

# LEPROSY REVIEW.

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## Editorial.

**A**MONG the series of articles in this number of the REVIEW, the one which will cause more than unusual comment is that entitled "Results of the Chaulmoogra Treatment in Very Early Cases of Leprosy," by no less an authority than Dr. Rodriguez, who is in charge of the skin clinic at Cebu in the Philippine Islands. The statement that "it does not necessarily follow that the earlier the case the better the results as far as treatment with chaulmoogra oil is concerned" is not only a startling one, but is one which will cause most of those who have given much thought to the therapeutics of leprosy furiously to think. We have more than once suggested that we feel that the best results, as far as the chaulmoogra derivatives are concerned, are seen in the early cutaneous cases showing signs of activity. Further, we have stated elsewhere that "because a child has signs of a leprotic infection it is not a *sine qua non* that it needs immediate treatment."\* By treatment is meant treatment by chaulmoogra derivatives. The facts laid down in this article seem to be beyond any reasonable doubt, but the explanation of these facts raises the whole question of the life history of the *Mycobacterium leprae*. Many workers hold that the organism of tuberculosis consists of three forms :—

- (1) Acid-fast rods.
- (2) Much's granules, also acid-fast.
- (3) Non-acid-fast granular forms.

Others go so far as to say that there is a mycelial form of the bacillus of tuberculosis, and still others state that the bacillus of tuberculosis in one phase is a filter passer. If any of these theories is proved for the organism of tuberculosis, then there would appear to be no reason why similar phases should not exist in the life of the *Mycobacterium leprae*. We have felt for some time that the *M. leprae* in many of its aspects can be looked upon as a cellular parasite, and if this is the case then, as with other parasitic diseases, a symbiosis tends to be set up between the parasite and its host. It is well known that specific therapeutic remedies, in the case of parasitic diseases, are apt to fail. This article, we feel sure, explains to some extent the many apparent failures of the chaulmoogra treatment, and will stimulate thought. We feel that it is more than ever being realised that the solution of the problem of treatment in leprosy will be found in the metabolic process of the body,

\* Leprosy Survey of Ceylon, 1933.

or, as Muir some years ago pointed out, it is the nature of the soil that causes the spread of the disease in the body, and until the causes that affect that factor are studied more closely, the successful treatment of leprosy is an impossibility in many cases. We still subscribe to the fact that the chaulmoogra derivatives are our stand-by, but the day has passed when we can consider them to be specific or effectual in every case, even in early cases. We may need to modify our statements concerning the necessity for the insistence on chaulmoogra treatment in early cases, and possibly confine this form of treatment more particularly to a certain group, especially those in which the bacillus is obviously in the well-known recognisable form. It seems evident that this remedy acts in some way on this form, but the factor of counter irritation appears also to be an important one. Take away this latter factor and the efficacy of the chaulmoogra remedies seems to be correspondingly diminished. Muir has also stressed this point.

Let us continue the search for better remedies but let us not forget that our most efficient remedies, still are the derivatives of hydnocarpus oil, and that these cannot be put into the limbo of forgotten things. We would strike this note of hopefulness—that while our ideas concerning specific treatment are apparently in the melting pot, we have never been more convinced of the value of leprosy work and the possibility of the control of this scourge than we are to-day. We must keep our vision clear, not letting our enthusiasm for treatment blur our view of prevention, or be so obsessed by apparently unfavourable reports that we lose our faith in the efficacy of all treatment. We plead for a sane outlook so that our view of the problem may be complete, and no part of the picture be out of focus because one aspect of the problem is stressed at the expense of another.

Dr. Moiser's article and report are full of interest, and it is refreshing to find the note of optimism contained therein. These two articles are not contradictory, but complementary, and it is only by seeing every side that we can ultimately attain unto a more perfect understanding of this most puzzling of human scourges.

The article on "Examination of Bone Marrow for M. Leprae," by Dr. Gass, reprinted from *Leprosy in India*, shows how completely the reticulo-endothelial system is invaded. We feel that the further study of the drugs affecting this system may lead us to the solution of the therapy of leprosy.

## Results of the Chaulmoogra Treatment in Very Early Cases of Leprosy.

JOSE RODRIGUEZ.

WHEN in 1925 we started treating individuals with incipient *bacteriologically negative* lesions, consisting of macules and localised anaesthesia, we expected that such cases, being early, would prove very amenable to the treatment. As a matter of fact, we felt confident that a considerable percentage of them would perhaps be definitely cured by the injections. These expectations were based on the results of our treatment obtained in many early *bacteriologically positive* cases whose cutaneous lesions cleared up rapidly following a series of injections with the iodised ethyl esters of chaulmoogra oil.

To-day, after a lapse of nine years, during which time most of our cases had been followed up even after apparent disappearance of the macules and the anaesthesia, we are no longer so sure that the chaulmoogra treatment is effective in this very early stage. On the contrary, it is perhaps useless, but as will be seen later in this paper, we are not yet in a position to discard this treatment entirely. We feel that a much larger number of cases than we have studied will have to be observed for a longer period of years before definite conclusions regarding the matter can be arrived at.

It became apparent early in the work that there was need of adopting a more dependable criterion for determining the efficacy of the treatment than by merely noting the changes in the size, number, appearance, nature, etc., of the leprotic lesions. This subject is dealt with in another article, which will be submitted to the Editor of the *LEPROSY REVIEW*, so that it need not be discussed here. Suffice it to say that in our opinion, the best criterion would be to observe the proportion progressing to the bacteriologically positive stage, both in treated and the untreated or trivially treated cases over a period of years. In other words, if a certain treatment were really efficacious, the treated cases should become truly "arrested," *i.e.*, none, or only very few, should become bacteriologically positive as compared with the number becoming positive in the control group.

We have studied two different groups of these early cases, totalling about 500 patients in all.

1. Three hundred and thirty-six children of leprous parents born in the Culsion Leprosy Colony previous to 1924,

followed for five years, during which treatment with iodized ethyl esters was intensively given to some, and none or hardly any to others. It must be stated, however, that the intracutaneous or "plancha" method was not employed in these children. (*Phil. Journ. Sci.*, 1932, Vol. 47, No. 2, pp. 245-258.) In this group, the proportion becoming positive among those receiving adequate treatment was about the same as among those who had received none or only trivial treatment. It was concluded in this study that the drug treatment as a rule was not effective in the "suspicious" or "prodromal," and the early "clinical leper" stages, but that its effects became more manifest when the organisms have appeared in their typical form in the lesions.

2. The second group consists of 225 out-patients of the Cebu Skin Dispensary, studied with Dr. Fidel Plantilla, for periods ranging from seven months to five years. In this group, the results of the special treatment seem to be more favourable, as can be judged from the following table:—

EFFECT OF TREATMENT WITH IODISED WIGHTIANA ETHYL ESTERS IN  
"CLOSED" CASES OF LEPROSY.

Duration of Treatment.	REGULARITY OF TREATMENT. (Percentage of expected number of injections actually received.)								
	0—60%			61%—100%			TOTAL.		
	Cases	Pos.	%	Cases	Pos.	%	Cases	Pos.	%
0—12 mo.	23	3	13	19	0	0	42	3	7.1 ± 3.96
13—24 „	40	4	10	10	1	10	50	5	10.0 ± 4.24
25—36 „	45	6	13.3	9	0	0	54	6	11.1 ± 4.27
37—48 „	60	14	23.3	14	2	14.2	74	16	21.5 ± 4.78
Over 48 „	5	1	20	0	0	0	5	1	20.0 ± 17.97
TOTAL ..	173	28	16.18	52	3	5.77	225	31	13.7 ± 2.16

In the above table, patients receiving less than 60 per cent. of their expected number of injections were considered inadequately treated; those receiving more than this amount were considered to have been treated regularly or adequately. It is seen that 16.18 per cent. of 173 receiving irregular treatment had become positive bacteriologically, while only 5.77 per cent. of those receiving adequate treatment became positive. The difference in percentage between the two groups ( $10.41\% \pm 2.88$ ) is statistically significant. In this out-patient group, therefore, the

results are undoubtedly in favour of the properly-treated group.

However, there is no direct correlation between duration of treatment and the percentage becoming positive. Even less became positive of those who have been treated less than one year than of those who have been treated from 35 to 36 months, although the difference is not statistically significant. There are too few of those who have been treated over 48 months to permit even tentative conclusions.

Moreover, we know that most of those who had been able to receive 60 per cent. or more of their injections, were better off financially than the rest, and could thus afford the transportation expenses necessary to report to the clinic weekly for treatment regularly. Furthermore, they naturally have been under our continual influence and care, while those seldom reporting did not get the benefits of medical advice of general nature. At almost every visit to the dispensary, these patients asked for and were given advice as to food, cleanliness, treatment of skin diseases and intercurrent illnesses, etc. Finally, these were too few cases observed properly so far, only 52 of them having received adequate treatment.

Summarising the results of the treatment in the two above groups of patients with incipient leprosy, totalling about 500 cases, observed for periods ranging from seven months to five years, we regret to have to admit that at the present time our experience is not yet sufficiently extensive to allow definite conclusion on this very important subject. However, we know now that the results have not come up to our original expectations. There is also very little doubt in our minds that if the criterion suggested in this paper were followed, the results with the chaulmoogra preparations are more disappointing in the early bacteriologically negative, neural or macular cases than in those with cutaneous lesions showing acid-fast bacilli.

In our experience the erythematous patches of clinical "tuberculoid" leprosy negative for acid-fast bacilli are as a rule more resistant to both the intramuscular and the intra-cutaneous injection of the chaulmoogra preparations than the red, acid-fast positive, infiltrated areas typical of the more advanced "cutaneous" stage. If these two types of lesions are followed histologically during a course of intensive treatment, it will be seen that in the case of the "positive" infiltration, there is fairly rapid granulation and fragmentation of the bacilli, disappearance of the globi, thinning out of the proliferated fibrous tissue, and diminu-

tion of the newly-formed small blood vessels, whereas there is very little change in the cellular structure of treated early macules from month to month.

Therefore, it does not necessarily follow that the earlier the case the better the results, so far as the treatment of leprosy with chaulmoogra oil is concerned.

The above results are certainly unexpected and paradoxical. A few years ago, it would have been impossible to explain these results even theoretically, but we believe that such an explanation is possible now.

The studies of Walker and Sweeney (*Journ. Inf. Dis.* 1920, Vol. 1, No. 1) and of Schöbl (*Phil. Journ. Sci.*, 1923, Vol. 23, No. 6, pp. 533-541) have shown that chaulmoogra oil and its derivatives inhibit *in vitro* the growth of acid-fast bacilli in dilutions that have no effect on the growth of non-acid-fast bacteria. These results have been confirmed in our laboratory in Cebu.

Manalang, as a result of his pathologic findings correlated with search for *M. leprae* in these incipient cases (*Monthly Bull. of the Phil. Health Serv.*, 1932, Vol. 12, No. 3, pp. 77-79) believes that "as in *M. tuberculosis*, *M. leprae* has a microscopically invisible ultra virus stage which is responsible for the so-called early lesions pathologically characterised by a perivascular infiltration. . . ." In other words, there may exist a cycle in the life history of the organism which develops within the body of the case of leprosy starting from an ultramicroscopic stage, found in the early macules to the solid, acid-fast, staining rods located in the cutaneous infiltrations and nodules.

By using the staining method of Much, my colleagues and I (*Phil. Journ. Sci.*, 1933, Vol. 51, No. 4, pp. 617-629), have been able to demonstrate the presence of Much-positive forms of *M. leprae* in a considerable percentage of leprotic lesions which do not contain acid-fast bacilli. Furthermore, we believe that these non-acid-fast bacilli are not merely degenerated forms because they are found in untreated "closed" or "incipient" cases of leprosy, as well as in previously positive and treated "quiescent" cases. We concluded that Much-positive non-acid-fast forms may represent another stage in the life cycle of the organism.

In the light of the above findings, may it not be possible that the chaulmoogra derivatives act in much the same way *in vivo* as *in vitro* (particularly when these drugs are injected intradermally) that is, may they not be more effective in lesions produced by acid-fast forms than in those

of earlier cases harboring chiefly non-acid phases in the life cycle of the *M. leprae*?

