

L E P R O S Y

A REVIEW OF THE SUBJECT BASED ON WORK AT  
THE LADY WILLINGDON LEPER SETTLEMENT  
CHINGLEPUT, SOUTH INDIA

by

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INTRODUCTION.

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I. REASON FOR CHOICE OF SUBJECT.

From November 1933 until the end of 1935 I acted as Chief Medical Officer of the Lady Willingdon Leper Settlement, Chingleput, South India, During that time I have been able to examine, study, and treat a large number of cases of leprosy. I have also been able to examine the records of an even greater number of patients who have been through this institution during the ten years from 1925 to 1935. It is on this experience and study that I base this thesis.

## II. DESCRIPTION OF LADY WILLINGDON LEPER SETTLEMENT.

The Lady Willingdon Leper Settlement was opened in 1925 by the Government of Madras for the care and treatment of those people suffering from leprosy who belong to Madras Presidency. The site chosen was one three miles south of the small railway junction town of Chingleput, and about forty miles south of Madras city. The Settlement is away from any large centre of population and is not on the main highways, but is easy of access both by rail and road - altogether an ideal situation for such an institution.

The Settlement, or colony, is in the form of a more or less self-contained village with the patients taking part in the communal activities as they would in their own houses. The capacity of the Settlement was originally 650, including men, women, and children. In 1933 extensions were added to accommodate another 100 children, thus raising the total capacity to 750. During 1935 the average numbers were 354 men, 104 women, and 227 children. The children are housed in dormitories and food is cooked for them. The adults live in small two-roomed cottages with

kitchen attached. They are issued with raw rations and arrange their own cooking. There are two central hospitals, one for children and the other for adults, for the treatment of acute illnesses. Schools and industrial classes are provided for the children. The adults are employed in the various forms of work necessary for the maintenance of such an institution - agriculture, carpentry, weaving, masons, shopkeepers, teachers, etc. A number are trained to help in the medical work as dressers, ward-boys, and injectors. In this way the necessary staff of healthy people is reduced to the minimum required for the offices and laboratory. Healthy people are employed for conservancy work, as only the "sweeper" caste will do that. No member of the healthy staff has ever shown any evidence of having contracted leprosy as a result of working in contact with leper patients, although several have been on the staff since the Settlement was opened in 1925.

During the ten years under review 2130 patients have been admitted for treatment in the proportion of 1347 men, 247 women and 536 children. Of this number 469 have been discharged with the disease arrested, 352 have left of their own accord, showing varying degrees of improvement,

improvement/132 have died, 492 have shown no improvement or have absconded, and 685 remain at present under treatment. These figures will be studied in more detail later on.

The majority of the patients belong to Madras Presidency, and are of the poorer classes. They have come from all over the Presidency, but naturally the greater number are from districts adjacent to the Settlement. Hindus predominate, and form 66% of the total. Christians make 12%, Muslims 8%, and Adi-Dravidas (Out-castes) 8%. In the minority are 3% Brahmins and 3% Angle-Indians. These last are of mixed blood, with the exception of three or four of pure European descent, but who are domiciled in the country. It is worth noting that almost all the Angle-Indian patients have been advanced cases in whom the disease has steadily progressed in spite of treatment. This suggests a very low resistance to leprosy in individuals of mixed European and Indian blood.

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### III. LEPROSY IN MADRAS PRESIDENCY.

#### I. Madras Presidency.

Madras Presidency, with an area of 143,370 square miles, comprises the greater part of South India. It is bounded on the east by the Bay of Bengal. On the north lie the provinces of Orissa and Central Province and the native states of Hyderabad and Mysore; and on the western boundary are the Travancore and Cochin States. Any study of leprosy in South India should include Mysore, Cochin, and Travancore, and the southern half of Hyderabad, but the statistical information from these states is not as complete as that of British India and therefore of less value, so only passing reference will be made to them. The greater area of the Presidency is low "plains" which rise gradually to the plateau of Hyderabad and Mysore. In the north of the Presidency lie the Eastern Ghats which reach about 4000 feet, and along the Travancore boundary are the Western Ghats which reach peaks of 8000 feet. The four main rivers are the Godaveri and Kistna in the north, the Pennar in the centre, and the Kavari in the south. All these have wide delta areas at their mouths. There is no great variation in the yearly temperature, which ranges from about 70°F. in the winter months to about 105°F. in the summer, although a few districts often rise to 115°F. Rainfall is on the whole



