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Editorial.

IN this number of the REVIEW we commence a short history of the Foundation and the First Decade's Work of the British Empire Leprosy Relief Association, by Sir Leonard Rogers. It is most appropriate that the Hon. Medical Adviser of the Association should write this history for, without his enthusiasm and excellent pioneer work, which the whole world has acclaimed, it would have been impossible for the Association to have been founded. We should like to place on record our very deep sense of appreciation of all the work which Sir Leonard Rogers has accomplished, and of his numerous extremely valuable contributions to the cause of leprosy. Sir Leonard Rogers' name is already well-known in research in many tropical diseases, and his contribution to leprosy research has been of the same value as his contribution along other lines, the best known of which being cholera and dysentery.

Dr. Cawston has contributed an article on "Nasal Hygiene in the Treatment of Leprosy and the Use of Antimony." We are very glad to publish this because we are anxious to draw attention to the necessity for very great care being exercised with regard to the nasal condition of patients. It is one of the most distressing of all complaints, and very much can be done towards its relief. We have in previous issues of the REVIEW published articles on this subject by Prof. Pavloff, of Vladivostock, and Dr. Rao, of Purulia. Dr. Cawston's advocacy of antimony has long been well known. At present we are endeavouring to test whether collosal antimony has the same effect in lepra reaction as potassium antimony tartrate. We have always agreed with the Calcutta School in their conclusion, that the benefit of antimony in leprosy is due to the fact that heavy metals in small doses tend to control lepra reaction.

The article on "Leprosy in India and Ceylon" is concluded in this number. It has been impossible to do more than briefly summarise a report presented by the Secretary to the Ceylon Government.

We would like to call our readers' special attention to the article by Dr. Roy on "Some Problems of Surgery in a Leprosy Colony." Much has been written of late concerning the treatment of leprosy, and one of the most pressing problems in a settlement is the surgical problem of how to deal with trophic manifestations of the disease.

This article describes in greater detail the method adopted at Purulia for dealing with necrotic metatarsal and other bones and shows how much can be done in this most distressing condition.

Miss Thornton's article on the " Treatment of Hookworm," is one of extreme importance, because in many settlements this problem is one of the most serious. It will be noted that many cases needed several doses of carbon tetrachloride before they could be considered free of ova. It is not sufficient in most cases to give patients just one treatment and, as indicated in the article, as many as fourteen treatments may be necessary. Not only does hookworm retard progress in the treatment of leprosy, but we feel certain that it is responsible for a certain number of heart disorders, especially disorders of the myocardia. As mentioned in this article, a number of cases of cardiac disorder were discovered, and in every case, on looking into the history of the case, it was found that at the time, or previously, the patient had suffered from hookworm.

The " Comparative Study of the Relative Efficacy of Special Esters and Ordinary Esters," is of importance only as it demonstrates that the attempt to overcome the staining properties of iodised esters has not been successful as yet, because the preparation which has been produced is too irritating for general use. The staining properties of iodised esters may be serious in light-skinned persons. In the darker skinned races it is a matter of no moment, but it is interesting to note that in a European the staining has lasted so far as long as 18 months. It is for this reason that we have in most instances in the treatment of light-coloured peoples reverted to pure hydnocarpus oil and creosote. As has been pointed out by others, the difficulty of its viscosity can be easily overcome by heating up to about 55 degrees F.

We have reprinted in full Dr. Muir's article on " The Leprolin Test," because we feel it is one of the most important advances which have been made within recent years. Dr. Muir has investigated very carefully this test, which was originally described by Bargehr and developed by Mitsude and Hayashi. We feel that this test will be of considerable value in estimating the relative resistance of patients to the disease, although in many respects we feel that the leprosy bacillus acts almost like a cellular parasite, and therefore, it may be premature to conclude that because a patient is negative to the Hayashi test, the prognosis is necessarily bad.

History of the Foundation and the First Decade's Work of the British Empire Leprosy Relief Association.

SIR LEONARD ROGERS.

THE completion of the first decade of the work of the British Empire Leprosy Relief Association (BELRA for short) affords a fitting opportunity for recording a brief history of its foundation and progress.

THE EVENTS THAT LED TO THE FORMATION OF THE ASSOCIATION.

Discovery of an improved treatment of leprosy.—It is not too much to say that a single decade before the foundation of the Association, in the latter part of 1923, the outlook for the unfortunate sufferer was little better than in the Middle Ages. The only prophylactic measure was compulsory segregation of all cases which was, in effect, a sentence of life-long imprisonment with no likelihood of recovery, in the vain hope that the disease might thus be stamped out in time. The innumerable remedies advised in its treatment bore witness to their small value, and none of them had ever sufficed to clear up the symptoms and remove the infectivity of any appreciable number of cases. This is shown in my Cameron Prize Lecture given before the University of Edinburgh in 1929*, which records with 88 references, the recent advances in treatment.

The most generally used of these methods was the old Indian remedy, chaulmoogra oil, which Ralph Hopkins of Lousiana showed to have some power of retarding the progress of the disease, but it was too nauseating to be curative. In the first decade of the present century the writer, working in Calcutta, had found gynocardic acid, the lower melting point fatty acids of chaulmoogra oil, to be less nauseating and more effective orally than the whole oil, and a medical colleague of his was cleared of a widespread leprosy rash by it. After demonstrating the great value of injections of emetine, the active principle of the ancient remedy ipecacuanha, he wrote in 1912 to a firm of manufacturing chemists, who had previously done valuable research in showing that chaulmoogra and hydnocarpus oils consisted mainly of chaulmoogric, hydnocarpic acids, and so-called gynocardic acid, to ask if they could prepare

* Edinburgh Medical Journal, January, 1930.

soluble products of these fatty acids suitable for injection, but a reply in the negative was received.

In the meantime, Dr. Victor G. Heiser, the founder of the great Culion leprosy segregation settlement of the Philippines, had been using very painful intramuscular injections of chaulmoogra oil with beneficial results, apparently of a temporary nature, as Dr. Wade later could find no evidence of any of the patients having been discharged recovered. In the middle of 1915, while on a visit to Calcutta, Dr. Heiser urged Rogers to undertake further work on the subject, with the result that soluble gynocardate of soda was made. This was reported by Rogers in February, 1916, to be of greater value by injection than the fatty acid orally. Later in the same year, he showed that it could safely be given with still better results intravenously, and that it thus might produce reactions in the leprous lesions with actual breaking up of the causative acid fast bacilli in the human tissues. A year later, Rogers was able to record, with photos and coloured plates, a series of 26 cases with complete disappearance of all the leprous lesions in 50 per cent. of cases of not more than 3 years duration, and in 25 per cent. of those of 3 to 5 years duration before treatment. Thus the important principle was established, that the injection of soluble preparations of the active principles of chaulmoogra and hydnocarpates constituted an effective treatment more especially of early cases of leprosy.

Subsequent improvements in the technical application of this principle may be briefly mentioned. During his four and a half years' investigations in Calcutta Rogers showed that hydnocarpates were more effective than chaulmoograte, and hydnocarpus wightiana oil from Western India was better than the chaulmoogra oil of Burma. After his return to England in 1920, he obtained a less irritating form of sodium hydnocarpate in the form of alepol, about half a million doses of which are being supplied yearly to British Possessions by BELRA. In the meantime in 1919 Hollmann and Dean, in Honolulu, after confirming the earlier work of Rogers, reported favourably on intramuscular injections of ethyl ester chaulmoograte and hydnocarpates, which have since been used very extensively by American workers, with the addition of iodine, and by E. Muir and others, with the addition of creosote as an antiseptic, although this modification is much more expensive than alepol. In 1925, E. Muir, who has been working since 1920 as leprosy research worker in the Calcutta

School of Tropical Medicine, founded by Rogers, established the value of a still simpler and cheaper modification in the form of fresh pure hydnocarpus wightiana oil with 4 per cent. creosote, which is most extensively used in India.

The leprosy problem in the British Empire.—Previous to the establishment of an improved treatment for the less advanced cases of leprosy, the problem of reducing materially the incidence of this justly dreaded disease, appeared to be so hopeless that it attracted little attention, and it was not until Muir and others sought out early cases for treatment that the magnitude of the problem became evident. Thus a survey of over 2½ million people in India has revealed 4½ times as many cases of leprosy as are returned in the census figures, mostly early ones, making a total of not less than 500,000 in India alone. In 1921, Rogers commenced a three years' study of the more important literature on leprosy during the previous half century on the distribution, epidemiology, infectivity and prophylaxis, which formed the basis of various papers and addresses, and a book on leprosy (published by John Wright and Sons, Bristol) in conjunction with Dr. E. Muir, who contributed the clinical and treatment sections. Among other things, these researches established a high incidence of leprosy in humid hot climates, with the highest rates per mille in tropical Africa, that the majority of infections occur in the first two decades of life, that 80 per cent. are contracted by living in the same house as a case of leprosy, but only 3 to 5 per cent. of those thus exposed develop leprosy, and that the incubation period averages two to three years and in 80 per cent. is under five years. He therefore advocated as the most rapid method of reducing leprosy incidence, the examination of the households and other contacts of known cases every few months for five to ten years, to enable the great majority of infections arising from them to be detected and cleared up by treatment in the early amenable stages. If nearly all these can be prevented from reaching an infective stage, within a single decade the sources of infection would be very greatly reduced by the infective cases present at the beginning of the decade either dying or passing into an uninfective nerve stage, for the more acute dermal cases are twenty times as infective as the chronic nerve ones. Recent trials of this plan in Naura Island and in the Sudan, described at the 1933 meeting of BELRA'S General Committee, indicate that the nearer this ideal can be approached the more rapidly and economically will leprosy be reduced in any area to easily manageable proportions.

The time had now come when it was essential to make the new knowledge known throughout the British Empire by means of an organized effort, and fortunately with the hour the men to carry it through were available.

THE FOUNDATION OF THE BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION.

The writer had already raised at council meetings of the Mission to Lepers, which had for long provided financial support to various missionary bodies engaged in administering a large proportion of the leprosy asylums in India, the question as to whether they could extend their work to providing out-patient clinics for the treatment of early cases of leprosy, but this was not considered to be practicable. On March 29th, 1923, Mr. Frank Oldrieve, for long Secretary for India to the Mission to Lepers, came to ask the writer to speak at a public meeting of the Mission in Cambridge, and he also broached the question of forming a new association to inaugurate leprosy work throughout the Empire. As Mr. Oldrieve no longer felt fit for whole time work in India, the Mission to Lepers were willing to release him on the completion of his deputation work in November, 1923, and his organizing abilities and personality as a whole-time Secretary of the proposed association would ensure its success and provide just what the writer had no time to undertake, so the opportunity was too good to be lost. Sir Frank Carter, a philanthropic Calcutta friend, was next enlisted in the good cause, and he has ever since been Treasurer of the Association. The writer next obtained the sympathy and support of a number of prominent public men of great weight, including Lord Chelmsford, who rendered invaluable service as Chairman of the General Committee, Lord Ronaldshay, Governor of Bengal, Sir Edward Gait, formerly Governor of Bihar and Orissa, who has proved a tower of strength as Chairman of the Executive Committee, Sir Humphrey Rolleston and Sir John Rose Bradford, each of whom has been President of the Royal College of Physicians of London, and the latter has throughout been Chairman of the Medical Committee, and many members of the Association whose names appear on our general and medical Committees. It is most gratifying to the writer that he cannot recall a single refusal to his appeals for the support of so many very busy men.

A meeting of a number of influential supporters was held at the India Office on July 12th, 1923, with Lord

Chelmsford in the chair, when the Association was inaugurated, and an Executive Committee, with Sir Edward Gait as Chairman, was constituted to complete the organization and to arrange for a public appeal to be made later at the Mansion House, permission for which had already been obtained. In September the writer drafted an appeal and a note on the medical policy, which were accepted by the Executive and Medical Committees, and a questionnaire on the incidence of leprosy and modes of prophylaxis in use was drawn up for circulation to all British Possessions. The Mansion House appeal had been fixed for December, but had to be postponed on account of an unexpected general election, to January 31st, 1924, when Lord Chelmsford, Lord Peel, Secretary for State for India, Sir Humphrey Rolleston, and the writer, spoke and asked for a considerable capital sum to enable the work of the Association to make a good start. By an unfortunate combination of adverse circumstances, including the recent subscription by the city of London of a quarter of a million pounds to the Japanese Earthquake Relief Fund, and the taking of office by the first Socialist Government, with fear of increased taxation, doubtless aided by the inexperience of the founders of our Association in the technique of appeals in Great Britain, this appeal brought in very little money and was most disappointing, so Mr. Oldrieve and the writer had to set to work to raise funds by other means.

