LEPROSY REVIEW.

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Editorial.

DR. ROSE'S article on " The Curability of Leprosy " will be read with a great deal of interest, especially in view of the conclusions of Dr. Rodriguez, which were published in the previous issue under the title " Results of the Chaulmoogra Treatment in Very Early Cases of Leprosy." It is, however, almost impossible to compare these two articles, as each authority is probably dealing with a different type of the disease. The majority of Dr. Rose's cases appear to be those in which the bacilli in the recognised acid-fast form could be detected, and it is in just these that Dr. Rodriguez appeared to hold out the most hope. Nevertheless, this contribution is of such interest that we have had the proofs circulated to a dozen or more well known leprologists and have asked for their comments. We publish some of these comments in this issue and expect to be able to publish others in the January number.

We would draw attention to one or two points which have struck us. In the first place, before coming to definite conclusions it would be imperative to visit British Guiana and see for ourselves the type of case, the conditions of treatment, etc., etc. The Secretary of the Association is at present in British Guiana, and we look forward to receiving his notes on the situation in that territory as well as in the British West Indies generally. Another matter that impresses us is the prolonged period of treatment which Dr. Rose advises patients to undergo. He is fortunate in having a well-organised community and an excellent anti-leprosy system, and therefore, can treat and observe cases for the periods suggested. In the less well developed countries and in those where the population is extremely vast, such a procedure is manifestly impossible, and therefore, comparable results, in Dr. Rose's opinion, could hardly be expected. It is of interest that the relapse rate in Dr. Rose's cases was greatest during the first two years after discharge, and that up to date no case has relapsed after six years. If this statement is substantiated, it will be of public health importance, for it will mean that the period of observation for contacts and those discharged on parole need not exceed six years. Sir Leonard Rogers fixed the period as five years, which appears to be very nearly correct.

Dr. Leggate's article on " Bonney's Blue Solution in the Treatment of Leprosy " illustrates very well the experience of many workers that as soon as a new remedy is tried in leprosy there is apparently a general improvement. We

await with keen interest further reports on Bonney's Blue Solution, and until these are forthcoming would reserve our comments.

We publish a further article from Dr. Rodriguez's pen on the " Evaluation of the Results of Treatment in Incipient Leprosy." In view of the interest created by the two previous articles in this issue, readers will be able to form a more considered judgment as a result of reading this contribution. We would like to underline heavily the following statement :—" Anyone advocating the expenditure of large sums of money on a campaign of leprosy control or eradication, based essentially on a treatment which has not been properly controlled nor sufficiently followed to determine the performance of the results, is assuming a very serious responsibility."

Readers will pass with a sense of relief to Dr. R. M. Wilson's essentially practical article on his work in Korea, and many will welcome the frank statement made therein concerning much of the discussion on " cure," a great deal of which is of an academic nature.

Dr. Welch's article, reprinted from the *East African Medical Journal*, is a very useful summary of general considerations in the treatment of leprosy.

The Secretary of the Association, when in India, was grateful for the help given him by Dr. Gass in the treatment of ectropion. Wishing to pass this knowledge on, he asked Dr. Gass to contribute a note on the operation he was doing and, therefore, we are glad to print his contribution on " Surgical Relief of Lagophthamos following Seventh Nerve Paralysis in Cases of Leprosy." The article is so clear and the description so excellent that it needs no further comment. We trust that those who are in charge of leprosy institutions will be encouraged to try this operation, as Dr. Cochrane was encouraged by Dr. Gass when in India last year.

The article by Dr. S. H. Martin and Dr. R. M. Wilson, on " Chest Diseases in Korean Cases of Leprosy," draws attention to the number of cases showing tachycardia. In a general routine examination at Purulia Leprosy Hospital last year, such a condition was noted, but the explanation was put down to the results of the chronic anæmia following severe ankylostomiasis, but the suggestion that it may be due to leprotic involvement of the vagus is interesting, and this should be followed up by those in a position to undertake post-mortem examinations.

The Curability of Leprosy.

F. G. ROSE.

OF late leprologists have been showing some pessimism as to the results of the treatment of leprosy with hydnocarpus oil and its derivatives. This pessimism seems to be due to the high percentage of relapses which have occurred, and has so far penetrated to the laity as sometimes to hinder the undertaking of prophylactic measures so far as they happen to be based on the curability of the disease. It is important that this atmosphere of doubt should be cleared as far as possible, and this paper has been written with that object in view.

The sparseness of the population (some 310,000 souls), the accessibility of the inhabited parts of the Colony, the spectacular results of treatment, especially in cutaneous cases, are some of the factors which have enabled us to keep in touch with the great majority of patients. Of 801 patients who have come under observation, 138 are dead, 16 have left the Colony, all but one being East Indian immigrants repatriated by the Government, and of the remaining 647, there are but 36 whose ultimate fate is not definitely known. The figures given here for relapse may therefore be taken as closely approaching complete accuracy. The "follow-up" is now done by means of out-patient clinics, of which there are six in different parts of the Colony. Here discharged patients are required to attend for periodical examination and treatment.

Originally treatment was not continued after discharge, but patients were required to visit the District Government Medical Officers at quarterly intervals for observation. It was not until 1929 that it became apparent that the percentage of relapses was so high as to cause grave doubts as to the permanence of the results achieved. It became necessary to ascertain to what cause these relapses were due. They occurred irrespective of the particular derivative of hydnocarpus oil used, the age of the patient, or the stage of the disease. Nor was it the return to unsuitable home-conditions and insufficient nutrition, for relapses occurred even in those who remained in the hospital and in some who lived in quite favourable conditions outside. We were driven to attribute their frequency to insufficient treatment.

Faced with the alternatives of retaining patients in hospital long after they had become negative, or of treating them for extended periods outside, for obvious reasons we adopted the latter. From 1929 we ceased to discharge

patients unconditionally. They are all now discharged on parole and are required to report at one of the out-patient clinics not only for examination, but also for continued treatment at monthly intervals. The results seem to bear out the correctness of our conclusions. If treatment is continued for many years—exactly how many has yet to be accurately ascertained—the relapse-rate is very far from excessive, as the accompanying tables will show.

Before proceeding, it seems desirable to make a few remarks on terminology. That recommended by the International Conference at Manila, which we follow, presents certain difficulties, to one of the most important of which attention must be drawn.

A case which has been "quiescent" for two consecutive years is termed "arrested." Thus, "arrested" cases will include not only neural cases with paralyses or loss of digits or limbs, but also cases in which function has been completely restored, the patient retaining no clinical evidence whatever of the disease. But the latter class of case is now in the majority in British Guiana, and reports wherein these are not separately tabulated may be very misleading to those not familiar with the real conditions.

It is therefore suggested that "arrested" and "quiescent" cases, that is to say, with complete restoration of function and elimination of all external evidence of the disease, should be termed "arrested and recovered" or "quiescent and recovered," as the case may be. Such expressions have been adopted for the purposes of this paper. The term "relapse" has been used in the accepted sense, and no reference is made to "interruptions" in quiescent cases.

Of the 647 known cases, 180 are cases which have been spontaneously arrested with deformity and have not received treatment during the last eight years. Thus, 467 have been under active treatment within this period, and of this number 381 have been under treatment long enough to receive 100 c.c. or more of oil or esters.

The fate of these 381 patients will now be considered. 257 were classed as "early" (C1, C1N1, C2, N1, and N2); 124 as "advanced" (C2N1, C2N2, C3, C3N1, C3N2, N2C1, N3, N3C1, N3C2, and Secondary Neural).

TABLE 1. (*Results in early cases*).

Arrested and recovered	50
Arrested but not recovered	26
Quiescent and recovered	50
Quiescent but not recovered	16
Improved	66
Worse or unchanged	49
Total	257

That is to say, of 257 early cases, 49 show no change or are worse, while all the rest have improved, 100 having become quiescent or arrested with complete restoration of function, while 66 show definite improvement, the majority with complete recovery of function, without having yet reached the stage of quiescence.

TABLE 2. (*Results in advanced cases*).

Arrested and recovered	6
Arrested but not recovered	16
Quiescent and recovered	4
Quiescent but not recovered	11
Improved	66
Worse or unchanged	21
Total	124

Thus, even advanced cases have a chance of recovery, though naturally much more slender than is the case in the early. They frequently require many years of treatment before showing definite signs of improvement. In our experience, in fact, hardly any advanced case of purely cutaneous nature is without hope of ultimate recovery.

It will appear from the tables given above that 98 arrested cases are now living; 13 of these, however, have eluded observation, leaving 85 whose fate is accurately known.

The following table shows the periods during which these patients have been under observation since discharge :—

Date of Discharge.	Period of Observation.	No. Arrested.	Relapsed.	Per cent.
1926–28	Between 5 and 7 years ...	13	2	15.4
1929	4 to 5 years	8	3	37.5
1930	3 to 4 years	18	11	61.1
1931	2 to 3 years	46	8	17.4
Total	... ...	85	24	28.2

Of the 24 relapsed cases, however, 12 have since recovered and are now again in the stage of arrest, so that up to date the number of relapsed cases is 12 out of 85, a percentage of 14.1, which cannot be regarded as excessive.

Most of these cases have received large quantities of oil or esters or both, from 100 to 1,200 c.c.

Oil or Esters, c.c.	No.	Relapsed.	Per cent.
100 to 200 ...	8	3	37.5
200 to 400 ...	24	14	58.3
400 to 800 ...	46	5	10.9
800 to 1,200 ...	6	2	33.3

Cases tend to relapse early, within the first two years after arrest.

