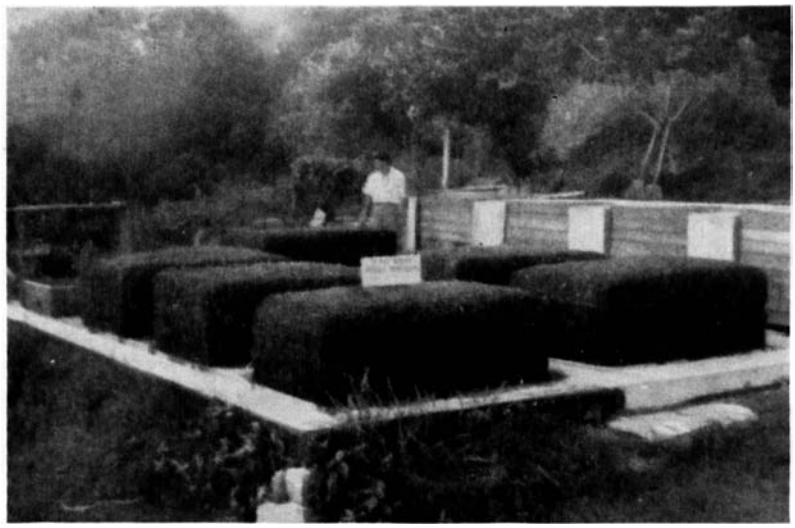
CONCRETE PLATFORM WITH GUTTERS AND SUMPS



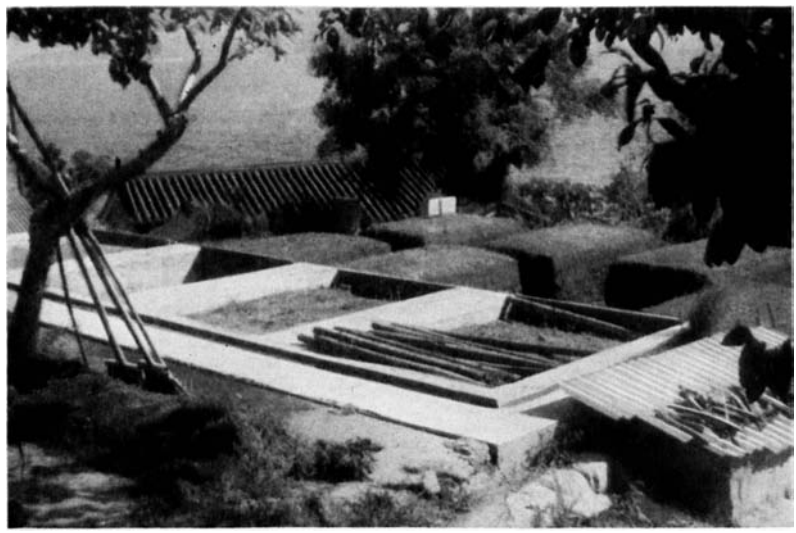
CONCRETE PLATFORM WITH GUTTERS AND SUMPS



12 WEEKS COMPOSTING



Looking at compost pits and piles from below.



Looking down on compost pits from above.

rectangular frame made from 4 boards, 8 ins. deep, is a useful " mould ": it can be raised as the pile grows, and then moved on to the next " bed ").

At the end of 8 weeks there are four pits filled and four heaps on the concrete beds.

At the end of 12 weeks there are four pits filled and 8 heaps in two rows on the concrete beds.

Thereafter each week one heap, having decomposed and matured for 12 weeks, is ready for removal, its place being filled in from the next row.

The contents of the pits and of the heaps are kept moist, with free drainage. In heavy rains some protection is needed: in the dry season they are watered daily and covered to diminish evaporation.

" Compost Activator " would speed up the process, but allowing 12 weeks for decomposition and maturation the resulting compost shows no offensive matter, is free from objectionable smell and does not encourage fly breeding. Dug into flower and vegetable beds it provides a rich nourishment for devitalised soil; and vegetables and flowers flourish.

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ABSTRACTS

Retention and Differentiation of Mycobacteria in Tissue Section. **J. H. Hanks.** Am. Rev. Tuberc., 1956, 74, 608.

Rapid deparaffinization and turbulent interactions between alcohol and solvents and alcohol and water cause the loss of mycobacteria from paraffin-embedded sections. This loss can be decreased by slowing the deparaffinization, by avoiding the use of alcohol, and by differentiating and decolourizing in aqueous reagents. Sulphuric acid differentiators and acidified sulphates as decolourizers are the best, because of their fixative action and their high selectivity in discharging carbolfuchsin from tissues, while leaving it in mycobacteria. A more sensitive and reliable method of obtaining essential information on mycobacterial lesions may be that of making impression films directly from the cut surfaces of organs.

Retention and Differentiation of Carbolfuchsin-stained Mycobacteria in Diagnostic Films. **J. H. Hanks.** Am. Rev. Tuberc., 1956, 74, 597.

The best demonstration of mycobacteria in diagnostic films depends more on other factors than the choice of the primary stain. These other factors comprise the use of protective protein films to cover or imbed the mycobacteria; the use of reagents which exert fixative rather than disruptive effects on cells and protein films, namely carbolfuchsin solutions, alcohol buffered at mild acidities, and acidified sulphates, whereas acid-alcohol is destructive; the use of judicious rather than excessive staining with carbolfuchsin; the use of decolourizing agents which keep the carbolfuchsin in mycobacteria while displacing it from cells, and in this matter acidified sulphates are better than acid-alcohol, alcohols buffered at mild acidities, and citric, hydrochoric and nitric acids; the use of sulphuric differentiators containing dilute methylene blue; the use of the differentiators in such concentrations as will permit of timing their action to end points. The paper gives details of materials and methods and discusses observations made and the factors concerned.

The Present State of the Leprosy Problem in Minas Gerais. **J. Mariano,** Arquivos Mineiros de Leprologia, Oct. 1956, No. 4, 416-426.

In the state of Minas Gerais, Brazil, there were 26,263 recorded cases at the end of 1955. Lepromatous cases comprise 66.89%,

tuberculoid 21.60%, and indeterminate 11.50%. The prevalence index varies in the 14 zones of the state from 4.2 to 40.1 per thousand, in a total population of 7,877,566. The 6 leprosaria in the state cost the Government about £337,000 in 1955, and for advances in the leprosy campaign it is estimated that an annual expenditure of about £50,000 will be needed, to cover staff including 14 leprologists, medication, equipment, food, etc. The leprosy service is to be interwoven with the general health service, and great benefits are expected to follow the introduction of domiciliary treatment, BCG vaccination of contacts, census of contacts and search for early cases, and health education of the people.

The Uptake of DDS by Leprosy Patients as Detected by Tracer Technique. **K. T. Chatterjee, R. K. Poddar, N. Mukerjee and R. Bose.** Bull. Cal. School of Trop. Med., 5: 4, 1957.

Studies on the DDS uptake by 22 leprosy patients using radioactive tracer technique showed that on oral administration there was initially a rapid increase to reach 8% of the dose in about 6 hours. The level then gradually decreased at an average of 62% a day to almost nothing in about 5 days. Excretion via the kidneys deals with about 78% of the drug within a week, at an average rate of excretion of 42% per day. The drug level in bone marrow and healthy tissues ran almost parallel to that in blood. The drug concentration was 10 times greater in affected than in healthy tissues. Findings after subcutaneous administration were similar to those after oral. The tracer technique was found to be 10 times more sensitive than the colorimetric.

Haemotological Effect of Adding Yeast and Iron to DDS in the Treatment of Lepromatous Cases. **N. Mukerjee and N. R. Sen.** Leprosy in India, Vol. XXVII, No. 4, Oct. 1956, 121-127.

The authors refer to the results of Dharmendra and Chatterjee, S. N. (1953) which showed that the routine use of yeast and iron was not necessary during the sulphone treatment of leprosy. They have studied 36 lepromatous cases to which a DDS product was administered, and of these 12 were given the DDS product alone, 12 had yeast added 0.5 gm. to each 50 mgm. tablet of DDS, and 12 had in addition 1.5 grains of ferrous sulphate. They found that the blood picture before and after gave no indication that these additions counteracted the tendency to produce anaemia, nor do they help very much in improving the blood picture subsequently.

Estados Reacionais na Lepra. (*Reactional States in Leprosy.*) **N. Souza Campos and P. Rath de Souza.** Rev. Brazil. de Leprologia, **25,** Jan.-March, 1957, pp. 3-18. 20 illustrations.

This paper represents a valiant attempt to bring order into the confusion in the clinical phenomena massed under the name of lepra reaction, or leprotic reaction. The authors make a comparative study under four heads: (1) lepra reaction (erythema nodosum); (2) tuberculoid reactivation; (3) reactional tuberculoid; (4) borderline lesions.

(a) As regards *origin, the first* only intervenes in lepromatous cases, in about 60% of them; it can be the initial manifestation of the disease; it begins acutely. *The second* intervenes in the course of the chronic evolution of quiescent tuberculoid macules; it begins slowly. *The third* begins acutely in the tuberculoid form and in rare cases may follow a reactivation attack; it can appear as a primary manifestation in apparently healthy persons. *The fourth* begins acutely, secondary to the reactional tuberculoid form in relapses, or in apparently healthy individuals as a primary manifestation.

(b) As regards the *type of the eruption, the first* shows lesions of erythema nodosum type, which are polymorphic with many degrees of swelling, and often there are neuritic, ocular, and orchitic complications, and frequent relapses. In *the second*, the pre-existing lesions show infiltrated reactivated margins, increase in size, and take on a reddish colour. New lesions may appear, and they never appear abruptly as in reactional tuberculoid. In *the third*, the lesions are polymorphic, there being tubercles, nodules, plaques, and patches of erythema. The colour is purple and vinous, and the lesions are strongly infiltrated, swollen, and succulent. There is a site of election on the palms and soles, eyebrows, and the naso-labial furrow. *The fourth* has the same aspect as the reactional tuberculoid. The colour tends to be rusty, and the outer borders are indistinct, and infiltration is less marked. Flat pigmented lesions often occur in association.

(c) As regards *systemic phenomena, the first* is always accompanied in the acute forms by fever, sepsis, arthralgias, headache, neuritis, gland swellings, weakness. These are less marked in the more chronic forms. *The second* does not show systemic phenomena. *The third* rarely shows them in the acute manner, but there are moderate joint pains, a mild increase in temperature, and a cutaneous hyperaesthesia. Some cases do not show any general effects at all. *The fourth* has almost always some general signs.

such as pains and oedema of the large joints, fever, and headache. Often these patients have to remain in bed.

(d) As regards *evolution, the first* tends to be chronic, relapsing acutely and subacutely, with residual ecchymoses and local thickening. *The second* stops in the reactivation phase and the case returns to its chronic evolution, often with the lesions increasing in size and number. Relapses can evolve into reactional tuberculoid. *The third* stops in the acute phase and most cases tend to clinical cure. Relapse cases have a tendency towards borderline lesions. *The fourth* stops in the acute phase and often the lesions take on the lepromatous aspect; rarely do they resolve or take on the characters of the reactional tuberculoid form.