Formation of provincial branches of BELRA.—As we had failed to obtain any substantial help in our great Empire work from its wealthy capital city, we turned to the provinces with happier results. In January to June, 1924, Mr. Oldrieve organized meetings at which we both spoke at Rotary Clubs and in Municipal Offices, etc. in Bristol, Glasgow, Liverpool, Birmingham, Dublin, Manchester and Edinburgh. The writer had hoped to get the support of particular cities for leprosy work in some part of the Empire overseas with which they traded, such as Liverpool to finance work in West Africa, but owing to a slump in trade the appeal there failed. Active branches were, however, formed in Edinburgh, Glasgow and Bristol.

During 1928, after his return from his East African tour, Mr. Oldrieve organized further branches in Aberdeen, Dundee, Plymouth, Cheltenham and Rugby, and Sir Edward Gait has also spoken at a number of our branch meetings. Up to 1933 no less than £13,400, out of the total receipts of £56,772, has been received from our branches.

To be continued.

Nasal Hygiene in the Treatment of Leprosy and the Use of Antimony.

F. GORDON CAWSTON.

THOUGH the relief of nasal catarrh is often associated with improvement of the health of otherwise normal patients, it would not appear that the importance of nasal hygiene has been sufficiently considered in the treatment of chronic diseases such as tuberculosis and leprosy, though the subject has repeatedly been emphasised by those in charge of consumptive homes and leprosy institutions.

Whether infection of the nasal passages should be regarded as primary focus of infection in leprosy or as secondary to a general infection, there can be no question that relief may be obtained by well regulated attempts to keep the nasal passages clear and relatively free from microbic infection, and that the secondary infection of nasal sinuses which are only too commonly associated with a simple nasal catarrh must lessen the chances of a patient overcoming a general infection.

Unfortunately, efforts to prevent infection during an epidemic of influenza have sometimes included the wholesale practice of washing the nasal cavity through with saline, thus tending to remove from normal persons the natural protection of the nasal mucus. Nasal lavage should be confined to persons suffering from infection of the nasal mucous membrane and, in these, a solution of sodium chloride or bicarbonate of soda is often of great service in removing infected matter and promoting the healing of ulcerated patches.

Nasal antiseptics are prepared as lotions, ointments and jellies. They should not be irritating to the mucous membrane and their use should not be unduly prolonged. It is conceivable that in using them one destroys micro-organisms which are of service in the protection of the body, and that relative immunity to nasal infection may sometimes be more readily effected by anti-catarrhal vaccines employed either as nasal sprays or for repeated injection.

Antiseptic lotions which suggest themselves as useful for chronic nasal infection are hydrogen peroxide, glycothermaline, boracic and hexylresorcinol. The addition of glycerine is often of value, whilst rectified spirit may sometimes be added where there is a tendency to polypoid formation.

As sprays, chloretone inhalant and hexylresorcinol are very useful indeed, whilst the occasional application of an antiseptic nasal ointment or jelly, such as ephregel or vix, renders nasal lavage less necessary and effects improvement by causing collapse of the turbinated bodies whose congestion prevents the ready escape of infected mucus or the normal ventilation of all parts of the nasal cavity.

Constant swelling of the turbinates may be produced by irritation during dust storms or in heated atmospheres with much humidity. Overclothing and over-eating aggravate the tendency, as does the presence of a deep-seated nasal infection. Where the nasal passages are kept clean and clear, many deep-seated nasal sinuses improve or may be cured without other measures being taken.

It is reasonable to suppose that careful attention to nasal infection in persons suffering from respiratory diseases and in cases of leprosy would enable the system more readily to deal with a chronic general infection. A leprologist tells me that he has obtained results which are definitely encouraging in a series of cases of leprosy treated with alkaline nasal douching and in the use of chloretone nasal sprays. Another informs me that he favours electrargol by spray in leprosy because of the definite improvement he has observed in ulceration of the nasal passages. I have myself observed improvement in the nasal condition of such cases whilst they were receiving a series of intramuscular injections of colloidal antimony. In the Leprosy Review for April, 1930, N. Pavloff mentions a 5 per cent. solution of chromic acid as particularly serviceable in the treatment of leprosy processes of the nose and throat.

Whilst a thorough investigation into the claims that are being made for nasal antiseptics in the control of respiratory disease is needed, there can be no doubt that conservative measures for the relief of nasal catarrh might be more widely used among chronic sufferers and incurables. It would be of great service if those who are in charge of leprosy institutions could undertake an investigation into the relative value of those remedies which are found to be of service in the treatment of chronic infection of the nasal passages, and report how far the improvement of the nose and throat may be associated with an arrest of the progress of the disease or with general improvement of the patient's power of resistance.

It is to be regretted that many officials are not encouraged to publish in the medical press the result of their own careful researches, and that so much of the work that

is being carried on is lost to science through being incorporated in inaccessible official returns.

I cannot find that antimony was used seriously with the object of overcoming the effects of leprosy previous to 1919, when the Secretary of the Indian Immigration Trust Board in Natal, with the concurrence of the two medical officers, granted me permission to treat a number of patients who were suffering from leprosy. The improvement shown in the general and local condition of these patients appealed to the authorities as well as to three medical men who had an opportunity of examining them, and it was on the recommendation of the Department of the Interior that I forwarded to Robbin Island a supply of the preparation of antimony which I had used in the treatment.

Other investigations which I have made on behalf of the British Medical Association convinced me that the most effective and least toxic preparation of antimony with which we are acquainted at the present time, is antimonium potassium tartrate given skilfully in carefully regulated doses in fresh solution intravenously, and that the injections should be given in the morning an hour or two after a light breakfast. I tested several others preparations of antimony including various colloidal preparations, but regarded all which might be administered orally or intramuscularly as somewhat uncertain in their action. About the same time, U. N. Brahmachari, in India, and R. G. Archibald, in the Sudan, recorded success from other preparations of antimony in the treatment of leprosy.

Unfortunately intravenous injections of antimonium potassium tartrate seem to have been responsible for undesirable consequences in the treatment of cases of leprosy in some countries, and this would seem to have been responsible for the discontinuance of antimony injections in the Amatikulu leprosy institution, where evident success was being obtained and where over 200 cases had received intravenous injections of an antimony preparation.

It is possible that local conditions have not been sufficiently considered in the reaction of leprous patients to treatment with antimony. When the beneficial effects of antimony injections in the treatment of leprosy in Natal had been published, the question was raised whether sufferers in Natal were affected with some parasitic infections which would reasonably respond to antimony therapy, irrespective of its influence on the leprosy bacillus. The late Sir Andrew Balfour, who was specially impressed with the return of sweating in leprotic areas among these Zululand

patients whilst under treatment with antimony, drew my attention to the extraordinarily contradictory reports of its value which were being received from various parts of the world. There would seem to be no doubt that intravenous injections of tartar emetic given at so great an altitude as that of Maseru in Basutoland, had a detrimental effect on the cases, though I have used it with success on other patients who were not cases of leprosy, in Southern Basutoland, in a dry mountainous climate of over 5,000 feet above sea level.

Antimony is closely allied to arsenic and, in therapeutic doses, it should prove to be a good hepatic stimulant besides being a useful remedy for schistosomiasis and for many skin diseases. Vin. antimonialis is a very useful expectorant which largely has fallen out of use. Personally, I much prefer it to tinc. camph. co., as its action over a few days is usually far superior. I was much impressed with the confidence patients at Westfort, Pretoria, had in this expectorant, and I have sometimes felt that where intravenous injections of antimonium potassium tartrate cannot readily be given, it might be better to rely on the use of vin. antimonialis than on other antimony injections.

Several of the newer antimony preparations, though less to be desired than tartar emetic for the treatment of schistosomiasis in spite of a good antimony content, would appear to be specially indicated in chronic skin conditions, and, if it becomes accessible, a new preparation of fouadin, which is now being tested, in view of its calcium content, would seem to be indicated in the treatment of leprosy where there is skin ulceration or other indication for the use of antimony. I am interested to learn that this drug is being tested in the Dutch Indies for the relief of leprosy.

I have not been afforded the opportunity of officially treating leprous patients in the Union for the last 15 years or since I obtained the success I reported to the British Medical Association in 1919; but where antimony has been used in South African institutions on a large scale, it has sometimes proved more beneficial than chaulmoogra oil, and this result has been recorded officially.

The improvement which was noted at the Amanzimtoti institution whilst the cases were under treatment with antimony injections, was continued for several years and until this method of treatment was no longer sanctioned.

Racial predisposition to disease has received careful attention, but the fact that the therapeutic doses of any drug may vary at different altitudes and among different

races seems to have been overlooked. When acting as medical officer under the Basutoland Government in 1931, during a prolonged winter drought, it seemed that almost any food or medicine had a beneficial effect in cases of deficiency disease. I found special use for injections of phosphorus, glucose, saline, and boiled sea-water and for tinc. rhei co., by the mouth. Intravenous injections of antimony, when called for, were difficult to administer because of the smallness of the superficial veins and the darkness of the skin, but I experienced no toxic effects. In Natal I have found Zulus able to tolerate large and repeated intravenous injections of antimonium potassium tartrate in fresh solution; the sodium salt is too frequently associated with shoulder pains and gastric disturbances for me to use it in private practice. Indians also tolerate larger doses than Europeans, but this may be due to the fact that they are small eaters. The toxic effects of antimony therapy which have been experienced in various parts of the world may possibly be due to unskilful regulation of the dose and to unreliable and stale solutions, but the idiosyncrasy of patients must be considered and, where a large number of patients have been found to respond to antimony therapy, it is unreasonable to condemn the use of the drug in that area because of unsatisfactory reports from its use in other countries.

Since antimony in the treatment of leprosy did not receive official approval in Zululand and was discontinued, official opinion has been guided by reports of its use in other countries and in other provinces of the Union and this may account for the recent official attitude towards its use.

In reply to a communication I am informed :—

" I am to state that antimony in its various forms has been given a thorough trial in our institutions, and that after such trial the Board was of opinion that the drug had no beneficial action whatever upon leprotic lesions. Its chief use was found to be in helping to clear up old-standing trophic ulcers, but no effect upon either nodular or anæsthetic conditions was ever noticed."

When it is impossible to find a suitable vein for administering tartar emetic to a patient suffering from creeping eruption or other condition for which antimony is indicated, I usually employ one or two intramuscular injections of antimosan, fouadin, Crookes' colloidal antimony or Comar's combined antimony and sulphur in colloidal condition.

Unfortunately, the term " tartar emetic " has sometimes been applied to the sodium salt which, in my experience,

is more commonly associated with toxic effects than tartar emetic. Where there is evident improvement in the general condition of a leprous patient, and where one observes, not only relief of the paralysis but healing of ulcerated patches and a return of sweating in anæsthetic areas, one is justified in continuing the use of the drug, but it must be administered with caution, and it is doubtful whether it should be given for more than a week or fortnight at a time, the general constitution being encouraged to exert itself in overcoming the infection.

REFERENCES.

(1) Cawston, F. G.—" Antimony in Leprosy," *British Medical Journal* 1920. December 4th, 1920.
1921. March 19th, 1921.

(2) Wildish, G. H.—" Antimony in Leprosy," *British Medical Journal.* 1922. January 14th, 1922.

Leprosy in India and Ceylon.

R. G. COCHRANE.

(*Continued from Vol. V, No.* 1).

IN the previous number of the REVIEW, I dealt quite briefly with the results of my tour in India, and in this concluding article I wish to consider the problem in Ceylon.

In view of the fact that Ceylon is an island, and on account of the comparative smallness of the territory, the leprosy problem is most limited, and therefore should be much more easily dealt with, and the possibility of controlling and eliminating the disease from such a country is a far more feasible proposition.

Leprosy has probably been in existence in Ceylon for many centuries. It was no doubt imported by invaders coming in from either India, or as some suggest, from Portuguese or Dutch sources. Owing to its proximity to the mainland, there seems to be no doubt that the disease has probably existed in Ceylon as long as it has in India. As so often occurs, the disease is patchy in its distribution, and the task which was set in attempting to sketch out a leprosy policy for Ceylon was no less than to attempt to find out where leprosy was prevalent and what measures should be taken in such areas. In the limited time at my disposal,

it was impossible to survey the whole of Ceylon, and therefore two areas were chosen, one a rural district and the other a municipality. The work was facilitated considerably by the fact that the Director of Medical and Sanitary Services put at my disposal the help of the two special officers who were appointed some months ago to develop leprosy work in Ceylon, and therefore, in summarising the situation in Ceylon, I wish to make it clear that this work could not have been done without their assistance. The best way, I feel, to clarify the situation for the readers of the REVIEW, is to abstract as briefly as possible the report which was submitted to the Government.