No. 1

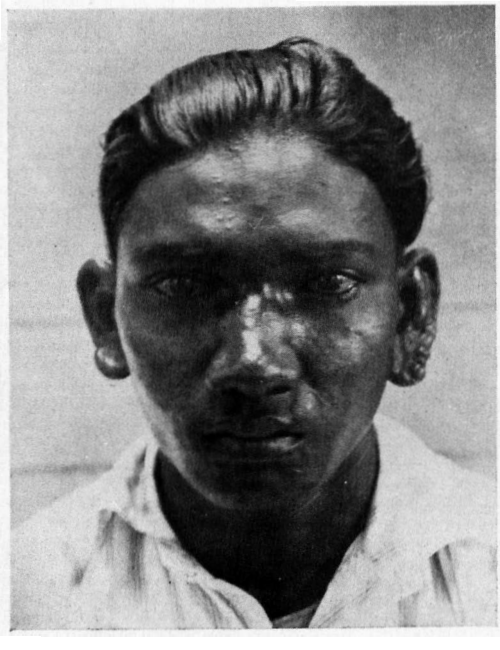
C_3 Case. On Admission

No. 1

Same Case after 12 months

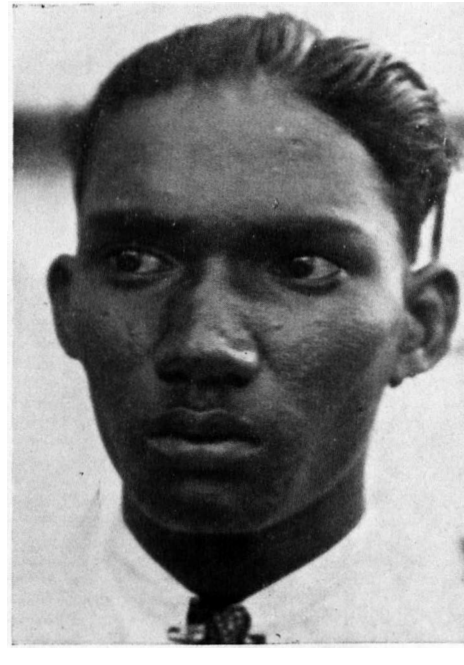
THE CURABILITY OF LEPROSY

No. 2



C_3N_1 Case. On Admission

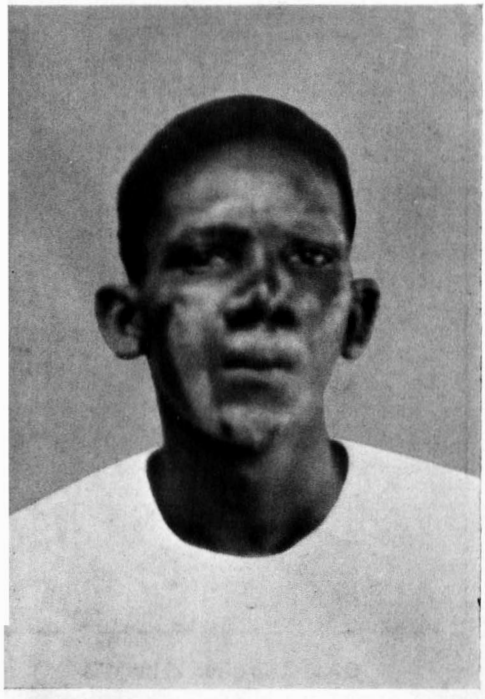
No. 2



After 12 Months. Ears Trimmed by Muirs Method

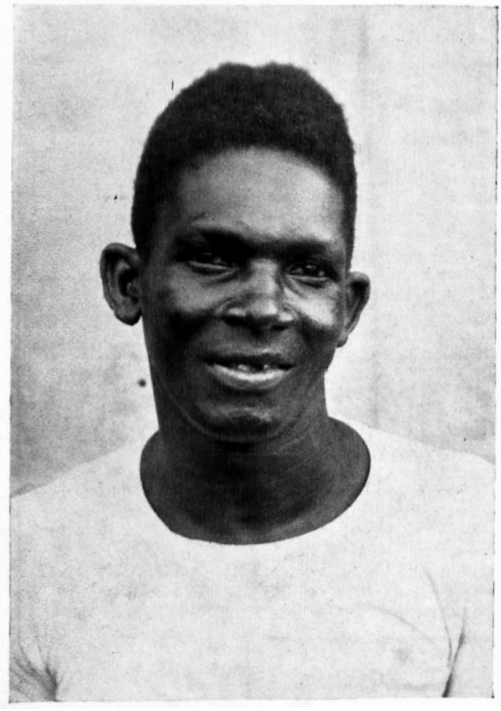
See also illustrations facing page 173

No. 3



C_3N_1 Case. Soon After Admission

No. 3



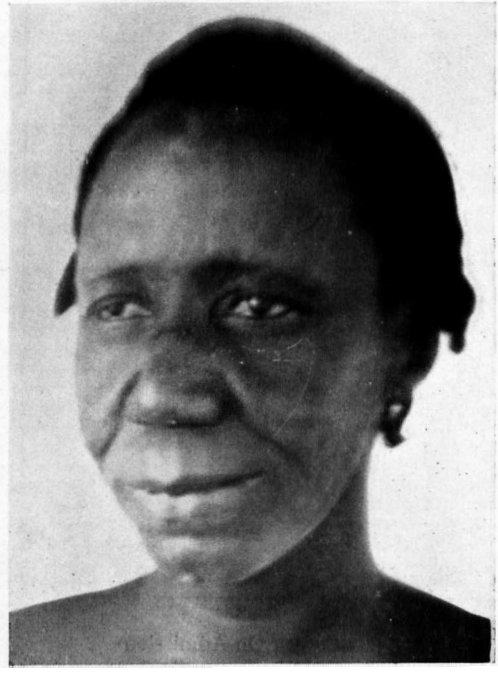
After 18 Months

THE CURABILITY OF LEPROSY

No. 4

C_3 Case. On Admission

No. 4



After 2 Years

Of the cases recorded above, 8 relapsed within 1 year, 11 between 1 and 2 years, 3 between 2 and 3 years, and 2 between 3 and 4 years of arrest. No case has relapsed after six consecutive years of inactivity, that is to say, after remaining arrested for four consecutive years, but the number under observation for such a period is at present so limited that it would be unsafe to draw any deductions from this fact. It seems, however, that the longer the period of inactivity, the less liability there is to relapse, and there is, moreover, another group of patients, the study of whom may help to a conclusion.

Earlier in this paper, mention was made of 180 patients who had become spontaneously arrested and had been under the writer's close observation for over eight years; indeed, some have been under his intermittent observation for some 18 years. It is true that nearly all are cases of the neural type, not more than four being mixed (in previous years, without treatment, the average duration of life of a cutaneous case was computed at only eight years). It is also true that in two similar cases examined post-mortem after some 15 to 20 years of alleged inactivity, M. Leprae were found in profusion in dissected nerves. Nevertheless such cases would not appear to be a menace to the public health, as far as our knowledge goes at present. Of these 180 cases, three have relapsed during the last eight years, but none after five consecutive years of inactivity.

Our policy in British Guiana, based on these facts, is therefore as follows :—Treatment is continued for six years after arrest, but at longer intervals after the first three years. Patients are discharged on parole after they have reached quiescence. During this stage and up to the end of three years after arrest, treatment is given at monthly intervals. During the next three years treatment at quarterly intervals appears to suffice, though we still insist on monthly examinations. We find that patients on the whole do not regard such lengthy periods of treatment as unduly exacting, and the regularity of their attendance leaves little to be desired. When a case has remained in the arrested stage for at least six consecutive years, it may safely be deemed "cured."

One more point remains to be considered. An examination of the histories, very carefully compiled, of some 1,000 patients admitted at Mahaica during several years past, shows that the large majority of infections are contracted in childhood. Cases treated in early childhood, moreover, yield more readily to treatment than the adult.

Latterly, therefore, our efforts in British Guiana have been directed more particularly towards discovering and treating childhood infections.

With the aid of the British Empire Leprosy Relief Association, we have established Out-patient Clinics, at which contacts are examined and uninfectious early cases treated, and we have now 102 children under active treatment, most of them either recovered or in a fair way to recovery. We have a special building for them within the leprosy hospital, erected by private subscription, and another is in prospect for children removed from leprous parents and orphan children in the arrested stage. When this has been completed, we shall have as effective a protection from leprosy as exists in any other country in which leprosy is indigenous.

SUMMARY.

1. Of 801 patients suffering from leprosy under observation in British Guiana from 1926 to 1934, 138 have died, and 16 have left the country.
2. Of the remaining 647, 180 are cases spontaneously arrested, leaving 467 who have undergone active treatment during this period.
3. Eighty-six of these received treatment for less than a year, leaving 381 whose ultimate fate is considered.
4. Two hundred and fifty-seven were early cases, of whom 76 are now arrested, 66 quiescent, and 66 improved.
5. One hundred and twenty-four were advanced cases, of whom 22 are arrested, 15 quiescent, and 66 improved.
6. It is suggested that arrested and quiescent cases in whom function has been completely restored should be termed recovered in addition.
7. Of the 142 early quiescent and arrested cases, 100, and of the 37 advanced cases 10 have completely recovered.
8. Ninety-eight cases have become arrested, of whom 13 have eluded observation.
9. Of these 85, 14.1% have relapsed and have not yet become re-arrested.
10. Relapse generally occurs within the first two years after the arrested stage has been reached.
11. Treatment should be continued for at least six years after arrest.
12. An arrested case may be deemed cured after six consecutive years of inactivity.
13. Special attention should be devoted to childhood infection.

* * *

We have received the following comments on Dr. Rose's article :

From Dr. J. M. H. MACLEOD, one of the leading dermatologists in this country :—

I was very glad to have your reprint of Rose's paper, but have some diffidence in appearing as a critic of it owing to my experience being so much confined to cases in this country. It seems to me, however, that this is a very fair paper, and so guarded and careful as to be more convincing than a good many I have read on the same subject.

I am not convinced, however, that it makes good the claim for specificity of hydnocarpus oil and its derivaties. It rather takes me back to the time when there was a very strong boom in cod liver oil in the treatment of tuberculosis. We are all familiar with cases of tubercle

which after a period of years have become quiescent and to all intents and purposes cured. This has happened in my experience in cases of *lupus vulgaris* associated with internal tuberculosis *foci*, and it is very familiar in cases of surgical tuberculosis. At one time we were inclined to attribute such occurrences to a specific action of the *ol. morrhuae*. Gradually the opinion gained ground that the oil was only of nutritive value. A paper such as Rose's, however, rather inclines one to think that there may be more in hydnocarpus in leprosy than there was in cod liver oil in tuberculosis, and this is emphasised by his results from continuing treatment for a number of years.

Unfortunately, in our experience so far as Moor House is concerned, the majority of the cases, in spite of all the treatment they have had, have either died or remained, in his terminology, "worse or unchanged." Only one case (Bishop) should be regarded as quiescent but not recovered, and another (Ventham) whom we have not seen for some years, who as far as I know may be regarded as quiescent and possibly recovered.

In view of these facts, it is impossible for me to do more than congratulate Dr. Rose on his results among the natives of British Guiana, and pray that a time may come when we can be as hopeful with regard to the treatment of the cases here.

From Dr. E. MUIR, Director of the Leprosy Research Department of the School of Tropical Medicine, Calcutta :—

Dr. Rose's paper, "The Curability of Leprosy," is of great interest to all who are engaged in anti-leprosy work.

(1) The geographical area involved has the advantage of being a limited one with a population of only 310,000. Only 801 cases of leprosy have come under observation, but no mention is made as to whether patients have been followed up to their homes and contacts examined. If this has not been done possibly such a survey, would lead to the detection of more cases.

(2) The table of results in early cases corresponds to the results that we obtain in India in places where the patients attend regularly and are efficiently treated.

(3) The results in advanced cases also correspond closely with results obtained in India under favourable circumstances.

(4) I thoroughly agree with Dr. Rose in his plan of keeping patients under treatment for six years after the disease has become "arrested" in the Manila Conference sense of the word. Routine examination only applies to examination of the skin and nasal mucosa. There is no doubt that, at least in patients who have been C2 or C3 cases, large numbers of bacilli may remain latent in the peripheral nerves without causing noticeable clinical signs. From the point of view of infecting others, these patients may not be immediately dangerous ; but any lowering of general health is apt to be followed by a relapse. In such cases, as Hayashi has pointed out, the leprolin test may continue negative or is only weakly positive. If the leprolin test from being weak or negative becomes moderately or strongly positive, this may be taken as a sign that infection has become almost or entirely eliminated from the body and that relapse is extremely unlikely to occur.

(5) "Cases treated in early childhood yield more readily to treatment than the adult." This is true if the treatment be begun early enough. What is far more important and likely to be effective than the *treatment*

of very young children is their isolation from infectious adults, this being begun, if possible, from birth. So far the chief stress has, I think rightly, been laid on treatment. Treatment is very important, but the isolation of children from infectious cases is far more important; more and more the chief emphasis must be laid on this aspect of the question.

From Dr. T. B. WELCH, Special Leprosy Officer of the British Empire Leprosy Relief Association in Zanzibar :—

Those concerned in the treatment of patients suffering from established leprosy will assuredly have welcomed Dr. Rose's interesting and important paper on "The Curability of Leprosy." Those, more particularly who, while fully recognising the limitations of oil of hydnocarpus and of its derivatives, retain their confidence in the value of these substances, will have found in that communication, at a time when that value is so extensively questioned, much to support their favourable opinion.

Oil of hydnocarpus and its derivatives are at present passing through the various phases through which they have been preceded by so many substances whose value has been first over-estimated and then unduly decried, but which have ultimately found their very real application in medicine. Perhaps the words "over estimated" do not here quite accurately describe the position; with greater exactitude it may be held that some of the earlier advocates of the use of these substances did not consider it necessary to stress the no lesser importance of the general management of the patient which, it is reasonable to suppose, they expected would assuredly receive the attention in leprosy in particular, the need for which is axiomatic in medicine in general; nevertheless, the primary importance of the general management has been emphasized over and over again. However, I have met not a few who have obviously been under the impression that these substances have been held out as being in some sense specifics which need only to be administered to the patient, irrespective of his general condition, for long enough for "cure" to follow; at any rate, where I have observed these substances most conspicuously to fail I have also seen inadequate attention being given to general management and to all that that implies, and this has appeared to be the prime cause of failure.

To emphasise the value of these substances, when associated with close attention to general management, I would here contrast their application in two institutions, of widely divergent types, whose activities I have had full opportunities of observing. In the first one, an asylum conducted on lines now long out of date, conditions were such as to render success inconceivable. Chronic intercurrent or concurrent disease, if obvious, received scanty consideration, while, if such condition was not obvious, its possible presence was ignored. Little was done to stimulate the inmates to take the exercise upon which their welfare so much depends. The dietary was markedly ill-balanced. Under such circumstances the inmates could not be restored to, and maintained in, a condition bringing the success of anti-leprotic measures within the bounds of possibility. However, such measures were attempted with little appreciation of their proper application, and with little discrimination in the judicious selection of patients. The results were entirely unsatisfactory and served only to create a profound scepticism regarding modern methods of treatment, though, obviously, these methods were not being applied. In the course

of many months I saw no instance of convincing progress towards arrest attributable to the treatment given.

The second institution was a settlement conducted on more progressive lines, and here a fair increase of success was gained in the treatment of well-established leprosy. Close attention was given to the restoration of patients to as satisfactory a general condition as was attainable. Considerable facilities for the detection and treatment of intercurrent and of concurrent diseases were available and were freely used, while very real efforts were made to gauge the results of treatment clinically and in the laboratory. The importance of exercise was stressed, and it was possible to provide many of the more promising patients with work for which they were paid. The food was of very good quality, though the dietaries were less well balanced than might have been desired. Under such circumstances it was possible to bring a very considerable number of patients to such a condition that a good deal might reasonably be expected of more particularly anti-leprotic measures based upon oil of hydnocarpus and its derivatives. These expectations were very fairly fulfilled. Anti-leprotic treatment of adults was voluntary ; in course of time it became increasingly appreciated. There were those, however, who were thought favourable subjects, but who consistently refused anti-leprotic treatment, and they served to some extent as controls.

Under systematic treatment, arrest was obtained in a fair number of cases even though their leprosy had, for the most part, manifested itself for several years. Patients were discharged only after repeated and consistently negative examination of smears, etc., made at moderately long intervals ; relapses after discharge were few, so far as is known, but unfortunately there was no effective follow-up system of those discharged, though a good many discharges were under casual observation. Some of the patients who had had general treatment only appeared to be approaching the stage of arrest with deformity, though the advantage undoubtedly rested with the more completely treated.

One group of patients proved consistently poorly responsive to anti-leprotic measures ; this consisted of children of either sex, aged 10—14 years, in whom leprosy was well-established. All these children had histories of symptoms of several years' duration, and the poor results of treatment were such as might have been anticipated since the early appearance of widespread lesions would seem to indicate particularly low resistance.

The conclusions to be drawn from the observations made under the conditions that have been detailed would seem to be :—(1) That oil of hydnocarpus and its derivatives have an important place in the adequate treatment of those suffering from leprosy, which is, however, limited by the need for patients being in or being brought to good general condition. (2) That these preparations are of little value in children who have shown well marked symptoms at an early age, *e.g.*, in the second five year period, which have persisted into the third five year period of life.