Our own studies lead us to advance the theory that the progress of leprosy in the human body and the effect of the treatment with chaulmoogra oil are probably somewhat as follows :—

In the very early depigmented macule as well as in the early anaesthetic or macule-anaesthetic type of leprosy, *M. leprae* may be present in an as yet undemonstrable form, which causes a distinct reaction in the tissues manifested by round-cell infiltration about the capillaries and arterioles. This unrecognised form has a distinct predilection for the cutaneous sensory nerves. It is possible that the organisms at this stage may be so minute as to be ultra-microscopic, or that no staining method has yet been perfected for their demonstration.

It is presumed that as the organisms gradually increase in size, the character of the tissue response also gradually changes, until by the time the former are demonstrable by the Much's stain, the pathological picture of the lesion will have become the typical "tuberculoid" arrangement. From the nature of the tissue response, characterised by proliferation of endothelial-like cells, it may be presumed that the main defence of the body during this phase lies in the phagocytic activity of these and similar cells of the reticulo-endothelial system.

Later, due perhaps to the evolution of a necessary step in the life cycle of the invading organism, or to some change in the tissues of the host, the bacilli become acid-fast and the phagocytes are no longer able to dispose of them properly. Consequently, the bacilli proliferate within the now powerless phagocytic cells to form the well-known "lepra" cells. Using supravital staining methods, Koike (*Jap. Journ. of Dermat. and Urol.*, 29, 1929) has shown these cells to be real histiocytes, following the classification of Sabin. The acid-fast bacilli may be phagocytosed also by the polymorphonuclear leucocytes of the blood and are thus distributed to other parts of the body.

When the acid-fast bacilli begin to appear, the lesions become thicker, due to accumulation of masses of "lepra cells" and to fibrosis, and also become reddish in colour, due to new formation of minute blood vessels. New lesions appear at the sites of predilection such as the earlobes, etc., due to dissemination of the bacilli by the polymorphonuclear leucocytes.



At this stage a variable proportion of the bacilli remain non-acid-fast.

It is possible that chaulmoogra oil may exercise an inhibitory effect *in vivo* against the acid-fast stage of *M. leprae*, as it does *in vitro*, but not against the non-acid-fast forms. Therefore, the administration of this oil, particularly by the intracutaneous or "plancha" method, where the drug is brought into more or less direct contact with the acid-fast organisms, may bring about their destruction and elimination, together with improvement or disappearance of the infiltrations, nodules, and other manifestations of "activity" of the disease. The patient may then become a "quiescent" or "negative" case, without any manifestations of "activity," and be negative for acid-fast, but still harbours Gram or Much-positive non-acid-fast bacilli.

When such negatives suffer a "relapse," it simply means that some of the Much-positive non-acid-fast bacilli have become acid-fast again.

It is realised that this hypothesis explaining the development of the leprotic lesions and the variable, paradoxical results of the chaulmoogra treatment, is based on incomplete evidence at the present time. However, this conception may prove useful to those who, like ourselves, have been long baffled by the conflicting and sometimes disheartening results following the use of the chaulmoogra preparations in the different types of this very difficult disease.

#### CONCLUSIONS.

1. The chaulmoogra preparations are of real value in the treatment of leprosy, but there is still much room for improvement with regard to our knowledge as to their proper indications, limitations, and action in the human body.

2. The chaulmoogra oil derivatives do not seem to be as effective in incipient leprosy as in the more advanced cases with lesions showing acid-fast bacilli. This paradoxical effect may be due to the fact that these drugs are not as a rule as effective against the non-acid-fast stages of the *M. leprae*, which are believed by some workers to be responsible for the earliest manifestations of leprosy, as against acid-fast forms of the organisms which produce the later lesions.

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

Sir LEONARD ROGERS.

(Continued from Vol. V, No. 2.)

### *Formation and Work of the Indian Branch of B.E.L.R.A.—*

As the result of a visit of Mr. Oldrieve to India, the Viceroy, Lord Reading, issued an appeal in January, 1925, in which he said : " I have convinced myself by personal observation that wonderful work is already being done in India on behalf of the lepers and for the prevention and cure of the disease. I ask all classes to join with me now in an earnest campaign to combat this dreadful disease." The result was remarkably good, for approximately £150,000 was raised, the interest on which has furnished an annual income of about £9,000 a year, with which the following advances have been made in less than one decade.

*Organisation* occupied the first year. Central and Provincial Councils were appointed and it was decided to hand over half the total income to the Provincial Councils in proportion to their original subscriptions to the Viceroy's fund, and this has been continued ever since as far as possible. Executive and Medical Committees were also formed.

*Research* has been throughout one of the main interests of the Central Council, which has largely financed the work of Dr. E. Muir, as a whole-time leprosy research worker in the Calcutta School of Tropical Medicine, and his staff. In 1927, Dr. J. M. Henderson was appointed to work with him and was succeeded on his retirement, in 1932, by Dr. Lowe, of the Dichpali Leprosy Institution. The research work done in Calcutta includes important improvements in treatment, such as the use of injections of Muir's creosoted hydnocarpus wightiana oil, a very cheap preparation suitable to Indian conditions, and avenyl, a combination of mercury and the oil, for use in cases complicated by specific disease. Work has also been done on the reactions produced by potassium iodide, thyroid extracts, the red corpuscle sedimentation test as a guide to prognosis and treatment, intradermal injections of hydnocarpates, together with much research in the pathology and bacteriology of human and rat leprosy. An average of £1,400 has been spent yearly on research during eight years.

*Training Doctors* in the improved treatment of leprosy has been an important feature of the work, for the Provincial Governments have deputed many of their medical officers to undergo short courses of training at the Calcutta School of Tropical Medicine, and latterly also at the Dichpali Leprosy Hospital in the Deccan, the cost of their training averaging £675 a year, including fares, being met by the Association, with totals of 655 doctors trained at Calcutta and 76 at Dichpali, up to 1932, or 731 in all. Another 850 are mentioned in the annual reports as having been trained by the survey parties in the provinces, many of whom are now treating leprosy at hospitals and clinics.

*Propaganda* has formed a most valuable part of the activities, and includes the preparation and display of films illustrating the progress and treatment of leprosy, and the use of wall charts and lantern slides illustrating the dangers of the disease and prophylactic measures against it. Many thousand copies have also been distributed of Muir's booklet on "Diagnosis, Treatment and Prevention," of a popular lecture on the disease, and pamphlets, on "Truths About Leprosy" and "What the Public should know about Leprosy." The annual average cost of propaganda has been £590.

*Surveys* have proved of even greater practical value and have been combined with propaganda and treatment in a most effective manner, as the following brief account will show. The returns of the 1921 census of the cases of leprosy in selected areas of each province were obtained, and the villages were visited to ascertain the real number of cases, as it was well known that only cases so advanced as to be evident to the lay enumerators are returned in the census figures. Between 1926 and 1931 no less than 2,435,610 persons were examined, and 16,499 cases of leprosy were discovered, or four times as many as the census figures of the areas dealt with, in accordance with the expectations of Dr. E. Muir. High incidence was found among backward aboriginal people and in labour forces. Markets and pilgrimages spread the disease, which is pre-disposed to by debilitating diseases and deficient diet. As a direct result of the surveys numerous clinics were started by the local authorities for the special treatment of cases of leprosy, and frequently several hundred patients were soon attending them. The provincial reports for 1932 show a total of 459 leprosy clinics and treatment centres in the six provinces which furnished returns. The Central Provinces alone reported 57,372 leprosy patients, and

Madras had the largest number of clinics, namely 180, with a total of 336,675 attendances, which, at the previous year's attendances per patient, would indicate 26,935 cases of leprosy. Bengal had 100 clinics, and in 1931 had 11,133 patients, so that the total number of cases treated at the special clinics cannot be much short of 100,000 annually at the present time, in addition to which an unknown number are being treated at the numerous clinics of provincial hospitals. When we recall that only about 8,000 advanced cases, mostly unsuitable

for in all the leprosy institutions of India, only one decade ago, the advance is most encouraging, although it must be admitted that the average number of attendances of the patients is still far too low, although the more suitable cases are likely to persist longest with it. A conference of leprosy workers was held in Calcutta in 1933, when it was decided to devote more attention to visiting the houses of the leprosy patients to advise their relations regarding preventative measures, and to trace contact cases with a view to their treatment in the early amenable stages. A very encouraging feature was the collection in the Salem district of Madras on a "Leper day" of over £2,000, mostly contributed by the poorest classes in coins of from one twelfth of a penny to one penny in value.

The Indian Branch are greatly indebted to the wise and experienced counsel of Dr. E. Muir, and also to the invaluable aid, as Chairman of the Executive Committee, of Sir Henry Moncrieff Scott, I.C.S., up to 1932, and later of Major-General J. D. Graham, I.M.S., Public Health Commissioner, India, Sir Ernest Burdon, I.C.S., as Hon. Treasurer. Sardar Bahadur Balwant Singh Puri has been Hon. Secretary, and it is noteworthy that the administrative expenses during the six years 1927-32, have averaged only £320.

*Organisation of Leprosy Work in British Possessions.*—Early in 1926 Mr. Oldrieve visited the British Colonies of Nigeria, the Gold Coast, and Sierra Leone, in West Africa, with the result that the Governments of the two former agreed to employ whole-time leprosy relief medical officers, who were selected by the Association and sent to Calcutta for special training under Dr. Muir, namely, Dr. T. F. G. Mayer and Dr. M. B. D. Dixey. Unfortunately, in 1931 their services were dispensed with owing to financial stringency, but a recent offer by B.E.L.R.A. to pay half the cost of whole-time leprosy officers in the medical

services of Nigeria and the Gold Coast has been accepted by the Colonial Office.

*Progress in Nigeria.*—Dr. Mayer began work here in 1927, and by 1930 nearly 6,000 lepers were being treated in 66 centres, with improvement in over 50 per cent., but with an estimated number of cases of leprosy in Nigeria of 95,000 much remains to be done. The largest leprosy colony is at Itu, in S. Nigeria, with about 1,000 cases, under Dr. J. Macdonald.

*Progress in the Gold Coast.*—Here Dr. Dixey made surveys and opened numerous out-patient clinics, as well as in Togoland, where there are 515 cases in a settlement, and 461 showed various degrees of improvement after nine months' treatment. In 1931 Dr. Dixey reported that out of 4,000 known cases of leprosy considerably over 2,000 were under treatment at 18 out-patient clinics and in a large settlement.

*Barbados, Trinidad, Jamaica and British Guiana* were visited later in 1926 by Mr. Oldrieve, an area in which rigorous compulsory segregation was still enforced, with the usual result that early amenable cases of leprosy were not found in the leprosy asylums and treatment was consequently greatly handicapped. The relaxation of the law to allow early mostly uninfected cases to be treated as out-patients at hospitals was urged, but so far only British Guiana, on the advice of Surgeon-General P. J. Kelly, has adopted the modern methods with great advantage. Trinidad has a good but costly island settlement for its segregated cases, which is an improvement on the former town prison-like asylum.

*British Guiana Progress.*—The results of adopting modern methods, as opposed to rigid isolation of all discovered cases of leprosy, is well shown in the report of Dr. F. G. Rose, on five years' leprosy work in British Guiana, recorded in Vol. IV, No. 1, of the Association's quarterly publication, THE LEPROSY REVIEW. Briefly, leprosy surveys were made and two leprosy clinics were erected at the cost of the Association, for treatment of early cases as out-patients, and two more have since been added. The more advanced and infective cases are sent for treatment to the leprosy hospital at Mahaica, where only cases suitable for treatment are now kept, the old hopeless crippled cases having been given separate accommodation. The result has been that over half the patients at what was formerly the Mahaica compulsory segregation asylum are now voluntary admissions for the sake of treatment, and of

491 treated patients, nearly all fairly advanced cases, 361 have improved, including 128 with the disease arrested, and out of 14 relapses only 6, or 4.7 per cent. of the released have failed to recover as yet. Moreover, in 132 further cases the disease has become quiescent. A number of hydnocarpus trees have been grown from seed sent by the Association, and some have already fruited, which will soon furnish a local supply of the oil for treatment.