This report deals with the whole situation, under six heads, and concludes with the usual summary and acknowledgments. The first section deals with the review of the present position, and it is pointed out that the anti-leprosy measures to date have been organised on the basis of the " Leper Ordinance " of 1901, which was enacted in accordance with the then known facts. It is shown that at that time the principle of compulsory segregation was very widely accepted, and because the clinical types of leprosy had not been clearly understood, the only possible measure consistent with the available knowledge was to make leprosy not only notifiable, but to enforce segregation of some kind upon every sufferer. It is mentioned that the basic principle of segregation does not necessarily need to be altered, for where the leprosy problem is of comparatively small dimensions, compulsory segregation must play a part in the preventive system. Under the " Leper Ordinance " segregation came under two heads :—(1) home isolation, and (2) institutional segregation. It is pointed out that the system was entirely unsatisfactory for the case in the infective stage of the disease and unnecessary for the case not in such a stage. The general conclusion in the first part of the report was that leprosy does not appear to be a serious menace in the island, but it seems fair to conclude that the measures at present in vogue would not control the disease. The reason for this is given that in the two asylums the admissions have remained at the same level or higher, and will probably continue so unless the system is modified. That is, every infective case existing in Ceylon may pass on the disease to at least one other person.

With regard to the types of cases segregated, the majority of these were of the cutaneous variety, but the survey party found sufficient evidence to justify the conclusions that earlier cases had existed, especially among

school children, and that the majority of late cases have probably passed through the earlier stage before being discovered. It is pointed out that it cannot be too strongly emphasised that unless leprosy is considered as only one of the many endemic diseases of the country needing special methods of control, the money spent on the prevention of this disease will be out of all proportion to its seriousness. On the other hand an apathetic attitude which involves the consideration of the problem as one of minor importance, and not worthy of serious attention leads to unnecessary expenditure on segregation and the formulation of too rigid a system of isolation. Leprosy, like tuberculosis, is probably only infective in the open stage; that is only those individuals discharging bacilli from the skin or mucuous membranes can be considered a danger to the public. It is known that in an endemic area only a percentage of those infected pass on to the advanced stage of the disease; there are as many, if not more, individuals who are never detected because their disease does not appear in a stage which is recognisable to the ordinary physician. No measures need necessarily be taken with regard to these individuals, but they form a very useful indication as to the resistance of the population. It has been suggested by some authorities that leprosy is a disease of childhood and early adolescence, and of those infected only a small percentage pass on to the more serious stages of the disease; in the others the disease becomes arrested by the time adult life is reached. In Ceylon, at present, it is only the more advanced cases that are discovered, the progress of those with early signs of a leprotic infection is neither known or watched; thus, up to now it has been impossible to control the spread of the disease, because many pass into the non-infective stage and remain in that stage, infecting others for months, or even years, before it is discovered. The recognition and observation of these early lesions in leprosy is a matter of utmost importance in any scheme of prevention; some of these will become arrested (the abortive lesion), others will advance, and as soon as activity has been noted in them, the case, usually a young person, can be placed under treatment at once.

This question with regard to the so-called abortive case is being dealt with in an article which will appear elsewhere.

The situation in the Eastern Province is then dealt with, and conclusions were based on surveys of two of the most populous districts, that of Kalmunai and Batticaloa. The method adopted was first the visitation of the contacts of

all known cases and those cases which had been granted home isolation or who had been discharged on parole. In addition to this an inspection was made of all available school children. The importance of this latter step cannot be too strongly emphasised because it is among school children that the index of infection can be estimated, and it is these persons who show the earliest type of lesion. It will be stressed more than once in this report that because a school child has signs of a leprotic infection, it is not a *sine qua non* that it needs immediate treatment. It is pointed out that in any survey, it is not the number of cases that is really important, but it is the age group and type of cases that should be stressed. For instance, an area where the cutaneous type is prevalent is probably much more serious than one where only neural cases are seen. It is further suggested that a high incidence amongst school children is possibly indicative that the disease is spreading and active measures should be undertaken, to endeavour to prevent further spread. Colonel Stewart, in an address at the Calcutta Leprosy Conference likened leprosy to an epidemic disease and suggested that it is important to know whether the epidemic is on the down curve or on the up curve. It is suggested that possibly if the age group is high and the proportion of infective cases not unduly great, then it is possible that the disease is on the down curve of the epidemic, and will in the course of time come under control. On the other hand, if the age group is low and the proportion of infective cases high, it may be legitimately concluded that the disease is spreading in such an area, and unless measures are taken, may infect a considerable number of people over the years. Because it is manifestly impossible to deal with every area, selected districts should be chosen, and if these are chosen along the above lines then it is felt that in all probability, if the disease is controlled in areas where it is spreading, leprosy in the other areas will tend to come under control. Viewing prevention in this light brings the problem within manageable proportions. The general conclusion with regard to the situation in the Eastern Province was that leprosy is probably no longer a serious menace in that area.

The situation at the Mantivu Leprosy Settlement is dealt with, and various recommendations are suggested.

The municipality which was chosen for investigation was that of Colombo, and the plan of campaign was along similar lines to that followed in the Eastern Province. The situation in the municipality of Colombo was extremely

interesting in that a higher proportion of school children were found to be infected. The average rate among the schools which were examined was just under three per thousand. In all 43 cases were discovered, 25 of whom were children. The brief survey of Colombo suggested that the disease may be spreading in certain areas. This is not at all unlikely, for when leprosy is introduced into an overcrowded municipal area, the chances of spread are considerable. It was in such areas that there appeared to be definite foci of leprosy which needed further investigation, and it was suggested that these areas should be surveyed in detail. It was suggested that all schools in Colombo should be examined, and thus it may be possible to discover other areas of spread. While the survey party was in the municipality some 13,700 children were examined.

During the time spent in Colombo, ten mornings were spent at the Hendala Settlement, and clinical demonstrations were conducted. In addition to this, a series of five lectures was given to the medical students at the Colombo Medical College. Recommendations with regard to the Hendala Settlement were also noted. The last part of the report deals with general recommendations regarding the situation in the island which will now be briefly alluded to.

RECOMMENDATION I.

This deals with the necessity for the modification of the present leprosy ordinance, as the system in effect appears to be too rigid. While Leprosy Ordinances are useful they should be looked upon in the same light as any other emergency measure, not to be applied unless it is unavoidable. The result of the enforcement of the Ordinance has been threefold :—

(1) Neural cases have been admitted, or readmitted, who, according to present knowledge, do not need segregation.

(2) The criteria for the discharge of a patient have, generally speaking, not been strict enough.

(3) The granting of home isolation, a provision made to avoid segregation, has resulted in an unsatisfactory state of affairs. In addition to this the formation of a Leprosy Board was suggested, consisting of the Director of Medical Services or his representative, two special leprosy officers, and the medical superintendents of the two settlements. The function of this Board would be to see all cases needing segregation or parole, and to decide with regard to the discharge of patients. It would also decide whether a

given patient needed isolation, treatment alone, or both. Thus every case would be seen by a group of men well versed in the diagnosis of leprosy, and mistakes would be avoided. It was suggested that only in a case where patients refused to go to a settlement, after the advice of the Board, should the Leprosy Ordinance be enforced. It was further stated that probably no closed case needed segregation, the only exception to such a principle would be in the case of children or adolescents who, in spite of treatment, were not improving, for active cases amongst children should always be taken seriously and be put under the best conditions if treatment is to be successful. Further suggestions were made concerning the duties of the medical superintendents of the asylums and concerning the period of treatment and conditions for discharge, and regulations for the following up of cases which were discharged. It was emphasised that in any scheme for the control of leprosy the examination of contacts was most important. When a case is first discovered the contacts should be traced, for it is easier to find them before suspicion is aroused, than after a period of time when the case has been isolated for some years, and all the members of his family live in fear of being isolated. Therefore, as soon as a suspected case has been reported, all possible contacts should at once be traced if the patient has been found to be suffering from leprosy. This applies whether the case is an open or closed one. The necessity for this step was illustrated on more than one occasion, when the source of some very early lesions in school children were traced to an infected member of the household who had never previously been suspected. It was not considered wise to bring pressure to bear on relatives to declare all contacts. Any form of compulsion at this stage defeats its own purpose, and when the public realise it is better for them to be examined, then they will come forward voluntarily for examination. When a previously unknown case is discovered it is better to try and persuade the individual to undergo voluntary isolation than to apply any Ordinance.

The next section of the report deals with the anti-leprosy measures in rural areas and anti-leprosy measures in municipalities. It was suggested that the districts in the Eastern Province, which needed special attention, were those of Kalmunai and Batticaloa, and at the hospitals in both these districts the medical officer in charge should have the necessary drugs available for the treatment of cases outside the settlements. Further, should cases be

found too far away to attend these hospitals, and treatment is needed, this should be made available at the nearest Government dispensary, provided the apothecary (dispenser) had some previous training. Unless large numbers of cases were discovered it was not considered necessary for the Eastern Province to establish a special leprosy centre, as it was thought that it would be better for the general hospitals to treat any cases. Further it was suggested that a complete leprosy prevention unit should be established which would make provision for the following :—

(1) Periodic examination of early cases, of contacts and parole cases.
(2) Further surveys.
(3) Propaganda and training.
(4) Treatment of early active cases.
(5) Isolation of infective cases.

Where there is a Medical Officer of Health, his department might be responsible for the first three items; the hospital would be the natural place for cases to go for treatment, and the settlement for those needing isolation. There should, therefore, be close co-operation between the Health Department, the Medical Department and the Medical Superintendent of the institution.

With regard to anti-leprosy measures in a municipality, conclusions were based on the results of the preliminary survey of Colombo. It was stated that there seemed to be no doubt that a sufficient number of early active cases would be discovered to warrant the organisation of a special leprosy prevention unit. This unit should be in charge of a medical officer with some special training in leprosy. When the Survey Officers have completed a more detailed survey of Colombo, one of their duties will be to organise such a unit, and they should be in charge until it is established. As much of the work of the unit will be connected with school children, it might be thought advisable to place a school medical officer in permanent charge after having special training in leprosy prevention and treatment. At this prevention centre all information concerning leprosy, its prevalence, distribution, etc., etc., will be kept, all contacts, suspicious cases, and paroled cases watched and examined, and early active neural cases will be treated. In addition, instruction courses for nurses, public health workers, school teachers and others, should be instituted, and propaganda measures for the education of the public carefully organised and supervised. There must, however, be a close liaison

between such a centre and the leprosy settlement, so that each is aware of the other's activities. When a case is discharged from Hendala, all details should be forwarded to the leprosy prevention centre.

Until the special leprosy prevention unit was organised, it was suggested that facilities might be made available at the general hospital in Colombo. It was emphasised that with regard to the investigation of cases of leprosy, this as far as possible should be confidential.

RECOMMENDATION II.

This deals with the place of institutions, and shows that ideally, provision should be made for five classes of institutions :—

(*a*) Early infective cases likely to improve under treatment.

(*b*) Late infective cases not likely to improve under treatment.

(*c*) Infective cases among children.

(*d*) Crippled cases who are a charge on the Government.

(*e*) Paying patients.

It was pointed out that on account of the expense it was hardly practical to develop these five types of institutions separately, but it should be possible to organise an institution for the first, third and last type of case, and one for the second and fourth. Further suggestions are made concerning the place the two existing institutions in Colombo would play in such a scheme.

RECOMMENDATION III.

This concerns the place of voluntary isolation in anti-leprosy schemes. There is no doubt that the nearer to a voluntary system any anti-leprosy scheme approaches the better it is. Inasmuch as leprosy is a limited problem in Ceylon it is desirable to have a Leprosy Ordinance for those who will not voluntarily put themselves under isolation. Every case, however, should have the option of being a voluntary patient and should be entitled to certain privileges. It was suggested that if a case either declares himself voluntarily or agrees, when discovered, to go into isolation, he should be considered a voluntary patient. Under the new system suggested this would result in a division of those cases isolated without the need of applying the Ordinance, and those cases segregated

under the Ordinance, the former would be considered voluntary inmates.

In addition to the voluntary institution, it was suggested that a dispensary school might be developed as has been done so successfully by the authorities in Dutch Guiana.

RECOMMENDATION IV.

The question of training and propaganda is considered the need for adequate instruction of all medical students in the treatment, diagnosis and prevention of leprosy is emphasised, and the necessity for the education of the general public and all who sway public opinion is stressed. The lines along which such education should be conducted are laid down.

RECOMMENDATION V.

This is concerned with the work of the Survey Officers, and divides the work under two heads :—(1) To ascertain as far as possible the incidence of leprosy in the island, and (2) to organise anti-leprosy measures in those areas where there is evidence of the spread of the disease.