Finally, I would stress the importance of careful discrimination in the selection of patients with these substances ; clinical observation, aided by procedures such as, more particularly, the erythroazte sedimentation test enables such selection to be made with a fair degree of certainty. Endless pessimism is produced among the patients and much disbelief among medical men and among the public generally by numerous failures following the promiscuous application of forms of treatment, however valuable within their limits. Few steps would do so much to commend their use, as would their restriction to those believed likely to benefit

thereby, as against their extension to those who, it is hoped rather than expected, might conceivably respond.

I do not wish to seem to assert that, where oil of hydnocarpus and its derivations have failed, there has necessarily been failure in general treatment or in the selection of patients. I have merely tried plainly to outline my experiences in the hope that by so doing I may contribute a little to that full discussion of the value of these substances and of their limitations in the treatment of those suffering from leprosy that is now so desirable.

Grants for Leprosy Work

The Executive Committee of the British Empire Leprosy Relief Association have recently made the following grants:

BRITISH GUIANA. Lady Denham—for work among children £200

INDIA. Mrs. Todd—for work among children ... £50

NYASALAND. U.M.C.A., Likwenu £20
Grant towards permanent water supply at Cholo £100

NORTHERN RHODESIA. U.M.C.A.—for buildings at Mapanza £45

SOUTHERN RHODESIA. Director of Medical and Sanitary Services, Salisbury—for development of Leprosy Institution at Mtoko £200

TANGANYIKA TERRITORY. Benedictine Mission, Peramiho £60

UGANDA. For distribution by Local Committee £300

Applications for financial aid will be sympathetically considered by the Committee, and all applications should, in the first place, be sent to the Director of Medical Services of the Colony concerned, who will forward them to the Secretary of the Association.

Literature

The following publications can be obtained from the Association:

THE SHADOW OF LEPROSY. Annual Report for 1933.

LEPROSY—SUMMARY OF RECENT WORK. Nos. 20—31. Reprints from the Leprosy Sections of the Tropical Diseases Bulletin.

LEPROSY REVIEW, Volumes I—V. Issued quarterly by the Association. Price 2s.

LEPROSY IN INDIA, Volumes II—VI. Issued quarterly by the Indian Council of the Association.

Bonney's Blue Solution in the Treatment of Leprosy.

JAMES LEGGATE.

STIMULATED by C. S. Ryles' article in the LEPROSY REVIEW of July, 1933, on his results with Brilliant Green and Crystal Violet, I had some of Bonney's Blue solution prepared according to the formula given :—

Brilliant Green, 0.5 grammes.
Crystal Violet, 0.5 grammes.
Absolute Alcohol, 25 c.c's.
Aq. Dist., to 2.500 c.c's.

and selected ten very bad C3 cases for experimental treatment.

Like Ryles I started on open leprotic ulceration (strongly positive) and used the ordinary " Flit " spray pump (as for tannic acid treatment of burns) as the means of application. The solution was sprayed on frequently during the day, and during the night the part was covered with lint soaked in the dye, and covered with water-proof silk. The results were dramatic. The purulent condition subsided in a matter of days, and the sores started healing.

It seemed possible that this was due to a general bactericidal action which was clearing up a secondary infection, so intramuscular injections were given to ordinary hard nodular C3 cases with marked, though not so rapid, effect. In addition, I gave intradermal injections into the nodules. Results in these cases were good. At Mtoko we noted rapid absorption of even firm, hard, fibrous nodules, and do not echo Dr. Ryles' disappointment at this method.

But the quickest results were in the soft purulent node. These were counter-punctured and irrigated through an intradermal needle with a stream of Bonney's Blue Solution. The pus rapidly subsided and the holes scabbed and healed. There was no suspicion of any systemic reaction and, in February the drug was given intravenously in view of the considerably less discomfort afforded the patient. The dose was first 3 c.c's to 5 c.c's, increasing rapidly till 10 c.c's and 12 c.c's were being given weekly.

This has been the procedure up to to-day with the selected cases who are given 12 c.c's weekly and 2 c.c's or

more into local lesions which are still outstanding. However, the remaining patients (some 500 odd) are so impressed with the results that they are clamouring for the new medicine, and this week it was determined to alternate Bonney's Blue with the iodised esters as routine treatment. This will necessitate reverting to the intramuscular route as being the only safe method for administration by orderlies, on whom the greater part of the work must, of necessity, devolve. One case developed a febrile reaction after an intravenous injection. This turned out to be malarious and yielded to quinine. The dose was halved at the next injection, but after that he was put on a full 12 c.c's dose with no untoward result.

Treatment of the N type is not so dramatic, though sufficient evidence is not yet forthcoming here. Edges of macules have reacted and subsided, and though no unilateral check has been kept, those particular areas subjected to intensive treatment would appear to show improvement. Whether this is due to the general systemic result of intravenous therapy or a local change it is impossible to say.

It would appear that Bonney's Blue solution is worthy of an extended trial. It may be that its greatest effect will be in countries with ample sunlight, and in Rhodesia, at least, the results have been most encouraging.

Microscopic examination seems to confirm the clinical improvement. Of the ten cases which started Bonney's Blue in January, two in particular, new patients who have had no other drug at any time, show definite fragmentation of bacilli and irregular staining after four months of weekly injections.

Laryngeal, throat and nose conditions have all responded well. One small youth admitted as a last stage C3 on March 20th, with the strained, husky whisper of throat involvement, demonstrated a marked improvement in speech in less than a month. I have not observed this very rapid improvement on admission with any other of the known preparations for the treatment of leprosy, and hitherto I have met no case of those changed over that has not done definitely better on the dye than on iodised esters.

Now that further experiments are to be made over a wider field, it is probable that some small percentage may do better on oil or esters as Ryles found, but up to the present I can only record with satisfaction an apparent superiority of Bonney's Blue over all other forms of treatment.

Evaluation of the Results of Treatment in Incipient Leprosy.

JOSE RODRIGUEZ.

LEPROSY workers are often baffled and confused by conflicting results obtained by different workers using apparently the same drugs or identical methods of treatment. One is impressed also by the long list of remedies which have been reported at one time (and these reports are usually supported by convincing statistical data and even by photographs) but which were later proven to be quite useless. The conclusion is inescapable that there is and has always been something seriously wrong somewhere about these reports.

The one serious defect common to practically all the published accounts on the treatment of leprosy so far has been the lack of proper criteria in evaluating the results of such treatment. In 1926, Acton wrote an article on the " Principles in the Testing of a Cure " (*The Indian Med. Gazette,* Vol. LXI, No. 6, pp. 1-26) which should be carefully read by everyone following the results of any treatment among cases of leprosy.

Admitting that the principles discussed by this authority are very difficult or may even seem to be impossible to apply in leprosy, workers in this disease must face the fact that unless these principles are applied to their work, their results will always be unreliable and subject to serious errors. The realisation of this fact is particularly important at this time when the treatment is being advocated with increasing insistence in schemes to control the disease in different countries. Anyone advocating the expenditure of large sums of money on a campaign of leprosy control or eradication, based essentially on a treatment which has not been properly controlled nor sufficiently followed to determine the permanency of the results, is assuming a very serious responsibility, to say the least.

It is not our intention to discuss in this short paper the principles already stated in the article of Lieut.-Col. Acton. We merely wish to call attention to the fact that particularly in cases of incipient or " macular " (?) leprosy it is necessary to take the utmost care in interpreting the results of the treatment, if grave errors are to be avoided.

In cutaneous leprosy, the criteria usually followed to test the efficacy of the treatment are the following :—

1. Disappearance of acid-fast M. leprae in smears from lesions previously positive for them.

2. Disappearance in true nodules or infiltrations of the signs of activity such as redness, thickening, granular appearance, etc. One would expect that only the rash or the inexperienced would base their judgment on the disappearance of the evanescent rashes of lepra reaction, but this weakness does not seem to be at all uncommon even among old workers, judging from photographs illustrating many articles.

The above tests of a cure or of improvement in cutaneous cases are perfectly reasonable, but the usual error lies in rushing to print before the permanency of the cure or even the improvement has been determined.

When it comes to pure neural and incipient cases, the criteria followed are even more unsatisfactory, as the lesions are bacteriologically negative to begin with, and the worker is forced to judge the effects of his treatment merely on the appearance of the macules or condition of the anæsthesia—whether they are progressing, retrogressing, or stationary.

If the development of the disease were a gradual process leading from the hazy hypopigmented patches or from a group of papules to the infiltrations and nodules of the bacteriologically positive stage, it would be not so difficult to follow and to check up the results of the treatment. Unfortunately, only a small proportion of the cases follow such regular course. Usually the progress is halting and irregular. A large number show alternating but irregular periods of activation and regression during which the patient seems to be either getting worse or is improving. In a considerable number of cases with depigmented macules, the lesions remain stationary for years; suddenly there appears a crop of new lesions which rapidly become positive, or else the patient discovers that his ears are becoming infiltrated. On the other hand, such macules, after developing to a certain stage become stationary or may disappear completely and the patient becomes apparently cured.

The reddish or pink macules are even more changeable than the depigmented ones, unless there is already distinct infiltration or nodulation, in which case the lesions become stationary or progressively worse.

A more or less sudden diminution or disappearance of localised anæsthesia observed on an otherwise apparently normal-looking skin, is of ominous import among our incipient cases; there usually follows a violent efflorescence of active lesions.

Thus, it is very easy to credit falsely apparent improvement of existing lesions to the treatment, unless the proper principles in the testing of a cure are strictly followed.

The above observations are based on a study of 336 children of leprous parents born in the Culion Leprosy Colony, most of whom had been followed personally by the writer for a period of nine years, and on 640 "incipient" or "closed" dispensary cases, 225 of whom had been repeatedly re-examined both clinically and bacteriologically for periods ranging from seven months to five years. The results of the chaulmoogra treatment among these cases are discussed in a separate paper submitted for publication in the REVIEW.*

It may be of interest to mention that when those who became positive were asked to describe the type, the size, site, etc., of lesion they had when first examined, and to tell the changes in their lesions during the period of observation, it was found that only very few of them could give these details with even approximate accuracy. In most of the cases their statements were so far from the actual observed facts that the writer has come to the conclusion that studies, based on the statements of patients as to the course of the disease and the progress of the lesions, are absolutely useless. Therefore, if one wants to study the development and progress of the disease in the early stages, there is no other alternative but to observe *personally* a sufficient number of them for many years.

In our opinion, the only safe method of determining the efficacy of a certain preparation among these early cases is to follow closely two groups of such cases, arranged as follows:

1. Adequately treated cases.
2. Cases receiving no treatment or an inadequate number of injections.

Fortunately, it is not difficult to arrange such a grouping of cases for study. In every dispensary for the treatment of incipient cases of leprosy there is always a number of patients who report for treatment quite regularly for a period of years, while others make only a few visits a year, and not a few will not be seen again after the initial visit.

At the close of the observation period, which should not be less than five years, all the cases should be re-examined. The efficacy of the treatment may then be determined by comparing the proportion progressing to the bacteriologically positive stage among the adequately treated patients as compared with that among the insufficiently treated group.

* Published in LEPROSY REVIEW, Vol. V., No. 3, July, 1934

Needless to say, the other precautions mentioned by Acton will have to be observed in such a study.

The nature of the disease we are dealing with is such that although it is certainly undesirable and very inconvenient, many years of observation are required before the efficacy of a certain treatment can be determined in leprosy, but this is the only safe way, particularly in the incipient stages. No short or easy methods are possible at the present time. It is precisely in this disease that the proper principles in testing a cure must be rigidly observed.

If these precautions were only followed, there would be less number of drugs so authoritatively endorsed for the treatment of leprosy, only to be finally discarded altogether or relegated to such secondary indication as control of reactions, treatment of ulcers or of eye complications, as a test to determine activity, etc.

(This article, also that which appeared in the July issue, by the same writer, is published with the approval of the Director of Health, Manila).

A Review of the Work at Soonchun Leprosy Settlement and Notes on the Leprosy Situation in Korea.

R. M. WILSON.

A REVIEW of our leprosy work for the past year may be of some interest to other institutions.

As to diagnosis, it is unfortunate that we do not have more positive diagnostic methods in the early stages of the disease. There are those border-line cases which prove a real problem. I have had three cases recently showing puffiness of the face, loss of eyebrows, etc., and while giving quite the picture of leprosy I could not give a positive decision for lack of any anæsthesia. I put all three cases on syphilitic treatment, asking them to return in a few months for further study. It would be a greater mistake to take such doubtful cases into the colony, than to delay diagnosis for a few months. On January 17th, a case was referred to me by Dr. L. K. Boggs, with the general appearance of leprosy; loss of eyebrows and some puffiness of face were the chief signs. Examination showed no anæsthesia, no pigmentation and bacillus negative. However, he had a four plus

Wasserman with some nose and throat trouble, and stated that after a few injections of 606, his eyebrows began to return in only a few months, much quicker than the return would be in cases of leprosy. So he was put on further syphilitic treatment.

Recently a young woman came, stating that her people had driven her out because her face resembled that of a "leper," due to loss of eyebrows. She stated that in the past she had applied medicine to her eyebrows to beautify them, and for this or other reasons they had fallen out. She was told to wait and watch for other signs. Two other cases came, thinking they were leprous, stating there was tingling of the skin, feeling like the crawling of ants, which is often an early sign. No positive symptoms could be located, and they were diagnosed as neuræsthenia.

If there is a positive anæsthetic spot I usually diagnose leprosy, unless this can be accounted for by some surgical trauma or injury in the nerve trunk.

Often cases who are leprous will try and deceive us, and cover up their symptoms, stating there is no anæsthesia when there is. Such will have to be blindfolded and tested. Some will claim to be leprous to get the benefits of the colony. This speaks more for the contentment of the inmates of the colony than for the individual's common sense.