It is interesting to note that the neighbouring colony, Dutch Guiana, has adopted the methods of British Guiana, and it is hoped that a visit of our Medical Secretary to the West Indies this year will result in our island possessions there adopting the modern methods.

#### WORK IN EAST AFRICA.

*Tour through East Africa.*—In 1927, Mr. Oldrieve made a 16,000 mile tour, which included Anglo-Egyptian Sudan, Uganda, Kenya, Zanzibar, Tanganyika, Nyasaland, North and South Rhodesia and Cape Colony, and he organised a number of Colonial branches of the Association, of which there are eleven, including seven in Africa, which have carried on leprosy relief work, and advised the Association regarding grants for providing treatment centres and accommodation for cases of leprosy under various missionary bodies in their territories. The following are some of the more striking advances made in this huge leprosy stricken area :—

*Uganda*, especially the western province bordering on Belgian Congo, is one of the most heavily infected areas in the Empire for its population, for a survey in 1931-32 showed 10,176 cases, which is probably only half the true figure. The Association financed the building of eight centres, in which Dr. C. A. Wiggins treated some 3,000 cases, motor-ing round to each every week, and has supplied a hospital where several hundred leprous children, taken out of schools, are being treated and educated under the C.M.S. Help has also been given towards founding the Lake Bunyoni leprosy hospital, under Dr. L. E. S. Sharp, of the C.M.S., in south-west Uganda, but much remains to be done.

*Kenya* is less infected than Uganda, and the coastal areas suffer most. Three leprosy settlements and a number of treatment centres are at work, but financial conditions have prevented much activity so far, and surveys to ascertain the number of cases are still required.

*Tanganyika* is believed to have at least 10,000 cases of leprosy, and in the absence of surveys the number is

probably much higher. No whole-time leprosy officer is available, but the Association has given financial assistance to a number of small leprosy settlements and treatment centres under medical missionaries of various denominations. By the end of 1933 the number of cases being cared for amounted to 3,462.

*Zanzibar* has at least 500 cases in an island population of 200,000, and affords a good opportunity to carry out the writer's suggestion to examine all the contacts of leprosy patients every few months for five to ten years, with a view to detecting and clearing up the 80 per cent. or so of household infections while still in an early stage, and thus to reduce the disease rapidly in a single decade. Early in 1933, Dr. T. B. Welch, with five years' experience in charge of the large Trinidad leprosy settlement, was sent to Zanzibar at the cost of the Association, with help as regards residence from the local government, to make a survey and carry out the above plan, which will be watched with great interest.

*Nyasaland and Northern Rhodesia* are estimated to have some 15,000 cases of leprosy and by 1930 no less than 59 treatment centres were being supplied with drugs and literature by the Association, nearly all under missionary care, as the Colonial Governments had no material funds to spare.

*Southern Rhodesia* is a much more progressive area, for in 1929 the Dominion Government appointed Dr. B. Moiser as a whole-time leprosy officer, and in 1932, 749 patients were being treated in two leprosy hospitals as well as a number of other treatment centres. The number of cases is estimated to be 10,000, and the Association has given repeated liberal grants to aid the work. The number of cases under treatment in leprosy colonies had risen from 136 in 1922 to 998 in 1932, and they have more than doubled in the last three years, while early cases are now coming voluntarily for treatment.

*The Anglo-Egyptian Sudan* has a leprosy area in the southern humid Bahr-el-Ghazal and Mongalla Provinces bordering on Uganda, where a remarkable campaign has been carried out under Dr. O. F. H. Atkey, who took advantage of a staff engaged in examining the scattered population yearly, for sleeping sickness, to note the incidence of leprosy. No less than 6,500 sufferers were found, mostly early cases; 4,800, including all considered to be infective, were moved to large settlements with 30 square miles of land, where they grow their own crops and are largely

self-supporting, while the remainder also receive treatment and are inspected regularly in their own villages. Thus, the plan long advocated by the writer of examining a whole population frequently and treating all the early cases and contacts, has been carried out on a large scale in the Southern Sudan, with the remarkable result that at the end of 1932 no less than 2,230 of the cases had been discharged during that year as free from all active signs of the disease, thanks to a large proportion of the cases being early mild ones. It is, therefore, now established that the nearer prophylactic measures approach the above ideal, the more rapidly and also the more economically will leprosy be reduced in the British Empire and elsewhere.

*The Union of South Africa* has at least 5,000 known cases of leprosy and for over a century past compulsory segregation has been more or less in force, during which time the disease appears to have much increased. As this system leads to hiding of all early cases for fear of life-long imprisonment, the leper asylums a few years ago contained only advanced cases unamenable to treatment, so it is not surprising that the medical authorities refused to acknowledge any material benefit from treatment. Fortunately earlier cases of leprosy are now being attracted by the improved treatment, and in 1930 the large Zululand leprosy institution at Emjanyana discharged no less than 20 per cent. of all their cases. Moreover, a decade ago all the 2,500 cases of leprosy then under control were examined bacteriologically, and one-third of the total were released as harmless, mostly chronic quiescent nerve cases, and room was thus found for many infective ones and a substantial saving was also effected. Our Secretaries have twice visited the Union and been given every facility for seeing the work being done there.

In 1925, 1926 and 1927, Colonial medical officers on leave were invited to meet the Medical Committee of the B.E.L.R.A., when the work of the Association was explained to them, and discussion invited, to the great advantage of all concerned.

After Dr. Robert Cochrane succeeded Mr. Oldrieve as Secretary, he toured through East Africa in 1930, from Egypt to the Cape, to consolidate and extend the work of the Association. In 1933 he visited India and Ceylon, the latter at the request of the Ceylon Government, and his work has been much appreciated wherever he went.

*Supply of Drugs and Hydnocarpus Seeds.*—A most important part of the work is the supply of drugs for the



treatment of leprosy to the various Empire colonies and clinics, chiefly in our African possessions. This has taken the form of the active sodium hydnocarpate, alepol, made for the writer by Burroughs, Wellcome & Co., as it can conveniently be sent out in powder form in 100 gramme bottles, one of which allows some 700 doses of the 3 per cent. solution to be made up for the weekly injections at a cost per patient of about half-a-crown a year. By 1928 the number of doses supplied to our Empire had risen to 255,000, and in 1932 it reached 635,000, or an average of just over 500,000 during the last four years, at an annual average cost of £760.

*Hydnocarpus Wightiana* and *H. Anthelminica* seeds have also been widely distributed to all our leprosy infected possessions with warm humid climates suitable for the growth of the oil-yielding trees, and several countries, such as Fiji and East Africa, now have 1,000 trees of the first variety that are already seeding, so that before long many of our colonies will be largely self-supporting as regards the use of the creosoted whole oil, and will also be able to prepare their own more expensive ethyl esters by Muir's economical cold process, as they are being increasingly used for injection into leprosy lesions by the intradermal method. The cost of distributing the seed has amounted to only about £200, so should prove to be a very good investment on similar lines to the importation of Cinchona seed from South America to Asia over half a century ago.

*Supply of Leprosy Literature.*—The organisation of leprosy colonies and treatment centres, and the supply of the new preparations required to be supplemented by information on the detailed treatment, early diagnosis and other essentials to success, as medical literature is scarce in many of our overseas possessions and practically non-existent in remote mission stations. The publication at a low price, by Rogers and Muir, of their book on "Leprosy," and of Muir's pamphlet in India, already mentioned, and subsequently of various papers by Dr. Cochrane, enabled information to be supplied to those who required it. So many inquiries were, however, received, that in 1928 the Association commenced publishing a small quarterly journal entitled "Leprosy Notes," and distributed 1,500 copies in the first year of issue. In 1930 this was slightly enlarged and brought out under the title of "Leprosy Review"; this completed its fourth volume in 1933, and has enabled the experience and results obtained in different parts of the British Empire, and far beyond its borders, to be recorded

and thus made available to other workers, and by 1930 its circulation was close on 2,000 copies.

The *Tropical Diseases Bulletin* has for many years published abstracts of the literature on leprosy (among other diseases), compiled by the writer, and he arranged, very shortly after the Association was formed, to obtain reprints at our cost, for distribution, which practice has been continued ever since to the number of about 750 copies annually to medical workers throughout our Empire, to enable them to keep up to date with the most recent literature on the subject. Since Dr. Robert Cochrane was appointed Secretary he has given much instruction on treatment during his foreign tours. In these various ways a great deal of highly important educative work has been accomplished by our Association at an average annual cost during 1928 to 1932 of nearly £500.

*Conclusion.*—The annual income of our Association during its first ten years has averaged in round figures £5,700. This sum has had to provide for the Empire-wide organisation and tours of our Secretaries, the yearly supply of half-a-million doses of drugs, and an immense amount of literature, and the housing and staffing of our headquarters (office accommodation during the first five years having been provided free of charge by a medical member of the Committee). Mention should here be made of the invaluable work of our Assistant-Secretary throughout, Miss Helen Wallich, on whom the main burden has fallen during the long absences on foreign tours of the Secretaries, assisted by Miss Jenkins from 1929-1932, and since by Miss Freda Robins, on whose indefatigable labours much of the Secretarial work and the sending out of immense numbers of appeals has depended. I also take this opportunity of thanking all those who, by personal service on various Committees, or by their generous contributions in difficult times, have rendered possible the good start of our Association in the work of mitigating and preventing such a distressing and ancient disease as leprosy. I trust this account of our labour will suffice to convince our supporters that our organisation is worthy of being entrusted with funds more commensurate with the immensity of the problem we are endeavouring to solve, a task in which we have always had the sympathetic and knowledgeable encouragement of our Patron, H.R.H. The Prince of Wales.

Fortunately, the Rev. P. B. Clayton, Founder Padre of Toc H, returned last year from an Empire tour impressed with the necessity for a great campaign, with a view to

abolishing leprosy from our Empire, much as the slave trade was abolished a century ago. After he had consulted the writer, a special Committee of Toc H and B.E.L.R.A. members was constituted to obtain volunteers for service in leprosy colonies and institutions, and funds to finance them for five years in the first place. There are already signs that such an appeal will not be in vain, so we may look forward confidently to a great extension of our work during the decade we have just entered on with redoubled enthusiasm in the cause of the half-a-million or more unfortunate sufferers from leprosy in our Empire.

## Ngomahuru Leprosy Hospital.

### ANNUAL REPORT FOR YEAR 1933.

B. MOISER.

	European Male.	Coloured Male.	Native Male.	Native Female.	Total.
Number of Patients on 1/1/34	1	1	259	138	399
Admitted .. .. .	—	—	78	49	127
Returned for further treatment	—	—	5	2	7
Returned for economic reasons	—	—	—	—	—
Discharged .. .. .	—	—	14	10	24
Died .. .. .	—	—	22	8	30
Deserted (Gone to Mnene) ..	—	—	1	—	—
Number of Patients at 31/12/33	1	1	305	171	478

It should be mentioned here that the Medical Officer was away on leave for six months of the year, and no discharges were made in his absence.

#### EUROPEAN STAFF.

The Staff has remained as before, i.e., four Europeans, including Mr. Burn, who is still a patient, and who has become negative to the microscope.

#### NATIVE STAFF.

This consists of a clerk, a builder, two trained hospital orderlies, a laboratory boy (Wilfred), and a varying number of labourers, the total being 19. The leprous native staff number 11, including five compound heads, school master, two dressers, an interpreter, gate-keeper, and vegetable garden superintendent. The total staff, European and Native, is thus 34.

## TREATMENT.

After a trial of various remedies during the past five years, ethyl esters of the oil of *hydnocarpus wightiana*, both iodised and non-iodised, have been chosen as giving by far the best results, and are now being used exclusively. Of the two kinds of esters, iodised and non-iodised, the former is much preferred. It can be given in heroic doses without any ill effects, it keeps well, it causes little or no pain, little or no induration, and does not tend to abscess formation.