whole/moderate. The West coast and Travancore side of the Western Ghats are the only parts of South India with more than 100 inches in the year. The East coast varies from 60 to 100 inches in the north and centre to 40 - 60 inches in the south. The inland districts adjoining Hyderabad and Mysore average less than 30 inches. The greater part of the Presidency enjoys the North East monsoon which comes in October and November. Drought occurs frequently in the inland districts, with consequent famine conditions, although the great famines of the past are now unknown, with the benefits of efficient administration and easy communications.

Madras Presidency has a population of 47 million, according to the census of 1931. Only six million are town dwellers and the other 41 million live in villages and small hamlets. The greater proportion of the people are of Aryan stock, of moderate physique, and have on the whole, a poor standard of living. The original Dravidian race are represented in the very poor "outcastes", and among the hills of the Ganjam and Vizagapatam districts and the Western Ghats are a sprinkling of even more primitive tribes whose origins are unknown.

unknown./ The caste system, with all its social evils, controls the lives of most of the people. With such a large rural population, the chief occupations are those connected with agriculture. The growth of industry in urban centres is attracting an increasing number into factories and workshops. The spread of the railway and the ubiquitous motor bus have left few communities in their old isolation and along with religious pilgrimages, have led to a greater mingling of the people. This has had a not inconsiderable effect in the spread of leprosy from endemic districts to others more or less free from the disease. Mention should be made of certain of the religious and social customs which have their effect on leprosy. The joint family system, although rapidly breaking down, undoubtedly influence the occurrence of the disease in families and has led to the common belief that it is hereditary. Child marriages lower the physique and general health. The clothing of the poorer classes is only a loin cloth or sari, which leaves the greater area of the body exposed to the possibility of infection. Abrasions and slight wounds are consequently daily occurrences, and the feet suffer most. I have observed that the lower limbs are commonly the site of the earliest lesions.

The habit of carrying children astride the mother's waist and hip explains the frequent occurrence of early lesions on the thighs and genitals in children.

The staple article of diet is rice. Among the higher classes the raw polished rice is preferred for caste reasons, but the poor eat the unpolished parboiled rice. Mutton is eaten by Muslims and Christians and the Hindu obtains his proteins from dhal. Milk is drunk by the better classes, and vegetables and fruits eaten by those who can afford to buy them. A millet-like cereal, called "ragi", is grown as a dry crop and is far more nutritious than rice, and contains a good store of vitamins A and B. Unfortunately this is regarded as "the poor man's food" and the majority of the population refuse to eat it. Those who do are usually more robust than the rice-eater. Fresh fish is eaten by those along the coast and rivers. In other districts the fish is salted or smoked and often it is half decomposed by the time it reaches the consumer. The decomposition evidently adds to the tastiness of the fish and in many districts this is regarded as a delicacy. Another source of decomposed food is the habit of leaving partly cooked rice soaking in water for 24 hours

or more in order to avoid cooking for every meal. The rice ferments and is regarded as more palatable in this state.

On the whole, the diet is a poor one. It consists very largely of carbohydrate. Fat is added in the form of "ghee", and proteins are insufficient in most cases. Vitamins are lacking for all but those who are able to afford milk and fresh fruits. There is little variety in the foodstuffs eaten and there is no one more conservative than the Indian in the matter of what he eats. It is thus very difficult to improve the diet and impossible to get any co-operation in dietetic propaganda or experiments.

Sanitation and public hygiene are non-existent, except in the larger cities, and even there they leave much to be desired. Conditions have greatly improved, within recent years, but it will take many generations of training to correct the habits and customs of centuries. The average middle and lower class town-dweller sees no reason why his house should have its own latrine when there is a convenient street drain at his front door. Fortunately for India, the sun does its work well.