(e) As regards *bacilli in smears from the skin and nasal mucosa, the first* is positive as a rule, rarely negative. *The second* remains negative before, during, and after the attack. Almost always positivity coincides with a tendency to change into reactional tuberculoid. *The third* is often positive in the beginning and during the acute phase, the bacilli being abundant and globi absent. The skin is more often positive than the mucosa. There is a tendency to negative smears in a variable length of time. *The fourth* is positive as a rule before and during the attack, with globi. In negative cases there is a tendency to regression to reactional tuberculoid.

(f) As regards *the lepromin reaction, the first* is always negative. *The second* is almost always frankly positive before, during and after the attack. *The third* is either positive or negative in the beginning and during the attack, tending to be more positive as the attack recedes. *The fourth* is always negative and remains so; in exceptional cases there may be a positive, but it is weak.

(g) As regards *structure, the first* shows an acute inflammatory exudate on top of the pre-existing lepromatous infiltrate. Bacilli are present, with a granular aspect, or absent, and lipids are present. *The second* shows acute inflammatory features added to the classic tuberculoid granuloma; there is a variable amount of vascular dilation, endothelial swelling, and oedema with consequent loosening up of the foci. In general bacilli and lipids are absent. *The third* shows a tuberculoid structure which is less typical than in tuberculoid reactivation, combined with vascular dilation, endothelial swelling, and intra- and extracellular oedema with consequent vacuolization and separation and loosening up of the infiltrative foci. Bacilli are almost always present, and lipids are absent. *The fourth* shows a picture intermediate between reactional tuberculoid and lepromatous. There are always plenty of bacilli, with globi. Lipids have not yet been studied sufficiently.

Histopathological Findings in a Case of Tuberculoid Leprosy. **D. G. Jamison and R. G. Cochrane.** Trans. Royal Soc. of Trop. Med. & Hygiene, **51**, July, 1957, p. 301.

This is a report of a demonstration specimen at a laboratory meeting of the Society. The lesion in a case of tuberculoid leprosy had been biopsied in the skin at the centre and at the margin; also the area adjacent to the lesion, and a segment of the nerve supplying the affected skin was removed. Silver-impregnated sections and haematoxylin and eosin stained sections were prepared. The former showed a relatively abrupt diminution of nerve fibres towards the zone of the lesion but there was a full complement of nerve fibres in the skin adjacent to the lesion. Silver-impregnated axis cylinders were much fewer at the margin of the lesion, and in its centre there were none at all. In both places empty and infiltrated Schwann cell pathways were still to be seen. Sections from the parent cutaneous nerve showed nerve destruction like that in the centre of the lesion.

Haematoxylin and eosin sections from the centre of the lesion showed a flattening of the epidermis, and in the subjacent dermis an extensive infiltration which included round cells, epithelial cells, and multinucleated giant cells, the picture typical of tuberculoid leprosy.

In the haematoxylin and eosin nerve section there was gross distortion of the pattern of bundles of nerve fibres. A central necrotic zone lay within the epineurium, surrounded by a cellular infiltration like that seen in the dermis of the centre of the lesion. Sensory tests (Lele, Sinclair and Weddell, 1954. J. Physiol., **123**, 187) showed that the skin adjacent to the lesion had normal sensation, but the centre of the lesion was anaesthetic to touch. The margin of the lesion had diminished sensation and impaired localization.

" Correlaçao Entre os Resultados da Leitura Clinica e do Exame Histopatalogico da Reação de Mitsuda ' (*Correlation between the results of the clinical reading and the histological examination of the Mitsuda reaction*). **L. M. Bechelli, P. Rath de Souza and R. Quagliato.** Revista Brasileira de Leprologia, **25**, Jan.-Mar., 1957, 21-58.

The authors have made a careful correlative study of the Mitsuda reaction in its clinical and histological aspects. They sought information on the following questions:—(1) Is the 1+ reaction always associated with a positive histology? (2) What is

the significance of a 1+ in prognosis? (3) Is there any difference in the histological picture of 1+ and 2+? (4) Does the reported unfavourable evolution in some 2+ cases contradict the prognostic value of the lepromin test? (5) What is the significance of a reaction with a slight thickening of the skin or a small papule under 3 mm. in diameter? (6) Can a new standard for reading the Mitsuda reaction emerge from the correlation with the histology?

In 118 cases of leprosy and 21 contacts the authors biopsied the site of the lepromin injection at about 30 days. Their histological interpretation was based on the following standards:—(a) *A positive histology* when there was a chronic inflammatory granulomatous infiltrate of a certain degree, with predominance of epitheloid cells, and tuberculoid structure, and the bacilli absent or very few; (b) *A negative histology* when there was a simple chronic inflammatory infiltrate with bacilli usually absent or few, or a granulomatous infiltrate without tuberculoid structure but made up of histiocytes and there being a great number of bacilli; (c) *A histology tending towards a positive* when the chronic inflammatory infiltrate is not totally granulomatous nor mostly made up of epithelioid cells, and these are grouped in places; giant cells may be present but are rare, and bacilli are absent or rare.

In their studies they found that the positivity in (c) above had a certain validity at the less definite end of the scale, especially if considered in relation to the clinical type. In their correlation of clinical with histological interpretations they found that the postitive histology was not seen at all *in the clinically negative lepromin tests*, but a negative histology in 90%, and in the rest the histology tending towards a positive. *In doubtful lepromin tests*, about 64% had a negative histology and the rest had the histology tending towards a positive. *In the 1+ lepromin tests*, about 60% had a positive histology, about 27% had the histology tending towards a positive, and the rest a negative histology. *In the 2+ lepromin tests*, about 58% had a positive histology, about 23% tended to a positive, and the rest had a negative histology. *In the 3+ lepromin tests*, about 84% had a positive histology and the rest the histology tending towards positive, and there was no case with negative histology. *In ulcerated lepromin tests* without nodule there was a negative histology in the 2 cases found. Considering their results the authors remark on the clear histological picture of the negative and 3+ lepromin reactions. They think that the doubtful clinical reading may be associated with a certain degree of body resistance in about one-third of the cases. They draw attention to the considerable similarity in the histology of the 1+ and 2+, in the intensity and

quality of the infiltrate, as well as the frequency of each type of infiltrate. There may sometimes be a negative histology in the 1+ and 2+ reactions. They think that the certificate of definite arrest of leprosy should include a consideration of the lepromin test, the aim being to reach 2+ for formerly indeterminate and lepromatous, though 1+ would do for patients where the histology was positive. They found that the pure histology did not enable them to distinguish the intensity of the reaction 1+ and 2+, but a 3+ can usually be distinguished. In lepromatous cases which were already bacteriologically negative a clinically positive lepromin was rare, and its histology was uncertain in significance; there was no frankly positive histology. In indeterminate and tuberculoid leprosy and in contacts there was a definite histological positivity in the 1+ and 2+ reactions. In quiescent tuberculoid leprosy negative histology was never seen, whether with the 1+, 2+, or 3+. Prognostic value of the reaction they think is indicated by the histology to be as follows:—for about a third of the doubtful reactions a certain degree of resistance; for 1+ and 2+ a definite degree of resistance, but not much difference between 1+ and 2+; for 3+ an efficient resistance.

They suggest that the lepromin test in future might be read in a new way, putting the 1+ and 2+ in the same group, so that there would be readings possible of negative, doubtful, 1+, and 2+, the last being the highest. The paper has 7 illustrations of histological findings, 3 tables of results and data of case histories of patients of the study grouped under their lepromin results.

Lepra Conjugal: Estudo Epidemiológico dos Casos Observados no Dispensario do D.P.L. en Campinas, S.P. (1934-1954)." **R. Quagliato.** (*Conjugal leprosy: epidemiological study of the cases observed in the dispensary of the Sao Paulo Leprosy Department at Campinas, Sao Paulo, 1934-1954*). Revista Brasileira de Leprologia, **25**, Jan.-Mar., 1957, pp. 59-68.

From the records of 7,062 contacts of leprosy patients of the twenty-year period, the following table emerged:—

Relation	Totals of contacts	Developed leprosy	%
Children of patients	2,064	206	9.9
Brothers or sisters of patients	1,365	121	8.8
Conjugal partners of patients	639	50	7.8
Parents of patients	400	36	9.0
Others	2,594	87	3.3
	7,062	500	

Of the 50 conjugal contacts who developed leprosy, 52% were males, and the lepromatous incidence was 37% in the males and 41% in the females. The duration of living contact was up to 10 years in 44%, and the apparent incubation period was up to 5 years in approximately 94%.

A *leading article* in the Lancet of Aug. 17, 1957, pp. 330-331, is worthy of study by leprosy workers, as it gives a valuable short account of *gamma-globulin deficiency*, with 42 references to the workers in this field. The interest of leprosy workers will be aroused by the possibility of using this congenital condition to enlarge our understanding of resistance to disease. Hypogammaglobulinaemia is however rare in occurrence, and if leprosy workers wish to be able to use this " experiment of nature " for studies to throw light on leprosy resistance, they should be prepared to be able to recognise it. Gamma-globulin ranges in normal children are 600 to 1300 mgm. per 100 ml. In hypogammaglobulinaemics values of 0 to 30 mgm. per 100 ml. will be found. As the serum antibodies occur in the gamma fraction, the importance of the grave deficiency in it will be seen. The defect seems to be one of production, and there is a remarkable associated deficiency of plasma cells in the tissues. It is accepted by most workers that antibodies are formed mainly in the plasma cells.

Maruskenie Temperatury i Electrosoprotioliajemosti Irmennenykh i Vneshne Zdorovykj Vchastkov Kozhy Rannikh Projavleniakh Lepry. (*Disturbance of Temperature and of Electrical Resistance in the Clinically Healthy Parts of the Skin, and in the Affected Parts of the Skin, in the Initial Stages of Leprosy.*) **A. Letichvskaia.** Sbornik Nauchnykh Rabot po Leprologii i Dermatologii (Collected Scientific Papers in Leprosy and Dermatology), N. 8, 1956, pp. 105-109. Rostov-on-Don Experimental and Clinical Leprosarium of the Ministry of Health of the U.S.S.R.

In the early stages of leprosy the study of autonomic disturbances in the skin by instrumental methods gives helpful information. The author measured the temperature of lesions and of outwardly healthy patches of skin, using an electric thermometer, and the electro-resistance by an ohmmeter. The electro-resistance of the skin indicated the degree of humidity of the skin. There were 73 patients in the investigation, of whom 14 were lepromatous, 13 tuberculoid, and 46 indeterminate. In erythematous and in

erythemato-hypopigmented lesions with definite outlines, it was found that the skin temperature was raised and the electro-resistance was lowered (corresponding to a raised skin humidity). In erythemato-hypopigmented lesions with a cyanotic edge but without clear outlines, and also in hypochromic, achromic, and dystrophic patches of skin, the skin temperature was relatively lowered, but the electro-resistance raised (meaning that the skin humidity was lowered). On skin patches showing some changes brought out by a nicotinic acid test, in some cases there was a rise in temperature and a lowering of electro-resistance (a rise in humidity). There was relatively less disturbance of temperature and electro-resistance than in the frank lesions. Thus the author thinks that instrumental methods of investigation make it possible to reveal the presence of autonomic changes in the early stages of leprosy, and to determine the degree of these disturbances, and so provide a valuable practical diagnostic method.