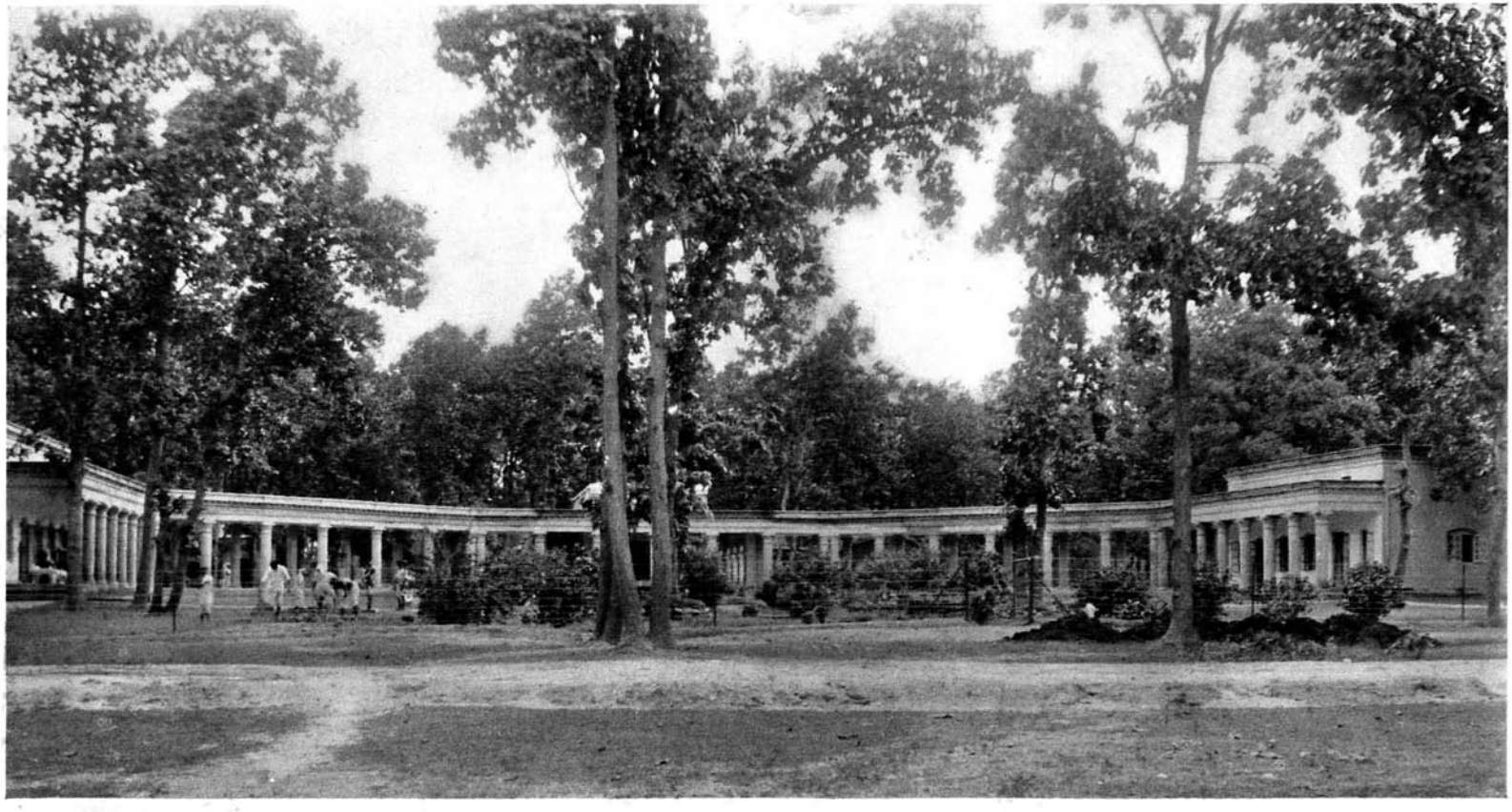
RECOMMENDATION VI.

This deals with the entrance of cases into the country, and notes that there is no doubt that an adequate inspection is made of immigrants from India at the Mandapam Camp. It is, however, stressed that it would be well for medical officers in charge of this camp and others who are dealing with immigrant persons, to have further instruction in the diagnosis of leprosy.

The last section of the report deals with the customary conclusions and acknowledgments, and special thanks are tendered to the Director of Medical and Sanitary Services, whose advice and help was at all times available, and to those officers who assisted in the field and the medical superintendents of the two institutions, without whose help and wholehearted support, the work which was accomplished would have been very difficult.

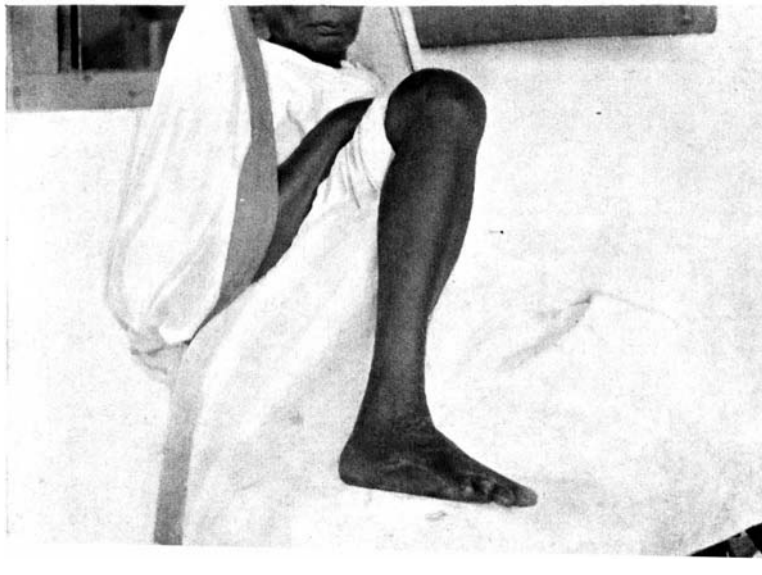
In concluding these articles on the leprosy situation in India and Ceylon, I should like to make acknowledgment to all those who assisted me while I was in India, and especially would I like to put on record the help that was given to me by Mrs. Miller, Consulting Surgeon to the leprosy hospital at Purulia, for her valuable aid and advice.

PURULIA LEPROSY COLONY



View of the Three Hospital Wards and Connecting Passages

Resulting Scar after Removal of Second and Third Metatarsals



The Fine Scar after Removal of Fifth Metatarsal.
(Mrs. Miller's Case).

Reproduced by kind permission of Mrs. Miller

Some Problems of Surgery in a Leprosy Colony.

A. ROY.

THE surgical aspect of the treatment of leprosy has not received much attention hitherto. The reasons for this are firstly, because this aspect of leprosy has practically nothing to do with its curative treatment. In this connection the only thing that has been commonly done is nerve stretching in the earlier neural cases, and this operation is done not necessarily with a view to treating leprosy, but in order that the nerve pain may be reduced and as an attempt to avoid later contractures to fingers and toes.

Secondly, the incentive for taking up surgical work in such cases is not strong, because a surgeon operates in order that he may relieve the patient's suffering and rid him of his complaint. In the case of those suffering from leprosy, surgical operations are often only palliative, and in many cases, such as the amputation of the leg, the patient's incapacity may be greater, not only because he has lost his limb, but the other leg may become worse owing to the greater strain placed on it. Further, in operating on those with crippled hands, the surgeon may prolong the patient's life, but in doing so he may increase his suffering, and one has to consider carefully such cases before operating, lest, as a result of the operation, incapacity may be actually increased. However, in many cases suffering is quite definitely prevented.

Thirdly, the results of operations are not always encouraging because few seem to heal up by first attention, even with the most asceptic care.

My plea for writing this note is mainly to show the difference not only in the results but also in the methods of dealing with the surgical aspect of the treatment. I have also noted that many doctors who have visited our colony mention their own methods of general treatment which are applicable to ordinary cases, but it is hard to convince them that general surgical methods are not always applicable to those suffering from leprosy. I shall now illustrate my remarks by referring to the following operations :—

Amputations.—These are the most common operations here. The incidence of cases which need amputation increases after the winter season.

Minor operations, (toes and fingers).—When there are ulcers on the tips of the toes and fingers a general practitioner may wonder why these tiny ulcers do not heal easily. When I was treating these cases in the general way I found a small percentage of cases did heal up though they took a longer time; but they were almost sure to break out again within a short period. Other cases did not heal up without snipping the tips off, but even some of these cases recurred after a longer period. I next started to disarticulate these bones at the nearest healthy joint. These efforts were more successful. Patients realised that as a result they no longer needed to visit the hospital daily for months together.

Trophic Ulcers.—In these cases I used to incise the tissues along the bone, snip off as far as I could, and at the same time cut off the tendens attached to the bone, pulling them out as far as possible. This method helped the patients, but the results were not permanent. Some returned for treatment after the next winter or even before that. Now we have discarded this method totally and instead dissect out the bone, which, though it appeared at first a barbarous procedure, is to my mind the best method of dealing with these cases. "There is only a tiny ulcer with slight necrosis of bone; what is the necessity of performing such big operations?" This was the complaint made by many of the sufferers, and even by some of our colleagues. But now our experience has shown us, after dealing with no less than 150 cases, the excellent permanent results obtained. We cannot but say "it is the method of choice."

DESCRIPTION OF TECHNIQUE.

Dr. Cochrane had conceived the idea of dissecting out the affected bones some years ago. I saw him trying this method in 1927. But he did not then give it an extensive trial probably for want of proper facilities. This time, owing to the able assistance and help of Mrs. Miller and the hospital staff at Purulia, all the beds in the hospital were filled up with such cases. The technique was as follows :—

Make an incision at the distal end of the necrosed bone on the dorsum of the foot or hand. Deepen the incision until the bone is reached, then extend it along the bone right up to its joint. Endeavour not to expose and damage the bone behind. Then disarticulate the joint carefully and dissect out the necrosed bone. Twisting the joint with lion forceps at the last stage makes the separation of the

bone easier. As far as possible clean up the ragged edges of the wound and snip away dead tissue, packing the wound with gauze soaked in 1–1000 acriflavine. One or two stitches may be inserted at the proximal end of the wound in order to cover the joint if exposed. Dress daily with acriflavine, but if there is sloughing change to eusol twice daily, or more often according to the requirements of the case. Wounds take on an average three weeks to heal up. The following points need emphasising :—

(1) Make a bold, clean incision.
(2) Try not to expose the next bone behind ; if exposed stitch the skin over it to cover.
(3) Deep sutures are of no use.
(4) Never try to do anything on the sole of the foot, or the palm of the hand.
(5) On opening the case the next day the edges may be found necrosed, probably due to repeated incisions in exposing the joint. Simple dressing with eusol will clear up this condition.

The advantages of this method are that the patients are saved daily visits to the hospital for dressing for a long period. They are also saved from the risk of sepsis, which in some cases may necessitate an amputation. Though it is troublesome and expensive in the beginning, it is more economical in the long run.

The disadvantages are that whatever precautions are taken the scalpel is sure to be useless for the next case. This may be avoided by using old scalpels to disarticulate the necrosed bone.

Lately we have improved the above technique to some extent ; on taking out the bone we plug the wound with acriflavine gauze as usual, but stitch the skin above. We have named these stitches " 24 hours' stitches," because we take out the stitches the next day. The object of putting them in is to prevent the wound from gaping too much. The big gap made by the tight plugging takes longer to granulate up.

MAJOR AMPUTATION OF LIMBS.

After amputating the limbs it is never safe to stitch from end to end. The patients have no vitality to absorb the oozing which accumulates beneath the stitches. A drainage tube is too irritating to the tissues. We have therefore found that a piece of fine gauze rolled up with a piece of fine rubber (a portion of torn glove) answers quite well.

Syme's amputation (an amputation at the ankle joint by a heel flap, with removal of malleoli) and Pirogoff's amputation (an amputation at the ankle joints in which the posterior part of the oscalsis is retained and united to the sawn surface of the tibia) are never advisable for cases of leprosy, where all the metatarsals are bad. In these cases amputation of the limb at the lower third is advisable. We tried these methods on two cases where all the metatarsals were necrosed. They still visit the hospital daily for dressing.

Cataracts.—We have not yet been able to find out any new method of operative technique for these, but we are sure that any lack of absolute rest for a fairly long period after the operation undoes the whole effort of operation. Before deciding to operate on cataract in a case of leprosy, it is necessary to make sure that the ultimate result of the operation would not be nullified by secondary infection lurking in the conjunctiva or in the lachrymal sacs and ducts, as in these places, especially in leprotic cases, rich bacterial flora almost always exist. A thorough cleaning of the conjunctiva, and rest to the eye for at least three or four days, should be an essential preliminary to any operative treatment on the eye. Strong antiseptics should never be used for cleaning the eyes, as the conjunctiva and the sclera in cases of leprosy are, in the majority of cases, devitalised already by the involvement of the ophthalmic branch of the fifth nerve, and there is usually superficial anæsthesia of the cornea with resultant loss of the protective influence exerted by the corneal reflex. Involvement of the other nerves supplying the orbital structures, as for example the supra-orbital, the orbital branches of the facial, indirectly influence the vitality of the conjunctiva and the sclera. The dirty nasal cavity in the vicinity of the eye may some time spoil the chance of recovery after operation by ascending the sepsis from the nasal cavity through the nasolachrymal duct.