Another aid in diagnosis, and often an early one, is the thickening of the nerve trunks, usually the ulnar. In the examination of 1,000 cases Chatterji found the ulnar nerve hard in 56 per cent., peroneal 53 per cent., and great auricular 18 per cent. A girl came to our General Hospital asking that a tumour be removed from her shoulder. I dissected out two masses about the size of a lead pencil running across her scapula and measuring 4½ inches in length, and later these showed bacilli. She confessed later to anæsthesia.

Treatment.—We have found nothing that has given so much benefit and satisfaction as the hydnocarpus oil, injected twice weekly, from 4 to 8 c.c. We get our supply direct from Siam, in 300 lb. tanks, about 33 cents per pound delivered. This should be made fresh from the summer fruit and not kept long enough to become rancid. It costs us about one yen per pound, but in the local market it is about three yen per pound. Our stronger workmen ask for large doses, and in one clinic where there are 150 cases, they asked that the dose should be increased from 5 to 7 c.c., stating that it made them feel better and more vigorous.

The esters have given so much pain that our cases refuse to take them. The stock of esters left over is proving very good in the local treatment of scabies and certain itching excemas, which I should like to ask others to try. We are now adding 2 per cent. esters to all scabies and excema ointments. I obtained a supply of the iodised esters from Manila and tried them, injecting directly into the nodules, which is so highly recommended. While it dried up many of the nodules it proved so painful a process that our cases could not continue with them.

In most of our cases we expect a very distinct improvement with three months' treatment. In another three months there is still more marked improvement and clearing up of the skin. Of course, in treatment there are many side lines such as diet, exercise, baths, sanitation, and complications that must be taken into consideration. Syphilitic complications are a big problem, and some of these will not respond to treatment. In many of the neural cases no special change or improvement can be expected, for these cases are often practically normal except for some small anæsthetic areas, and these may continue so for many years, neither better nor worse.

Pellagra.—Many of our cases show a pellagroid condition breaking out, and this is often the case in the spring. I wonder if other institutions experience this ! It is quite like pellagra with a sunburn rash on the wrists, neck and exposed parts with stomatitis and intestinal disturbances. Our cases usually clear up quickly upon being given plenty of pork in their diet.

Another useful adjunct we find are the swimming clubs. These seem to prove beneficial and it is fine exercise, and it is not difficult to get the patients to enter into this sport with zeal. We are on the seaside, and the hot sand rubs and then a good swim are popular. In neuritis we find atophan, cinamomin and terrotodoxin give the best relief in the order named. Calcium chloride intravenously is also beneficial. Some cases seem to be helped by nothing, and have to suffer intensely.

One discharged case came to us this week saying he had been entirely well for 14 years, and that he has a good farm and is very happy. During the past year 82 cases have returned to their homes. Many more are quite able to return were it not for the fact that they are so feared and dreaded in their villages that it is almost impossible to get them re-established in society. One big problem is what to do with the " cured " case.

We are doing vasectomy upon a number of cases and allowing them to marry and live within the colony, both parties being arrested cases. These support themselves on the land except for an allowance of one yen a month per person. This couple also adopts a child, and thus the home idea is made more perfect.

The youngest case I have seen was nine months old, but it is quite unusual to see them under the age of four years. It is generally accepted that leprosy is a disease of childhood and youth, even though it may not appear until later in life, the innoculation probably taking place in early years. It is probably the most mildly infective disease known, and innoculation is by *long* and *close* contact. At the Manila Leprosy Conference the disease was divided into two classes, " open " cases, which may spread the disease, and " closed " cases in which the bacillus is not found in scrapings from the skin, and therefore non-infective. Rogers claims that 60 per cent. are house infections. Humidity has much to do with the incidence of leprosy. It is a very striking fact that most of the 20,000 cases of leprosy in Korea are in the southern half of the country, and only a very few north of Seoul.

It was very encouraging to attend the Tokio Leprosy Conference and see the earnest zeal and interest taken in this subject. Eighty papers were presented, and over one hundred were in attendance. These energetic students are working upon almost every line imaginable. At this conference, just as throughout the world, there are two classes of men—those believing that " once a leper, always a leper " and others with a bright and hopeful outlook, believing in a probable cure. Some men feel that one treatment is about as poor as another and that isolation, good food and sanitation are the essential things. Others feel that chaulmoogra oil has a very definite place in treatment. It was good to see how the Government is backing the work through the Empire, and doing its part. The Japanese are quite like the Germans in their minute detail of study. I look to see the Japanese take a lead in the advancement of this line of work. I should like to make one or two criticisms in a kindly spirit of some of the work I saw, one being that the institutions did not have the thought or idea or hope of a cure, but were places in which the sad creatures could spend the rest of their days in isolation. At one such place I found two big husky Koreans in the early stages of the disease, asleep in their beds at 11 a.m. These men stated that there had been no improvement in their condition,

and apparently none was expected. In most cases treated there should be a very definite improvement seen in three months. It is a most important thing to get one's staff and the entire colony into the *spirit of a cure.* Every case should make this his first aim. If the doctor does not expect a cure, what can be expected of the patient! Doctors spend too much time debating the word " cure." What if a few leprosy germs are discovered at post-mortem. If 70 per cent. to 80 per cent. of the cases discovered early show marked improvement, this is the thing we want. Call it " arrested " or anything else, but let us have a little more faith in improvement. My patients are just as keen and interested in their improvement as I am. We keep posted a list of the essentials in treatment. Even our blind cases have their tasks, and are not allowed to remain in bed, but stir about. Some own and care for rabbits, which interests them and shortens the days.

Another criticism I wish to make is that while the doctors and visitors must wear rubber boots, masks and gowns, and are sprayed from top to bottom, yet, on the other hand, there are attractive little non-leprous nurses taking pulses, making beds, and caring for the patients. Some were carelessly leaning upon the patients' beds. I noticed also that some of the homes and cottages used by the doctors and attendants were not screened against flies and mosquitoes, and were only a couple of hundred feet away. In our institution, the homes of the attendants are half a mile away from the colony, and are screened.

In our institution also, no healthy person comes in contact with cases, except the two doctors, and all are taught not to touch a door knob or anything used by inmates. All injections, dressings and nursing is done by the leprous staff, and here is a splendid opportunity to provide work for the " closed " cases. I think it was reported that none of the workers in Japan had been infected, yet there is a slight danger that could be avoided. I believe that every institution should have a nurses' training school, and a few good nurses given the task of training the inmates to do this work. In one institution there were healthy cooks, and I noticed that these received and handled the dishes which came back from the wards. It is a good policy to keep the number of healthy workers in leprosy institutions down to the minimum. 95 per cent. of the jobs about such places can be filled by closed cases, and laundry, cooking and nursing can all be done by healed patients.

Some Considerations on Diagnosis in Leprosy and on the Treatment of Lepers.

T. B. WELCH.

(*Reprinted, by kind permission of the editor, from "East African Medical Journal," Vol. 2, No. 3, June,* 1934).

OVER-OPTIMISTIC reports circulated from time to time, subsequently exaggerated, have done a great deal to injure the prestige of modern methods in the treatment of lepers. Further damage has been done by the application of these methods to patients hopelessly involved. Valuable though these methods are, their indiscriminate application is to be deprecated, and it behoves those undertaking such treatment to exercise a judicious discrimination in their selection of patients.

I propose to-day to stress the importance of adequate diagnosis and treatment, and particularly to emphasise the fact that the leper is rarely *only* a leper—a fact unfortunately often overlooked, and so such prospects of success as may be present are rendered remote.

The leper whose disease is clinically only recognisable is in great danger, however slight its manifestations ; in much greater peril is he in whose tissues *M. leprae* are found, while the more readily they are demonstrated the more precarious is his condition. Nevertheless, in a very considerable number of early cases and in a fair number of those that are only moderately advanced, arrest of leprosy without residual deformity follows careful attention to the making of a full diagnosis and to the provision of adequate treatment. In still more advanced cases arrest may similarly be obtained but with the persistence of more or less residual deformity. Little, however, is to be expected of more particularly anti-leprotic measures unless the patient is in fairly good general condition before bringing them into use ; if such condition cannot be attained, these measures, helpful as they are within their limited field, should be withheld, since their use, inevitably followed by failure, tends to bring them into unmerited disrepute because their limitations have not been duly appreciated.

M. leprae establishes itself readily in children ; less readily in adolescents, and with difficulty in otherwise healthy adults, the difficulty increasing with advancing years. Successful invasion may, however, take place in adults whose resistance is lowered by one or more predisposing causes, though usually only after prolonged and

close association with another leper. Such causes may be transient, such as acute illness; or they may be of long-standing, such as chronic disease, habitual under-feeding, an ill-balanced diet, and so on.

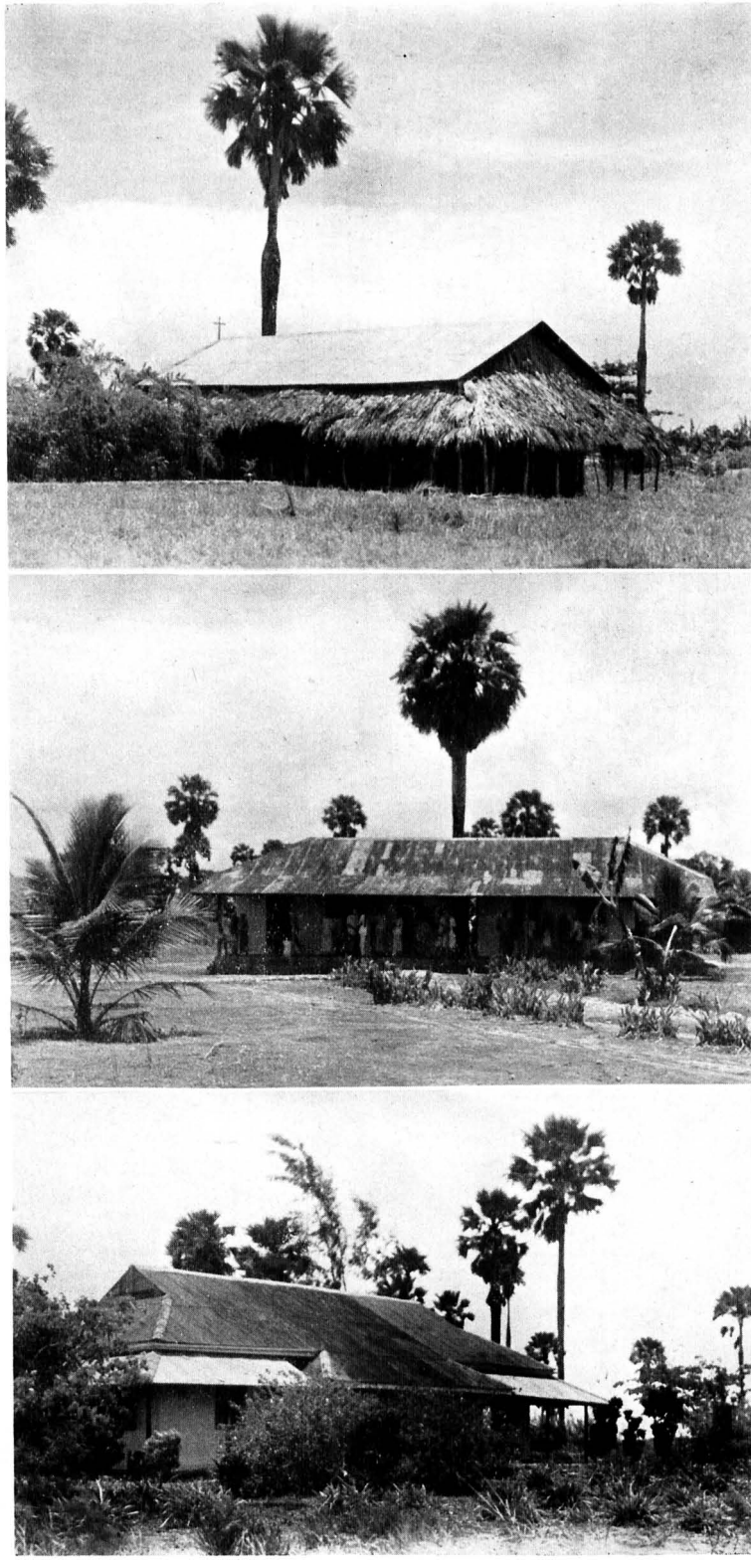
Not only does *M. leprae* become established with difficulty, but also it shows a definite tendency to die out. Abortive cases, in which leprosy is manifested by one or two macules only, that have remained unchanged for years, are not rare; cases in which progress has been exceedingly slow and in which elimination has ultimately taken place, leaving the patient comparatively undamaged are more common; while even more frequent are cases that have passed on to the non-infective stage of late neural leprosy with residual mutilation after a prolonged course. In all these cases, successful invasion has been followed sooner or later by the dying off of the invaders.

Since normally healthy persons living under good conditions, rarely, if ever, acquire leprosy, and since some ascertainable predisposing cause usually, and perhaps always, precedes successful invasion by *M. leprae*, it seems possible that the removal of such causes may contribute to the arrest of leprosy, and this is found to be so in practice. In some cases of early leprosy such removal may be all that is required, while in more advanced cases a good deal may be expected of more particularly anti-leprotic measures after any other unfavourable conditions present have been set right.

It is important to remember that often there is more than one predisposing cause present. Thus ankylostomiasis and some dietetic deficiency such as hypovitaminosis frequently occur in the same patient.