Iodised esters are given here in doses up to 10 c.c. intramuscularly, with or without a portion given intradermally twice a week without causing any ill effects whatever. Six-ounce bottles are opened as required and fluid taken direct into the syringe from the bottle and the bottle kept corked until finished, and it has been found to keep well for two weeks or more under these conditions. As far as can be seen, no change takes place after admission of air to the bottle, so that I cannot support the statement that a bottle of iodised esters, when once opened, cannot be used again. Our experience here is in direct contradiction of this belief, and is an important point. The preparation is not treated with ultra-violet light, or in any other way. It is simply kept in a cupboard, or on a shelf in the laboratory.

Our supply of iodised esters comes from two sources. (1) Burroughs Wellcome's "Moogrol." (2) Government Chemical Laboratory, Cape Town.

A preference is held for the former, but so far, we have not found a great deal of difference between them. Both are quite satisfactory and are producing results much in advance of other preparations.

In the case of non-iodised esters, the maximum dose has been about 5 c.c. twice weekly, but such doses cause a good deal of pain and induration, a few general reactions and abscesses. The conclusion has thus been drawn here that the iodised ester is the best remedy. It is expensive, but results show that it is worth the money. Dosage is not determined by weight of patient, but simply judged by condition of site of last injection. If indurated and painful the dose is lessened or withheld; if the patient has general febrile reaction (very rare) the dose is withheld. It is found that most patients become "saturated" at the end of about six or seven weeks, and no injections are given for a week or even a fortnight.

Trichloroacetic acid is applied to nodules, and raised edges of maculae, and is much desired by the patients themselves. I consider it to be of great value in cauterising nodules and infiltrations.

In addition to the above specific treatment, other diseases are sought out and remedied. Malaria is countered by mass quininisation during the rainy season, intestinal parasites (which are not common) being got rid of by appropriate treatment, and syphilis controlled where necessary, such cases being very few in number.

#### RESULTS OF TREATMENT.

It can be stated definitely that results with modern treatment (in this case iodised esters) are far better than I have ever seen in an experience of 25 years' active work. Even the apparently hopeless cases are given treatment, for it is impossible to state beforehand which cases are likely to improve and which are unlikely. Some of the very worst cases have shown remarkable improvement. It is true that here and there one comes across a case, generally not of the worst type, who exhibits no improvement whatever, no matter what drug is employed, or he even becomes worse. But it is very seldom that such cases desire cessation of injections. The drug, although it fails to control the disease, appears to give the patients a feeling of well-being. This applies specially to the worst nodular type.

I think it is a mistake to assume that any case is not likely to improve. Here, every new patient is given treatment, *i.e.*, increasing injections twice weekly, and changes of drug made if no improvement noted. The number of cases that remain stationary or become worse are very few, and we have less than half-a-dozen cases of active disease who are not receiving treatment. We have a few completely burnt-out cases who are settled here for purely economic reasons, and these receive no specific treatment. The earlier the stage of the disease the better the results. I believe that almost all early cases are easily curable. Experience here shows this conclusively. Sometimes the results are spectacular, all symptoms clearing up completely in six months.

But curability is by no means confined to early cases. Later stages require more prolonged treatment, but eventually many are apparently cured and are discharged on parole and followed up to a certain extent, which is much less than could be desired.

The number of cases discharged, who are not seen again, is far too great, and it is in this respect that we fail here rather lamentably.

I might mention here, too, a second failure, namely, the omission to examine contacts. The Medical Officer should tour his district in the dry season to examine all discharged cases and contacts of new admissions. Many early cases would surely be discovered by this means, and I'm afraid that a number of relapses would be brought to light.

#### BACTERIOLOGICAL.

The rule to examine smears from every patient four times a year still holds good, but owing to the absence of the Medical Officer for six months the patients have been examined only twice this year. This routine microscopic examination occupies a great deal of time each day, but I consider it to be of the greatest importance, and the best indication of the progress of the patient. The appearance, arrangement, size, degree of staining, etc., of the bacilli, under the microscope are, I believe, reliable indications of the state of the disease in the patient. Severe cases show masses of large closely-packed clumps, deeply stained, whilst, as the patient improves, the clumps become smaller, less compact, less deeply stained, and the bacilli become scattered and dotted. If bacilli are present in any numbers, it takes only a very short time to ascertain the fact, but 15 minutes examination is necessary before a case can be declared negative.

Smears are taken from the lobe of the ear (small portion snipped off with scissors, and raw surface lightly scraped with knife) ; from the nose (mucus membrane scraped until it bleeds), palate (scraped), nodules (incised), enlarged glands (syringe aspirations), and skin ulcers and raised edges of maculae (small incisions and scrapings).

#### GENERAL.

Regular occupation and exercise is insisted upon for everybody, the patients are kept busy out of doors four mornings in the week from 6.30 a.m. to 11 a.m. In the afternoon they have to fetch their own wood and water, cook their food, and till their small farms. They are also taken to bathe and wash their clothes once a week. They construct and repair roads, drains, keep the place clean, make and tend plantations, nurseries, vegetable gardens,

build houses, tend cattle, make clothing, etc. It is not practicable for them to grow cereal food for the hospital, neither would it be economical. Seasons are so uncertain, and mealie meal can be bought more cheaply than it can be grown at Ngomahuru.

#### SCHOOL.

This is now attended by boys only, from 2—4 p.m. on five days of the week. The number of pupils on the register is 16, and attendances are very regular, illness interfering but little.

#### TAILORING AND DRESSMAKING.

This year the method of obtaining clothing has been radically altered, and a great saving of expense effected. Formerly, clothing of all kinds was bought ready-made from local suppliers, but this year the material has been imported direct from England and the clothing made up here with our own labour. Three tailors using two treadle machines cut and make all jumpers and shorts for the men, and cut them to measure, whilst the Matron, with her class of about ten girls, make all blouses and skirts for the women. By this method we can now supply each patient with two suits a year for less money than one suit a year formerly. One suit per annum is insufficient. Instead of patients going about in absolute rags, they are now decently and warmly clothed. I should like to mention that the credit for this innovation is entirely due to Mr. Burn, who has had many years experience of this sort of thing in West Africa.

Vests and blankets are still bought as before. All sacks in which mealie meal is supplied are made use of as rain-coats and bedding and are most useful. Shoes are necessary and are cut out from old motor tyres.

#### HOUSING.

The number of separate villages is now six, the additional one being set apart for early closed cases, and for those nearing discharge. More than 70 new huts have been built during the year, made of Kimberley bricks and thatched, the work done entirely with our own labour.

#### BUILDINGS.

The only new brick and iron building erected is the mealie meal store, which has been connected to the distributing shed, and the two together now form a very

convenient arrangement. This was erected with our own labour.

Close by is the new butchery, made of Kimberley bricks and thatch, with cement floor. This should last a few years, but should later be replaced by a brick and iron structure.

#### WATER SUPPLY.

The pump has given a good deal of trouble on occasions, but there has been no lack of water in the bore hole.

#### CHILDREN AND CRÛCHE.

The number of healthy infants born here is 10, seven being illegitimate ; brought in by mothers, 13, the number sent home being 12, died 2, remaining 23, one leprous contracted outside.

There is no crêche in existence as yet, and the difficulty of separating infants from mothers remains as acute as before. It is an exceedingly difficult problem, but it is hoped to build a new crêche near the women's compound, and that this will prove effective.

The cost per head per day, including staff salaries, works out at 5.98d.

#### ANALYSIS OF 722 NATIVE CASES OF LEPROSY.

At Ngomahuru there are no out-patients, all patients living within the hospital fence in six villages, arranged according to type of case. The total number who have been treated here since the records began (about 1913) is 909.

The preparations that have been mainly used are alepol, plain esters of hydnocarpus oil, and iodised esters. The last named is now being used to the exclusion of the others.

The total number of patients who have been discharged as "arrested" cases is 271, of whom six have been re-admitted for further treatment. Of these 909 patients, 722 have been fairly completely recorded in the books, sufficient data being available for analysis.

The patients are classified in the following table according to the types recommended by the International Leprosy Association, N representing purely neural cases, NC representing mixed cases, whilst the purely cutaneous cases are indicated by C. In each case the numeral following indicates the degree of severity. This numeral would vary with different observers, and thus is not strictly comparable with the records of others, but differences would not be great.



## MALE AND FEMALE.

Type of Case	Number	Discharged	Improved	Stationary	Worse	Died	No. become Negative
N1. .. ..	98	55	38	2	—	3	—
N2. .. ..	203	126	52	2	—	23	—
N3. .. ..	22	12	7	1	—	2	—
N1 C1. .. ..	106	8	87	3	2	6	49
N1 C2. .. ..	47	1	28	8	2	8	11
N1 C3. .. ..	4	—	2	1	—	1	—
N2 C1. .. ..	135	13	88	5	1	28	47
N2 C2. .. ..	54	—	22	22	—	10	5
N2 C3. .. ..	15	—	3	5	2	5	—
N3 C1. .. ..	14	—	6	5	—	3	8
N3 C2. .. ..	8	—	3	1	—	4	—
N3 C3. .. ..	2	—	—	1	—	1	—
C1. .. ..	5	1	4	—	—	—	2
C2. .. ..	4	—	1	—	—	3	—
C3. .. ..	5	—	1	1	1	2	1
Total .. ..	722	216	342	57	8	99	123
Percentages ..	%	30.0	47.3	7.9	1.1	13.7	30.8

Total Admitted to 31/12/33. 909

,, Discharged ,, 271

From the table it will be seen that—

Neural cases total 323 ... 45%

Mixed cases total 395 ... 53%

Cutaneous cases total 14 ... 2%

Mixed cases predominate, whilst purely cutaneous cases are very rare.

The 98 N1 cases are all early cases. Of them 55 have been discharged as "arrested" (56%) whilst 38 showing improvement are still here and will probably all be discharged. Thus 95% of these cases have been or will be discharged. Only two remain stationary. The three deaths were not caused by leprosy. (I may interpolate here that the causes of deaths at this hospital are not always definitely

known. Autopsies are never performed for reasons of policy, and sudden deaths are not uncommon).

The N1 is the type of case that we should have here in much larger numbers. They are easily curable, and the simplest way to find them is to examine contacts at the homes of infectious cases. I believe this method of examination of contacts is much better than surveys, as a practicable way of getting early cases under treatment. Very early cases are difficult to diagnose, and require time and detailed examination, which cannot possibly be given during a survey. Surveys produce interesting information, and they show up advanced cases, but they do not produce the early cases. These are certain to be found at the kraals of infectious cases, so why not go straight for them and examine each individual carefully? We have had the experience of two surveys in this country, but I advise examination of contacts in preference to surveys.

N1 C1 are also early cases, but not so easily amenable to treatment as N1. We have had 106 N1 C1 cases, of whom only eight have been discharged, but 87 have improved, and most of these will be discharged in time.

So it can be said that over 90% of early cases will be "arrested," and called "cured" if we do not quibble about the word. How important it is to get hold of the early case!

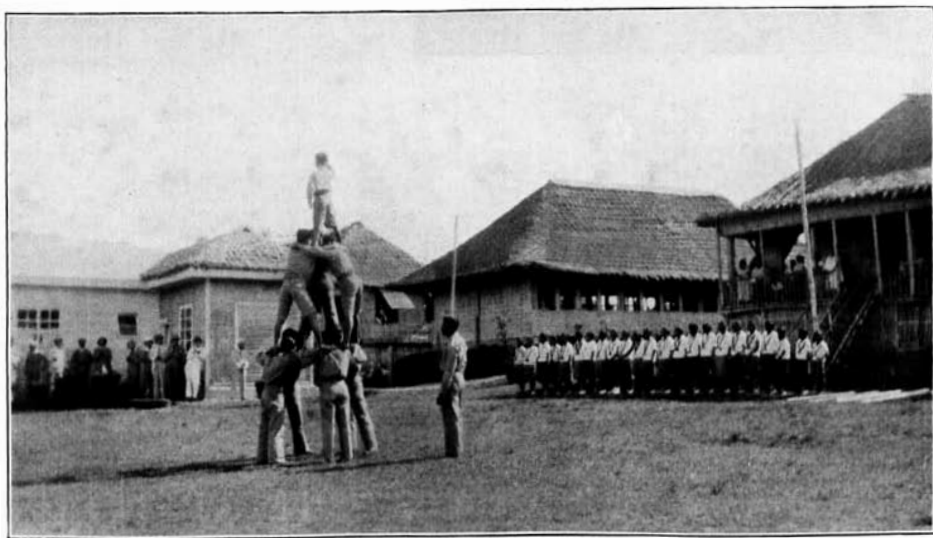
As noted above, the purely cutaneous case is very rare. We have only had 14 cases of all degrees of this type, and of these only one has been discharged, and six others have improved. These cases are treated intradermally, and generally improve. The four C1 "improved" cases will probably all be discharged later.