The occurrence of ectropion in the late neural stages of the disease marks the crowning tragedy of leprosy, as this inevitably leads on to corneal ulcers resulting in leucoma and loss or diminution of vision of varying degrees. Palliative measures usually advocated in similar cases in non-leprotic cases, as for example, wearing a shade, frequent antiseptic washings and smearing of the eyelids at bed time with liquid paraffin, etc., prove unavailing in cases of leprosy, as in the latter there are several other factors that complicate the ectropion. By the time the ectropion is detected in a case

of leprosy there is usually some degree of anæsthesia of the cornea and devitalisation of the conjunctiva and sclera. As a result of loss of corneal reflex there is already some latent infection of the conjunctiva and some injury to the cornea. In these cases palliative measures are worse than useless.

Application of paraffin to the eyelids of these cases has been known to afford a shelter to the secondary organisms which were enabled to multiply in the canthi and in the fornices of the conjunctiva, and produce a purulent exudation.

After a visit from Dr. Gass, of Chandkuri, he demonstrated an operation on lateral tarsorrophy. We continued to perform this operation, and have found since then that great care has to be taken in the selection of cases. A cripple patient cannot be expected to keep his eyes clean after the operation. If the eye is not kept clean, the artificial protection afforded to the bulber conjunctiva and the cornea by the operation will form a pocket in which secondary organisms can multiply vigorously and make the result of operation worse than the original ectropion itself. We have had experience of this lately, and therefore, in crippled cases one should hesitate before attempting a canthorraphy.

Finally, to secure uniformly successful results after operation it is essential to examine the stools for hookworm ova and erradicate them if they exist, otherwise wounds do not heal up quickly owing to the paucity of hœmoglobin.

Acknowledgments are due to Mrs. Miller, Dr. Rao, and to Miss Thornton, for their kind help and guidance, and also to Mr. A. D. Miller for supplying the photos.

Literature.

LEPROSY REVIEW. Vols. I-IV. Vol. V, No. I Issued Quarterly by the Association. Price 2s.

LEPROSY, SUMMARY OF RECENT WORK. Nos. 20-30. Reprints from the Leprosy Sections of the Tropical Diseases Bulletin.

THE SHADOW OF LEPROSY. Annual Report, 1933.

LEPROSY IN INDIA. Vols. II-V. Issued Quarterly by the Indian Council of the Association.

REPORT, 1932. Annual Report of the Indian Council.

Treatment of Hookworm.

M. P. THORNTON.

THE commencement of the campaign against hookworm infection in the Purulia Leper Homes began in 1929, when the responsibility for treatment was handed over to the Sister in charge of the hospital. Previous to this time the method of procedure was for all patients in the homes, including the children, to have one dose of carbon tetrachloride in March or April each year. The late Dr. Landeman was very dissatisfied with this method, as hardly any examinations were made, with the exception of a few severe cases of infection. He had all the inmates of the leper homes before him, house by house, and from these he collected the names of 372 patients who appeared to have severe hookworm infection. Subsequent examination of stools found all positive. These patients were treated a few at a time, and as they became negative others were put on the treatment list. All admissions to hospital were likewise treated, whether their names were on the list or not. (A good maxim for this hospital is to push the hookworm treatment in all septic cases and the troubles will clear up themselves.) These cases, at the rate of 6—12 examinations per day (the microscopical examinations being chiefly undertaken by Solomon Laurenga, the head-compounder) occupied the remaining months of 1929 and all of 1930. During 1931 Miss Krogh made an intensive campaign throughout the entire homes. All inmates were examined and treated where necessary. In 1932 I again took over the work, concentrating on new admissions to the homes, hospital patients, all children in the seven homes and some of the weekly out-patients.

In January, 1933, a systematic house by house examination was again commenced, and at the request of Dr. R. G. Cochrane, statistics were kept. At the beginning of each month a list was sent to hospital of all new cases. These are always put on the treatment list as soon as received. Hospital patients continue to be examined on admission, whether with a previous history of negative stools or not. Drs. Roy and Rao, and Solomon Laurenga, have done the microscopical work.

I did not manage to get all the cases examined last year but percentages to date show :—

Patients admitted before January 1st, 1933 : 37.19% H.W. ova positive.

Patients admitted after January 1st, 1933: 89.89% H.W. ova positive.

Patients admitted after January 1st, 1933, for hospital treatment only: 70.83% H.W. ova positive.

(Some of these latter cases were given treatment before examination.)

626 patients were examined in 1933. Of these, 318 were positive. The following is a list of the number of treatments required to produce negative stools.

Name	1st time discovered H.W. Pos.	No. of doses required	For 1st time Neg. Result	Again Pos.	Treated	Subsequent examinations
Mukta ...	12/27 } Only 1/28 } partially treated	3	7/29 Exam.? Faulty.	'30, '31 Treated till clear 13 times	2	/6/32, /5/33, /1/34
Absalom ...	/3/30	1	/3/30	—	—	/8/33, /1/34
Kusum ...	/10/32	5	/4/33	—	—	/1/34
Sunimia ...	/11/30	(?)	/1/30	—	—	/6/31, /1/34
Magdolini ...	/6/30	(?)	/8/30	/6/31	1	/1/34
Matongini	/5/30	(?)	/11/30	—	—	/5/31, /1/34
Raphael ...	/5/30	1	/5/30	—	—	/6/31, /1/33, /1/34
XDulal ...	/2/28	(?)	/4/29	/7/31	2	/9/33, /1/34
Haradon ...	/6/30	2	/11/30	/7/31	1	/6/33, /1/34
Biswapoti	/1/29	2	/6/29	—	—	/8/31, /1/34
Sarbananda	/5/29	3	/7/29	—	—	/11/29, /1/31, /8/31, /8/33, /1/34
Peter ...	/8/30	4	/11/30	—	—	/7/31, /6/33, /1/34
Khonka ...	/7/30	(?)	/11/30	—	—	/8/31, /9/32, /7/33, /1/34
Baroda ...	/11/30	(?)	/11/30	—	—	/5/31, /1/33
Raya ...	/3/32	2	/7/32	—	—	/1/34
Krishnadas	/7/30	2	/9/30	—	—	/7/31, /1/34
Horipad ...	/7/30	5	/11/30	—	—	/7/31, /9/33, /1/34
Simson ...	/11/29	(?)	/6/30	/7/31	1	/5/33, /1/34
Sichoria ...	/4/29	10	/7/30	/1/34	1	/7/31, /7/32, 16/1/34
Kironbala	1927	14	'30	—	—	'31, '32, '33, /1/34
Daud ...	10/32	8	'33	—	—	/1/34

H.W. TREATMENTS.—Carbon Tetrachloride m. 40.

Old Patients.	*Out-patients and New Admissions.*
Cleared 88 with 1 treatment	Cleared 30 with 1 treatment
,, 37 ,, 2 ,,	,, 25 ,, 2 ,,
,, 16 ,, 3 ,,	,, 14 ,, 3 ,,
,, 5 ,, 4 ,,	,, 5 ,, 4 ,,
,, 4 ,, 5 ,,	,, 2 ,, 6 ,,
,, 2 ,, 7 ,,	,, 3 ,, 7 ,,
,, 1 ,, 8 ,,	,, 1 ,, 12 ,,
,, 1 ,, 9 ,,	

41 patients under treatment at present time.

The method of treatment is carbon tetrachloride, with three exceptions, when beta napthol grs. 40 was administered. The usual dose given of C.T. is m. 40. In severe

cases of weakness m. 30 was given as the initial dose. The carbon tetrachloride is mixed with an equal quantity of milk or rice-water and administered to the patient in this way; children according to age, a child of twelve taking m. 20 if normal size for age. I find the patients are less likely to vomit afterwards if the treatment is given in the morning after fasting all night. C.T. is followed one hour later by an ordinary dose of magnesium sulphate, except in the old or weak, when a smaller dose suffices. After an action of the bowels all patients are instructed to take one pao of milk (this is supplied to each one from hospital and is an encouragement to come along for treatment). I find the milk prevents any toxic effects from arising. One patient was troubled with vomiting for 24 hours. Subsequent information elicited the fact that he had not taken his milk as prescribed, but kept it for the evening. Mid-day he had his rice as usual. A similar patient in hospital had the same trouble for six hours. His milk was found in his locker. Both patients soon recovered when kept on milk for 24 hours.

An examination is made two weeks after treatment, positive cases continuing treatment and examinations in this manner until a negative stool is found. Cases requiring four treatments and over are examined again three months after a stool has been found negative. In two cases only have ova been found and this has cleared up entirely in one more treatment. Several persistent cases have had a long period free from infection, as particulars given in table will show. One casualty occurred, but whether due entirely to treatment by C.T. is uncertain.

A fairly new admission case had taken his treatment and returned to his house. Diarrhœa was reported the following day and unfortunately the man was not admitted to hospital, neither did I hear of his trouble until he collapsed and died before help was available. He had appeared in fairly good condition except for some anæmia.

Dr. R. G. Cochrane, during his physical examination of female patients in 1933, discovered a number of slight heart disorders. Practically all of these women had a history of previous hookworm infection and in some cases examination proved a present history.

I have found it worth while concentrating on a group of patients at a time until they are negative to hookworm ova, rather than giving treatment all round and then beginning all over again. Anæmic and new admissions are always put in the current treatment group. 30—60 patients at a

time are under treatment, additions being made as others pass on to the "negative" group. Treatment is on the whole much appreciated and is shown by the concern some patients show if they have not been called down for treatment after having delivered their specimen at the dispensary. Only this week I have two requests to give more treatment. One was from an ex-sepoy, who begged to have treatment once again and not to trouble to see whether it was needed or not. He said he felt so much better after the last course, that he wished to take another. Some little time ago we had difficulty in getting an old man back to his house because he was demanding treatment ! He said he had never felt so well in his life as he did the weeks after taking his two treatments. He was given Mist. Iron Tonic to quieten him. This latter is given for one month to all patients requiring three treatments or over. Some of the others have it too, if they appear anæmic.

A Comparative Study of the Relative Efficacy of "Special Esters" and the Ordinary Ethyl Esters of Hydnocarpus Wightiana.

G. R. RAO.

MESSRS. Burroughs Welcome & Co., Ltd., requested Dr. R. G. Cochrane, the Medical Secretary of the British Empire Leprosy Relief Association, to try the "Special Esters" prepared by them, against the ordinary Ethyl Esters, from Hydnocarpus Wightiana, used in the treatment of leprosy; and ascertain if the Special Esters were in any way better than the ordinary Ethyl Esters. For this purpose, a liberal supply of both the special and the ordinary esters prepared by them, was sent to Dr. R. G. Cochrane. Both the Esters were iodised with iodine.

Eleven cases of leprosy, mostly out-patients attending the out-patient clinic of the Purulia Leprosy Colony, were selected for this experimental study. Of these eleven cases four were very irregular in attendance and this experiment was not continued. The remaining seven cases were fairly regular and had fairly symmetrical, bacteriologically posi-

tive and leprotic infiltrated type of lesions on both sides of the body. The special esters were injected into the lesions on the right side of the body intradermally, and the ordinary esters into the left side lesions, also intradermally, once a week. The resulting local and general reactions as well as improvements (clinical), if any, were noted carefully week by week. The table appended herewith gives all the relevant particulars about the cases studied. The experiment was carried on for from six to eight months.

CONCLUSIONS.—The special esters were found to be too irritating (producing keloids in some cases), and could not be used for any length of time; and the improvement in the injected lesions was not commensurate with the irritation produced. The special esters were found to be therapeutically inferior to the ordinary Ethyl Esters.

TABLE.

Serial Nos.	Name	Type	No. of injections	Period of Treatment	Range of dosage in c.c.m.	Results	Remarks
1	Karuna Kansari	C_2	20	6½ mnths	Spl. ½–2½ ccm Ord. ½–3 ccm	Spl. too irritating	Improvem't more marked on the left side
2	Soma Muchi	C_2	18	7 mnths	Spl. ½–2 ccm Ord. ½–2 ccm	do.	do.
3	Parama Rajwar	C_2–N_1	23	7½ mnths	Spl. ½–2½ ccm Ord. ½–2½ ccm	do.	do.
4	Narayan Singh	C_3–N_1	23	6½ mnths	Spl. ½–2½ ccm Ord. ½–2½ ccm	do.	do.
5	Narayan Bouri	C_3–N_2	21	7½ mnths	Spl. ½–2½ ccm Ord. ½–2½ ccm	do.	do.
6	Goju Mahato	C_3–N_2	18	7½ mnths	Spl. 1–2 ccm Ord. 1–2 ccm	do.	do.
7	Ballu Ram	C_2–N_2	23	7 mnths	Spl. 1½–3 ccm Ord. 1½–3½ ccm	do.	do.