The importance of dietetic deficiency in relation to leprosy is gaining increasing recognition. Muir (1932) states that in twenty-nine early cases he has brought about arrest of leprosy by putting the patients on a properly balanced diet. Dietetic deficiency is, however, not uncommon in institutions, while it is common in lepers at large, and it is apt to be overlooked. The importance of some factor is easily exaggerated at the expense of others of no lesser significance; but it is probable that syphilis or ankylostomiasis often in the presence of some dietetic deficiency are by far the most usual causes predisposing the leprosy.

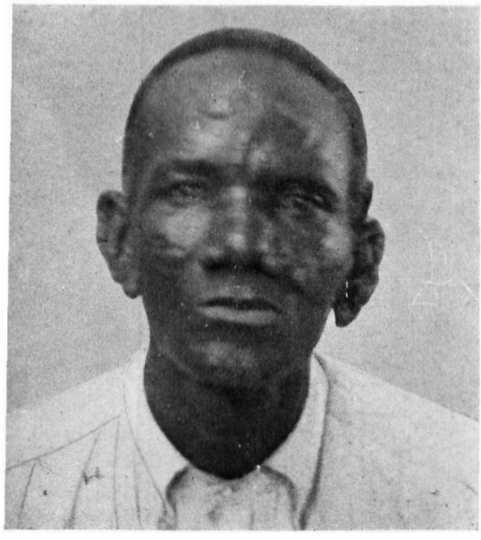
That diet might be a factor in determining the incidence of leprosy was suggested long before these days of progress in rational dietetics. Gilbert White (1778) in a letter later included in The Natural History of Selborne (1789) described



FUNZI LEPROSY SETTLEMENT, ZANZIBAR.

1.—Church. 2.—Dispensary. 3.—Sisters' House

No. 5



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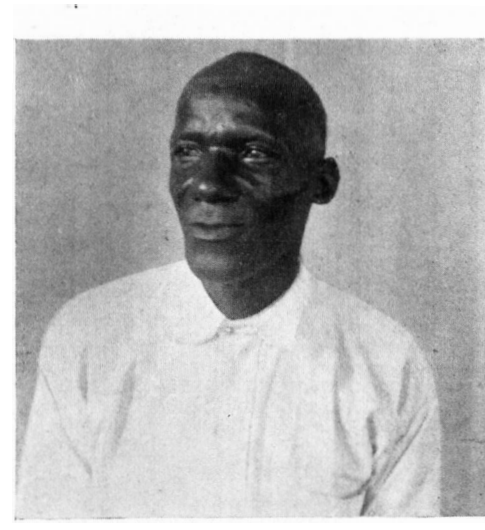
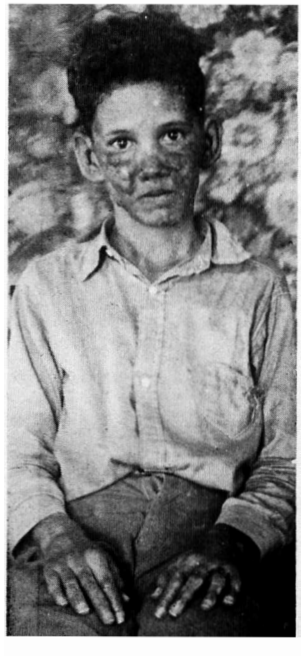
No. 5



After 3 Years

THE CURABILITY OF LEPROSY

No. 6



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After 18 Months

in some detail a man whom he believed to be suffering from a typical leprosy ; after briefly reviewing the occurrence of leprosy as related in history and in the scriptures, he refers to the leper hospitals that had existed in England and to large legacies that had been left for the benefit of their inmates. Thereafter, he states his views as to the causes that had almost eliminated leprosy from the British Isles in a passage that I think worth quoting. He writes, " It must therefore, in these days, be to a humane and thinking person a matter of equal wonder and satisfaction when he contemplates how nearly this pest is eradicated, and observes that a leper is now a rare sight. He will, moreover, when engaged in such a train of thought naturally enquire for the reason. This happy change, perhaps, may have originated and been continued from the much smaller quantity of salted meat and fish now eaten in these kingdoms ; from the use of linen next the skin ; from the plenty of better bread ; and from the profusion of fruits, roots, legumes and greens, so common in every family." White then enlarges upon this subject, but the above passage contains his essential points, and considerations of time forbid further quotation.

When it has been concluded that a patient is suffering from leprosy, it becomes necessary to recognise the type of his disease, whether neural or cutaneous and, if the latter, whether he has also neural manifestations which, if present, may be primary when they are evidence of a still active pathological process, whether progressive or retrogressive, or they may be secondary when they are the result of past nerve involvement ending in nerve destruction. Next, in respect of cutaneous manifestations the stage of his cutaneous leprosy has to be determined, whether it is in the first stage, presenting lesions which are not anæsthetic and which contain few *M. leprae,* or in the second stage with the appearance of nodular lesions or of diffuse infiltrations containing numerous organisms, or in the third stage when elimination has set in and the lesions are obsolescent. Then the phase of the disease has to be determined, whether it is quiescent, of which the principal characteristic is the absence of constitutional disturbance ; or, it may be reactionary, characterised by constitutional disturbance associated with exacerbation of old lesions and the appearance of new lesions ; these manifestations, in the first and second stages of cutaneous leprosy, remain after the cessation of the constitutional disturbance, but in the third stage, that is the stage of elimination, they disappear as the constitutional disturbance subsides, often with marked

improvement in the patient's condition ; or, again, the phase of resolution may be present in which a return from the reactionary to the quiescent phase is taking place.

The observations bearing on the patient's leprosy that I have just outlined have their ultimate importance. Of no less moment and of more immediate concern is a very strict search for any predisposing causes that may be present. The need for searching investigation has to be emphasised, because the patient's leprosy is too often allowed completely to overshadow other conditions from which he is suffering, though the overlooking of these is likely to have far reaching repercussions upon his prospects. Such other conditions may not be obvious. Thorough physical examination is essential, as also are routine examinations of the urine, of the faeces for ova and cysts, and also of the blood including hæmoglobin estimation ; further, the performance of the Kahn Test is necessary and that of the Wassermann Test is desirable. Determination of the erythrocyte sedimentation index will be needed, but usually at rather a later stage. Further, I would stress the importance of the appraisement of the results of treatment, in due course, by laboratory methods, in addition to the previous application of these means for diagnostic purposes.

By the above procedures one or more unfavourable but perhaps rectifiable factors will usually have been brought to light. The work is rather laborious, but it is fully repaid by results, while its thorough performance forms the very foundation of success ; and the rectification, in so far as possible, of unfavourable conditions is the first step in treatment.

The thorough treatment of any unfavourable intercurrent conditions is as essential as is that of persistent predisposing conditions. Leprosy *per se* is not a cause of severe debility unless the disease is very advanced. Patients are not infrequently seen who may fairly be described as fit persons who have the misfortune to harbour *M. leprae* in their tissues ; it is those who are in or who can be brought to such condition who may benefit from more particularly anti-leprotic measures, while any application of such measures to patients in poor condition leads to certain failure.

It is difficult to over-estimate the importance of the recognition and of the thorough treatment of persistent conditions that have given the opportunity for *M. leprae* to establish itself and flourish in the patient's tissues. Sometimes, however, a patient is found in whom the predisposing

cause has been transient, and that patient is likely to do well. Sometimes some condition is found whose very treatment is apt to aggravate the patient's leprosy ; for instance, many advanced lepers who are also suffering from syphilis, do badly on organic arsenical compounds, while potassium iodide in doses appropriate to syphilis may prove disastrous to the patient. Again, the prolonged presence of some predisposing cause may have brought the patient to a condition such that no treatment will restore him sufficiently for him to benefit by anti-leprotic measures, as happens not infrequently where ankylostomiasis of long-standing and of great severity is present. Further, some condition may be found which is in itself a contra-indication for anti-leprotic measures as, for instance, chronic nephritis or pulmonary tuberculosis.

The question of more particularly anti-leprotic measures arises when the patient is already in, or has been restored to good general condition. The results of physical examination, of the laboratory examinations to which reference has already been made, and of the determination of the Erythrocyte Sedimentation Index, show when this condition is attained.

It may be well here briefly to consider the determination of the sedimentation index and its bearing on prognosis and on treatment.

A thorough mixture of four parts of the patient's blood with one part of a five per cent. solution of sodium citrate is drawn up into a sedimentation pipette which is placed vertically in a stand. The length of the column of citrated blood is measured ; then, at the end of one and a half hours and again at the end of two and a half hours, the amount of sedimentation that has taken place is measured, and the mean of these two readings is expressed as a percentage of the length of the column of citrated blood. The sedimentation index so determined is an indication of the degree of debility from whatever causes from which the patient is suffering. In the extremely debilitated the sedimentation index is very high, and the less the patient's debility, the lower is his sedimentation index. In leprosy, with one or more concurrent conditions present, the sedimentation index is a measure of the gross amount of debility and, as the effects of the concurrent conditions are eliminated under treatment, the sedimentation index falls. Further, the sedimentation indices in uncomplicated quiescent leprosy have been ascertained with sufficient accuracy to be helpful. In normal man, or in the ex-leper with or without residual

deformity, the sedimentation index is about 10, and it is but little higher in primary neural leprosy ; in early cutaneous leprosy the sedimentation index is below 20 ; in more heavily involved cases it is below 30 ; and in very heavily involved cases it is below 50.

Approximate only though these figures are, they are of very great value in determining treatment. Thus, if a patient is found to have a higher sedimentation index than is appropriate for his stage of leprosy, then the following possibilities are indicated :—(*a*) That concurrent conditions have not yet been successfully treated, or that, perhaps, they have been missed. (*b*) That the patient may be in the phase of reaction ; and here the determination of the sedimentation index is of particular value, since it begins to rise before other signs become manifest.

It is important, however, to remember that when anti-leprotic measures are being taken that involve the production of the least clinically recognizable reactions at short regular intervals, the sedimentation index, if determined within a day or so of treatment, will be higher than the figures that I have given which apply to quiescent leprosy, but that thereafter it should rapidly fall to the quiescent figure ; and, further, that as favourable progress is made, the sedimentation index in the quiescent phase will itself fall.

The sedimentation index should first be determined when the patient's general condition gives reason to suppose that he may now benefit by more particularly anti-leprotic measures ; supposing his sedimentation index shows him to be in such condition, these measures are instituted, and the sedimentation index should subsequently be determined as a matter of routine at quarterly intervals, and at other times when there is lack of progress without obvious cause, or when it is wished once more to begin anti-leprotic measures after they have for any reason been discontinued.

The immediate object in treatment, as regards the patient's leprosy, is to expose to dissolution such small numbers of mycobacteria as the patient's general defensive powers can destroy, and to enable specific immunity gradually to develop. In primary neural leprosy, general treatment may be all that is necessary ; but, if not, then anti-leprotic measures are instituted ; extreme care is necessary, or dissemination of *M. leprae* and extension of the disease will result.

In early cutaneous leprosy it is desired to produce very slight and transient evidence of reaction at short regular intervals, manifested by a rise of temperature of a degree or

so associated with appearances of slight activity in existing lesions. This slight constitutional disturbance should, at most, not last more than 36 hours; anything more than this is likely to cause the patient's condition to progress to the second stage. Similar manifestations are desired in the second stage, and injudicious treatment carries with it the risk of further extension of the disease.

In the third stage, that is in Muir's stage of elimination, treatment may be a little more energetic, since a considerable degree of specific immunity has been attained and elimination is taking place; but, even so, care must be taken not to push treatment too hard lest the patient become unduly debilitated.

I have assumed that the patient's leprosy is in the quiescent phase; should the reactionary phase be manifesting itself, then the position resembles that arising from over-energetic treatment; measures appropriate to the quiescent phase are now contra-indicated and those calculated to restore that phase are required.

The treatment of the leper, even when he is in good general condition, is beset with pitfalls. Anti-leprotic measures have carefully to be adjusted to each patient, while any attempt at mass-treatment inevitably leads to failure. The difficulty is to avoid alike the dangers of excess and the uselessness of inadequacy in treatment. Much is done to attain this object by physical examination of the patient, and more if his temperature is regularly recorded and if his erythrocyte sedimentation index is frequently determined; by these means unfavourable conditions are detected and can often be dealt with before they have done much harm.

There is, undoubtedly, much disappointment with the results of treatment. Many failures are due to the fact that the patients concerned have not been, and were perhaps incapable of being restored to such general condition as would enable them to benefit by anti-leprotic measures. Patients who cannot be so restored should frankly be recognised; to submit such to prolonged anti-leprotic treatment wastes the time of those responsible for their care and does them no good; they become very understandably dissatisfied, and their discontent spreads far and wide, causing other and perhaps more hopeful lepers to refrain from coming forward. It is far better to concentrate upon the more promising cases, since every leper whose disease under treatment has undergone arrest is a propagandist whose very presence in a population whose leper-content can as yet

only be guessed at, will encourage the early lepers, who alone respond fairly readily to treatment, to reveal themselves.

Adequate treatment of lepers is time-consuming, and in established leprosy, results are attained but slowly. The hopeful fact remains that an increasing amount of success is being won even in fairly advanced cases, while the more attention is paid to the patient's general condition and all that implies, the greater the probability of arrest of his leprosy.

Surgical Relief of Lagophthamos following Seventh Nerve Paralysis in Cases of Leprosy.