It will be noticed in the table that 203 is the highest number of any one type, the type being N2 in this case, and it must be explained that the great majority of these come under the heading of "secondary neural," *i.e.*, they have been "mixed" cases, and have lost all signs of cutaneous involvement. They have not been N1 cases that have become N2 through extension of the disease to other nerves.

Improvement has been shown by all types except N3 C3. These are really hopeless cases, and fortunately they are few. The table does not show that we do any good at all by giving these people treatment, but I do not consider it justifiable to withhold treatment, for it produces a feeling of well-being and comfort in the wretchedness of their lives,



EVERSLEY CHILD TREATMENT CENTRE, CEBU,  
PHILIPPINE ISLAND



WESTERN VISAYAN TREATMENT CENTRE, ILOILO,  
PHILIPPINE ISLANDS

NGOMOHURU LEPROSY HOSPITAL, S. RHODESIA



CASES WITHOUT MUTILATION, ABOUT TO BE DISCHARGED



CASE OF NODULAR LEPROSY WITH MASSIVE ENLARGEMENT  
OF CERVICAL AND THYROID GLANDS

and is not a great expense when the smallness of the numbers is considered.

The rest of the table is self-explanatory, and it only remains to give an indication of age and sex.

0—10 years of age	...	2.6%
11—20    "   "	...	11.9%
21—30    "   "	...	34.1%
31—40    "   "	...	26.8%
41—50    "   "	...	15.5%
51—60    "   "	...	6.2%
61—70    "   "	...	2.9%

The peak is reached in the decade 20—30. This is too old. We ought to have many more between 10 and 20, for this is the most susceptible age. The figures are another indication of desirability of examination of contacts. To my mind, this is the "royal road" in any leprosy campaign and is quite practical with the help of Native Department.

With regard to sex, 469 were males, 253 were females, *i.e.*, in the proportion of 1.8 to 1. Number of cases positive that became negative, is 123, *i.e.*, 30.8% of positives.

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## Case of Nodular Leprosy, with Massive Enlargement of Cervical and Thyroid Glands.

BERNARD MOISER.

**P**ATIENT, named Nyambi, was a well-nourished man of about 20 years when admitted to Ngomahuru Leprosy Hospital, on October 31st, 1930. A younger brother was admitted later. Primary lesion had been an ulcer on outer side of left wrist.

*The Skin* was very nodular all over exterior surfaces, with very little hypopigmentation. Face and ears nodular, scrotum enlarged and thickened, and both testes were nodulated. He spoke in a whisper.

*Nerves*.—Auriculars, ulnars, and peroneals all thickened and tender.

*Anaesthesia*.—Extensive in both forearms and hands, outer side of lower extremities from hip down. Cervical and femoral glands enlarged. Tongue nodular, and there were some small ulcers on the palate. Nose and ear both very positive, with large rods. He was classified N3 C3,

and treated with alepol at that time, later with esters. He improved for a time and regained his voice.

By early 1932, the cervical glands had become very large, with one or two sinuses discharging yellow pus. This was examined on several occasions for actinomycosis, but none was found. About this time the thyroid gland began to enlarge, and with the cervical glands formed a very large swelling in the neck. General condition remained remarkably good.

He absented himself in February, 1933, without permission, and returned in April, when it was found that he had a syphilitic ulcer, for which he was given a full course of spirobismol and kharsulphan, which cleared up all syphilitic manifestations. The glands in neck and thyroid continued to enlarge, discharging masses of mycobacteria, and the patient died on January 22nd, 1934.

The glandular enlargement was apparently entirely due to leprosy.

The photograph shows the patient's condition on 25/5/32, and on 24/10/33, and it will be observed that the thyroid did not begin to enlarge until the cervical glands had already assumed very large proportions. Glands in other parts of the body were not enlarged, except the femoral, and these only to a slight extent.

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## An Apology.

In an article which was published in the April number of the REVIEW, on "Some Problems of Surgery in a Leprosy Colony," we apologise that in printing a photograph of Purulia Leprosy Hospital we inadvertently omitted to acknowledge that this was reproduced by the kind permission of The Mission to Lepers.

We should like to take this opportunity of saying that this institution is the largest that the Mission has in India, and we would remind our readers of a fact which tends to be overlooked, namely, that the Mission to Lepers was the first organisation to engage in leprosy work on an extensive scale. It was largely their work in India that stimulated further aid on behalf of the cause of leprosy. The Mission to Lepers maintains 47 homes and has under its care some 10,000 cases.

## Ethyl Esters of "Pongamia Glabra" in the Treatment of Leprosy.

G. R. RAO.

*Introduction.*—In the Ayurvedic system of medicine five oils have been recommended as curatives in the treatment of leprosy ; and of these five, *Hydnocarpus wightiana* is given the first place. Next in importance comes "Pongamia Glabra." *Hydnocarpus wightiana* is already in universal use in the treatment of leprosy, and so far there is no reference in the literature to the use of *pongamia glabra*. It was, therefore, considered desirable to try the effect of *pongamia glabra* in leprosy, and Dr. E. Muir, of the Calcutta School of Tropical Medicine, was consulted about the advisability of using the oil. He told the writer that some years back he had himself tried the oil and found it to be too irritating when injected. He therefore advised caution in using it.

A pure sample of the oil was obtained from Messrs. Ernakulam Trading Co., Ltd., and was filtered and sterilised before use. Olive oil free from fatty acids was used as a dilutant, and a one in ten dilution of the oil was injected in a few selected cases, subcutaneously. Gradually the dilution was weakened and the pure oil was used. No marked irritant effect was noticed and it was therefore considered safe for use. As the oil was too viscid it could not be used intradermally. Ethyl esters had to be prepared, but there was no known technique for preparing the esters of *pongamia glabra*, and the optimum proportion of the oil, alcohol and acid had to be worked out by actual experiments. Preliminary experiments with different proportions of the oil, the acid and the alcohol, were carried out, and a satisfactory method of preparing the esters was arrived at.

*Technique of Preparation (in brief).*—The optimum proportion of the oil, alcohol (absolute) and sulphuric acid pure (sp. Gr. 1.845) was found to be 1, 1.25, 0.015 or 100, 125, 1.5. On this proportion the oil, alcohol and acid were mixed and the mixture boiled for 24 hours in a flask fitted with a reflux condenser. The separated esters were then washed with distilled water thrice and neutralised with 0.4 per cent. anhydrous sodium carbonate repeatedly, until no free acidity could be detected by titration with N/20 sodium hydroxide. After a second washing with distilled water, thrice, steam was passed into the esters for half-an-hour, to remove the volatile impurities. After filtering again,

the esters were dried in an open pan type of container, in oil bath and filtered once again and sterilised by heating to 130 deg. C. for half-an-hour. Plain sterilised esters were used.

*Technique of Administration.*—With a view to ascertaining the therapeutic efficacy of the esters when administered by different routes, three batches of cases were selected. In the first batch of eight cases the pongamia esters alone were given intradermally in all the active lesions found on their bodies ; in the second batch of six cases the pongamia esters alone were given intramuscularly and no other anti-leprotic remedies were used, not even trichloroacetic acid painting externally. One case of this batch had to be given occasional intradermal injections just to satisfy him. In the third batch of three cases, the pongamia esters were injected intradermally into the lesions on the right side and, for the sake of comparison, the ordinary half per cent. ethyl esters of *Hydnocarpus wightiana* injected similarly into the lesions on the left side. For this batch, only cases with fairly symmetrical lesions on both sides of the body were selected, so as to render the comparison of results easy and fair.

*Results of Treatment.*—Of the 17 cases treated for periods varying from six to eighteen months, seven showed apparent clinical improvement, but there was no appreciable effect on the bacteriological findings. The *M. leprae* in the lesions did not seem to have been affected by the drug. Next, comparing the results obtained by the different methods of administration, it was noted that those treated by the intradermal method had shown comparatively greater improvement than those having intramuscular injections only. Probably this comparatively greater improvement (clinical) obtained by those having intradermal injections is due to the fact that such injections in hypopigmented and, or erythematous patches, exert a rapid and noteworthy effect in restoring the normal pigment of the skin in such patches. In fact, the chief effect of this drug seems to be to produce a localised hyperpigmentation of the skin, when injected intradermally, in the injected areas ; and when injected intramuscularly also, the same hyperpigmentation is noticed all over the skin surface, and it takes longer to produce this hyperpigmentation. This melanogenetic or melanopoietic action seems to be a special feature of the drug ; and is *not* due to the irritation caused by injections of a foreign body into the skin. When injected into the healthy skin it first produces a hyperpigmentation



at the site of injection, which remains for a month or two and then gets slowly absorbed, finally leaving the injected area slightly darker than the surrounding skin. The hyperpigmentation produced by the drug was directly proportional to the natural complexion of the case treated with it. Dark complexioned cases showed a literally "coal-black" hyperpigmentation, and lighter complexioned cases showed a lighter black and brownish-black sort of hue. This noteworthy melanogenetic or melanopoietic effect can be utilised in cases of leucoderma—and it is hoped that this drug may have a future before it, as an effective remedy in leucoderma.

To ascertain the efficacy of this drug in cases of leucoderma, three cases of leucoderma of not more than two or three years duration, were given intradermal injections of the esters into the leucodermic areas. With weekly intradermal injections, all the leucodermic areas became hyperpigmented. But the drug failed to exert any effect in a case of leucoderma of 20 years' standing. Probably in such long-standing cases the melanoblasts are dead. In recent cases it seems to have a noteworthy effect.

All the relevant particulars regarding the cases of leprosy treated by this drug are given overleaf in tabular form.

### *Summary and Conclusions.*

(1) *Pongamia glabra* oil and ethyl esters were tried in 17 cases of leprosy by three different methods of administration.

(2) The pure oil and its ethyl esters can be used intradermally as well as intramuscularly.

(3) When injected intradermally into hypopigmented or erythematous patches of leprosy, or in leucodermic areas, it produces an intense hyperpigmentation, presumably by stimulating the melanoblasts.

(4) When injected intramuscularly, a general darkening of the complexion all over, results, and this takes some time to become evident.

(5) The drug has no effect, apparently, on the *M. leprae*, the causative organism of leprosy.

(6) Its melanogenetic or melanopoietic action may bring the drug into therapeutic prominence in cases of leucoderma, which are not very long standing.