Perforation of Gall-bladder during Prednisone Treatment. **G. L. Mouzas and J. H. Briggs.** Brit. Med. J., Aug. 24, 1957, 450-451.

They report the first case of this under corticosteroid therapy. The subject was a man of 45 years with psoriasis and rheumatoid arthritis. He had received previous treatment with cortisone in 1953, and prednisone acetate in 1955, and again in 1956. During the last he developed an acute abdominal condition which came to operation, where a posterolateral perforation of the wall of the gall-bladder was found. Cholecystectomy was carried out and hydrocortisone was given during the operation and corticotrophin post-operatively. Proteinuria was present up to the 10th day and was traced to amyloid involvement of the kidney. The histological study of the gall-bladder revealed amyloidosis. The patient made a good recovery.

Ensaios de Imunização contra a Lepra pela BCG. (*Trials of BCG in immunization against leprosy.*) **A. C. Pereira Filho.** Thesis published at Juiz de Fora, Brazil, 1955, pp. 151. 22 illustrations. Faculty of Medicine of Juiz de Fora.

Prof. Pereira Filho in his thesis studies the subject fully and reports much original work, and gives full attention to the work of others. He thinks the dispensary and the preventorium were of great value in the leprosy campaign, but with the advent of the sulphones and more particularly of BCG, the dispensary draws

ahead in importance. The favourable protective results of BCG even make it possible to dispense with the preventorium, and after protection by BCG the children can be cared for in a creche. In his studies of the Mitsuda reaction in leprosy he finds that it is universally valuable in prognosis, and it indicates the degree of resistance to leprosy for subjects of it as well as those who are free of it. The early Fernandez reading indicates only the degree of allergy, whereas the Mitsuda indicates the immunity. Children from a leprosy focus, or children not from such a focus, usually become reactive to the Mitsuda from 2 years of age. The reaction falls off rapidly in intensity after 60 years of age. Even 2 years after its application the Mitsuda may exert a mild influence towards awakening or reinforcing the immunity. The Mitsuda is especially valuable for separating contacts into immune and non-immune, and in discovering the grave cases. The author found that tuberculosis is a definite factor which directly or indirectly changes the Mitsuda reaction from positive to negative, and confirms the immunological connection between tuberculosis and leprosy, and that BCG can bring allergy and immunity towards *M. leprae*, as shown in data from preventoria and dispensaries. There is, however, a dissociation between tuberculin allergy and the Mitsuda reaction, and leprosy does not give immunity against tuberculosis. The origin of the immunity indicated by the Mitsuda is still not entirely understood: children living in an environment free of tuberculosis and leprosy can give a positive response. The practice of giving BCG by mouth in 3 doses of 0.2 gm. monthly was found to be effective 100% in conversion to a positive Mitsuda. BCG was also found to help the therapeutic action of the sulphones. Mitsuda conversions obtained by BCG were maintained over 4 years of observation.

REVIEWS

La Lepro. Official Organ of the Japanese Leprosy Association. Vol. 25, No. 5, Sept. 1956.

Y. Kawaguchi has studied *the correlation of tuberculosis to leprosy*, and reports that vaccination of mice with phenol-killed tubercle bacilli did not elicit a resistance to murine leprosy, but a liquid paraffin vaccine of tubercle or of murine leprosy bacilli did cause in the mice a degree of resistance to murine leprosy. A still higher grade of resistance was obtained in mice by vaccination with living BCG. On the other hand, injection of mice with a liquid paraffin vaccine of killed murine leprosy bacilli had no effect on tuberculous infection.

N. Harada reports on *electron microscopy of ultra-thin sections of M. ulcerans*. The internal structure of this organism is very similar to that of *M. leprae*, *M. leprae murium*, and *M. tuberculosis*. It has two types of bacillary bodies, one of homogeneous solid type, and one with various internal structures, and there are intermediate forms between these. There is an enveloping cell wall to the bacillary body, and inside it are large electron-dense granules, small granules, and electron-transparent vacuolated structures. There are also reticular, tubular, and branching string-like structures. (Illustrated by 26 figures.)

N. Hirano and K. Sushida studied *the chemotherapeutic effect of isonicotinoyl-3-methoxy-4-hydroxybenzal hydrazone in murine leprosy* and report that it acts as a bacteriocidal drug in this disease. Subcutaneous or oral administration had a marked effect in a few months. When discontinued, there was sometimes relapse and retreatment seems to have no effect. They postulate the development of drug-resistance by incomplete treatment. They also showed that daily inoculation of the drug for a week could prevent the onset of the disease in mice inoculated with murine leprosy bacilli.

M. Uchida and E. Shionuma discuss *the relation between acute iridocyclitis and erythema nodosum in leprosy patients*. They think they have a close relation, and their seasonal frequency is the same, namely lowest in the winter and greatest in the spring. They also noted in their leprosarium that the two conditions corresponded in general and seasonal frequency both in the chaulmoogra and the sulphone era. They think both conditions have an allergic significance. They were able to examine the histology of 4 eyes which were enucleated from cases which happened to have both acute leprous iridocyclitis and erythema nodosum leprosum: the histo-

logical changes were similar to those observed in erythema nodosum leprosum of the skin.

K. Takeda reports on an investigation of *the spreading reaction of hyaluronidase*. They studied the intracutaneous hyaluronidase spreading reaction in 357 leprosy patients. The reaction is much less in leprosy patients than the normal. It is most marked in the lepromatous type, and is least in childhood and adolescence. The fact that the reaction gradually increases with age is a specific phenomenon in leprosy patients. The height of the erythema nodosum leprosum reaction goes with the lowest intensity of the hyaluronidase reaction.

K. Sugai and K. Fukushi discuss *foamy cells*. The character of the lepra cells or foamy cells of Virchow was previously understood to be due to the action of the leprosy bacilli and their products, but now in the era of efficient antileprotic drugs foamy cells occur in lesions where there are few or no bacilli. By reference to the foamy cells of pneumonia, pulmonary tuberculosis, and lung cancer, it is shown that the presence of a bacterium is not always necessary for the activation of the reticuloendothelial system. Phagocytosis of pathologically isolated lipid was the essential process, and the protoplasm of the cell accumulates fatty substances to form foamy cells. The same thing must be the case in the formation of lepra foamy cells.

International Journal of Leprosy. Vol. 24, No. 3, July-Sept., 1956.

C. B. Lara and J. O. Nolasco of Culion Sanitarium, Philippines, report on further studies of Culion-born children as regards *Self-healing, or Abortive, and Residual Forms of Childhood Leprosy and Their Probable Significance*. Children born of leprosy patients at Culion have been under practically continuous observation over the past 24 years. There were 287 cases who developed lesions of leprosy. The findings are summarized in four tables correlating the course of the disease with the clinical morphology of the initial lesions, the early bacteriology, the Mitsuda reaction, and the histology. About three-fourths of the cases of infection healed spontaneously, and this was apparently permanent. The process of healing seemed to be best and surest in those who had initial lesions of papulonodular and other thickening and definitely circumscribed forms. The infiltrated and diffuse lesions went with the lowest proportion of healing, and the wheal-like and raised and flat macular lesions were intermediate. A higher proportion of healed cases was associated also with low bacterial content of the

lesion and a strong Mitsuda reactivity. Histologically, lesions with undifferentiated round-cell or monocyte infiltrates showed earlier healing than those with the tuberculoid structure, except with the papulonodules. Relapses were chiefly noted within less than three years of apparent healing, became rarer after that, and were hardly seen at all after ten years. Relapses occurred more often where the early lesions were of tuberculoid histology, and also where the early lesions were wheal-like and macular. A small number of apparently healed cases showed inconspicuous residual signs, such as enlarged or tender nerve trunks with or without anaesthesia, and micropapules on or near anaesthetic atrophic scars. Most of them are probably benign, but they could reactivate in later life. An investigation of repeated intracutaneous injection of lepromin in a group of children against controls showed some advantage for those who had received the injections before the appearance of leprous lesions, but the evidence so far is inconclusive, and a further study of this matter is proposed.

The authors raise many interesting and valuable points in their discussion, and the whole paper merits close study.

K. Mitsuda, director of the Aisei-en National Leprosarium, Japan, writes on *Primary and Secondary Tuberculoid Leprosy*, with 1 text figure. He advocates the name "secondary tuberculoid" for the appearance of the tuberculoid histological picture in treated and healing lepromatous leprosy. The tissue granuloma of tuberculoid leprosy replaces the former histopathology and is associated with disappearance of the bacilli and the return of a positive lepromin reaction. Also a biopsy of the lepromin reaction nodule shows a histology very similar to that of the ordinary tuberculoid lesion. If thickened sensory nerves are found, the biopsy of such nerve will also reveal tuberculoid structure.

J. Convit of Venezuela gives his fifth report of *Studies of Leprosy in the German Ethnic Group of Colonia Tovar, Venezuela*, dealing with the morbidity rates in BCG-vaccinated and unvaccinated groups during five years. In the first group there were 584 persons and in the control group 522. All lived in close contact with infectious forms of leprosy. Records began in 1950 and full clinical and laboratory observation was maintained. The vaccinated group yielded three cases of leprosy, which were of the tuberculoid type and healed rapidly, whereas the unvaccinated group produced 25 cases, including 9 infectious cases and 6 indeterminate. The morbidity coefficients of 5, 11 and 45.70 respectively indicate strongly that BCG vaccination has a decided preventive action

against leprosy, as also the fact that no infectious form of the disease was found in the vaccinated group.

A. R. Davison of Westfort Institution, Pretoria, contributes an interesting and provocative paper on *Infections in Leprosy Institutions.* He disagrees with the ideas that leprosy is acquired only or mostly in infancy, and that adults do not need to take precautions against infection. He reviews the literature of infections of members of the staff of leprosaria and gives details of South African cases within his knowledge. Two doctors of the Pretoria leprosarium contracted leprosy. One of these actually injected suspensions of nodules into ten members of the Bantu staff, and probably himself, to prove that leprosy could not be transmitted. The other doctor apparently acquired the infection from a chance operation wound, resulting in a tuberculoid lesion in one finger a few months after the prick. Three European overseers and a nurse who had worked in South African leprosaria also developed leprosy, also ten Bantu males who had no family history of the disease, at ages suggesting they were infected when adult. The danger of exposing a child to infection for as little as six weeks is illustrated by an infant with that short contact with a leprous mother, who developed lesions 1 year after removal from its mother. The author advocates the observance of hygienic rules by staff, and that infected individuals should not come into contact with children.