H. H. GASS.

ANYONE working in a leprosy settlement where there are a considerable percentage of N3 cases, is well aware of the distressing ocular conditions resulting from seventh nerve paralysis. The process does not always stop at the irritative stage but often goes on to corneal ulceration, irido-cyclitis, and finally to total destruction of the eye. In the more chronic cases, usually the first sign of corneal involvement is the vascularisation of the lower pole of the cornea. This is in contradistinction to trachoma, which usually shows pannus at the superior pole. Palliative treatment consisting of bandaging the affected eye, or eyes, at night with absorbent cotton soaked with liquid paraffin does give relief. But patients tire of this and get lax in continuing this form of treatment. A more permanent form of treatment is desired.

The operative procedure which we have found of value in Chandkhuri, is the one described in Oxford Looseleaf Surgery," Vol. 4, Part I., page 290, and is called Canthorrhaphy.

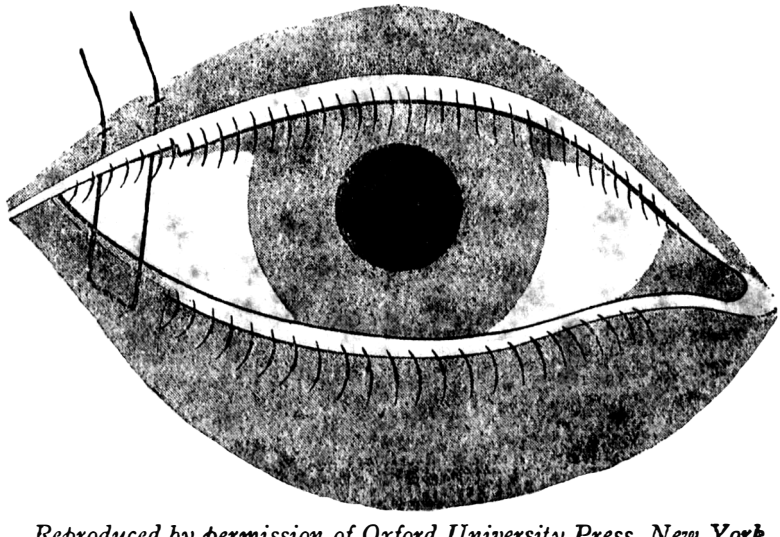
Indication: Paralysis of the orbicularis oculi which prevents the lids from completely covering the cornea.

Preparation: Iodine paint over skin surface of the lower lid which is to be excised. Thorough washing of the eye with corrosive sublimate solution 1—5,000.

Anaesthesia: Two drops of 4% cocaine solution dropped into the eye every five minutes, three times. 1% novocaine solution for skin and subconjunctival infiltration. We find it useful to add a few drops of adrenaline, 1—1,000 solution for the control of bleeding. We first evert the upper lid and inject the portion of conjunctiva which is to be excised

with enough novocaine solution to produce moderate ballooning. The skin area of the lower lid is dealt with similarly.

Operation: Before beginning the operation it is advisable to determine where the new lateral canthus is to be. This point is marked on the upper and lower lids. The upper lid is now everted and an incision 5 mm. deep is made along the intermarginal line and carried out to the lateral canthus. Then an incision sufficiently deep to excise the conjunctiva is carried upwards for about five millimetres, after which it is carried out to the lateral canthus. The incision being in the form of a triangle with its base towards the medial part of the eye, and its apex at the lateral canthus. A similar incision is made over the skin of the lower lid as shown in diagram. It is very important at this time to remove the lash bearing area of the lower lid, which is to be included in the suture. I have had cases in which I failed to be thorough about this procedure with the result that lashes grew again with much discomfort to the patient. The union of the two corresponding raw surfaces is merely the matter of a mattress suture. The suture material which we use is silk. The suture should be armed with two fine eye needles with a full curve. The first needle with suture is passed from the under or conjunctival surface of the lower lid and out through the excised area of skin, then through the raw or under surface of the upper lid to the outside. This procedure is repeated with the needle at the other end of the suture at a distance of about 4 mm. from the point of entry of the first needle. This procedure is illustrated in the following diagram:—



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It is wise to tie the two ends of the mattress stitch over a small ball of cotton so as to avoid cutting into the skin. A short continuous stitch may be taken to approximate the margins of the lids. This is, however, not necessary if there is proper approximation with the mattress stitch. The eye or eyes should be kept bandaged for about ten days. We usually remove the mattress stitch on the twelfth day. The eye may be washed with weak antiseptic solutions after the fourth or fifth day. Of course, the less meddling there is after the operation the less danger there is of non-union of the two surfaces. When dressings are changed, it is important to avoid any pulling or tugging. Before removing the eye-pad it should be thoroughly soaked with warm sterile boric lotion.

The cosmetic result of the operation is better if a bilateral canthorrhaphy is done. It is, however, not always necessary to do both sides.

General Light Treatment of Leprosy.

P. H. J. LAMPE.[1]

IN Netherlands India, special interest has been aroused by a new method of treating leprosy, based upon the diffuse application of ultra-violet light in such a weak dose, that the patients could be treated with those rays for 8 to 10 hours per day. This original method of treatment, by which the entire body instead of the local affected area is intentionally exposed to the light, was used by Dr. Denis Mulder from 1924 to 1929, for individual treatments in Bandoeng and for mass treatment in the leprosy hospital at Pelantoengan, near Semarang.

Although, according to Mulder's plan, the treatment should be continued for three years at least, the mass treatment at Pelantoengan was not prolonged. Nevertheless good results were seen, partly generally, as for example, improvement of the general condition, increase of body-weight, etc., and partly locally, as for example, the disappearance of macules, the levelling of lepromata, noticeable healing of wounds, etc.

These results were published by the promoter of this method of treatment in a monograph, which appeared in the Dutch language. This monograph entitled " Het Kruis der

1 This is a short note on a preliminary report by Dr. Lampe of an investigation by him on the scientific and practical technique value of ultra-violet in leprosy, using Mulder's.—EDITOR

Leprozen " (1930), contains among other particulars a number of photographs of patients before and after treatment, that demonstrate very surprising results, which well deserve further attention.

Under instruction from Government, Dr. Lampe prepared a report (1934) on the scientific value and the practical usefulness of Mulder's treatment.

This report ends with the following conclusions :—

1. *Source of Study and Investigation* : The adjudging of the scientific value and the practical usefulness of Mulder's light treatment of leprosy has been based mainly upon a study of the data, reported in monograph.

2. *Theoretical Basis* : The theoretical basis of the method, founded on personal experience with other tropical diseases, can be formulated as an expectation, that also with leprosy the natural powers of defence of the organism will be activated by stimulation with light, and that the localised symptoms of the disease will be lessened ; the present-day views concerning light-therapy as stimulation-therapy are not contrary to this " expectation."

3. *Technique* : The principle of the treatment and its application depend upon a weak dose of an even, diffuse exposure or total-lighting with artificially produced ultra-violet rays ; this method is, under certain circumstances, applied in mass in a room, suitable for the purpose, where the patient has freedom of movement during the treatment. The purely medical precautions to be taken, individual dosage, desired or undesired individual reactions, etc., are not specified ; it does seem, that with the burners placed at a distance of 2.5 m. such a weak dose is used, that the patients apparently can be exposed without inconvenience for as long as 8 to 10 hours daily, during a series of six days of exposure, with a free interval of 10 to 14 days.

4. *Claims of Priority* : This treatment of cases—called general light treatment by Mulder—is original ; no other application in conformance with that principle is mentioned in the leprosy literature and the " very " weak dosage of light employed is on the whole unusual.

5. *Scientifical Value* : In view of the present stage of the development of the therapy of leprosy and the modern knowledge concerning the possible reaction of leprosy patients to it, a (new) method of treatment is only to be considered

valuable in so far as a regular and conscientious verification has proved the durability of the effect of treatment. Since Mulder did not check his observations in the above sense, before drawing conclusions and publishing them, the publication, *i.e.*, " Het Kruis der Leprozen " can only be called premature, and the data mentioned therein can never be included in the basis of recognition, that the method has scientific value and supplies a need.

6. *Practical Usefulness*: Only in connection with a recognition of scientific value can investigation show whether this value is of more than academic significance and if the treatment in question lends itself to practical application. *A fortiori*, therefore, it holds true, for Mulder's light treatment of leprosy, as described and explained in " Het Kruis der Leprozen," that through a non-recognition of a proven scientific value, a practical usefulness cannot be accepted.

7. *Further interpretation of the effect of the first general light treatment at Bandoeng*: As far as the effect of treatment ascribed by Mulder to light is concerned, one may consider that neither a casual connection between light-treatment and the course of the disease has been shown, nor has real recovery been proven.

8. *Further interpretation of the effect of the mass-exposure at Pelantoengan*: The circumstances under which this mass-treatment took place were bad; nevertheless, good results were observed. The photographically fixed clinical picture of 12 or 13 patients before and after treatment undeniably points to very important improvements, the duration of which, however, was not verified.

9. *Possible significance of the effect of treatment*: The effect of Mulder's general light treatment of leprosy may apparently—waiving differences of degree and as far as the duration of the observation goes—be compared partly with the general effect of tonic strengthening measures, and partly with the local effect of other methods of physical treatment.

10. *Possible " apparent " value of the effect of treatment*: Without further observations, it cannot moreover be excluded, that the results observed by Mulder, for the greater part have a psychic foundation in direct casual connection with the suggestive power of a new therapy, applied with conviction and great enthusiasm.

11. *Further trial desirable*: The omission up to the

present of a further trial of Mulder's general light treatment of leprosy must be regretted, because, on the basis of the known experience, the practical usefulness of the treatment can not be considered to have been excluded or proved.

12. *Publication of this report recommended* : The further trial is thought to be desirable of the general light treatment of leprosy, especially in combination with other methods of treatment.

Final conclusion : Formulated in reply to the question, asked in the Government resolution of 26th November, 1933, No. 1, the final conclusion of this investigation is :—

(*a*) The scientific value and the practical usefulness of the light exposure treatment of leprosy, applied by Dr. Denis Mulder, cannot be judged in any other manner than by the data and explanation furnished by Dr. Denis Mulder, as published in " Het Kruis der Leprozen," second edition ;

(*b*) On the strength of those data and explanations it cannot be determined that that method possesses scientific value or practical usefulness.

* * * *

Under Dr. Lampe's supervision the general light treatment of leprosy will again be tried in Netherlands India on a large scale, along with other methods, in a number of leprosy hospitals. With the idea of stimulating others in other places also to test the value of this method, and to report on it, Dr. Lampe has requested the publication of this summary.

Agent : Ultra-violet rays applied as general light bath ;

Dosage : Regulated in such a way that, placing the burners at a height of 2.5m, the patients can be exposed to the light for 8 or 10 hours per day without inconvenient external reaction.

Scheme of treatment : For example, periods of six successive days of exposure, alternating with free intervals of one to two weeks.

Details : During the treatment efforts should be made to obtain free bodily movement and physical exercise in a general way.

Duration : According to Mulder, at least three years.

Chest Diseases in Korean Cases of Leprosy With Special Reference to Tachycardia

S. H. MARTIN and R. M. WILSON.

(*Preliminary Report.*)

IN the Christmas vacation a special study of diseases of the chest was made at the leprosy colony, 15 miles from Soonchun. The houses of the inmates are arranged in two large crescents facing the South and are built on an elevation overlooking an inland bay. There are 800 inmates housed in about one hundred houses, larger than the average Korean home. These facts must be remembered when we consider the possible effect of environment on the cases to be studied. Their food consists of rice, meal, barley and beans all mixed and cooked together. They get also quite a variety of vegetables, grown in the colony, and meat or fish once or twice a week. The patients in this preliminary report were especially examined with a view to :—

(1) Determining exactly how much pulmonary tuberculosis could be found in patients in Korea suffering from leprosy.

(2) What possible relation there could be between tuberculosis and leprosy.

(3) Amount of lung leprosy.

(4) The effect of chaulmoogra treatment of leprosy with tuberculosis.

(5) Number of deaths due to tuberculosis.

The patients were all assembled at the large church, and all between the ages of thirty and ten were asked to come to the hospital at the colony in regular turn, and others who were suspicious of chest conditions, not included in this group, were picked out by inspection.

The following notes will give a general idea of our findings :—

Laryngeal Involvement.—Some twenty patients, mostly above twenty years of age, were found suffering with leprous involvement of larynx. The appearance was very much like that of tuberculosis. There was ulceration and erosion of the laryngeal wall and posterior pharynx. Three of the cases were so much involved that tracheotomy was necessary, and this was done at the time, the patients receiving immediate relief. One of these patients was completely deaf and blind, with complete loss of hair all over the body and marked nodules all over the face.

Breast Changes.—A number of cases were noted with

abnormal mammary development. These cases invariably showed a tendency to female secondary characteristics, *viz.*, enlarged breasts, female distribution of pubic hair, female fat distribution over pubis. All of this was due to atrophy—more or less marked, of the testicles. Most of these cases are sterile and have lost sexual power. Women were not so affected.

Scars of various kinds were seen on the chest due to old abscesses and burns, when the patient could not feel heat due to anæsthesia of skin and to broken down nodules.

Palpation of the neck often showed some fibrosis tissue spread from nearby cervical glands, causing an increase of vocal fremitus which was not due to lung changes.

In those examined, definite tuberculosis was found in only seven cases—all of whom were males.

All of these cases probably had tuberculosis when they entered the colony, and only one boy of fourteen, who had been in the colony a year, showed a lung lesion, and his sputum was negative for tuberculosis. He has been having chaulmoogra treatment. The other six cases showed quite definite tuberculosis, two of them in the second stage of the disease with cavitation, and one with probable intestinal involvement. These cases had some lung involvement before entering the colony.