Serial No.	Name.	Type on admission.	Nature of infection.	Period of treatment.	Total No. of injections.	Dose range in c. cms.	Result of final examination.	Bacteriological examination Final result.	Remarks.
1	Jhunki	C1 N2	I.D.I.	yr. mth. 1 2½	57	2 to 5½	Improved	RAE 1/20, LHE 1/M RTBS 4 6/1, nose 1/M	
2	Champa	C3 N2	I.D.I.	1 1wk	49	½ to 4	Stationary	All M/1	
3	Robni	C3 N2	I.D.I.	0 10	40	1 to 4	Improved	—	
4	Muchi Dhumi	C3 N1	I.D.I.	1 2½	58	1 to 4½	Stationary	RHE 4/1, LHE 4/1, chin 11/5, nose M/1	Intracellular forms
5	Bilasi	N2 N3	I.D.I.	0 10	40	½ to 2½	Stationary	—	
6	Bishtu	C3 N2	I.D.I.	1 3½	61	2 to 6	Improved	Rt. eyelid M/1	Intracellular forms
7	Magru	N2	I.D.I.	1 1	52	2 to 6	Improved	chin 3/1, nose M/1 —	
8	Rajoni Kanto	C3 N1	I.D.I.	1 ½	50	½ to 4	Improved	RHE M/1, LHE M/1 nose M/1	Granular forms Intracellular
9	Sodai	C1 N3	I.M.	1 1½	54	2 to 3	Stationary	Nose 1/1, chin 4/1 RHE 1/1, Lt. eye- brow 10/1	Granular
10	Ahlad	C3 N2	I.M.	0 10	40	½ to 2	Slightly Improved	Skin of nose 30/1 chin 6/1, RHE 4/1 LHE 10/1, nose M/1	Intracellular
11	Ashari	C1 N2	I.M.	0 7½	30	1 to 2½	Improved	Nose 1/10, RHF neg., RTBS neg.	
12	Dileswar	C1 N2	I.M.	1 2	56	2 to 2	Slightly Improved	LHE M/1, RHE M/1 nose M/1, rt. eye- brow M/1	Intracellular
13	Sukua Sordar	C3 N2	I.M.	0 10	40	2 to 4	Slightly Improved	Chin M/1, nose M/1, skin of nose M/1, lt. eyebrow M/1	
14	Band- hona	C3 N2	I.M. & I.D.I.	1 1wk	49	2 to 5	Improved	Chin M/1, RHE M/1	
15	Pano	C3 N2	K.E., Rt.I.D. H.E. Lt.I.D.	0 6½	27	½ to 1	Improved	LHF 10/1, RHF 4/1 RHE and LHE 8/1, nose	Intracellular
16	Sombhu Revajali	C3 N2 N2	„ „	0 8½ 1 5	35 43	½ to 1 ½ to 3½	Slightly Improved Improved	M/1 all over —	

I.D.I.—Intradermal injections. I.M.—Intramuscular injections. yr.—year. mth.—months.  
 M/1—many bacilli per field. 4/1—four bacilli per field, and so on, the numerator indicating the  
 average, the number of bacilli per field. At least 10 fields were examined for the average.

#### ACKNOWLEDGMENTS.

My thanks are due to Dr. M. Wardman, M.B., Ch.B., the previous Chief Medical Officer of this Colony, for the supply of the oil, and for advice and encouragement received. I am also indebted to the Rev. E. B. Sharpe, the Superintendent of this Colony, for continuing the supply of the oil for this experiment. I am also grateful to Dr. E. Muir, and Dr. R. G. Cochrane, for the encouragement received from them.

## The Treatment of Leprosy.

D. F. BAXTER.

*A Paper read at the Calcutta Leprosy Conference on 27th March, 1933.*

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

**T**HE main lines of the subject can be conveniently divided into three heads.

First of all, what are the directions along which institutions with no facilities for research and experiment should direct their treatment?

Secondly, where facilities for experiment are available, what should be the treatment?

Lastly, we shall consider briefly the results of treatment.

1. In the first place it may be stated that the treatment at the smaller treatment centres, and particularly the out-patient clinics, should be such as to combine ease of administration with economy and effectiveness.

Hydnocarpus Oil and its derivatives are the drugs that have received the most attention, and rightly so, because of all the numerous drugs that have been tried, they have given the most consistently satisfactory results, in the average case. Because of expense, the pure oil may have to be relied on entirely. The Medical Stores in Madras are preparing and selling the ethyl-esters at Re. 1 per pound. Such a price makes its use possible for the smaller out-patient clinics and dispensaries. The ester is stable in quality, easy to inject and suitable for intra-dermal administration. It may be found that a mixture formed by the addition of olive oil is better tolerated by certain highly infected skin cases. As a preservative, creosote is necessary.

2. For the institutions with facilities for experiment and research, certain centres should be chosen to try out any preparation that may have offered prospects of therapeutic advance. One difficulty is that patients with faith in the present treatment are with difficulty persuaded to co-operate in an experiment with a new drug whose efficacy is unknown. It is probable that this difficulty may be partly overcome through a frank explanation being given beforehand, and by asking for volunteers.

In such a way it may be possible to carry out, in certain centres, the crucial control-experiment of keeping two batches of similar patients under identical conditions, giving one batch general treatment only, and the other batch general treatment plus special leprosy treatment.

The result would demonstrate the value or otherwise of special treatment. It may be possible to compare the findings so obtained in an in-patient institution, with a third group of out-patients, to represent the benefits of treatment without any general treatment at all, beyond what can be advised to certain cases.

3. *Results of Treatment.*—There are several considerations and possibilities that make the question of evaluating the results of leprosy treatment difficult.

(a) The course of the disease is a long one and slow one. The progress of the disease is usually so slow that it is often impossible to be certain from clinical examination whether a case is improving or is just stationary or is getting worse. Bacteriological findings do give a certain amount of assistance. The general impression gained from watching most cases of leprosy is that one is watching an exceedingly slow-moving condition and thus one may consider a case as "disease-arrested," when the disease is still active.

Such an error is obviously easy when one considers that the disease is essentially one of the lymphatic system. That being so, it is the activity or non-activity of the lesions in the lymphatic glands that determines permanent quiescence or not. And we have no methods of judging with certainty the activity or non-activity of such lesions.

(b) In addition to the course of the disease being a slow one, it is possible that there is a swinging character about the active physical signs. The lymphatic system is chronically involved, but skin and nerve tissue obtain floods of bacilli from time to time. These are repeatedly killed off or reduced to such a state that they are invisible. During such periods of latency, the case may be sent away as a "disease-arrested" case, to return some time later, with a relapse. Such an alternating condition of activity and latency may be found to be the normal course of events in the average case of leprosy, especially in the skin type. Naturally permanent quiescence is possible at any one of these clinically and bacteriologically latent periods. The only way of learning the truth of this surmise is the observation of large numbers of cases, receiving treatment over periods of ten to fifteen years, along with controls not receiving treatment at all.

(c) The third difficulty is that the observation period of six months, which we now consider necessary for the granting of a discharge certificate, is too short a period. Thus cases leave too soon after treatment, and relapses

occur, but they are not discovered owing to the fact that they do not return. A good number of the relapse cases at Chingleput are those who have been compelled to return for varying reasons. To lengthen the observation period by doubling it, would be almost to halve the annual turn-over of cases in institutions that already find it difficult to cope with the large numbers desiring admission.

What are going to be the criteria for the efficiency of the treatment? It can be stated with confidence that it is very difficult to draw any conclusions from the results of treatment in purely nerve cases, because we have no way of discovering whether a nerve lesion is an active lesion or not before treatment is actually commenced. But in the skin case, pure or mixed with nerve symptoms and signs, we do have an accurate test, it being taken for granted that the presence of bacilli indicates activity.

Therefore, there will be concentration on the skin case in most figures that will be presented. It may be argued that such concentration is putting an unfair strain on the reputation of our treatment. Such is probably so, but my main object is to show the limitations of the treatment, particularly in the skin case. It is impossible to state with confidence whether treatment prevents the incidence or onset of skin symptoms in early cases, until we have got knowledge regarding the average frequency of such progression from nerve to skin, in untreated cases.

*Present population of the Settlement.*

<i>Adults.</i>	Early and middle nerve	84 or 19 per cent.	
	Skin, all stages ...	236 „ 54	„
	Advanced nerve ...	117 „ 27	„
<i>Children.</i>	Early and middle nerve	36 „ 40	„
	Skin, all stages ...	45 „ 50	„
	Advanced nerve	11 „ 10	„

*Discharges with Certificates—*

<i>In 1930.</i>	10 skin cases obtained	S.F.	cert. or 1.8 per ct.
	16 „ „	D.A.	„ 2.6 „
	31 nerve cases „	D.A.	„ 5 „
	19 „ „	S.F.	„ 3 „
<i>In 1931.</i>	9 C. cases „	S.F.	„ 1.5 „
	33 „ „	D.A.	„ 5.5 „
	23 N. „	S.F.	„ 4 „
	74 N. „	D.A.	„ 12.3 „

(This latter figure contains a number of *burnt outs*.)

<i>In 1932.</i>	7 C.	cases obtained	S.F.	cert. or 1	per ct.
	15 C.	" "	D.A.	"	2.5 "
	24 N.	" "	S.F.	"	4 "
	37 N.	" "	D.A.	"	6 "

It may be noticed that in the later years a less number of skin cases have been discharged with certificates. This is due to more thorough bacteriological examinations.

Let us now examine the present-day adult population with skin leprosy and attempt to discover what has been the result of treatment on them over prolonged periods of time.

238 of the present adult inmates are skin cases, who have been in the Settlement for varying lengths of time, and have remained so ever since they were admitted.

30 cases have had treatment for 7 years and over.

10	" "	6	" "
13	" "	5	" "
15	" "	4	" "
20	" "	3	" "
34	" "	2	" "
62	" "	1	" "
54	" "	1 year and under.	

Four cases not in this series were originally pure nerve cases, but have developed into the skin type, while under treatment.

74 skin cases have recently become bacilli-free, with the following lengths of treatment :—

4 cases have had treatment for 7 years or more.

10	" "	6-7	" "
9	" "	5-6	" "
10	" "	4-5	" "
8	" "	3-4	" "
9	" "	2-3	" "
16	" "	1-2	" "
8	" "	1 year and under.	

Ten cases, now under treatment, are cases who have relapsed.

#### *General Conclusions—*

1. 24 per cent. of those who came in originally as skin cases became bacilli-negative under treatment with an average length of 3.2 years.

The remaining 76 per cent. have remained bacilli-positive, under treatment with an average length of 2.7 years.

Therefore, roughly one skin case in four may become bacilli-negative, in a seven-year period, with an average treatment period of 3.2 years.

2. Such a finding should make us chary of hoping that by treatment alone can leprosy be removed from any given district.

3. Therefore the basis of our attack on the disease must rest, until some more effective remedy is found, on voluntary isolation, either at home when possible, or elsewhere.

The soundest foundation for our campaign then, is not therapeutics, but propaganda leading to the prevention of spread of infection from the infectious skin case.

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## The Treatment of Leprosy.

Dr. R. G. COCHRANE.

*A Paper read at the Calcutta Leprosy Conference  
on 27th March, 1933.*

(A) *Standard treatment for centres with no facilities for experiment.*

In considering the best type of treatment to lay down in centres where it is impossible to experiment, the following four principles should as far as possible be adhered to :—

- (1) Relative efficacy.
- (2) Cheapness.
- (3) Relative painlessness.
- (4) Ease of administration.

(1) *Relative efficacy.*

As will be said later, it is extremely difficult to evaluate the results of any of the special lines of treatment in leprosy, but there are certain preparations which have been used long enough for us to be able to say that they are, as far as we know at present, the most effective drugs in the treatment of leprosy. In order of their efficacy I think most workers would place them thus :—

- (i) Iodised or creosoted esters.
- (ii) Pure hydnocarpus oil and creosote.
- (iii) Alepol or the sodium salts of the hydnocarpic acids.

(2) *Cheapness.*

One must always remember when recommending a certain line of treatment to a centre of the type we are considering, that the cost of the remedy is an important factor. Therefore, as the iodised esters are the most

expensive, it might be better to use hydnocarpus oil, unless the centre is sufficiently well equipped to make its own esters, or to produce them at inexpensive rates from a neighbouring source. As we are considering Indian conditions where the oil is easily obtainable, one hardly needs to consider alepol. The advantage of the latter preparation is that the drug occupies a small bulk and it can easily be transported, whereas the pure oil is more difficult to transport. Again, alepol is easily injected, being a watery solution and easily made up ; all that is required is distilled water and a little carbolic acid.

(3) *Relative painlessness.*

This factor is of most importance, for if a drug is painful, patients will be discouraged to attend the dispensary. The least painful of the drugs is the hydnocarpus oil ; esters are very slightly more painful, and alepol is liable to be the most painful.

(4) *Ease of administration.*

The methods of administration are well known and are as follows :—

- (a) Intravenous.
- (b) Intramuscular.
- (c) Subcutaneous.
- (d) Intradermal.

The intravenous route is little used, and the two chief methods are intradermal and subcutaneous. The method of subcutaneous infiltration being easy and comparatively painless is often the method of choice. The intradermal method is the most painful and it takes a longer time to administer compared to the subcutaneous route. Further there is the question whether intradermal methods alone are as efficacious as intradermal injections combined with subcutaneous and intramuscular injections. I should personally recommend the subcutaneous route as a routine, with the painting of the patches with trichlor-acetic acid. In cases with infiltrated erythematous patches and in those patches where bacilli can be demonstrated, I should suggest that these should be given intradermal injections.