Sister Hilary Ross of Carville reports on a study of *Magnesium Metabolism in Leprosy.* She investigated 177 cases of leprosy, and 27 non-patients as controls, and found that 132 of the leprosy cases had magnesium levels in the serum within the normal range. Low concentrations were found in 27 lepromatous cases and 1 tuberculoid case, and slightly raised levels were seen in 16 lepromatous and 1 tuberculoid. A clinical diagnosis of amyloid nephrosis was associated with 8 of the low level and 6 of the raised level cases. Leprosy *per se* does not appear to affect magnesium metabolism.

R. Chaussinand of the Institut Pasteur, Paris, discusses the *Standardisation of Lepromin.* He mentions the decline in the ready supply of lepromatous nodules because of the efficacy of the sulphones in treatment, but declares that he himself is less pessimistic than others in this matter. It has led some workers to use high dilutions of the lepromin, and though he thinks many of these are quite effective, he does not approve of the very high dilutions, nor of the addition of reinforcing substances which have no antigenic value. To solve the problem that leprosy workers in

many places are not well equipped, the author has undertaken to prepare a standardized lepromin from sterile nodules that are sent him from overseas. The Mitsuda-Hayashi technique as modified by Wade will be used, and care taken to attain uniformity in the preparation of the different lots for distribution, and the final concentration will be determined by optical density. This product does cause some false reactions, attributable to tissue elements. An attempt was made to secure a more homogeneous suspension of the bacilli by ultrasonic treatment, but it was found that the activity of the product was reduced. From the author's experience with dilutions, he thinks that 1:50 can be used for clinical work and 1:200 for epidemiological studies. The optimal dilution for universal use will be revealed only when dilutions are standardized and studied in various parts of the world.

H. Floch of the Institut Pasteur of Cayenne writes of *The Mitsuda Reaction Using a Phenol Extract of Normal Skin.* Recently Kooij (Internat. J. of Leprosy, **24** (1956), 171-182), and earlier de Faria (Rio de Janeiro, Serviço Nacional de Lepra, 1953) reported Mitsuda-type reactions to a preparation of normal skin. Floch now reports results obtained with a 1:40 suspension of normal skin, comparing it with a 1:750 dilution of lepromin. In 12 lepromatous cases he obtained a few positive early reactions with both antigens. In 145 other leprosy cases, which were indeterminate and tuberculoid, over a half gave early positive reactions to the normal skin suspension, and less than a half gave them to the dilute lepromin. Late reactions occurred in over a half with the normal skin suspension, and in 72% of indeterminate and 90% of the tuberculoid cases with the diluted lepromin.

W. A. Hadler and L. M. Ziti of Brazil report on *Histological Reactions Produced by Experimental Inoculation of M. Leprae Murium into the Golden Hamster*, and include 2 plates with 14 figures. They inoculated intraperitoneally 6 mgm. of *M. leprae murium* into golden hamsters, and this caused a disease which developed slowly and ended with the death of the animal. There was an initial phase of small inconspicuous macroscopic lesions which were histologically of retrogressive nature, and after the 150th day a late phase with larger lesions of a progressive nature. In the early lesions the bacilli are few and show morphological changes, and the lysis of bacilli is probably due to active participation of macrophages. In the late lesions the bacilli multiply actively and do not show lysis. The cells of early lesions have characters between the epithelioid cell of the guinea-pig on the one hand, and the lepra cell of the rat

on the other. The cells of the late lesions have only the characters of the rat lepra cell. The deposition of a " hyalin substance " causes secondary lesions in various organs in the initial phase, and asteroid bodies may be seen in the lesions in the late phase.

Y. T. Chang of Maryland reports further from his studies in the *Chemotherapy of Murine Leprosy*. This is the 5th and deals with the effects of various combinations of DDS, Streptomycin, and INH on mouse leprosy. He found that the suppressive effects of these combinations were definitely superior to those obtained with the individual drugs alone. Arranged in decreasing order of effectiveness the following groups emerged: (1) streptomycin, INH and DDS; (2) INH and DDS; (3) streptomycin and INH; (4) streptomycin and DDS; (5) streptomycin alone; (6) INH; (7) DDS.

In the Editorials, J. M. M. Fernandez discusses *the use of BCG in the prophylaxis of leprosy*, who should be vaccinated, and how and when, and suggests the urgent need of decision on the matter at the next international meetings. H. W. Wade discusses the new and piquant subject of *the cause of damaged ear cartilage in cases of leprosy*. He had submitted this question to many workers and the Correspondence section of the Journal contains varied replies from 21. Dr. Wade analyses these replies. It seems that this " nibbled " or serrated condition of the ear cartilage (a Plate with 10 figures is given as illustration) is rare, and some workers have not seen it. It seems more likely to be associated with lepromatous and borderline leprosy. Most agree that breakdown and ulceration of lesions are involved, and several bring in secondary infections, local disturbance of blood supply, and complicating conditions. It seems worthwhile for all workers to examine their records and to seek to elucidate this condition further. Dr. Wade thinks that it will help our understanding of borderline leprosy.

BOOK REVIEW. **BCG and Vole Vaccination,** by K. Neville Irvine. 2nd Edition 1957, 103 pp., 10 plates in colour, 4 figures. Published by the National Association for the Prevention of Tuberculosis, Tavistock House North, London, W.C.1. (Price 15/-.)

Dr. K. Neville Irvine, adviser in BCG vaccination to the Oxford Regional Hospital Board, has brought up to date this wonderfully concise and clear little book on BCG and Vole Vaccination. Over 200 alterations have been made in the text, and new sections added to deal with the treatment of the normal

vaccination reaction, and of complications. The 8 chapters of the book and the adequate illustrations should leave any worker with a very satisfactory knowledge of the subject. The summary and reference appended to each chapter are of additional value. Every leprosy worker should study this book, because of comparable techniques in his field, and because so much can be learned from these advances in the field of tuberculosis. The use of BCG as a possible preventive inoculation against leprosy makes this book of the highest importance for the leprosy worker.

The Rumanian Medical Review, Jan.-Mar., 1957, the first number of its first year, deserves a warm welcome from all medical workers. It is published in English and contains original and summarized articles on subjects in physiology and pathology, public health, microbiology, parasitology, internal medicine, tuberculosis, neurology, neurosurgery, psychiatry, endocrinology, dermatology, and surgery. It is to be hoped that in such an inclusive Review articles on leprosy will eventually be provided.

La Lepro. Official Organ of the Japanese Leprosy Association. Vol. 26, No. 1, Sept. 1957.

M. Nakamura reports on his studies on *the chemical composition of the murine leprosy bacillus.* The method of trypsin digestion was used to obtain the murine leprosy bacilli from the subcutaneous tissues of rats. Chemical analysis showed a less amount of total nitrogen, carbohydrate, and nucleic acid, and a greater amount of phospholipid and substances extractable by alcohol—ether, than with other cultivable acidfast bacilli.

Y. Takayama studied *the onset of murine leprosy as influenced by previous use of X-rays, cortisone, and other drugs.* It was found that cortisone administration after X-ray irradiation, and cortisone alone, suppress the murine leprosy granuloma to some degree. Toluidin blue or toluidin blue mixed with alum did not accelerate the onset of murine leprosy. Egg yellow or a mixture of ox-serum albumin and ferment extract do accelerate the granuloma to some extent. The same author also studied *intramuscular DDS and Promin intravenously* in murine leprosy and found the latter was superior in effect, and in method of administration and doseage.

K. Ushio, Y. Takayama, and K. Ikeda have studied the effects of 3 drugs in murine leprosy. The first was *isonicotinyl-3-methoxy-4 hydroxybenzal hydrazone.* This had a striking effect both in inhibi-

tion of the disease and treatment. The second was *4:4'-diamino-diphenyl sulphoxide,* and the third was *neo-minophagen AT:* both had small inhibitory effect.

T. Kitagawa and T. Nagata discuss *lower limb amputations* in leprosy. They think that the need for surgical treatment is increasing because of the advance in the chemotherapy of leprosy. They studied 114 patients and found that amputation of both legs had been necessary in 33, and that 71 patients with tuberculoid leprosy had required amputations against 43 lepromatous. The essential cause for most amputations was perforating ulcer of the foot. The site of amputation in most cases was the middle or lower third of the leg. The sequelae were neuralgia and pains on pressure or contusion in half the cases, and ulcer of the amputation stump in half the cases, and there was considerable wasting of muscles and no benefit in this regard from a prosthesis. Fall in temperature in the amputation stump was not invariable, but it did occur in the lepromatous patients, to a 3.7° C. decrease.

International Journal of Leprosy. Vol. 24, No. 4, Oct.-Dec. 1956.

J. Convit, C. Sisiruca, and P. Lapenta of Cabo Blanco Leprosarium, Venezuela, give *Some Observations on Borderline Leprosy.* They point out that the inclusion of the borderline group in classification is a valuable contribution to the understanding of leprosy. They collected 286 cases from their area for study and note that they constituted 3.2% of the known cases of the disease. They closely studied 100 dimorphous cases in hospital, and found that 43 of them had a "facies dimorpha," consisting of a bat-like configuration of the infiltration on the forehead, between the eyebrows, on the bridge of the nose, and on the chin and cheeks. Also they noted hypochromic halos round some lesions in 27 cases, and think it is a process secondary to regression of lesions. Hyperchromic patches, secondary to the regression of infiltrated lesions, were very typical, and found in 61 cases. It is important to distinguish them from those of indeterminate leprosy. The borderline hypochromic patches have the features of possessing a possibility of growth, and will show a borderline histopathology: the nerve disturbances are variable. They can evolve into lepromatous (which is the more frequent) or into tuberculoid (infrequent) or progress centrifugally as hyperchromic patches. Such lesions can exist from the beginning with borderline histology.

In 21 cases the authors tried out daily intravenous injections of methylene blue, and found that the dye was retained where

histologically-proved lepromatous changes existed, and pure borderline lesions did not retain it.

Electrophoresis tests of the plasma of 30 cases showed a normal albumin-globulin ratio in 60% of them, which were in regressive activity. In the rest the ratio was below the normal value, and in this group the lesions were tending to persist and spread.

C. B. Lara, C. A. Palafox, J. L. Ignacio, and J. O. Nolasco, of Culion Sanitarium, Philippines, give their first report on their *study of Children of Leprosy Patients Isolated at Birth, given Lepromin and BCG Injections, then Returned to the Colony.*

In an 8 years study so far, 100 children born at Culion of leprosy parents have been isolated at birth. Later 55 have been returned to their parents in the leprosarium after their Mitsuda reactions have become moderate to strong, and 11 have been released to their families outside the leprosarium: by March 1956 there were 33 remaining in isolation and 1 had died.

Repeated lepromin tests were given to 40 children: by this means 16 did not attain 3+ reactivity and BCG was used for them.