We can therefore say that out of the 800 cases in this colony there are only seven suffering from tuberculosis of the lungs, and of these cases all but one brought the disease with them to the leprosarium. This means that the percentage of tuberculosis is less than 1 per cent. in this colony, which is less than in the average Korean village.

The reasons why there is so little tuberculosis in this colony are :—

(1) The healthy site of the colony.

(2) The industrial and farming work which keeps most of the patients out all day in the fresh air and sunshine.

(3) Good food and the excellent sanitary condition of their houses.

(4) Practically all of them have had treatment by chaulmoogra oil, which has been proved a benefit in tuberculous cases.

There are three main types of leprosy. In Korea we have not so many of the nodular type, but more of the neural and maculo-neural types. In the Philippines, death due to tuberculosis was as high as 45 per cent.[1], being marked in the nodular type. The Director of our Pathology department, Dr. I. S. Yun, says that in the post mortem

findings at this and other hospitals, the lungs were not found involved as much as the intestines, messentery, and lymph glands.

While the main idea of the study was to see how much tuberculosis was present, we were exceedingly surprised to find a very large number of cases of *tachycardia*. At first we thought it was due to nervousness, but these patients with hearts beating at 130-150 per minute, ten minutes to one half hour later—would be almost as fast—120-140 beats per minute. There were four cases of definite mitral stenosis and one of myocarditis.

These thirty rapid pulse cases showed no signs of tuberculosis, exophthalmic goitre, neurasthenia, beri beri, influenza, alcohol or tobacco poisoning. There were no signs of heart failure and only in ten cases were there definite murmurs present. Two showed a marked increase in the mitral second sound. There were a number of cases that had kidney involvement which seems a fairly common complication in leprosy; in these cases heart involvement could be expected. Nearly all of the kidney cases were in the far advanced stages of leprosy. Heart involvement is not unknown in leprosy. The Culion Leper Colony reports 23 per cent. of their autopsy cases as having died from heart dilatation, etc.[2]

The leprous involvement of ulnars, frontal and peroneal nerves is well-known—also of optic neuritis and destruction of that nerve, but the possibility of the involvement of the vagus and other nerves of the autonomic or entero fector nervous system has been up to the present not an important question. In my study of heart lesions in 500 beri beri heart cases I have found many cases of vagus nerve pathology causing tachycardia, which, however, is different from that found in leprous lesions. In lesions of motor and mixed nerves (extro fector nerves) in leprosy we find them greatly thickened, with granulomatous cords and giant cell formation which may break down into caseation,[3] and in other cases we find evidence of vacuole degeneration.

After careful elimination of all causes, we believe that the tachycardia that we are finding in the leprous cases in Soonchun, Korea, to be due to an inhibition of the vagus or pneumo-gastric nerve. The final proof is by post mortem examination, which has not been done on any of the cases of leprosy in this colony as yet, but at the first opportunity we plan to obtain specimens of these nerves from patients showing this heart condition and report on the same.

NOTE.—March 1st: Within the last two months the

heart rate of these tachycardia cases has not changed.—(S.H.M.).

NOTE.—June 1st: Re-examination shows the heart rate unaltered.—(S.H.M.)

REFERENCES.

(1) Report of "Culion" Leper Colony, Philippines. (*Leprosy Survey*).
(2) The same.
(3) Muir, E. and Chatterji Sin. "Leprous Nerve Lesions." (*International Journal of Leprosy*), 1933, Vol. 1, No. 2.

A Note on the Action of Chaulmoogra (Hydnocarpus) Preparations on *M. Leprae Muris*

JOHN LOWE.

(*Reprinted from "Leprosy in India," April,* 1934.)

WE seek in this note to examine the grounds for the common belief that the preparations of chaulmoogra and hydnocarpus oils have an inhibitory and bactericidal action on *M. leprae,* to point out how unsatisfactory is the evidence on which the belief is founded, and to describe certain experiments which do not support this belief. This note is therefore mainly destructive criticism, but we hope it may help in clearing the ground for a more rational view of leprosy treatment.

Chaulmoogra oil inunction was used empirically for many centuries in the treatment of leprosy. According to Tomb (1933) injections of the oil were first given by Tourtoulis Bey in 1894; the ethyl esters of the oil were first used by Engel Bey about 1908; sodium salts of the fatty acids were made by Moss in 1879 and were used orally from 1891 and by injection from about 1912. All these developments were purely empirical, and the first work done in investigating the action of these preparations on *M. leprae* was done by Walker and Sweeney (1920). They investigated the action of soluble preparations of chaulmoogra oil on acid-fast bacilli in a liquid culture medium (glycerol-veal broth). They found that the presence in the medium of the sodium salts of the total fatty acids of the oil in high dilutions (up to 1 in 75,000) inhibited growth and made subculture impossible. The acid-fast bacilli used were "*B. leprae muris* (*Hollmann*)" and "*B. leprae hominis* (*Levy*)" in addition to *B. smegmatis,* and the bacilli of human, bovine, and avian tuberculosis. They considered that these findings indicated the antiseptic and bactericidal

activity of chaulmoogra oil on the acid-fast group of organisms. This activity was found to be one hundred times greater than that of phenol.

There are various criticisms which may be made of this work. Firstly, the cultures of leprosy organisms which Walker and Sweeney used, are not generally accepted as genuine. In fact, "*B. leprae muris (Hollmann)*" was considered by Hollmann himself (Currie and Hollmann, 1913) as being not a true culture but a contamination. Secondly, the impossibility of subculture is not a sound criterion of death of the bacilli. A far sounder criterion would be the failure of the bacilli to produce the disease when injected into susceptible animals. Walker and Sweeney attempted to demonstrate this with *M. tuberculosis*, but their results were, in our opinion, inconclusive.

This work of Walker and Sweeney stimulated other work of a similar kind. Such work is reported by Schobl. (1923 and 1924) who confirmed Walker and Sweeney's findings; his work is open to the same criticism that we have made of Walker and Sweeney's work. Recently Cummins and Weatherall (1933) investigated the action on *M. tuberculosis* of *Alepol*, a preparation of a selected fraction of the lower-melting-point fatty acids of hydnocarpus oil. They found that the presence in Besredka's fluid egg medium of alepol in a dilution of 1 in 1,000,000 inhibited growth; after thirty-five days material from the culture tube was injected into a guinea-pig which was sacrificed nine months later and showed no disease. A control tube of the same medium showed growth which, when injected into a guinea-pig, caused general tuberculosis. A similar result was obtained in a second experiment. Attempts to treat rabbits suffering from experimentally induced tuberculosis by intravenous injections of alepol gave inconclusive results.

The work of Walker and Sweeney, while it is suggestive of a bactericidal action of chaulmoogra preparations on *M. tuberculosis*, fails to prove any bactericidal action on *M. leprae*, for they were almost undoubtedly not dealing with *M. leprae* or *M. leprae muris*. We therefore fail to see what grounds they have for the statement :—" These facts supply a scientific basis for the use of chaulmoogra oil and its products in leprosy." The acceptance of this statement makes necessary three assumptions: (1) that the hydnocarpus preparations have an inhibiting and bactericidal action on *M. tuberculosis* in vitro; (2) that because *M. leprae* and *M. tuberculosis* are similar in structure and staining properties, the action of hydnocarpates on both

these organisms is the same, and (3) that the action of hydnocarpus preparations in vivo is the same as in vitro. While the first assumption may, on the evidence available, be considered a possible one, the second and third assumptions are mere guesses and based on no sound evidence.

Before expressing any definite opinion regarding the action of hydnocarpates on *M. leprae* in vitro, we must obtain evidence regarding their action on genuine *M. leprae*, using the method of injection of treated bacilli into susceptible experimental animals, in order to investigate whether the treated bacilli are alive or dead. We have no satisfactory method of culturing *M. leprae*, but since we can obtain large numbers of bacilli from the nodules of leprosy patients, this difficulty can be overcome. There still remains, however, the insuperable difficulty presented by the fact that we have no experimental animal susceptible to human leprosy. Therefore the action of hydnocarpus preparations on *M. leprae hominis* cannot be properly investigated at present.

With rat leprosy, however, the major difficulties disappear. We can get enormous numbers of *M. leprae muris* from the tissues of infected rats, and we have in the rat an animal highly susceptible to this organism. We have therefore been able to carry out a careful investigation of the action of hydnocarpus preparations on *M. leprae muris*, and the results of this work we report here. We should be quite clear, however, that since the relation between *M. leprae* and *M. leprae muris* is undetermined, we do not know whether the results of these experiments can be interpreted as indicating what is the action of the hydnocarpus preparations on *M. leprae hominis*.

Experiment 1.

A rat in the advanced stages of rat leprosy was sacrificed and portions of the spleen and liver were emulsified in normal saline. To different lots of the emulsion was added sodium hydnocarpate (the sodium salts of the total fatty acids of hydnocarpus wightiana oil) in dilutions 1 in 200, 1 in 2,000, 1 in 20,000, 1 in 200,000, and 1 in 2,000,000. The emulsions showed large numbers of acid-fast bacilli. The various emulsions were kept at room temperature for three hours. At the end of this time some of the treated bacilli were injected into rats. (With the lower dilutions the sodium hydnocarpate was washed out before the bacilli were injected into rats.)

In all, 32 rats were used, five lots of four rats being

inoculated with bacilli treated with five different dilutions of sodium hydnocarpate and twelve control rats being inoculated with untreated bacilli.

Of the experimental rats, three died in the first month, showing acid-fast bacilli in the tissues. These we will ignore. The remaining 17 all lived for three months or more and at death all showed a generalised infection with rat leprosy.

In connection with the interpretation of post-mortem findings we would point out that the findings of a few acid-fast bacilli is no proof that the animal has rat leprosy. Bacilli may be found for more than a year after the injection of killed bacilli. The presence of a progressive systemic infection, with very large numbers of multiplying bacilli, is the criterion we use in all our rat leprosy work.

Experiment 2.

In a similar way bacilli were treated with a 5% solution of sodium hydnocarpate, for periods of 3 hours and 20 hours, and were then injected into rats. Control rats were injected with untreated bacilli.

Of four rats injected with bacilli treated for three hours, all developed a generalised rat leprosy infection.

Of seven rats injected with bacilli treated for 20 hours, all developed a generalised rat leprosy infection, but in several of them the development of the disease was much retarded.

Experiment 3.

Eleven rats were injected with bacilli treated with 5% sodium hydnocarpate for three hours. Four died within two months. The remainder lived for three months or more, and all showed a massive general infection with rat leprosy.

In our experience the only fact suggesting a bactericidal action is that in a few rats injected with bacilli treated with 5% sodium hydnocarpate acting for 20 hours, a generalised rat leprosy did not develop till very late, while in all rats injected with bacilli treated with the same dilution of sodium hydnocarpate for three hours, generalised rat leprosy developed fairly quickly. This suggests that the time factor may be of importance, and that even weak dilutions might kill the bacilli if longer time were allowed. Even if this is so, we have to be sure that such bactericidal activity is peculiar to hydnocarpus preparations, and is not due to a simple soap action. We are therefore making further experiments, treating bacilli with sodium hydno-

carpate in various dilutions for long periods before injection into rats, and using as controls rats injected with bacilli similarly treated with sodium oleate. One such experiment has already shown little or no difference in the bactericidal powers of these two preparations.

If we compare our results with those reported by Walker and Sweeney we see a great difference. According to our experiments, even 5% sodium hydnocarpate acting for 20 hours did not give a complete bactericidal action while, according to Walker and Sweeney, a supposed culture of *M. leprae muris* was killed by a dilution of 1 in 75,000 acting for 24 hours. The reasons for the difference we judge to be (1) we were dealing with true *M. leprae muris* direct from the tissues of an infected rat, while Walker and Sweeney were using a culture of a bacillus of doubtful nature isolated from rat leprosy material many years previously, (2) the criterion of death of bacilli used by Walker and Sweeney was failure to grow in subculture. We used the test of pathogenicity in susceptible animals.

We cannot help feeling that our results are more reliable than those obtained by Walker and Sweeney.

Conclusions.

We are led to the conclusion that up to the present no conclusive evidence has been obtained of any special inhibiting or bactericidal activity of sodium hydnocarpate on *M. leprae muris* in vitro. We believe that " the scientific basis for the use of chaulmoogra oil and its products in leprosy " provided by the work of Walker and Sweeney is unsound.

The apparent lack of bactericidal activity of sodium hydnocarpate on *M. leprae* in vitro does not prove that it has no effect in vivo. Quinine does not kill malaria parasites in vitro, emetine does not kill *Entamoeba histolytica* in vitro, antimony does not kill *Leishmania donovani* in vitro, yet the efficacy of these preparations in treatment is established. We should note, however, that these are delicate protozoa, the killing of which is a very different matter from the killing of an extremely resistant acid-fast bacillus, such as *M. leprae*. *M. leprae muris* can be treated with 5% sulphuric acid for several hours and still remain viable (Marchoux and Chorine, 1932).

We think it is unlikely that hydnocarpus preparations have any special inhibitory or bactericidal action on *M. leprae* either in vitro or in vivo. Nevertheless we believe that hydnocarpus preparations are valuable in leprosy

treatment. The action is probably indirect. If this is so, the proof of the efficacy of any preparation is to be obtained only by accurate observation of the results of treatment of patients. In such a chronic disease as leprosy this is not easy, but under the circumstances it is probably the nearest we can get to a scientific basis for the use of hydnocarpus or any other preparations in treatment.

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Trypan Blue in the Treatment of Leprous Eye Lesions.

E. MUIR and S. P. CHATTERJI.

(*Reprinted from "Leprosy in India," January,* 1934.)