(B). *Experimental Treatment with suitable staff and equipment.*

This is a subject which is difficult to deal with in a limited space, and therefore I can only express thoughts running through my mind.



Leprosy treatment has tended to follow along one line. By this I mean that one line or method of treatment tends to be pushed to the exclusion of others. The method now recommended is intradermal injection, while previously it was subcutaneous infiltration plus trichlor-acetic acid. Effective as intradermal injections are, is it a sound policy to confine oneself largely to this method alone? It has been suggested that all we do in intradermal injections is to scar up the local lesion leaving the deep foci untouched. It is known that the ester or oil remains in the tissue for months after injections. Have properly controlled experiments ever been done to show that intradermal injections alone are as efficacious as subcutaneous, combined with intradermal? Further, what is the optimum of dose of ester or oil? There is a tendency not to exceed 5 or 6 c.c. of the remedy because of the pain of the injection, but it has been known for some time that those patients who can take large quantities of oil by mouth usually improve. Therefore I suggest that perhaps our doses tend to be too small. It would therefore be helpful to have evidence as to the optimum dose of the drugs used. Further, have there been any properly controlled experiments giving evidence that intradermal injections are superior to trichlor-acetic acid? If there have not, then the pain of the intradermal method is a decided drawback.

The tendency to adhere to the chaulmoogra oil derivatives has been marked. There have, however, been one or two breakaways from well-trodden paths, and institutions with suitable equipment should be encouraged to experiment along profitable lines. Two lines of treatment suggest themselves to me. The first is the aniline dyes. Dr. Ryles reports favourably on the use of brilliant green, and is now using Bonny's blue, which is a mixture of brilliant green and crystal violet. It is well known that it is possible by the eosin and other aniline dyes to sensitize living cells and to cause by the action of visible light abnormal conditions, similar to those produced by ultra-violet radiation.

A vast field of experimentation is opened out here; further, there is a considerable amount of ultra-violet radiation which can be used in the sun's rays. This suggestion is thrown out in order to open up the way for experimentation, by the intradermal injections of aniline dyes and the deliberate exposure of the areas to the sun's rays.

Although the therapeutics of leprosy are much more satisfactory than ten years ago, workers in well-equipped

institutions should ever be on the look out for other remedies, and if the indigenous systems of medicine recommend any particular remedy, this should afford a basis for trial. Dr. Rao mentioned the use of esters made from *Pongamia glabra*.

These are some lines along which experiments might be initiated, and institutions sufficiently well equipped should be ready to try out lines of experiments which appear to be fruitful. On the other hand, some supervision should be exercised or else much valuable time and money will be wasted. Finally, it cannot be too strongly emphasised that cases which have a good chance of recovery should be treated along well-tried lines and not be subjected to excessive experimentation by an over-zealous doctor, lest they pass to the stage when treatment is of no avail. The fact remains that in our treatment of leprosy our resources must be almost limitless, for hardly any two cases react to exactly the same line of treatment, and it is impossible to outline all the possible methods. In the discussion to follow I hope this will be brought out.

#### *Results of treatment.*

It is extremely difficult to evaluate the results of anti-leprosy treatment, and the sceptic has ample opportunity of saying that no treatment has been definitely proved to be of any value. In assessing the results we must steer between the Scylla of excessive optimism and the Charybdis of extreme pessimism. I think a fair statement may be made that the modern therapeutics of leprosy will bring a large number of early cases to a state of complete freedom from the disease, and that the majority of infective cases, in the course of time, will become non-infective. In our endeavours to encourage workers we must not be blind to the fact that we are a very long way off a specific remedy for the disease, in the sense that arsenic is for syphilis, or quinine for malaria. Leprosy may become arrested not only in the late stage, the type which has long been known in India as "burnt-out," but also in the early stage.

If we admit that the so-called abortive case occurs in the early stage and that many late cases become self-arrested without treatment, there remain that large group of cases, chiefly in the cutaneous stage, which, without adequate treatment, would become more advanced, in this latter group are we able to assess the value of the treatment at all accurately. Percentages are difficult to estimate. In Purulia in 1932, the percentage of symptom-free cases

among the in-patients was 6% and among the out-patients 3.8%. Such results are not encouraging. Institutions such as Dichpali, where there are fewer advanced cutaneous cases, report better results, but how much is due to the better conditions rather than to any specific action of the drug used?

Again, the reports of the relapse rates both in Hawaii, and I believe now in Culion, are somewhat alarming, and therefore this question arises. In our treatment of cutaneous cases are we merely scarring up superficial lesions or are we getting at the deep foci of infection? We know as in tubercle, so in leprosy, when patients return to their former surroundings they are very liable to relapse, hence the importance of a settlement where they can gradually become accustomed to ordinary conditions of life.

One must confess that we have a long way to go in our search for better remedies for the disease. It may be that leprosy does not lend itself to specific treatment and that our greatest advance will be along epidemiological and preventive lines.

While expressing these doubts I do wish to emphasise most clearly that I am not pessimistic. I have seen a great change in the therapeutics of leprosy, but I am, as others are, only too much aware of the distance yet to be travelled, and therefore we must keep an open mind and be ever on the look out for new and better remedies.

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## Cases of Leprosy seen in the Federated Malay States.

G. RYRIE.

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

**T**WO things, I think, justify the presentation of this collection of oddments from the Federated Malay States to readers in India. One is, that there are definite variations in the type of leprosy—and to some extent in the treatment—in different countries, so that the platitudes of one leper hospital may be the surprises of the next. The other is that the study of leprosy in Malaya demands not merely an observation of its effects on Malays, but also on Southern Indians and Chinese. Fourteen per cent. of the population of Malaya are Indians, nearly forty per cent. are Chinese. One is thus able to form an inter-racial picture of leprosy that is in some ways unique.

This immigrant Chinese and Indian population supply a good deal of Malaya's leprosy problem. The normal prosperity of the country, its high standard of public health work, and the lack of anything but very mild seasonal variation, ensure much more stable health and economic standards than exist in many parts of India or China. One can study the incidence and course of leprosy therefore under steady conditions as well as see it inter-racially—see leprosy steadily and see it whole, so to speak.

An observation of groups of Southern Indian and Chinese lepers reveals at once the fact that there is a striking racial difference in their types of leprosy. Out of a hundred and fifty Southern Indians (mainly Tamils and Telegus) examined this year, forty per cent. were almost wholly nerve cases. A similar examination of Chinese patients for comparison showed that less than twenty-five per cent. were predominantly nerve type. To this we must add two further observations. One is that the incidence of lepra-reaction is very much lower in the Indian section of Sungei Buloh and that the severity of advancing or acute phases of the disease seems generally much greater among the Chinese. The other is that the death-rate (not from leprosy) among Indians in Sungei Buloh is roughly about forty per mille; that of Chinese is nearly eighty per mille. These figures are roughly calculated from the percentage death-rate in the last eighteen months.

On the other hand, it must be remembered that these figures and observations are made from cases under institutional control, under the same type of treatment and in receipt of an adequate diet.

We cannot, of course, assess the effect, if any, of comparative racial immunity in accounting for these striking differences. The Southern Indian labourer outside the Leper Settlement sticks to his traditional diet—a diet deficient in vitamins, fats, proteins, and mineral salts. If the exacerbation of leprosy had any close connection with faulty diet, he would certainly be worse off than the Chinese labourer, who is singularly broad-minded about what he can eat.

There are, however, three other differences in racial habits which may to some extent throw light on this question.

1. The Southern Indian takes care of his skin. He has a medicated oil massage to the body every week. And the Indian—who oils and massages his skin—is relatively free from skin leprosy.

2. Diseases of the teeth and gums are less common among Southern Indians: At least seventy per cent. of Chinese patients in Sungei Buloh have pyorrhœa. My attention was drawn to the possible importance of this during the examination of arrested cases. No single person discharged this year (about 150 cases) has shown marked signs of pyorrhœa although other septic conditions were occasionally present. The suggestion is that pyorrhœa definitely exacerbates leprosy.

3. Southern Indians have a regular morning system of bowel hygiene, reinforced with all the religious and physiological weight of custom.

These characteristics of the Southern Indian, his poor diet and his more effective mouth, bowel, and skin hygiene (if we suppose that they are connected with the comparative mildness of his leprosy) seem to indicate that freedom from toxæmia is of more importance to a leper than the correction of faulty nutrition—that in the leper's metabolism cleanliness is more important than adequacy.

One or two interesting points arise from a consideration of the concomitant diseases of lepers observed in Sungei Buloh. It is difficult to avoid two conclusions. One is that in Sungei Buloh some diseases do not seem to be concomitant with leprosy; the other is that leprosy does not seem to be a concomitant of certain other diseases.

For instance, although the examination of the urine is a frequent routine procedure here, we have no record of glycosuria occurring in an active leper. In general hospitals in Malaya diabetes is not infrequent, especially among the carbohydrate-eating Southern Indians. It would be interesting to know the experience of other workers with regard to the absence or comparative rarity of diabetes among lepers.

Arterio-sclerosis is comparatively rarely found here, although not uncommonly observed among Chinese patients in general hospitals. Chronic nephritis is, of course, frequent in Sungei Buloh, as in leper hospitals elsewhere.

Manifestations of leprosy, as has been often observed, frequently disappear in the course of acute tuberculous toxæmia. This is almost invariably the case here, and similar retrogression of leprotic lesions is often observed with coincident grave toxæmia from disease of the liver or kidneys. I have noticed on four or five occasions a rapid resolution of leprosy in cases of severe jaundice.

These observations on the tendency of leprosy to disappear in the presence of certain systemic poisons are of

passing interest in the case of Father Damien. Father Damien, as is well known, contracted leprosy in Molokai. It was observed after his death that all signs of leprosy had disappeared from his face. This was considered to be a result of the sanctity of Father Damien's life. I have not observed sanctity as a concomitant factor in cases in the Federated Malay States showing a similar recession of lesions, and I suggest that Father Damien's death was due to chronic uræmia, in the presence of which the lesions disappeared.

This interaction of other diseases with leprosy seems full of interest, if we may conclude that certain poisons in the circulation can, and do, cause the disappearance of leprotic lesions.

A further point of interest rises from survey work in the Federated Malay States. The examination of over five hundred non-leper Chinese housed in the Federated Malay States Decrepit Settlement, and a further examination of some thousands of Indian labourers in rubber estates, revealed the fact that about ten per cent. of the total had palpable auricular nerves. There were no other clinical signs of leprosy. If the fact that an auricular nerve is definitely visible on stretching the skin, be taken as evidence of present or past leprosy,\* the suggestion is that minimal infections are very much more common than is sometimes realised. Further work on this is being done as autopsies become available. It seems feasible, however, that, just as in tuberculosis, slight infections are not uncommon and that the disease may often become self-limited at a very immature stage. Among the poorer classes both leprosy infections and families tend to multiply: in both there may be a high infantile mortality.

The treatment of nerve pains and trophic ulcers deserves comment for two reasons. One is that these subsidiary scourges of leprosy form constant problems everywhere, and practical experience in their treatment is seldom inter-changed or pooled. In this connection the recent symposium of views on ulcer treatment in this journal is of particular value. The other reason is that prolonged and unnecessary misery can be and is caused by unskilled treatment. In nerve pains I have observed physical and mental damage caused by prolonged and uncontrolled administration of aspirin, ephedrine, and narcotics. In trophic ulcers one has observed with distress the effect of daily applications of external antiseptics based on the fetish of "keeping the wound clean" while extensive caries of bone within

\*We think that such evidence is not conclusive—Ed.

remains untreated. With equal distress one has seen daily plugging of ulcers, blocking drainage, and driving infection up the interfascial sheaths, resulting in inevitable amputation or septicæmia. In the treatment of trophic ulcers the main reliance in Sungei Buloh is placed on strapping. If on palpation the exudation from a trophic ulcer contains tiny bubbles of gas this is held to be indicative of caries of bone. The bone is then thoroughly scraped, the wound cleaned and the cavity syringed with a solution of acriflavine in spirit. The limb is then strapped. Ulcers involving soft tissues are similarly cleansed with an alcoholic solution of acriflavine and strapping applied. Grossly contaminated putrefying ulcers are cleansed with 1 per cent. Chloramine which we have found especially effective as a deodorant and disinfectant. It is not necessary to buy expensive strapping. Any hospital can make up a cheap composition of wax, resin, zinc, and spirit, which can be smeared on bandages, applied, and left untouched for a week. The saving in daily dressings, and the results, more than justify a trial of this treatment.