Of the 11 children released to guardians, 5 were lost to observation, and 4 have remained free of leprosy, but 2 who returned to the leprosarium at 3-9/12 and 1-7/12 years of age later developed leprosy after exposure periods of 2-5/12 and 3 years respectively. These periods are similar to the average incubation periods for children unisolated and under constant exposure. Neither of these positive cases of the development of leprosy had received breast feeding: one had attained only 1+ lepromin positivity: the other had not received lepromin, nor BCG. No child developed leprosy while still in isolation, though 51 of them have been isolated for 3 to 6 years. By contrast, in slightly younger unisolated children 46 or 36.2% developed leprosy. Congenital transmission therefore seems of no importance.

Of the 55 children returned to the leprosarium, 46 show no evidence of leprosy after an exposure of 1 to 1½ years: longer observation is needed (3 more years) before it will be possible to assess the protective value of prolonged isolation from birth, and of lepromin and BCG injections. The authors think that much more careful study and evaluation of BCG is needed before it can be given a sure place in prevention of leprosy, and more consideration should be given to the sensitizing action of previously-injected lepromin on young children who are Mitsuda-negative, as they have regularly observed this beneficial effect.

A. R. Davison reports on a *Clinical Evaluation of INH as an Adjuvant in the Treatment of Lepromatous Leprosy*, with a note on the *Detrimental effect of Erythema Nodosum Leprosum Reactions*. The study was carried out on 129 lepromatous patients. Of these, one group of 40 received only sulphones, and served as the control. Another group of 40 received sulphone plus INH. The third group of 39 patients received INH, DHSM (dihydrostreptomycin), and PAS. The fourth group contained 10 patients for a pilot study of streptohydrazid, of which each vial contains 1 gm. of streptomycin and 266 mgm. of INH combined in one molecule. A previous investigation under the auspices of the Leonard Wood Memorial Foundation showed that the sulphones alone, and DHSM and PAS, had been the most efficacious. Therefore in the present investigation INH has been added to these drug plans. The duration of the present study was 2 years. The author found that the previous method of giving numerical values for clinical improvement was not satisfactory, as the degrees of activity of lesions is more important than their mere presence, and he suggests that the bacteriological index is the only reliable standard.

In the present series there was clinical improvement in almost all the forms of lesions in all the four groups under treatment. Taking the infiltrations as being the most typical form of lesion and the most susceptible to clinical change and assessment of the same, it was noted that the degree of improvement was almost identical in all the groups, and the bacterial indices were also very similar in all groups.

The author observes that erythema nodosum leprosum has increased tenfold since the sulphones were introduced, that it is not an allergy to sulphones, and occurs almost exclusively in bacilliferous cases. He found 59 cases with ENL, and found that the reduction in the bacterial index was much less than in the 58 cases who did not have ENL (12% against 42%), and hence this reaction is detrimental to the patient and calls for control, in which corticosteroids should be considered.

D. L. Leiker reports on 2 cases of the *Mononucleosis Syndrome in Leprosy Patients Treated with Sulphones*. The patients, both aged 25 years, were under treatment with DDS for major tuberculoid and atypical lepromatous leprosy respectively. Five weeks after the treatment was begun they showed severe symptoms typical of infectious mononucleosis, with accompanying high white cell count and high percentage of mononuclears. One patient had a short relapse but recovered completely. The other patient died after 10

days with severe liver damage and agranulocytosis, after having a bullous dermatitis which subsided under cortisone. In Nigeria in 1949 Lowe described the occurrence of the mononucleosis syndrome in sulphone-treated leprosy patients, but considered it to be a true infectious mononucleosis precipitated by the sulphone treatment: it has not been mentioned by other workers since then. The condition seems to be limited to the first 2 months of treatment: a true infectious mononucleosis should turn up in later periods of treatment as part of a wider endemia. Further, within 2 months of PAS administration, similar syndromes have been reported. In Netherlands New Guineas not a single case of infectious mononucleosis has been reported in the past. From all this the author thinks that the syndrome is not the true infectious form but is a delayed allergic reaction of the reticuloendothelial system induced by sulphones and other drugs, and prefers to call it " mononucleosis syndrome." Early treatment with antihistamines, cortisone, or ACTH seems indicated.

In an addendum the author reports a third case, æt. 26, in whom the syndrome began about 7 weeks after sulphone treatment had been started. There was also a generalized exfoliative dermatitis. Cortisone treatment was used at once, with speedy relief of all symptoms. The blood picture at onset was, white cell count 9,800 with 66% mononuclears; at 2 weeks after onset, leucocytes 21,500, mononuclears approaching normal, at 5 weeks after onset, leucocytes 8,600 and mononuclears 30%.

C. H. Payne gives a clinical note on a case of *Leprosy and Granuloma Annulare in the Same Patient.* This was a female of 42 years who presented skin lesions of the lower limbs of many years duration. She had spent 3 years in various clinics and received a number of diagnoses, but finally leprosy was recognised. The lesions appeared to be tuberculoid, but all smears were strongly positive for bacilli. After 9 months of sulphone therapy the smears became negative and remained so, but the lesions persisted without change in size. Their appearance changed in the direction of flattening, and the assumption of a bluish tinge, and a biospy specimen suggested granuloma annulare. Under corticosteroid therapy there was considerable improvement. The author enquires if other cases have been experienced of this conjunction of granuloma annulare with leprosy.

Prof. Sabura Sato, of Tokoku University, Sendai, Japan, reports on a case of *Nerve Abscess in Lepromatous Leprosy*, and reviews the reports of *Nerve Abscess in Japan.*

The nerve abscess in the case of lepromatous leprosy occurred in two ulnar cutaneous nerves of a male æt. 18. The abscess swelling contained purulent matter made up chiefly of lepra cells, particularly foamy cells, but few leucocytes, and there were many leprosy bacilli. There were no cultivable bacteria. The histological picture showed a highly infiltrated and thickened nerve sheath, with an increase in the fine fibrils in delicate networks, round cells and lepra cells being contained among the fibrils. The nerve cord as a whole had become a lepromatous granuloma consisting of lepra cells and many large foamy cells. Round cells and polymorph leucocytes were very scanty. There was a widespread destruction of nerve fibres, so that only a few or traces of them remained in the increased fibroblasts and connective tissue fibres. No trace of tuberculoid structure or caseous necrosis was seen, such as strikingly occur in the nerve abscess of tuberculoid cases.

Two other cases of lepromatous nerve abscess recorded in Japan are mentioned which had the same essential features, and the rarity of abscess of the cold type in lepromatous leprosy is reported. Reports of cold abscess in tuberculoid leprosy are given for 13 cases in the Japanese literature. This tuberculoid cold abscess is derived from liquefaction of the caseous nerve lesions, and lepra reaction is one of the main causes of the development of abscess. The caseous neuritis, which is the basis of abscess formation, is common in Japan, whereas the typical nerve abscess is rather rare.

T. F. Davey contributes an analysis of the data of Lowe and McNulty on *Tuberculin and Lepromin Reaction in Nigeria.* Special attention is given to the results of low dose tuberculin tests and later of high dose tests in the negatives. The results are correlated with the lepromin reaction.

Out of 278 healthy adults, 79 or 29% were positive to the low dose von Pirquet test, and 96% of these positives also reacted to lepromin. However a large proportion of the negatives were also negative to lepromin. Of the 199 persons negative to the first tuberculin test, 144 or 73% were positive to the high dose tuberculin. The greater part of these positives (84%) reacted to lepromin, and a half of the negatives were also negative to lepromin.

There was a basic similarity in the results of 81 children who were tested, though with important quantitative differences. Only 10, or 12% of the children reacted to the low dose tuberculin, but as before almost all (90%) were positive to lepromin. Of the 75 negative to the low dose tuberculin a bare majority of 52% reacted

to the high dose tuberculin. Again, of these positives 59% were also positive to lepromin, but all who reacted to the high dose tuberculin were negative to lepromin.

It is clear that in almost all subjects who had high sensitivity to tuberculin there was an associated positivity to lepromin, and the correlation was marked for those who were only positive to high dose tuberculin. There was no such correlation for those who were absolutely negative to tuberculin. It is thought possible, and even probable in the case of children, that some of the reactions to high dose tuberculin were of non-specific nature. A point of great interest which requires deeper study is the specific inability of lepromateous patients to convert into lepromin reactors, though hypersensitive to tuberculin and having been inoculated with BCG.

J. H. Hanks of the Leonard Wood Memorial Laboratory, Harvard, has studied and reports on *Quantitative Aspects of Sampling Leprosy Skin Lesions by the Scraped Incision Method.* The scraped incision method of Wade is simple, convenient, and efficient. Hanks has found that a simple modification of the habitual method of making a film can improve still further the uniformity and senstivity of the bacteriological examination. This modification consists in spreading each sample of material to the greatest limit before drying begins, though not forcing it, so as to allow of a natural spread of the cells which make up the material. If desired, still further sensitivity can be obtained by increasing the thickness of the film up to 4 times that recommended for routine purposes. He found that such films may be 14 times more sensitive than average films, and 56 times more sensitive than the thinnest clinical films. Finally, to examine all tissue fragments and cell clusters in each film is another method of increasing sensitivity.

T. Tanimura, H. Honda, and T. Oshima, of the Department of Dermatology of Osaka University Medical School, in their *Studies in the Serology of Leprosy,* report on the *Complement Fixation Reaction by a Modified Antigen.* The authors review previous work on cephalin among the antigens used for carrying out the leprosy complement fixation test, and go on fully to describe their construction of an antigen which contains cholesterin, cardiolipin, and a mixture of cephalin fractions, with added kaolin, which antigen shows a great deal of specificity for leprous sera. The cephalin fractions are those obtained by Folch's method, namely phosphatidyl-ethanolamine diphospho-inositide, and phosphatidyl-serine. In trials to find out the best proportions of these fractions for use in the cephalin part of the antigen, they found these should be 29:10:1 respectively, of solutions of 1% in ether.

With this mixture of cephalin (1% in ether), Cardiolipin (0.2% in alcohol), and cholesterol (1% in alcohol) in the same way they found that the best proportion of the 3 basic solutions was 10:5:1 respectively.

Tests in 110 leprous sera produced high percentages of positives in the three forms of the disease (the lowest in the tuberculoid, but even then 74%), and the total positives were 87.3%. Negative results came from all the sera from healthy subjects, 19 tuberculous and 6 cancer cases. Three or 7.3% of syphilitic sera were positive, and 2 out of 10 pregnancy cases, or 20% were positive.

Tests repeated after an intervals of 6 months in 4 lepromatous cases who were improving clinically showed no material decrease of positivity of the tests. In so short a time it seems that serological improvement in leprosy should not be looked for. The authors think that the cephalin-cardiolipin-cholesterol antigens are suitable for clinical use, as they possess high antigenicity in all forms of leprosy, but give few group haemolytic reactions with sera of tuberculosis, syphilis, and cancer, and normal persons with the exception of pregnancy. The reaction has been called the Handai method, after Honda.