Spl. — Special Esters of Hydnocarpus Wightiana.
Ord.— Ordinary Ethyl Esters of Hydnocarpus Wightiana.

The Leprolin Test.

E. MUIR.

(*Reprinted from "Leprosy in India," Oct.,* 1933.)

INTRODUCTORY.

IT is sought in this paper to review briefly the literature on the subject, to describe the technique, and to describe certain experiments which the writer has carried out by means of the test. The main object of the paper is, however, to suggest lines along which the leprolin test may be used with a view to elucidating certain problems connected with the resistance to leprosy, the method of transmission, and the factors determining the type of leprosy. A list of these suggestions will be found at the end of the paper. There are many leprosy institutions and clinics in India which furnish excellent clinical material for investigation along the lines we have indicated. It is hoped that this paper will be of use to the doctors in charge of these institutions who are interested in these problems.

WORK DONE BY OTHERS.

The leprolin test has been used by Mitsuda in Japan for many years. Hayashi (1933) has recently developed the use of this test. An article by him was abstracted in the July, 1933, number of this journal, so we have not detailed his methods further here.

Mariani (1924) made a suspension from a leprous nodule and inoculated it intradermally in 10 cases of leprosy, 8 of which were of the nodular and 2 of the nerve type. In the former there were no signs except a little erythema and infiltration which disappeared by the 8—12th day. In the nerve cases after the 10th day there was infiltration and swelling locally, followed by the formation of a central vesicle. On the 20th it reached the size of an orange pip and was surrounded by a red dense border. It cleared up with some loss of tissue by the 60th day. There was no fever or constitutional disturbance.

Bargehr (1926) originally recommended using a suspension similar to Mitsuda's ; but instead of injecting he applied it by sacrificing the skin and rubbing in the suspension. In our own experience and that of others, this method of carrying out the test is not as satisfactory as that of intradermal injection. Bargehr tested 162 patients with the following results : Of 82 showing bacilli, all gave a negative test ; of 80 showing no bacilli (a large number of whom showed definite signs of leprosy), 45 gave negative results, and 35

gave positive results; the 35 giving positive reactions either showed no signs of active leprosy (though they had been in contact with lepers) or were lepers with mutilated fingers and toes apparently recovered from the disease. Bargehr does not mention the type of case (common in India, Japan, and other countries) with red, swollen, annular lesions, which invariably gives a positive reaction. This may be due to absence of this type of case from the leprosy institution in which he worked.

de Langen (1929) prepared a dried powder prepared from nodules and stored in vacuum tubes. From this he prepared his leprolin. He concluded that the reaction is specific and that it may be of use in the diagnosis of early cases. He used it for distinguishing between active and inactive cases, as the former gave a negative and the latter a positive result. He considered that a positive reaction in a person who had frequently been in contact with lepers justifies the opinion that he has acquired resistance against the infection. He also suggested that the test may be of use in taking prophylactic measures.

Chiyuto tried out the leprolin test in three groups: (1) 169 children of leprous parents, their ages varying from under 1 to over 16 years. There were signs suggestive of leprosy in 168 of these, but bacteriological examinations were negative. Under 2 years all were negative; over 16 only 5.5% were negative. Between 2 and 16 results varied. (2) 97 healthy children. Those under 1 year all were negative. Those from 3 to 14 years were all positive, as compared with only 85.5% positive in the children of lepers of the same age. (3) 10 healthy adults without history of leprosy. Of these all were positive, though one was only slightly positive.

A positive reaction is indicated by an inflamed, button-like induration at the point of leprolin inoculation, which does not appear when the result is negative. This is explained below in detail.

It must be clearly understood that the specific nature of the test is shown not by the positive results, but by the negative results obtained in leprous cases of the cutaneous type. Suspensions of other acid-fast bacilli, such as Koch's bacillus, Stefansky's bacillus (M. Lep. mur.), etc., give positive results in non-lepers and also in leprous patients both of the neural and cutaneous type. Hansen's leprolin gives positive results, varying in degree, in many non-lepers, more strongly positive results in neural cases of leprosy, and negative results in skin cases. The leprolin

test is therefore not entirely dependent on an allergic condition as is the tuberculin test in tuberculosis, though in cases of leprosy the reaction may possibly be increased or diminished by the action of specific immunity or of allergy. The objection may be raised that positive results in non-lepers are due to their having unknowingly been subjected to small infections, which have produced some specific immunity. To prove or disprove the validity of this objection, we are arranging to have the test tried out in a country where leprosy is non-endemic.

With non-leprous subjects, negative results are more common in children, especially very young children, than in adults.

The strongest reactions with the leprolin test are in patients with indurated, raised, erythematous lesions of the nerve type, *i.e.*, the tuberculoid lesion of Klingmüller (1900, 1930) and others, which is very common in Japan and N. India, but less familiar in some other endemic countries. Clinically the indurated nodule produced by the intradermal injection of Hansen's bacillus suspension resembles a small lesion of this type (see Figs. 1 to 6). Histologically there is a difference. In the former, if we examine it a few days after inoculation, we find an extensive hyaline area at the centre, which may or may not become necrotic, and round this there is a dense cellular infiltration, in which it is difficult or impossible to find bacilli. In the natural lesion the granuloma is arranged in a cord-like form round the vessels and nerves, and instead of the large hyaline area there are giant cells, though occasionally small hyaline areas are found. This difference is accounted for by the trauma caused by the needle and the massive number of bacilli suddenly introduced by inoculation.

TECHNIQUE.

Preparation of Leprolin.—We have adopted the following technique in preparing leproma suspension for the leprolin test. Many cases of the C_3 type have thickened pendulous ear lobules which have a very high content of lepra bacilli. These patients are generally eager to have their ears trimmed. This is done as follows: After sterilising the skin of the ear lobe with tinct. iodi, a special curved clamp is applied, leaving exposed on its conclave margin the superfluous tissue. This tissue is removed with a sharp knife and placed in a Petri dish. Pure carbolic is applied to the cut surface and the clamp removed. Several pieces of tissue are removed in a similar manner from other

patients. These are boiled in water for 45 minutes and then cut up into small pieces, which are dried for a few hours under a fan and thereafter in a vacuum dessicator over pure sulphuric acid. The dried material is ground up to a fine powder in a glass mortar and stored in a dessicator.

In preparing the suspension, 0.4 gramme of the dry powder is ground up with about 10 c.c. of saline ; the fluid suspension is pipetted off ; the solid residue in the mortar is again ground up with saline, and the fluid suspension pipetted off and added to the rest of the suspension, this process being repeated three or four times. The whole suspension is then shaken up in a large test tube and allowed to sediment for 10 minutes, after which the fluid is again pipetted off, the sediment being discarded. Saline is added to make 100 c.c. along with 0.5% carbolic. The suspension is then made up in 1 c.c. ampoules which are sealed and heated at 120 deg. C. for half-an-hour. This forms Hansen's (H) leprolin.

The control leprolin is made by the same method, the spleen and liver of a rat which had been inoculated intra-abdominally with rat leprosy five or six months previously, being used in place of the lepromatous skin. This forms the Stefansky (S) leprolin.

It is difficult to understand leprolin accurately, as in neither of the organisms used is an *in vitro* culture yet available. For practical purposes, however, the above technique is sufficiently accurate. This is shown by making a series of intradermal tests with full strength standard leprolin and dilutions 1 in 2, 1 in 4, 1 in 8. While the stronger suspensions give a somewhat stronger reaction, the difference in the reaction is not in proportion to the difference in dilution, 1 in 8 giving + where the full strength gives ++. For the sake of uniformity, however, we keep a standard smear of each suspension, which has been prepared by spreading out a standard loopful over a given area of microscopic slide. When fresh leprolin is prepared, a similar loopful of the suspension is spread over an equal area of slide and the concentration of bacilli compared. No attempt at counting the bacilli is made, but it is possible to tell whether the numbers are approximately equal. By making several such examinations before diluting the suspension, it is possible to adjust the strength by adding more or less saline.

It is important in preparing the powder for leprolin to make a large amount at one time, so as to ensure, as far as possible, uniformity of results.

The usual dose used for inoculation is 0.2 c.c. Care should be taken that it is injected into and not under the skin.

Reading the Results.—In doing this it must be remembered that even in cutaneous cases there is slight serious effusion due to local irritation, which lasts a few days. The actual results should be read off at weekly intervals for six weeks after inoculation. Four criteria may be used : (*a*) The size of the red flush round the point of inoculation ; (*b*) the feeling of a raised area on passing the finger over the infiltrated spot ; (*c*) the button-like feeling of induration on picking up the affected skin between the finger and thumb ; (*d*) desquamation, vesication, and pustulation in the more severe reactions.

The degree of reaction is indicated as follows :—

− (negative) with no reaction showing.
± (doubtful) slightly raised skin felt on passing the finger over the area, slight erythema noticeable in light coloured skins.
\+ (one plus) definitely raised skin, erythema and induration to the extent of 5 mm. diameter.
++ (two plus) the same as the last with induration up to 10 mm. diameter.
+++ (three plus) as the last with pustulation at the centre.

Those who carry out the test in all types of cases will soon learn how to divide their results into the five groups. Some idea can also be gained from the photographs, Figs. 1 to 6, which have been enlarged to life size. The reaction frequently is definite by the 7th day, though it may be delayed till the 21st day. Thereafter it takes 1 or 2 weeks to reach its maximum.

The reactions to Hansen's and to Stefansky's leprolin are similar in type, though they may vary in degree.

EXPERIMENTS.

Six experiments with the leprolin test are recorded in this paper. The first of these was carried out with the single leprolin test, using H leprolin alone. In experiments 2 to 4, the double leprolin test was used with both H and S leprolin. Unfortunately, the former of these had a much lower bacillary content than the latter, and thus in cases in which the disturbing specific factors connected with leprous infection were absent (*i.e.*, in non-lepers), it tended to give a weaker reaction.

The sixth experiment shows the effect of injections of H. leprolin filtrates and of a leprolin prepared from Kedrowsky's bacillus.

Experiment (1).—The leprolin test was carried out in 84 children of leprous parents in the Purulia Leper Home. These are divided into 5 series : (*a*) Inmates of a home for the

healthy girls of lepers. The girls themselves did not show any signs of leprosy, though some of them had in the past shown such signs. (*b*) Infants in a nursery connected with the last-mentioned home. These were free from signs of leprosy. (*c*) Inmates of a boys' home similar to that of the girls. (*d*) Girls under observation, *i.e.*, showing slight signs of leprosy, though negative to bacteriological examination. (*e*) Boys under observation, similar to the last.

This experiment was carried out with the single leprolin test, only H leprolin being used.

The results are shown in Table I.

TABLE I.

	+++	++	+	±	—	Total	Average age in years
(*a*) Healthy girls	15 ; 42.8%	1 ; 2.8%	12 ; 34.2%	5 ; 14.2%	2 ; 5.6%	35	13.4
(*b*) Children in nursery	0 ; 0%	1 ; 12.5%	0 ; 0%	1 ; 12.5%	6 ; 75%	8	3.5
(*c*) Healthy boys	3 ; 15%	3 ; 15%	5 ; 25%	7 ; 35%	2 ; 10%	20	11.2
(*d*) Observation girls	0 ; 0%	2 ; 13.3%	5 ; 33.3%	1 ; 6.6%	7 ; 46.6%	15	12.2
(*e*) Observation boys	1 ; 66.6%	1 ; 16.6%	2 ; 33.3%	0 ; 0%	2 ; 33.3%	6	11.1
TOTAL	19	8	24	14	19	84	

In series (*a*), the average age of which was 13.4 years, there were only two negatives, while 42.8 per cent. gave very strong positives. These reactions are seen to be stronger than are generally found in cases which have not been in contact with leprosy (compare Tables II and III), and may probably be taken as an indication of increased resistance to leprosy.