In nerve pains we have found that a 10 per cent. solution of menthol in spirit rubbed along the line of the nerve sometimes produces effective relief. We have given up the administration of ephedrine or any other sedative by the mouth: ephedrine is used here only as an injection round the nerve. Injections of Cylophyllum oil 2-6 c.c. intramuscularly are often effective here and are the most popular form of treatment—they appear to have been a failure in some hospitals. We have found the operation of stripping the fibrous capsule from the ulnar nerve (which Dr. Lowe very kindly demonstrated to me in Dichpali) an invaluable procedure in thickened resistant cases.

In lepra reaction the routine administration of alkalis has been given up, as no benefit from alkali was found on comparison with control cases on acids. Potassium Antimony Tartrate, though undoubtedly useful, has been given up in favour of intravenous injections of Fluorescein in doses of 20 c.c. of a 2 per cent. solution bi-weekly. We have given as much as 100 c.c. of a 2 per cent. solution in a few acute cases without apparent ill-effects. (In a non-reaction case I have given as much as 350 c.c. of a 2 per cent. solution in a single dose.)

These reflections are neither scientific nor original. We have, however, so often found the benefit of informal views of visitors from other countries that we feel these random notes may be of some interest to other workers.

## Examination of Bone Marrow for *M. Lepræ*.

H. H. GASS, M.D., and D. P. RISHI.

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

**T**HIS report is based on the microscopic examination of the bone marrow of 69 cases of leprosy in the Chandkhuri Leprosy Hospital. Most of the material was gotten from necrosed bone which had to be removed surgically. The remainder was gotten from post-mortem material. The bones examined included the phalanges of the upper and lower extremities, metatarsals, radius and ulna, and tibia. The investigation was carried out taking as a basis the fact that *M. lepræ* has been found in abundance in the cells of the reticulo-endothelial system.

To ensure against the factor of extraneous contamination, the cut end of the bone to be examined was always cleaned with antiseptic fluid and the marrow removed by means of a probe. To be very sure, we took a tibia, cleaned the bone thoroughly, immersed it in spirit for 48 hours; then made a fresh cut with a clean saw, and removed the bone marrow by means of a probe. This upon examination showed *M. lepræ* in practically every field. Slides and instruments were always scrupulously cleaned before examining any material.

The bone marrow of seventeen out of twenty-one mixed cases (cutaneous and neural) was positive for *M. lepræ*. Three of the four that were negative were from smears taken from phalanges or parts of phalanges, and one from a metatarsal. Of the forty-eight cases which were classified as neural not a single smear of bone marrow was positive for acid-fast bacilli.

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### Corrigendum.

Dr. F. G. Cawston has drawn our attention to the fact that owing to an error in the manuscript of his article, entitled "Nasal Hygiene in the Treatment of Leprosy and the Use of Antimony," which appeared in the April number of *LEPROSY REVIEW*, the name of the institution recorded on page 62 as Amanzimtoti, should have read Amatikulu, no cases of leprosy being treated at the former institute.



## Leprosy in the Republic of Paraguay.

IT is interesting to hear that active measures are being considered for the development of modern anti-leprosy work in the Republic of Paraguay. We have received a memorandum from Dr. J. Nairn Hay indicating the lines along which measures are to be enforced.

The population of Paraguay is approximately one million, and the number of cases of leprosy is estimated to be between 2,000 and 4,500. This appears to be relatively small, but at the same time there seems to be evidence that the disease is spreading. It is for this reason that the authorities are considering putting into force active measures with regard to the control of the disease. It has been decided to build a colony near Sapucaí, on the railway about 80 miles from Asunción, on a piece of land of about 2,500 acres, excellently suited for the growing of crops and plantations, and with a good water supply. It has been pointed out to us that this decision is due to the far-sighted and wise attitude taken by Dr. Eusabio Ayala, the President of the Republic, who is being ably and enthusiastically supported by Dr. Justo Prieto, the Minister of Education, and Dr. Ricardo Odrioso, Dean of the Faculty of Medicine of the National University. The colony will consist of some 36 houses, each accommodating four patients, and a modern treatment block with dispensary and laboratory. Each patient will have his or her own plot of land in which to grow the usual food stuffs, and will be free to live in his or her own house without any restrictions. The point that is being stressed is that patients will be attracted there by persuasion rather than brought by force. This will open up the possibility of giving first place to segregation and treatment on modern lines, and emphasis will be placed on the voluntary attraction of open cases to the settlement.

The main objects of the colony are stated to be as follows :—

- (1) A centre for the modern treatment of early and advanced cases.
- (2) A centre for research work in leprosy.
- (3) A centre for training students and others.
- (4) A centre for agriculture—to provide occupation for the patients.

(1) *A Centre for Modern Treatment.*—As there are some 100 advanced cases already under treatment, provision will have to be made for them. As their health is not good they

will be housed in a part of the colony where it will be possible to carry out their treatment without difficulty. They will also be allowed sufficient ground to grow the food stuffs to which they are accustomed. As early cases are attracted to the colony, provision will be made for them in other parts of the colony, apart from the advanced cases.

(2) *A Centre for Research*.—The first object of research will be :—

- (a) To ascertain the number of sufferers from the disease in the country.
- (b) The districts most infected and the type predominating.
- (c) The factors influencing location and type.

(3) *A Centre for Training*.

- (a) For the medical students of the National University—laying stress on the practical rather than on the theoretical side.
- (b) For others taking up leprosy.

(4) *A Centre for Agriculture*.—It is necessary that the patient under treatment be occupied in useful work, physically active and mentally tranquil. For this reason it is necessary to provide him with work that will prove fruitful in his hands. The product of such work, however, can be of little financial value to the colony.

The general policy for the country will be as follows :—

- (1) Segregation of all open cases.
- (2) Early diagnosis and observation of new cases, with facilities for immediate treatment of those needing it.
- (3) Examination of all contacts every six months over a period of five years.

The programme includes, in addition to institutional work and the training of students and medical men, opportunities for the investigation of the situation in the field.

It appears to us that this Central American State is organising its leprosy policy on essentially modern lines, and this comes as a refreshing piece of news, for the chief information to reach countries abroad concerning the situation in Paraguay is usually information regarding the Chaco War. We should like to congratulate the authorities in Paraguay, and trust that Dr. J. Nairn Hay's memorandum will be speedily implemented.

## Reviews

"INTERNATIONAL JOURNAL OF LEPROSY." Vol. 1, No. 3. July, 1933.

Among the original articles in this issue there is one by Dr. Molesworth on "The Influence of Natural Selection on the Incidence of Leprosy," which is a development of a paper which was read before the Australasian Association for the Advancement of Science in Sydney in August, 1932, which was published in the *Acta Venereologica*, in August, 1932. Muir criticised the paper in the same Journal, and a reply by Molesworth to Muir's criticism appeared in *Leprosy in India*, in July, 1933. The present article is largely rewritten with a view to meeting Muir's further arguments. It is in itself an attractive theory, and while the existence of racial or tribal resistance cannot be disputed, whether this is due actually to the laws of natural selection or to the general resistance in the tribe being raised by economic conditions, or the disappearance of predisposing causes, such as famine and disease, etc., would be difficult to prove. It would be an injustice to the theory to attempt to detail Muir's arguments, and our readers are referred to the original communications if they wish to study the subject in more detail. Suffice it to say that countries such as Japan, where the factor of natural resistance should be beginning to come into play, there should be some evidence of the commencing disappearance of leprosy. On the contrary, however, leprosy apparently is still prevalent, and, furthermore, the non-resistant form, generally considered to be the advanced cutaneous form, is still very prevalent.

Dr. Chatterji contributes an article on "Thickened Nerves in Leprosy in Relation to Skin Lesions." This is an extremely interesting article and we reproduce Dr. Chatterji's summary and conclusion:—

"Observations have been made on thickened nerves in relation to skin lesions as seen in a clinical study of 3,079 cases of leprosy.

"The area of deep analgesia is usually less than that of superficial anæsthesia. As repair progresses, the anæsthesia usually persists longer than the analgesia.

"From the clinical findings it seems that in the ascending type of nerve lesion the infection spreads by lymphatics from the skin lesion. The reasons why the nerves are found thickened in their superficial course, like the ulnar behind the elbow, are that there is space for the nerve to swell, and that because the lymphatics and blood vessels of the part are not under the pressure of muscles, stagnation may occur and therefore the infection finds time to work out its course. This also explains aberrant findings in which infection may spread by collateral branches of lymphatics to the nerves adjacent to the skin lesion.

"The nerve supplying the leprous patch should be palpated, as far as practicable, throughout its whole course because only a particular part may be affected, though the whole trunk may be involved. The adjacent nerves should also be examined for any aberrant findings.

"Sometimes a case of leprosy with thickened nerves may serve as a living model for the anatomists; even the finer nerve branches of a nerve may be so thickened that their course can be demonstrated easily by palpation. On the other hand, a nerve may be missed entirely because it has an abnormal course, as when the ulnar is found on the medial epicondyle.

"The importance of the nerve findings in relation to diagnosis, prognosis and treatment is emphasised. If the wide possibilities of cutaneous nerve involvement are kept in mind the *diagnosis* of an early case of leprosy is often facilitated, especially when superficial anæsthesia is not marked, or when the affected part is burned or disfigured by a local corrosive application.

Dr. Read, of the Henry Lester Institute of Medical Research, Shanghai, contributes an article on "The Toxicity of Sodium Hydno-carpate." He points out that there is a cumulative action of the drugs, and that this is clearly seen in the slowly developing toxic action in the kidneys of rabbits and dogs, small doses producing albuminuria and possibly hemoglobinuria. He further points out that the prolonged sub-cutaneous treatment in dogs, instead of lessening the toxic effects, *i.e.*, nausea and vomiting, gradually increased them until the animals eventually vomited their meals and showed blood in the urine. Dr. Read considers that the hydnocarpates are probably excreted in the saliva, and concludes that there are indications that with continued treatment there is a gradual saturation of the organism with this foreign oil, which is gradually excreted in small dosage through the kidney and is not burnt up in the body like ordinary fats.

As a result of these experiments he suggests that care is needed in selecting suitable concentrations. It is difficult to apply animal experiments to man as one very seldom sees any toxic results from the use of preparations of hydnocarpus oil (*chaulmoogra*). It is known that the oil by mouth does produce toxic effects, but there has been very little evidence of actual toxic effects arising from any methods of injection. It would assist clinicians enormously if an optimum dose of the various drugs could be discovered. At present the size of dose is largely arbitrary.

Further articles in this issue are "Statistics of Leprosy in the Krutyje Rutschji Leprosarium, Leningrad," by Dr. A. A. Stein, and "Leprosy in St. Croix," by Dr. Howard Fox. Dr. Fox suggests that owing to climatic and other conditions St. Croix should be an excellent place in which to undertake an intensive laboratory and clinical study of the disease.

Dr. Gonzales Uruena gives a Summary of the First Leprosy Census in the Republic of Mexico, and points out that the distribution of centres in that country seems to indicate a stream which starts at the Pacific coast and continues through the States of Jalisco, Guanajuato and Querétaro until it arrives at the Federal District. He suggests that this current might coincide with the route followed by the active colonial trade during the Spanish rule. He further suggests that the disease may have originated in the West Indies, there having been frequent relations with Cuba. The large incidence suggests that cases are probably not discovered until they have reached adult life. The largest group of cases comes under the age period of 20—29, giving further support to the theory that the majority of cases acquire the disease during adolescence or earlier.

Dr. Rose contributes an article on "The Incidence and Treatment of Leprosy in British Guiana and the British West Indies," which is an interesting review of the present position of leprosy in those isles.

The remainder of this Journal is confined to reprinted articles from other sources, among which is a further note on the "Cultivation of *Mycobacterium Lepre*," which will be of interest to research workers.