L. Kátó and B. Gôzsy, of the University of Montreal Institute of Microbiology and Hygiene, have studied the *Action of Histamine and Antihistamine on the Ingestion of Murine Leprosy Bacilli by Macrophages of the Rat and the Guinea-pig.* The antihistamine used was synthetic, mepyramine maleate. The influence of the histamine and the antihistamine was studied on the power of the macrophages of peritoneal exudates of guinea-pigs and albino rats to phagocytize the tubercle bacillus from a culture of BCG and the murine leprosy bacillus from a suspension of leproma. The ingestion of BCG by the cells of both animals was stimulated by the histamine and inhibited by the antihistamine. On the other hand, the phagocytosis of the murine bacillus was not affected by either of the two substances, and this applies to both exudates. A crude aqueous extract, free of bacilli, from the rat leproma, inhibited the phagocytosis of BCG by guinea-pig monocytes. The extract of rat lepromin and the antihistamine cause similar morphological and functional changes in the monocytes, namely deficiency of pseudopodia and vacuoles, contraction of the cell, and passive behaviour with BCG. (5 illustrations.)

G. L. Fite discusses *Leprosy, Society, and Hansen's Disease.* He mentions the great vogue of the use of the term " Hansen's disease " and acknowledges the successful spread of this name for

leprosy. In analysing the cause of this success he traces it mainly to social attitudes. The social forces in leprosy are more powerful than the individuals or agencies involved, and these forces tend, not only to stigmatize leprosy, but also to throw a veil of magic over it instead of getting down to matter-of-fact control of it in the light of what knowledge and resources we have. The physician who is genuinely interested in leprosy is baffled, frustrated, and wearied by the false attitudes to it and the inevitable counter-arguments. He mentions leprophobia as one of these false attitudes and says that even education is not a sure cure for it; nor is it wise to adopt the counter-attitude of condemnation of anyone who has this foible. There is also the negative leprophobe who treats the danger of contagion with contempt, and the infectious leprophobe who spreads his fear on to others. Leprophobia does not exist, except as the occasion for it may arise, but it can then develop with extreme rapidity, for there is always a latent background attitude of hatred or loathing. He points out that in the case of poliomyelitis and cancer publicity campaigns have been run, and have taken advantage of the fear of them already existing in the public mind, with good effect, in that vaccination and early treatment have been "got across." The similar social fear of leprosy can be used to give a similar good result. The campaigns against poliomyelitis and cancer had something solid to offer, and in leprosy we should similarly point to the treatment of leprosy by the sulphones, and not make too much in propaganda of coining new names for leprosy or curing leprophobia. As regards the use of "Hansen's disease" for leprosy, the trend is away from using personal names, and the author thinks that the use of this name will never be more than a temporary expedient. The physician's duty is to apply himself to the immediate problem of leprosy as a chronic infectious disease, without permitting himself to be diverted by the social complexities.

The *Editorial*, by H. W. Wade, on the *Lepromin Reaction and Non-Specific Reactivity to Tuberculin*, provokes deep thought on the relationship between leprosy and tuberculosis and suggests study along the lines of lepromin reactivity correlated with two-dose tuberculin testing. Wade refers to the work of Lowe in Nigeria and Guinto in the Philippines on the relationship between the lepromin and tuberculin reactions, and the emergence from their work of the possibility that high-dose reactions to tuberculin may be non-specific in nature, which idea is also developed by Palmer and coworkers. McFadzean prepared a report on Lowe's subsequent findings in tests of 621 children æt. 5 to 16 years. A high total tuberculin-positive rate was found, with no evidence of a

relation to leprosy infection, yet the prevalence of tuberculosis in the community was low. On the whole, there was a significant correlation between the lepromin and tuberculin reactions, but the correlation was relatively poor among subjects who reacted only to high dose tuberculin. It looks as if the unknown antigenic factor behind the high dose tuberculin positives is not so effective for lepromin reactivity: on the other hand a very large proportion of the few who failed to show even the low-grade sensitivity to tuberculin failed also to react to a single dose of lepromin.

Wade then turns again to the Lowe data, as re-examined by Davey, and compares them with a similar study made by Guinto, Doull, and Mabalay. In adults a very large number of positive lepromin reactions went with only mild degrees of tuberculin sensitivity, and many with none at all, and in children the results strongly indicated the existence of non-specific reactions to tuberculin. As regards the reasons behind the large dose reactions one cannot assume they are necessarily due to infection with the tubercle bacillus, and that they are due to mycobacteria other than the tubercle bacillus does not seem likely. Wade postulates that an individual may be *conditioned* to react by non-specific means. He points out that BCG is a non-specific means of inducing lepromin reactivity, and this reactivity is widely held to be protective, even as the " natural " form of it is supposed to be. He sees no reason why the lepromin positivity associated with non-specific tuberculin sensitivity to high doses should not contribute to resistance to leprosy infection.

There is suggestive further evidence of the existence of non-specific reactivity in the report of the Medical Research Council (U.K.) on tests of 56,7000 schoolchildren with low and high tuberculin doses, though the idea is not discussed in the report.

In the *Correspondence* section Dharmendra and K. R. Chatterjee correct and amplify their previous article on the *Prognostic Value of the Lepromin Test in Contacts* (Internat. J. of Leprosy, **24**, 1956, pp. 315-318). Dr. Huldah Bancroft add a note from the statistical point of view. Dharmendra does not think that the results given in his addendum provide an indication of any protective value on the part of the repeated lepromin tests. Dr. Huldah Bancroft, on the other hand, thinks the evidence is statistically strong enough to suggest that there is.

G. Basombrío of Buenos Aires raises questions of the *significance of lepromin positivity*, referring to a statement by Prof. J. Gay Prieto which mentioned exceptional positive Mitsuda reactions in lepro-

matous cases. Basombrío asks for answers from workers on (1) Has it been proved that the immunity state of children with a positive Mitsuda is of no significance? (2) Are there lepromatous cases which give spontaneous positive Mitsuda reactions? (3) Information from the experience of other leprologists on children with positive Mitsuda who later developed lepromatous leprosy? The Editor adds a comment to remind us about lepromin-reactive lepromatous cases being possibly borderline previously.

J. M. Fernández defends his *choice of the right scapular region of the back for routine testing with lepromin*, giving his opinion that the thicker firmer skin is more suitable for nodular reactions like the Mitsuda, there is more room on the back for multiple testing when required, and the patient cannot see what happens to injections on the back.

D. E. Morton reports such details as are available of a case of *activation of leprosy associated with ACTH and Cortisone Treatment*. The corticosteroids were apparently given to a female æt. 71 in the quiescent stage of lepromatous leprosy and continued for several months. The patient felt that her condition grew steadily worse on these drugs, and the records of her clinical condition support that this was so. There was no check available of bacterial index during the period covered by cortisone therapy.

Boletim do Serviço Nacional da Lepra, XV, Special Number, 1956. pp. 106, 17 illustrations. Rio de Janeiro, Brazil.

This special number contains a *symposium on erythema nodosum leprosum*. Prof. J. Ramos e Silva in his presidential address defined the syndrome and its relations. Dr. L. M. Bechelli in his paper studied the clinical features and differential diagnosis and the frequency of its occurence in leprosy patients, which in his experience is considerable in lepromatous cases. Prof. H. Portugal reported on *histological and laboratory findings*. In 9 cases out of 12 studied, the lesions were similar or equivalent to the granuloma described by Miescher (Acta Derm. Ven., 27: 447, 1947), comprising a histiocytic infiltration in the adipose tissue or collagen. Dr. A. Porto Marques also discusses the histology and laboratory data. Out of 7 cases bacilli were present in 5, and the bacilli showed granulation and changes in shape and size. In parts of the subcutaneous adipose tissue there were many vacuolated cells full of bacilli, and similar cells could be found round the sweat glands. Clumps of bacilli or small globi could be observed in vacuolated cells in the suppurative and necrotic foci. Dr. P. Rath de Souza

dealt with the same subject. In sections he found vascular dilation with interstitial oedema and exudation of neutrophil and sometimes eosinophil polymorphs. This exudate is always in relation to lepromatous infiltrations, and these are regressive, since the cells appear vacuolized from the presence of lipids and show a pyknotic nucleus. Bacilli may be numerous or few or absent, and granular forms predominate. He thinks there is a constant relation between the reactive lesion and the lepromatous lesions, and that the latter show regressive features, and this is confirmed by Wade and others. He thinks there must be always a lepromatous lesion in existence to precede the reactional one. He found no example of the granuloma of Miescher in the biopsies he examined. He defines the leprotic reaction as an intercurrent exudative process implanted on a pre-existing lepromatous granulomatous process. It seems as if in lepromatous lesions in regression, a leucocyte-stimulating substance arises. Whether it is bacillary or cellular in origin is unknown.

Prof. F. E. Rabello took up the *general pathology* of the condition. He points out that the erythema nodosum phenomenon is not confined to leprosy, but can occur in connection with tuberculosis, BCG inoculation, coccidiosis, streptococcal tonsillitis scarlatina, cerebrospinal meningitis, ganglionar lympho-reticulosis, venereal lymphogranuloma, and sarcoidosis. In connection with all these he detects a factor of basic infection as the primary specific stimulus, a homologous or heterologous factor which builds up the state, and a precipitating factor which brings it out and which is almost always some drug which is used. Dr. Nelson Souza Campos discusses the same subject. He points out that erythema nodosum leprosum exclusively occurs in the lepromatous type, in which the leprosy bacillus is living practically as a saphrophyte, with the miniumum of indication of any resistance on the part of the body. In this state an apparently allergic reaction supervenes, and the cause of it is by no means clear. An intercurrent tuberculous infection has been suggested, as tuberculin sensitivity is common in reacting lepromatous cases, and the use of BCG seems to desensitize such cases and improve and attenuate the reactions.

Prof. R. D. Azulay discusses the *immunology* of the condition. It only occurs in the lepromatous form, but many lepromatous cases escape it. Bacteriological and histological findings are discordant, and either specific or non-specific causes can release the reactions: hence erythema nodosum leprosum is the clinical expression of a different way of reacting for some of the lepromatous cases. There is contained in the picture a factor of allergy or para-allergy. Dr.

Candido Silva discusses the same aspect and describes his findings in cases of lepromatous leprosy subject to attacks of leprotic reaction and erythema nodosum who were tested with haemagglutinins and antigens made from the leprosy and other mycrobacteria. Attempts at desensitization were made with polysaccharides of *Pseudomonas aeruginosa*, colon bacillus antigen, and autogenous streptococcal vaccine. The results were not suggestive, though there were indications of some difference between erythma nodosum and ordinary lepromatous cases. The clinical diversity and the rhythm of the evolution of the disease are parallel with the immunological findings.

Dr. J. Baptista Risi studies the *prognosis*. While it is impossible to be dogmatic, he thinks the prognosis tends to the favourable side. The deadly equilibrium and indifference to the bacillus on the part of the body at least is broken and the level of resistance is raised. Non-leprotic forms of erythema nodosum do not aggravate the respective diseases associated with them, and it may be the same with the leprosum form. Furthermore, it is an acute manifestation, not so bad a thing as progressive lepromatization, and it is absent in advanced lepromatous cases. He thinks that haemagglutination studies do reinforce this idea of the harmlessness of the reaction and cites clinical comparative studies where the reactive group made better progress in the long-term view.