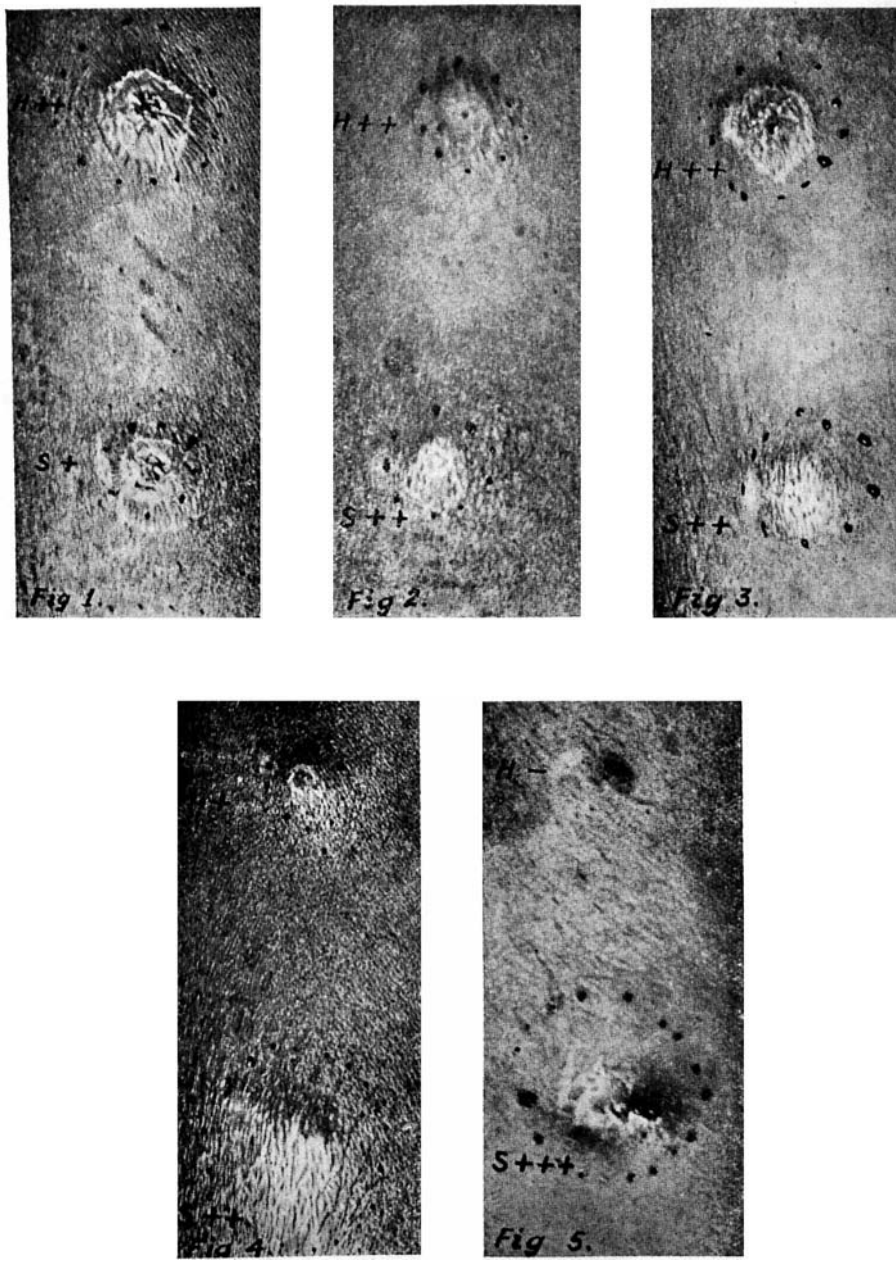
In series (*b*), *i.e.*, the nursery children, 6 out of 8 were negative. The other two were a child of three years of age with ++, and a child of six years, with +.

Series (*c*) shows a slightly higher number of negatives, but this may be accounted for by the lower average age.

The last two series (*d*) and (*e*) show a very different condition, having respectively 46.6 and 33.3 per cent. of negatives. Apparently they contain the less resistant children.

This experiment seems to indicate that the leprolin test may be of value in making a prognosis in the case of leprous contacts, whether they show slight signs of leprosy or not. These results are similar to those in Chiyuto's first group.

If the negative leprolin test in infants indicates low resistance to leprosy, it helps to explain the generally



FIGS. 1–5. H = test made with Hansen's leprolin, S = test made with Stefansky's leprolin. The dotted lines indicate the limit of induration as felt by picking up the skin between finger and thumb.

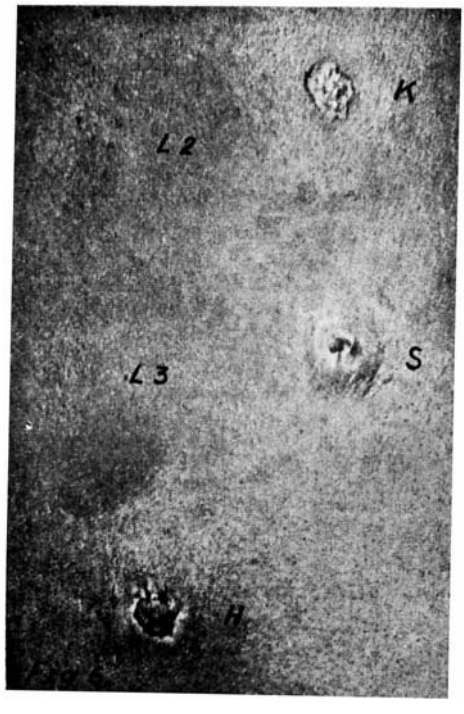


FIG. 6. Shows the leprolin reaction.

K = test with leprolin prepared with Kedrowsky's culture.
S = " " " " Stefansky's "
H = " " " " Hansen's "
L_2 = " " filtrate from suspension of Hansen's bacillus filtered through an L_2 Chamberland candle.
L_1 = " " filtrate from suspension of Hansen's bacillus filtered through an L_3 candle.

acknowledged greater frequency of infection in children than adults. We have discussed below the possible connection between this and the types of disease.

Experiment (2).—Twenty-nine children, average age 3.4 years, at a children's clinic in Calcutta were inoculated, the double test with H and S leprolins being used. The results were as follow :—

TABLE II

Result	*H leprolin*	*S leprolin*
−	15	5
±	7	10
+	5	7
++	2	4
+++	0	3

Among the 21 children of three years old and under there were 15 negative to H leprolin, *i.e.*, 76.2 per cent. Of the 8 who were over three years none were negative to H leprolin. Of the 5 giving negative results to S leprolin 4 were under one year and 1 was 18 months of age. It was noticed, however, that 3 children gave unusually high results, viz :—

No. 9, age 3, H leprolin +, S leprolin +++;
,, 18, ,, 3, ,, ,, ++, ,, ,, +++;
,, 19, ,, 1, ,, ,, ++, ,, ,, +++.

On enquiry it was found that numbers 9 and 19 were sisters, and on examining their relations, a single anæsthetic macule, diagnostic of leprosy, was found on the body of their father. Careful enquiry, however, failed to reveal any other sign of leprosy among relations or other contacts. It should be mentioned that those attending this children's clinic are drawn from the homes of coolies working in a large industrial concern. A careful survey of the labour staff of this factory two years previously showed 0.75 per cent. of leprosy.

It was noticed that almost without exception the result of H leprolin bore a definite proportion to that of S leprolin, the former being one point lower than the latter except when both were negative. This is accounted for by the fact that the former contained fewer bacilli than the latter. Thus the two children who gave ++ with H leprolin gave +++ with S leprolin, the other child giving +++ with S leprolin (the sister of one of the latter) was an exception, and gave only + with H leprolin.

This experiment suggests that reaction to Hansen's bacilli, when it occurs in non-lepers, is generally not due to previous contact with human leprosy, any more than a positive reaction to Stefansky's bacillus is due to previous contact with rat leprosy, but is of the nature of a non-specific reaction to acid-fast bacilli. Conversely, the

lowered or absent reaction to Hansen's bacillus in very young children is of the same nature as the lowered or absent reaction to rat leprosy organisms in such children.

Experiment (3).—We found the same relationship between H leprolin and S leprolin in six older patients who were sent to our leprosy clinic with a mistaken diagnosis of leprosy. The following table gives the particulars :—

TABLE III

	Name	*Age*	*Disease*	*H leprolin*	*S leprolin*
1.	Surju	45	nil	+	++
2.	C.N.	11	Lichen	−	+
3.	A.M.	30	,,	++	+++
4.	A.D.	35	Syphilis	+	++
5.	Akhay	32	,,	+	++
6.	Bishnu	28	,,	+	++

From this, as well as from the previous experiment, it is seen that the degree of reaction to both H and S leprolin varies in strength in non-leprous individuals.

As is mentioned above, the S leprolin had a higher bacillary content than the H leprolin, and therefore gave a stronger reaction ; but there is a definite relation between the reactions to the two types of bacilli, a stronger or weaker reaction with the one being linked respectively with a stronger or weaker reaction with the other.

Experiment (4).—In this experiment the double leprolin test was carried out in three cases of neural and two cases of cutaneous leprosy. The readings recorded week by week are given in Table IV.

TABLE IV

No.	Name	Age	Type	H Leprolin Reading in days after injection				S Leprolin Reading in days after				
				7	14	21	28	7	14	21	28	
1	S.R.	36	N_1	−	+	+	++	+	+	+	+	(See Fig. 1)
2	R.M.	32	N_1	+	+	+	++	+	+	+	++	(See Fig. 2)
3	D.S.	21	N_1	±	+	++	++	+	++	++	++	(See Fig. 3)
4	M.K.	32	C_1	±	+	+		+	++	++		(See Fig. 4)
5	K.U.	34	C_2	±	−	−	−	±	++	++	+++	(See Fig. 5)

We see here that in neural and cutaneous leprosy the relative degree of reaction given with H and S leprolin is different from the relative degree of reaction given in non-lepers, as shown in Tables II and III.

In case 1 (see Fig. 1) the H reaction is stronger than the S, though the former took a longer time than the latter to develop its full strength. In cases 2 and 3 (see Figs. 2 and 3)

they are equal. In case 4 (see Fig. 4), one of the slight cutaneous leprosy, S is stronger than H, as it is in non-lepers. In case 5, a C_2 case, in spite of a +++ reaction with S leprolin, the H leprolin gave a negative result.

Thus, by carrying out a double test with H and S suspensions, we have :—

(*a*) in neural cases a relatively strong H leprolin reaction,
(*b*) in cutaneous cases a relatively weak or negative H leprolin reaction,
(*c*) in non-lepers an intermediate place, the two reactions being approximately equal, if the bacillary content of the suspensions is the same.

The weekly readings show that the H leprolin reaction came on more slowly than the S leprolin reaction. Thus the former was at first weaker than the latter, while in the fourth reading it had become stronger. This is found in most neural cases of leprosy, but not in non-lepers.

This would seem to show that, while in non-lepers the positive results with both suspensions indicate a non-specific reaction due to natural immunity, in neural cases there is in addition to this an element of acquired immunity or allergy which supplements the natural reaction to H leprolin and makes it stronger. This factor, however, takes longer to act than the non-specific reaction. Hence the delay of increased reaction with H leprolin in these cases. From this we may argue that there is in cutaneous cases an analogous force acting in the opposite direction, which removes or cancels out the natural reacting power.

Experiment (5).—In this experiment the double leprolin test was carried out in 120 cases of all types of leprosy at the Gobra Hospital and the Calcutta School of Tropical Medicine leprosy clinic. The results with H leprolin, classified under the subtype of case and strength of reaction, are shown in Table V.

TABLE V

Subtype	Maximum reading of test					Total
	+++	++	+	±	−	
N_1 ...	11	14	7	3	1	36
N_2 ...	8	11	12	0	0	31
N_3 ...	1	0	0	1	0	2
C_1 ...	0	0	4	4	8	16
C_2 ...	0	0	2	1	23	26
C_3 ...	0	1	0	0	8	9
TOTAL ...	20	26	25	9	40	120

There are 86.2 per cent. of negatives and doubtfuls in the cutaneous cases, but only 7.2 per cent. in the neural cases. There is only one completely negative among the neural cases, and this case when re-inoculated with a slightly stronger leprolin gave a $\pm$ result. Notice that in this case the reaction to leprolin was only $+$.

While advanced cutaneous cases almost always give a negative result with H leprolin, it will be noticed that one C_3 case gave a positive. This nodular case had been given a prolonged course of intravenous injections of 1 per cent. mercurochrome. This, after the first few injections, improved the patient's condition, but later it caused necrosis, liquefaction, and bursting of cutaneous and subcutaneous nodules producing lesions similar to those found in very strong reactions to leprolin. In spite of this the general condition of the patient remained good. It was then found that H leprolin produced a $++$ reaction. Unfortunately this test was not carried out before the course of mercurochrome. The above would seem to indicate that this line of treatment had increased the patient's resistance to the disease.

The other cutaneous cases giving positive H leprolin tests were chiefly patients in excellent health making satisfactory progress towards recovery.

In some other cases, which were at first supposed to be of the neural type and in which the routine bacteriological examination had been negative, the H leprolin test was negative; but on repeated, very careful bacteriological examinations, lepra bacilli were found in the skin and nasal mucosa, showing them to be actually cutaneous cases. This shows the usefulness of the test in classifying cases.

Experiment (6).—A quantity of H leprolin was divided into three portions, *a*, *b* and *c*; *a* was filtered through a Seitz filter, *b* through a Chamberland L_2 filter, and *c* through an L_3 filter. Eight patients suffering from different types of leprosy were each inoculated with 0.2 c.c. of each of these filtrates, and also at the same time with H leprolin, S leprolin, and a leprolin prepared from Kedrowsky's so-called culture of Hansen's bacillus. None of the cases reacted to any of the filtrates; all of them, both neural and cutaneous types, reacted strongly to both S leprolin and Kedrowsky's suspension; the neural cases reacted to H leprolin, but the cutaneous cases did not (see Fig. 6).