INFECTION of the eye-ball, especially when complicated by lepra reaction, is perhaps the most painful and distressing condition caused by leprosy. Sometimes the leprous condition will heal up, but leave the patient blind. It is therefore very important that in every case of cutaneous leprosy the eye should be carefully and repeatedly examined under atropine to find out if there is any involvement or not. The early signs of ocular involvement are :—(1) Failure of the pupil to dilate fully and symmetrically on the application of atropine ; (2) Thickening or congestion of the bulbar conjunctiva ; (3) Involvement of the cornea, in the form of a pterygium-like growth, nodule or interstitial keratitis ; (4) Redness or photophobia. If there are signs

of active disease, atropine should be given at least once a week, after excluding the presence of high intra-ocular pressure.

Many remedies have been tried in the treatment of eye lesions. Dizon (1930) recommends subconjunctival injections of adrenalin and atropine to break down early adhesions of the iris. Wood (1925) mentions benefit, such as he had not seen before, in one case which he treated by injecting 1 per cent. sodium taurocholate with 1 in 2,500 bicyanide of mercury dissolved in 2 per cent. saline. Other workers (Hoffmann, 1927) obtained good results with krysolgan and other gold preparations.

Kirwan (1927) recommends for corneal infiltration due to leprous granuloma and associated with the growth of new blood vessels, a complete peridectomy, resecting a piece of conjunctiva down to the sclera. He states that this operation produces excellent results and often prevents extension of the disease. In cases in which the pupil is prevented from dilating by posterior synechiæ, Kirwan recommends a broad optical iridectomy. He has performed this operation in many cases, all of whom got a temporary improvement in sight, but in the majority of cases the results have been disappointing. In many of the cases the ciliary infection lit up afresh with the formation of plastic exudation in the new pupil. On the other hand, vision was considerably improved in a number of cases.

But in our experience, while many of these remedies give a certain degree of temporary relief, none of them can be relied upon to control the inflammation.

Recently we have been using trypan blue injections at the Gobra Leprosy Hospital with excellent results. Two methods have been used in its administration, viz. (*a*) 0.1 per cent. solution in normal saline injected subconjunctivally, sufficient being given to balloon the conjunctiva; (*b*) 1 per cent. solution in normal saline intravenously, 3 to 20 c.c. being given once or twice a week according to the tolerance of the patient. It is well to use Grübler's preparation, and the solution should be fresh.

The intravenous method can only be used for a limited time, as trypan blue has a selective action for leprous granuloma; and when a certain concentration is reached, the cutaneous lesions begin to ulcerate and gastro-intestinal disturbances appear in many cases. Trypan blue is not eliminated by the kidneys, and it takes a considerable time to be eliminated from the body. When, therefore, there is a concentration in the skin lesions sufficient to begin to cause

ulceration, intravenous injection of this drug should cease and only small doses (3 or 5 c.c. of the 1 per cent. solution) be given once a week. Some patients are rather sensitive about the colour of the skin produced by trypan blue, but are reassured when they find that the blue colour is not permanent. Intravenous injections of trypan blue are valuable in leprosy for other reasons, but we shall not refer to these in this paper.

The other method of giving trypan blue, viz., subconjunctivally, seems to be simpler and, as far as our limited experience goes, equally effective. Such injections may be repeated if necessary at intervals varying from one to two weeks according to the condition of the patient's eye.

The following is a complete list of the cases treated and the results obtained :—

(1) L. R. Type C.3 ; pain and inflammation in both eyes. He was given one injection subconjunctivally in the right eye and five in the left eye. Pain and inflammation subsided immediately after the first injection and never came back again.

(2) Godadhar. Type C.3 ; right pupil fixed and pain does not react to light ; the left eye shows irregular dilation of pupil. Ten injections of T. blue 2—5 c.c. were given intravenously. He was given one injection into the right eye subconjunctivally and two in the left eye. The patient was in constant pain due to his eye inflammation. After T. blue the pain has gone and the vision is slightly improved.

(3) Gorai. Type C.3 ; right pupil occluded, left pupil showed a small aperture in the lower and outer sector ; there was pain and inflammation and very hazy vision. Three subconjunctivally injections of T. blue were given into the right eye and two into the left. The vision of the left eye has much improved and the inflammation has subsided. There was no marked improvement of vision in the right eye, but the pain is less than before.

(4) Surendra Das. Type C.3 ; right pupil slightly irregular in shape, both pupils react to light. There was pain, redness and irritation. Two subconjunctival injections of T. blue were given in the left eye, after which pain and inflammation subsided.

(5) Jamiruddin. Type C.3 ; there were pain, redness, and irritation ; right pupil irregular with slight reaction to light, left pupil quite fixed to light and irregular in shape. Three injections were given subconjunctivally into the left eye. Pain and inflammation is very much less.

(6) Bhaskar. Type C.3 ; with the right eye he can just count figures ; left pupil is fully dilated and oval in shape. There was acute pain and inflammation which became less during 14 intravenous injections of T. blue and two subconjunctival injections.

(7) Mohapatra. Type C.3 ; leprous nodule in the right cornea and constantly suffering from painful eyes. Since giving two injections of T. blue into the right eye he is almost free from acute pain and inflammation and vision has improved.

(8) Upendra Mondal. Type C.2 N.3 ; this patient cannot close his right eye and had in consequence constant pain and irritation. After one injection of T. blue subconjunctivally into the right eye the pain and redness have gone, and he says that his vision has improved.

(9) Rajendra Chatterji. Type C.3. The patient had cataract in both eyes. After operation iritis set in. He had constant pain and inflammation, especially in the right eye for some years. After five injections of T. blue into the right eye and one into the left, pain and watering have ceased and redness is less. There is also disease of the lids, which has so far prevented complete recovery.

(10) A. Bhasker. Type C.2; there was acute inflammation of the right eye. All pain and inflammation have subsided after one injection of T. blue subconjunctivally.

(11) Gokul Saha. Type C.2; this patient was admitted with acute inflammation of the right eye and severe pain in the head. Atropine, etc. failed to give relief. One injection of T. blue subconjunctivally removed all pain and irritation.

While trypan blue is not an infallible remedy in the treatment of all leprous eye conditions, it is certainly superior in our opinion to the many other remedies we have tried. Even in Case No. 8, with the other type of eye lesion caused by paresis of the lids and anæthesia of the cornea, it was of great value. In the series of eleven cases, without a single exception, there was partial or complete relief from pain, and improvement of vision.

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The Editor, "Leprosy Review."

DEAR SIR,—Knowing that you believe in giving credit where credit is due, I venture to call your attention to a reversal in this respect in your editorial on the "leprolin" skin test, in the April number of LEPROSY REVIEW. You speak of the Hayashi test, and say that it was originally described by Bargehr and developed by Mitsuda (sic !) and Hayashi. It is to be noted that the title of Hayashi's article on the test in the first number of the *International Journal of Leprosy*, last year, was "Mitsuda's skin reaction in leprosy," so he does not claim it himself.

In that article he stated that Mitsuda had first reported on it in 1916 in the *Japanese Journal of Dermatology and Urology*. A fact easily verified is that Mitsuda described it at the last (third) International Conference on Leprosy, which was held at Strasbourg in 1923. His report, which is brief but adequate, is to be found on page 219 of the transactions of that conference. That volume, by the way, should be in the library of every leprologist and can be procured from J. B. Bailliere et Fils, Paris, or from Professor Marchoux, of the Institute Pasteur, who was secretary of the conference. To return to the skin reaction, the earliest reference that I have found to anything by Bargehr on the subject is 1925. I am, yours, etc., H. W. WADE, M.D.

Reviews.

"INTERNATIONAL JOURNAL OF LEPROSY," Vol. 1, No. 4. October, 1933.

Dr. Keil, of Leprosy Polyclinic, Paramaribo, writes on the importance of nutrition in the prevention and cure of leprosy. This article emphasises the well-known fact of the importance of diet in leprosy and appends the diet used in the Polyclinic School. The authorities are fortunate in being able to put the children on such a diet. Many of the institutions in the tropics would find such a scale not only financially impracticable, but impossible during many months of the year. However, there is a temptation to sacrifice quantity for quality, and the diets used in Surinam should be of value as a basis in the regulation of the diets elsewhere.

Dr. Denney, of Carville, contributes an article on the work of the United States National Leper Home. This article reviews the work of the Technical Services, the Dermatological Service, Ear, Nose and Throat, Neuro-psychiatric, Orthopædic, Dental, Laboratory, X-ray, Nursing and Dietetic Services. The whole article reflects the immense work which is undertaken and demonstrates the efficient way in which this home is organised.

Dr. Muir contributes the second of the reviews which are to appear on the "Treatment of Leprosy." This is a contribution which covers some fifty pages with bibliography of 257 references. The review is one of the most exhaustive which has ever been done and is of immense value. No attempt will be made to summarise it as readers are advised to consult the original article.

Dr. Robineau writes on leprosy in French West Africa, giving a summary of publications during the past thirty years.

The reprinted articles include a condensation of Dr. Ryrie's contribution to the Transactions of the Royal Society of Tropical Medicine and Hygiene (1933). A condensation of an article by Denney & Eddy, which appeared in the archives of Dermatology and Syphilology (1933), on the *in vitro* behaviour of lepra and certain other acid fast organisms in the presence of leukocytes. The following is a summary given by the authors :—

"Acid-fast bacilli in Tyrode's solution have been subjected to rabbits' leukocytes from peptone pleural effusions.

"Bacilli of the tuberculosis group proliferated readily in the presence of both living and subsequently dead leukocytes. Phagocytosed bacilli proliferated until the death of the phagocyte. Both intra- and extracellular colonization produced irregular stellate clumps.

"Bacilli of the non-pathogenic group proliferated readily, but were not greedily phagocytosed. Colonization was predominantly extracellular, and the colonies were irregular and often stellate.

"Of the bacilli cultivated by others from lepers, eleven strains were distinctly attracted to the leukocytes; fourteen were not. With the former, intra-cellular proliferation continued until eventually the phagocyte was ruptured. The latter grew principally extra-cellularly, and when phagocytosed appeared not to proliferate rapidly, if at all.

"Rat leprosy bacilli were readily phagocytosed, as single rods and small clumps. Within the cell proliferation continued until the phagocyte was distended to the point of rupture, the intracellular growth sometimes being dense and distinctly globular. Extra-cellular colonies progressively increased in size and some of the dense, spherical masses were indistinguishable from globi.

"Leprosy bacilli and globi obtained from an incision in a nodule

showed chemotactic affinity with the rabbits' leukocytes, but no proliferation of the single rods or increase in the size of the globi.

" Pus from leprous abscesses also underwent phagocytosis. There was no definite increase of free bacilli, but a definite increase in the number and size of globi. Subsequent additions of fresh leukocytes appeared to cause a progressive increase in the size of the globi, and the formation of additional small ones ; this formation of new globi apparently ceased when free organisms were no longer present in the suspension."

" CUTANEOUS SENSITIVITY TO ACID-FAST BACILLI IN SUSPENSION," Prof. S. L. CUMMINS, LL.D., M.D., and ENID M. WILLIAMS, M.D. (*British Medical Journal*, April 21st, 1934).

This article was prepared as a result of a suggestion of Muir's as to whether healthy adults in countries where leprosy is no longer endemic react to Mitsuda's Leprolin Test in the same way as non-leprous adults in India. To perform this test, twenty-five non-tubercular male adults at the Cardiff City Mental Hospital were chosen, and for sake of comparison each patient was tested both with " leprolin " and an intracutaneous innoculation of 0.1 c.c. of tubercle bacillary suspension equivalent to 10 million dead bacilli. In addition, to see how tuberculous patients reacted to a tubercle bacillary suspension, it was decided to test the same suspension diluted so that 0.1 c.c. contained one million bacilli only, and five adult males with relative chronic pulmonary tuberculosis and three children with non-pulmonary lesions were chosen. The following is the summary of observations by the authors :—

" The factors determining the responses noted to the intradermal inoculation of heat-killed acid-fast bacillary suspensions in persons free from the signs of clinically active tuberculosis call for further study, and can only be discussed as a part of the larger subject of bacterial hypersensibility. Here it will suffice to summarise the points brought to light in the series of observations described.

" 1. The typical reaction to tubercle suspension resembles the typical intradermal tuberculin reaction in reaching its maximum on or about the third day. It differs from the tuberculin reaction in persisting longer and showing a tendency to late central necrosis. The writers have noted central necrosis as a rare occurrence after intracutaneous tuberculin tests, but these have been marked at the third day at the height of the reaction, whereas the central necrosis caused by bacillary suspension comes on as the initial inflammatory reaction is fading.

" 2. The typical reaction to leprolin (suspension of heat-killed leprosy bacilli and leprous tissue), when applied to healthy persons in an area free from endemic leprosy, differs from the intracutaneous tuberculin reaction in remaining for some days negative or doubtful, gradually developing to a maximum between the eighth and the fifteenth day, and lasting on for from four to six weeks as a diminishing zone of inflammatory oedema, often showing late central necrosis.

" 3. Six out of twenty-five persons tested with leprolin reacted to the injection in a manner similar to the usual response to intracutaneous tuberculin or to tubercle bacillary suspension, showing that they were hypersensitive to a bacillary antigen to which, presumably, their tissues were " virgin soil." This result suggests that " group " sensitivity must play a definite part in reactions to acid-fast bacillary constituents.

" 4. It is of interest that, in two probably non-tuberculous children tested with intracutaneous tubercle bacillary suspension, no reaction was observed either late or early, the bacilli being disposed of without inflammatory response."

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