Dr. Gilberto Mangeon discusses *treatment*. There is no entirely satisfactory method of removing the reaction and preventing its recurrence, and some workers think it should be stimulated rather than suppressed, because it is beneficial. He thinks each case should be decided on its own merits, after careful clinical study. Treatments which are used to control the syndrome are many, and include (1) Change to injectable sulphone for mild attacks of erythema nodosum leprosum occurring in the course of sulphone therapy. (2) Anti-allergic, desensitizing, and stimulant treatments include (a) daily intravenous injections of 2% calcium chloride up to 20 c.c., (b) injections of 10% sodium hyposulphite and magnesium hyposulphite up to 10 c.c., (c) intravenous 10% calcium gluconate, (d) daily intravenous glucose saline, isotonic, 25, 30, or 40%, (e) the desensitizing and detoxicating action of strontium in form of a series of 10 daily injections intravenously of 0.45 in 5 c.c. of methylglioxilate of diethylenediamine, (f) auto- and heterohaemotherapy in increasing doses, (g) intramuscular or intravenous injections of Vitamin C in daily doses of 50, 100, and 500 mgm., (h) antihistamines such as benadryl, (i) transfusion of whole blood, 250 c.c., has good results which are evident in the first 24 hours,

with disappearance of the skin manifestations. (3) Alkaline therapy, such as intravenous 5% sodium bicarbonate in 20 c.c. doses. (4) Intravenous doses of 5 to 10 c.c. of 1% tartar emetic, or other antimony preparations intramuscularly, are not much used. (5) Various substances have been used to stimulate the reticulo-endothelial system, such as urotropine, gonacrine, colloidal suspension of benzine charcoal in physiological saline (5 c.c. every 2 days), omnadin, ichthyol, pituitrin, a vaccine made from lepromas. (6) Chemical substances and dyestuffs have been used as intravenous 1% methylene blue solution in distilled water, dose 0.2; gentian violet 0.18 to 0.24 oral for adults; 1% intravenous mercurochrome. (7) A great variety of sera and vaccines. (8) Perez and Orbaneja use intravenous succinic acid, 5 c.c. daily of a 2% solution, and think that it has a cortisone-like action. The results are sometimes good, but it does not prevent relapses. (9) Chloropromazine has good results from its neuroplegic and ganglioplegic action, but has the disadvantage of being hypotensive. (10) INH in doses of 5 mgm. per kilo of body weight (about 4 or 5 tablets orally a day) has good results in 80% cases with some workers, but has failed with others. (11) Injectable Vitamin D with calcium chloride by mouth and a lacto-vegetarian diet has been recommended by Herrera and has a high percentage of good results. There are relapses. (12) Vitamin PP has given good results with Floch. (13) Irgapyrine has been used by some, but has no efficacy. (14) Cortisone acetate and ACTH. Cortisone has been used in doses of 50 mgm. six-hourly (200 mgm. in the first 24 hours, and reduced after control of the symptoms to 100, 75 and 50 mgm. daily). It acts on the connective tissues and not on the disease, and sulphone therapy can be continued during its use. The special precautions peculiar to cortisone therapy must be observed. Cases suitable for cortisone are those with intense reaction which endanger the general state of the patient. The use of ACTH is necessary in association with cortisone in order to avoid prolonged inertia and consequent atrophy of the suprarenal. It is injected in doses of 100 to 150 mgm. after 10 days of cortisone therapy. (15) Candido Silva has been making experiments in the use of biological products (see reference to his paper at an earlier stage of this Abstract). (16) Use of BCG as a desensitizer at various places in Brazil resulted in preliminary aggravation of the reactions but went on to considerable improvemtent, even accompanied in some by improvement in the general state. The BCG was given by mouth in doses of 0.2 mgm. weekly for 15 weeks, in one or more courses. The method is perfectly tolerated and is thought to be so efficient as to be part

of the solution of the problem of erythema nodosum leprosum reactions. (17) As recommended by Muir and Jeanselme, methods are applied to provoke the reactions, in the belief that they are beneficial. Muir gave 1 to 2 gm. daily of potassium iodide, increasing daily by 1 to 2 gm. up to 6 to 7 gm. If there is no reaction, the treatment is suspended. Usually a reaction begins on the second day, and the treatment is kept up for 2 weeks if there is no deterioration in the general condition. Three reaction periods can be provoked in this way in 4 to 7 months. The method seems precarious and risky.

All the above methods are tarred with the brush of empiricism. More basic research and comparative clinical studies are needed. When we do use any of the above methods, we should do so on the basis of a careful study of the course of the disease in each individual patient.

Dr. A. M. Alonso gives a careful clinical study of erythema nodosum leprosum. He says it is really an extensive polymorph erythema with associated and important involvement of nerves, joints, and certain organs, and it always calls for observation and care of the patient in hospital. Prof. R. N. Miranda points out in his paper that a positive lepromin reaction in a case of erythema nodosum will make it unlikely that it is the leprotic form. He thinks that peripheral nerves in lepromatous cases can be attacked by erythema nodosum leprosum and such cases should be called acute nodosis of leprosy.

The symposium concluded with an interesting discussion which focalized many of the aspects of the problem, and some of the points in dispute. There seemed general agreement, as Dr. P. P. de Oliveira pointed out, that the condition only appears in th lepromatous, that lepromatous cases who have erythema nodosum have a high rate of tuberculin hypersensitivity, that the incidence of the condition has increased since the introduction of sulphone therapy, that the condition often seems beneficial in the course of the disease, that leprosy is not the only factor in the appearance of the condition. Dr. H. C. de Souza-Aranjo made reference to the possible role of granules in the leprosy bacilli, which from phase-contact microscopic studies he thinks to be regenerative elements in the bacilli which have been seen to form new bacilli, and such granular bacilli are common in leprosy cases which are in regression.

REPORTS

Annual Report of the Rajah Sir Charles Brook Memorial Settlement, 1956.

The Superintendent of this leprosarium at Kuching, Sarawak, is Mr. Hamish MacGregor, M.B.E., and Drs. Pillai, Finlayson, Glyn, Kraszewsky, and Murray visited weekly during the year. Hospital assistants and other staff number 9. The year began with 387 patients and ended with 372, and 68 were discharged symptom-free during the year. Sea-Dayak and Chinese are the most prominent in the racial classification of inpatients, though Land-Dayaks, Kayans, Malays, Melanaus, and Javanese are also represented. Children numbered 39. There were 8 children born in the settlement in the year; their care was arranged for outside the leprosarium, with family or friends for preference. The main form of treatment is oral DDS, and a few received injectable sulphones, and interest is being shown in hydnosulphone, a combination of sulphone and hydnocarpus, for patients who show intolerance or do not do well on oral sulphone. Cases of lepra reaction and longstanding trophic ulcers show some decline in number. Tuberculosis and cancer were the most important of the intercurrent diseases. There is a small laboratory which is aided by the Pathological Laboratory, Kuching. The internal activities of the settlement seem numerous, cheerful and co-operative, resulting in many improvements to the amenities. Besides the special care and interest of the Medical Department, the settlement has received advice and solid help from the Public Works Department and the Forestry Department and others, and the visits and interest of H.E. the Governor, as well as many visitors from overseas.

The Work of WHO, 1956.

This annual report of the Director-General is full of interest, as it describes current and projected work in communicable diseases and public health in the world, and does not omit attention to such important sections as maternal and child health, nutrition, mental health, education and training, etc. Leprosy is given increasing attention by WHO, who aid many countries in their leprosy control schemes. For example, one reads in the project list of leprosy control schemes in Ceylon, the Caribbean, Iraq, Thailand, Indonesia, French Equatorial Africa, Nigeria, Gambia, Uganda. On page 54 of the Report there is interesting comment on some aspects of leprosy control schemes, in particular on the wide use in the French territories of fortnightly injections of oil suspensions of

DDS. It is commented that it seems very useful in the organisation of mass treatment under rural conditions, because it enables patients in remote foci to be reached and treated regularly, and cuts down the number of contacts between patients and treatment staff, and so enables the latter to cover a greater number of patients.

From the Report it is clear that WHO has become an enormous force for good in world health.

International Digest of Health Legislation, WHO. Vol. 8, No. 1, 1957.

The regulations of 23rd June, 1955, of Mexico on the control of leprosy appear on pages 68-71. They provide for the establishment of a National Leprosy Control Service which brings into harmonious co-operation the dispensaries, sanatoria, preventoria, and health units, as well as specialised physicians and staff. The leprosy dispensaries, giving due regard to Mexican conditions, are chosen as the basic and most important units of the Leprosy Control Service, and full staffing is apportioned to them, including a laboratory technician. Sanatoria and preventoria are by no means abolished, and are considered still to have important functions. The existence of private institutions is also welcomed. Statistics and records, education of the public, special training of physicians and staff, are also provided, and the whole is co-ordinated by a central technical office. It is clearly stated that any form of coercion of patients and relatives is to be avoided, and the first recourse must be to education and persuasion.

The Leprosy Centre at Paramaribo, Surinam.

A report on a visit to this centre has been issued by Sister A. French-Augustin, who apparently went there on a WHO Fellowship. She describes a fine piece of work, well staffed, well organised and equipped. The superintending leprologist is Dr. Bueno de Mesquita, assisted by Dr. Jacob and Dr. Pinas, Sister Markiet and 12 nurses, also a dentist and eye specialist. There are 3 leprosaria, and hospital care, housing, social welfare, schooling, gardens, and radio are all available. There are about 370 inpatients and 700 outpatients. There are 30 model cottages built for patients who have reached arrest of the disease, but have no home to which to go.

The Chronicle of the World Health Organisation, March, 1957, Vol. 11, No. 3, page 63.

A discussion is described of *leprosy in the Americas* at the meeting in September, 1956, of the WHO Regional Committee for

the Americas, at Antigua, Guatemala. A table is given of statistics of the prevalence of leprosy in the Americas, from which it is evident that (for the 18 countries given) Brazil has the heaviest burden, with Mexico next, then Argentina, Colombia, and Paraguay. It was agreed that there is a need for active measures in combating leprosy, and leprosy demands a higher priority under national public health programmes. The representatives of Brazil stated that the techniques used to date for leprosy control in Brazil had not produced the results expected, in spite of its 36 leprosaria, 31 preventoria, and 80 regional dispensaries in operation, and a revision of operating methods is in progress. In Venezuela, BCG vaccination had been applied for many years to the entire population in leprosy areas in one programme, and to the population under 15 in leprosy foci for 4 consecutive years, in another programme.

R.C.M. Leprosy Colony, Ndanda, Tanganyika, 1956 Report.