This experiment confirms Hayashi's findings, and shows that the leprolin is not caused by any filtrable element in

the suspension. It also seems to prove that Kedrowsky's so-called culture is not actually a culture of M. lepræ, and that a culture of non-pathogenic acid-fast bacillus (which we believe this culture to be) gives a positive leprolin reaction similar to that produced by Stefansky's bacillus.

DISCUSSION AND CONCLUSIONS.

We have tabulated and explained six series of experiments with the leprolin test and tried to indicate the nature of the test. We also suggest certain lines along which it may be usefully employed. These may be summarised as follows :—

1. Acid-fast bacilli, when injected in suspension intradermally in healthy human subjects, tend to produce at the site of injection a reaction indicated by a raised, red, indurated swelling, from 5—20 mm. in diameter, sometimes followed by vesication, pustulation, and loss of tissue, but without noticeable general constitutional disturbance. This is generally true of both pathogenic and non-pathogenic organisms. It applies also to suspensions of leproma taken from lepers, and to suspensions of tissue of rats suffering from rat leprosy, if these contain large numbers of acid-fast bacilli.

2. Experiments 2 and 3 seem to indicate that in those who have not been infected with leprosy, the degree of reaction to Hansen's and to Stefansky's bacilli is approximately the same, the one or the other being greater according to the number of bacilli inoculated. The degree of reaction is not, however, in exact proportion to the number of bacilli, a dilution of 1 in 8 giving a reaction of about half the strength given by an undiluted suspension.

3. In very young children the reactions both with Hansen's and Stefansky's leprolins are as a rule either negative or very much less than those observed in adults. If this indicates weak resistance to leprosy, it will help to explain the frequency of leprous infections in early childhood compared with those in adult life.

4. In cases of nerve leprosy with few bacilli, especially in those of the macular type, the reaction to Hansen's leprolin is increased, but that to Stefansky's leprolin remains the same. The increased reacting power is, however, delayed in showing itself.

5. In cases of cutaneous leprosy with numerous bacilli, the reaction to Hansen's leprolin is diminished or absent, but that to Stefansky's leprolin is apparently not diminished.

6. This relative increase and diminution of reaction to Hansen's leprolin seems to indicate the presence of a specific factor connected with immunity or allergy.

It is generally acknowledged that neural leprosy, especially of the macular type, is associated with a higher degree of resistance to the disease than cutaneous leprosy, the lesion of the former showing few or no bacilli and those of the latter many. For this reason the strong leprolin reaction in neural leprosy may be taken to indicate comparatively strong resistance to the disease.

7. We cannot agree with those who consider that a positive test, carried out with H leprolin alone, is, in the case of non-lepers, an indication of a previous infection with leprosy. Apparently in non-contacts the reaction may be present or absent, and, when present, may vary in strength to a considerable degree. Using the double leprolin test, however, with two leprolins of approximately equal bacillary content, a reaction with H leprolin stronger than that with S leprolin justifies a suspicion of immunization through previous infection with leprosy in the case of non-lepers.

8. A strong positive leprolin reaction may be taken as an indication for a favourable prognosis, as it indicates resistance to the infecting organism. This would seem to indicate that any drug or line of treatment which changes a negative reaction with H leprolin into a positive, or strengthens the degree of reaction, may be looked upon as of therapeutic value in leprosy.

9. Experiment 6 suggests that the leprolin test may be used to show whether or not a culture obtained from leprotic tissue is a true culture of M. lepræ.

SUGGESTIONS FOR FURTHER INVESTIGATIONS.

1. Improvement in preparation of leprolin. It may be argued from the statements made in paragraphs 4 and 7 of the *Discussion* that a dilution of H leprolin, too weak to give a reaction in a non-contact, should react positively in a case of neural (N_1 or N_2) leprosy, the signs beginning to appear later than with a stronger suspension. S leprolin of equal bacillary content would, however, fail to give a reaction. Such a modification of the leprolin test would require delicate uniform standardisation. If recent claims to have cultured M. lepræ are confirmed, it may be possible to obtain more uniformly standardised leprolin prepared from such a culture.

2. Acid-fast bacilli, supposed to be M. lepræ, have been found by various workers in newly-born infants. It is generally agreed that children separated from their leprous mothers at birth and kept free from leprous infection thereafter, seldom, if ever, develop leprosy. If young infants have low resistance to leprosy, as is indicated by experiments 1 and 2, why does the pre-natal infection not develop into active leprosy in children who have been protected from post-natal infection? Is it possible that immediately after birth there is, as in certain other diseases, a short period of high resistance, followed by a longer period of low resistance? This is a matter for careful investigation.

3. Experiments 2 and 3 seem to show that the degree of reaction to Hansen's bacilli, and therefore presumably resistance to leprosy, varies in non-contacts. What is the reason for this? Is this reacting power hereditary; is it connected with families, tribes or races; is there a sex variance; is it raised or lowered by the general health of the patient; is it changed by disease, diet or habits?

4. Are those who have naturally an absent or weak leprolin reaction before contact with leprosy more liable to develop leprosy after infection than those who give a strong leprolin reaction previous to infection?

5. Our experiments seem to show that in non-contacts equal quantities of Hansen's and Stefansky's bacilli produce approximately equal reactions. We have shown that in cases of neural leprosy there is an increased reaction with H leprolin. Our experiments show that a stronger reaction to Hansen's bacilli than to an equal number of Stefansky's bacilli is characteristic of neural leprosy and also probably of increased resistance to leprosy. Are we justified in assuming, however, that those non-contacts who give a strong reaction to S leprolin (and also therefore to H leprolin) are more resistant to human leprosy than those who give a weak reaction or none at all? Also, conversely, are we justified in assuming (as we have been inclined to do in this paper) that very young children with weak or negative reactions to both forms of leprolin have a weak resistance to leprosy?

6. If a weak or negative leprolin test in early childhood indicates weak resistance to leprosy, then infants in contact with infectious cases are likely to become highly infected before they reach the more resistant condition found in maturer age. A high degree of infection also causes a weak leprolin test, which, we assume, indicates low resistance to

leprosy. There is thus primarily low resistance due to the age factor, and secondarily low resistance maintained by the heavy infection which has taken place during infancy. We should therefore expect such cases to develop the more severe cutaneous form of leprosy. If our hypotheses are true we may take it that high infection in infancy and early childhood leads to the cutaneous type of leprosy with numerous bacilli ; whereas later infection, taking place after greater natural resistance has developed, is more likely to produce the less severe neural type. This is a matter waiting for confirmation or disproof. We would suggest careful enquiry as to the likely age of infection in every case, and comparison of this with the type of disease.

7. Attention is drawn to the interesting case (mentioned under experiment 5) of C_3 leprosy with a ++ leprolin test after treatment with mercurochrome, and to the remarks in paragraph 8 of the *Discussion*. This suggests a wide avenue for investigation.

8. In this paper we have associated a negative leprolin test, as found in C_2 and C_3 cases of leprosy, with low resistance to leprosy, because in these cases there is comparatively little reaction to M. lepræ—whether it be the bacilli which are found in large numbers in such cases, or whether it be the dead bacilli of the leprolin.

How is it then that sometimes with or without special treatment, such cases become bacteriologically negative, though it is only after the disappearance of the bacilli, or when they have become very much reduced in number, that the leprolin test begins to become positive ? What then is the relationship of the factor which causes the elimination of Hansen's bacilli to the factor which causes the reaction to H leprolin ?

9. This suggests another question : Is there any connection between the condition commonly known as " lepra reaction " and the factor which causes a positive leprolin test ? Can it be that, while in C_3 cases this factor is ordinarily absent, under certain circumstances it becomes temporarily present, and that " lepra reaction " is analogous to the positive leprolin test, the bacilli present in the tissues acting in a manner similar to those inoculated in the leprolin test ?

If this is so, the debility produced by " lepra reaction " may be responsible for destroying the above-mentioned factor, resulting in the usual spontaneous subsidence of " lepra reaction." This hypothesis is put forward for

investigation as a possible explanation of this mysterious phenomenon for which no satisfactory explanation has yet been offered.

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REFERENCES.

(1) Mariani (Giuseppe).—" A special form of cutaneous anaphylaxis in leprosy." Pathologica, 1924, Sept. 15th, Vol. 16, No. 380, pp. 471-477

(2) Bargehr (P.).—" Natural Cure in Leprosy." Gansesk Tijdschr. v. Nederl.-Indie, 1926.

(3) de Langen (C. D.).—" Specific skin reactions in leprosy." Meded. Dienst d. Volksgezondheid in Nederl.-Indie, 1929, Vol. 18, No. 1, pp. 113-119.

(4) Chiyuto (Sulpicio).—" Leprolin test." Philippine Health Service. Bulletin for July, 1932, Vol. XII, No. 7.

(5) Hayashi (Fumio).—" Mitsuda's Skin Reaction and Leprosy Classification," (abstract), 1933.

(6) Hayashi (Fumio).—" International Journal of Leprosy," 1933, Vol. 1, No. 1, pp. 31-38.

(7) Klingmüller (V.)—" Lepra," 1900, Vol. 1, p. 30.

(8) Klingmüller (V.).—" Die Lepra," Handbuch Der Haut—und Geschlechtskrankheiten, 1930.

Correspondence

The Secretary, B.E.L.R.A. March 9th, 1934.

I think the claims of Gold Chloride should be considered for trial in leprosy. It has already been found useful in Nigeria by the late Dr. Robertson.

It has certain advantages over the organic compounds among which are :—

1. Cheapness.
2. Ease of obtaining it (it is one of the testing reagents used in Public Health work).
3. Solutions of it are antiseptic.
4. It is relatively a-toxic. Up to ¼ grain may be given, though the dose in leprosy is round about 1/20th grain.

T. F. G. MAYER.

Reviews.

"INTERNATIONAL JOURNAL OF LEPROSY." Vol. 1, No. 2. April, 1933.

This number is one of extreme interest to leprosy workers, and they are urged to join the International Leprosy Association, in order that the excellent material which is contained in this quarterly publication, may be made available to them. We feel that no one who wishes to take a serious interest in leprosy should hesitate to join this Association.

The April number of the Journal contains an excellent article on "Leprous Nerve Lesions," by Muir and Chatterjee, in which they describe the early neural lesions and discuss the nature of the so-called tuberculoid type (leproid). Their conclusions are of the utmost interest, the two main ones being :—

(1) That the tuberculoid lesion is essentially a neural lesion, the infection entering by way of the nerve terminals and "spreading collaterally through the cutaneous and subcutaneous communications, and at the same time finding its way up into the main nerves."

(2) That such lesions are produced by a hitherto undiscovered neurophilic virus or form of the M.B. lepræ, and that this "living germ or virus" has a predilection for the connective tissue of peripheral nerves, and "under certain circumstances generally associated with lowering of the general health of the patient, it can be transformed into the well-known acid-fast rod of Hansen."

It is impossible to summarise the article for, apart from the exigences of space, it can best be appreciated by reading it in full.

This article is followed by one on the "Granular Forms of the Leprosy Bacillus," by W. H. Hoffman, in which he states that the granular forms may be of extreme importance, and follows up the suggestion in the previous article that the bacillus may pass into the non-acid fast form and possibly be a filter passer.

One suggestion that is made, but is not followed up, is the possibility of the leprosy bacillus being a cellular parasite. We feel that many aspects of leprosy can only be explained by such a phenomenon, and that the possible parasitic nature of the disease needs investigating.

It is impossible to summarise Dr. Cole's most excellent review on the "Chemistry of Leprosy Drugs." This is the first series of such reviews, and others are promised on "Treatment, Epidemiology and Prophylaxis" as they are made available. These articles are followed by a short description of "Leprosy in Finland and Esthonia and Latvia," by Drs. Axel Cedercreutz and A. Paldrock.

"EDUCATION, HEALTH AND AGRICULTURE IN INDIA SINCE 1921."
By The Duchess of Atholl.

The above pamphlet has been brought to our notice by the India Defence League. This document is of interest to us, in that under the section dealing with health it is mentioned that a recent survey showed that leprosy had increased fourfold since 1921. While such a statement draws attention to the importance of the problem in India it, however, is not quite correct. What has happened is that, as a result of the modern methods of diagnosis, a larger number of cases of leprosy can be recognised. It is important in evaluating a survey, to endeavour to estimate whether the increased number of cases is due to the fact that cases which were previously unknown had become revealed, or was due to an actual increase in the disease; for, unless this differentiation is made, the conclusions drawn from actual statistics, may be erroneous.