There were 464 inpatients under treatment, and 101 patients were discharged after 2½ to 3 years' treatment or more, and most were symptom-free or much improved. The treatment given included DDS, sulphetrone injections, conteben, INH and TB1, and hydnocarpus oil injections intradermally. There were 4 cases of drug intolerance to DDS in the shape of severe exfoliative dermatitis, and 2 cases of hepatitis, one severe, one mild. Only a few patients had reactions. Five patients had the complication of pulmonary tuberculosis, and are being treated with dihydrostreptomycine and INH, or INH and TB1. There was one infant who showed tuberculoid macules in 1955, 5 months after birth. She has been treated with oral DDS for 10 months now, and the macules are repigmented almost completely. All of the 17 patients who have been given Conteben make good progress: this drug is considered of value in those who have repeated reactions under the sulphones, or are drug sensitive to them, or do not respond satisfactorily to them. It is noted that 50 patients under the sulphones since February, 1951, and still under observation, show a disappointing persistence of positive skin smears, and in some, of still active skin lesions. There was 1 case of relapse in a patient discharged in 1954 after 3 years on DDS. The relapse occurred 9 months later, and after 12 months more of DDS has again had disappearance of his lesions; this was apparently a tuberculoid case.

The Report of the Medical Services, Ministry of Health, Sudan Government, for the year 1954-55, contains a brief reference to leprosy. There has been a change of method towards domiciliary

treatment of leprosy patients with sulphones, but 14 leprosy settlements continue to function as homes for the multilated and incapacitated; of the inmates of these former leprosaria there were 2,098. It is reported that 77% of cases in the Ingasana Hills of the Blue Nile Province are of the tuberculoid type. During the year 1,106 new cases were diagnosed, of which 175 came from Equatoria, the known heavily endemic zone. The policy is to make supplies of sulphone available in all dispensaries, and special record cards.

The Report for 1956 of the Mission to Lepers, Hong Kong Auxiliary, which conducts the leprosy work at **Hay Ling Chau,** describes a very fruitful, well organised, and wel-staffed work. In addition to an honorary consultant staff comprising a pathologist, a dental surgeon, a radiologist, and a plastic surgeon, the Superintendent (Dr. N. D. Fraser) has the aid of 3 Medical Officers, a nursing supervisor, a matron, and 2 nurses, 2 laboratory technicians, and many other staff and voluntary workers. The interest of H.E. the Governor, Sir Alexander Grantham, and Lady Grantham and their team of workers in the Auxiliary must be of greatest value. Maintenance and construction of the buildings and settlement also seems to be in very good hands. Patients treated at Sandy Bay and Hay Ling Chau between 1950 and 1956 numbered 785, and of these 187 were discharged "arrested." The transfer of patients to Hay Ling Chau was completed in August, 1952. For Hay Ling Chau the year 1956 ended with 388 patients, and 35 had been discharged "arrested." Good therapeutic results are obtained in the majority of patients treated. There is limited accommodation in the Shap Lung Centre for those discharged "arrested," but permanently crippled, so that many such have to remain on in Hay Ling Chau. Persistent lepra reaction in patients has been treated with considerable success by the method suggested by Dr. E. J. Currant, that of giving the sulphones in minimal doses with a view to desensitization. It was found that previously reactive patients actually responded to treatment with such doses, with a steady fall in bacillary index. The laboratory work is very active and full, and time has been given to research in pathology and immunology of leprosy. The teaching of medical students in leprology also goes on.

Annual Report, 1956, The Victoria Leprosy Hospital, Dichpali, India.

Dr. A. L. Furniss reports encouraging development in surgical work for the correction and prevention of deformities, and notes

the great psychological value of the cosmetic result of operations. There were 2,632 people who came for examination for leprosy. The average number of inpatients was 490. Patients discharged with the disease arrested numbered 69. Orthopaedic operations number 94, and rhinoplastics 24. The laboratory work flourishes, and X-ray examinations were 157. The report mentions that it is quite impossible to admit everyone who comes, because of the lack of resources.

Report for 1956 of the Nigeria Leprosy Service Research Unit, Uzuakoli, Eastern Region, Nigeria.

Dr. T. F. Davey, the Senior Specialist, describes a fruitful year. He points out that the Research Unit possesses all essential facilities for basic leprosy research, and adequate numbers of highly co-operative patients are available. The region is also one of great immunological interest. Therefore the research programme has been directed to pilot trials of new anti-leprosy drugs, biochemistry in especial relation to new leprosy drugs, immunological studies in the field, and some aspects of epidemiology. The therapeutic trials included diphenyl-thiourea (Ciba Compound 15095E), diamino-diphenyl sulphoxide, and pyrazinamide. All these have been assessed against the standard of DDS, and the first and second are promising, while the third seems of little value. As regards DDS itself, the remarkable fact is reported that there is still no evidence of the development of drug resistance. Early cases respond rapidly to it, but the treatment must be continued for a long period. The distressing complication of neuritis in the later stages seems to be less severe if a steady dosage of 100 mgm. daily is given, rather than 300 or 400 mgm. twice weekly. A minority of cases of relapse occur among macular cases, especially in atypical tuberculoid, but no case has been yet encountered of relapse in lepromatous cases who have had adequate treatment. In immunological studies, Dr. Davey draws attention to the decline in leprosy prevalence in the region, and raises the question of the possible influence of tuberculosis on this. Tuberculin testing among school children has been undertaken, and lepromin tests side by side with them. It is too early for definite conclusions. The effect of BCG on conversion of lepromin is also being studied. In biochemistry, careful study of the absorption, excretion, and metabolism of the new drugs has been made. There is yet no satisfactory means for estimating the concentration of diphenyl thiourea in the blood. In epidemiology, work continues of a special study of a group of villages which began in 1941. It is proposed to submit these

villages to tuberculin and lepromin testing. New equipment at the Unit includes an X-ray and a good camera. Training of workers goes on in the more technical aspects of leprosy.

The Chronicle of the World Health Organization, Vol. 11, No. 6-7, June-July, 1957, p. 179.

At the 10th World Health Assembly of May, 1957, the subject of leprosy was discussed among the many activities of WHO. The delegate of India expressed the hope that WHO would adopt a leprosy programme as broad in scope as those undertaken for malaria and tuberculosis. The problem in India was so large, with an estimated number of 1½ million leprosy cases, that help was needed. The Thailand delegate gave the estimated number for his country as 100,000. In the Philippines there are about 20,000 and much social ostracism of leprosy sufferers, and in rehabilitation it is hoped that plastic surgery will contribute to the patients being accepted back into civil life. In Egypt they have moved away from compulsory isolation, and when the patient is contagious his isolation is now optional, and in any case after becoming non-contagious he is treated through outpatient services. They now have 10 central and 40 branch clinics for leprosy treatment. In French Equatorial Africa the problem is large and has been met by mobile teams, which now treat 100,000 cases after 2 years of operation. Similarly 300,000 patients are expected to begin treatment this year in French West Africa, and the number may soon rise to 500,000. French Cameroons is preparing an attack on similar lines. In Nigeria a plan is in operation for the treatment of 200,000 patients, based on temporary isolation and treatment given from the permanent or mobile services. Also in the Belgian Congo 250,000 cases are being treated, and injection methods are used as well as oral administration of the drugs. Greece had modified the leprosy law to permit the treatment of patients at home.

The Report for 1956 of the Medical Department of the Leonard Wood Memorial, Washington, reprinted from Leprosy Briefs, has been issued by the Medical Director, Dr. James A. Doull. He refers to increasing interest in leprosy research in the U.S. and abroad, and in rehabilitation of leprosy patients. In connection with the latter, Dr. Doull has suggested a clinical conference on orthopaedics, physiotherapy, and plastic surgery in leprosy, which could possibly be held at Sungei Buloh in a year or two.

As regards the research work carried on in 1956, in *microbiology*

and biochemistry, Drs. Hanks, Gray, Brodie and Wallace have continued their studies at the Leonard Wood Memorial Bacteriological Laboratory, Havard Medical School. The work of Dr. Hanks is directed to finding a practical method of distinguishing active from inactive *M. leprae,* by reducing tetrazolium in slide preparations under strict anaerobiosis, and microscopic observation of the reduced salt (formazan) in the mycobacteria. The formation of formazan artefacts has been troublesome, likewise contaminating micro-organisms have to be inactivated and distinguished. Dr. Wallace with Dr. Elek have studied the propagation of *M. leprae murium* in cell cultures on the lines of (a) protection of bacilli from extracellular environment and serum inhibitors; (b) stimulation of bacillary activity; (c) modication of host cell metabolism. Drs. Gray and Brodie continue their studies on the mechanism of coupled oxidative phosphorylation in mycobacteria. Active fractions have been obtained.

In *pathology,* at the Leonard Wood Memorial Pathological Laboratory, Culion, Philippines, Dr. Wade's work continues on the improvement in staining of *M. leprae* in tissue sections, on the standardization of lepromin, and on the intradermal injection of *M. leprae* and *M. lepraemurium* in young monkeys. Dr. Wade is also editor of the International Journal of Leprosy.

In *epidemiology* Drs. Guinto and Mabalay in the Cebu unit, Philippines, studied the results obtained with different lepromins, and showed that patients who have been negative to ordinary lepromin will sometimes respond to a lepromin containing larger numbers of bacilli. They found that Wade's purified lepromin, a purified bacillary suspension, was suitable for practical use, as it was comparable with ordinary lepromin but gave fewer strong reactions. Dr. Kluth reported from the Unit at Corpus Christi, Texas, on the epidemiology of the disease in Texas. Though the known leprosy case, and particularly the lepromatous, seems to be the important source of infection, it does not account satisfactorily for about 70% of the leprosy that is occurring in Texas. The disease may spread from casual contacts with lepromatous cases in the non-recognized period of such, or with quite unrecognized cases. There may even be a self-limited type of missed infectious case. There was no evidence justifying the suspicion of healthy carriers. He postulates a dormant stage of leprosy, possibly of long duration. Dr. Doull and Miss Derrom pursued their enquiries in broad epidemiology and obtained remarkable and useful results which have been recorded in Leprosy Briefs. Field studies in Cebu are also being directed to investigating the apparent trend to a disease

of more benign type, and to investigating the reactivity in young children to lepromin and tuberculin, with relation to the effectiveness of BCG, the lepromin test, and unknown natural causes.

In *chemotherapy* Dr. Chang tested a number of compounds for effectiveness in murine leprosy, including cycloserine, paromonycin, cortisone, and a number of chemical compounds. He has newly developed a 3 weeks' screening technique, and is experimenting with slide culture preparations of monocytes in the hope of devising a quicker screening technique. Drs. Doull, Rodriguez, Davison and Tolentino continued their comparative study of DDS with DDS plus additions of nicotinamide or BCG vaccination (the Third Series of such trials). The fourth series will study intramuscular DDS and diphenylthiourea (SU 1906 Ciba), also Compound 377 of the Connaught Laboratories of the University of Toronto: this compound is the isonicotinyl hydrazone of 2-carboxymethoxybenzaldehyde. The results so far may be described as unexciting. Methods of evaluation are to be improved by attention to clinical points like the healing of ulcers, to bacteriological findings, and to serological and biochemical changes, such as the relative excess of gamma globulin in lepromatous leprosy.

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