The Hindu religion teaches that all

all/the misfortunes of life are the punishment of the gods for sins committed in a previous existence. It is a man's "fate" if he develops leprosy. Such a philosophy breeds an astonishing indifference to disease. This is the greatest obstacle to the improvement of public health and the control of disease in the country.

All things considered, it is little wonder that the people are of only moderate physique and have a low resistance to disease. Conditions are favourable for the occurrence and spread of leprosy, and for many centuries that disease has taken its toll.

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## 2. DISTRIBUTION OF LEPROSY.

The 1931 Census gives a total of 33,321 lepers in the Presidency. This is obviously a gross underestimate, as the Census returns are dependent on diagnosis by lay people and the wish, or not, of the individual to record himself or herself as a leper. As a rule, only those people with marked evidence of the disease\* will record it in the Census as they know it is useless to attempt to hide their condition. Consequently, most of these cases are probably the deformed "burnt-outs" and the advanced nodular cases. The earlier and less severe cases are not recorded, either deliberately or from ignorance of the true condition. Since 1931 leprosy surveys have been carried out in many districts and by July 1935 no fewer than 120,000 cases had been registered by the Chief Leprosy officer for the Presidency. It is not unreasonable to assume that there are at least 150,000 lepers in Madras Presidency alone. The Chief Leprosy Officer for Travancore has carried out similar surveys, registered 35,000 cases, and says there are many more. The States of Cochin and southern Hyderabad are known to be highly endemic centres, and

and/Mysore has its quota, but reliable figures for these areas are not available. From information I have received from various authorities and my experience of more local conditions I do not consider it an exaggeration to say that there are not less than 200,000 lepers in South India. On the basis of these figures it appears that the Presidency has an incidence of 3.19 per mille, or .3%, indicating a fairly high endemic centre of the disease.

The accompanying map shows the distribution of leprosy according to the 1931 Census returns. Although these returns are below the true figures, there is no reason to suppose that they do not indicate with some degree of reliability the distribution of the disease. The areas that appear most affected are the northern districts, and the west coast. Travancore and Cochin are among the most highly endemic centres in the world, some districts having an incidence of 1 in 7. There are several factors which probably influence this distribution.

(I) Density of population.

Leprosy is a disease spread by contact, and in all such diseases there is an obvious

obvious/ connection with density of population. The incidence is heaviest in those districts with the densest population. This occurs along the northern coastline and delta areas - Ganjam, Vizagapatam, and the Godaveris; in the more industrial districts in the centre - Chingleput, the Arcots and Tanjore; and the very fertile west coast. These appear to be the chief foci of infection and the incidence falls as <sup>we</sup> leave these districts, and enter, for example, the less fertile inland districts Anantapur, Kurnool, and Coimbatore, or the slopes of the Eastern Ghats. The incidence in the large cities is high. An example of this is seen in Saidapet, a suburb of Madras with a population of 33,000. In 1934 I was connected, in a consultant capacity, with a very thorough leprosy survey of Saidapet, and 2% of the population were found to have signs of leprosy, including 5% of school children.

(II). Racial and Social Factors.

Leprosy is a disease affecting chiefly the poor and middle classes. The well-to-do are less affected and also the very primitive. The disease is comparatively uncommon among the primitive tribes dwelling in the hill districts, but when these migrate down to the plains and come



come/in contact with the low degree of civilization there, they are extremely susceptible. Such people returning to their homes have introduced the disease into their villages, where it has spread rapidly. The factory workers show a high infection. A survey of one industrial centre in East Godaverri gave an incidence of 5%. A high incidence was found among the weaving community of Saidapet. Although the disease is undoubtedly commonest among the poor, no community is free from it. There is probably no family in the country which has not at least one leper in it. There died recently a well known Maharaja of considerable political importance who was an obvious leper. The seriousness of the disease is well known, but there exists an extraordinary indifference to it. It is generally regarded as the punishment of the gods and the individual's "fate". There has come to me on several occasions an educated and cultured Brahmin in an advanced stage of the disease and highly infectious. On each occasion I have advised treatment and pointed out to him the danger of infecting his children. He has always politely agreed with me, but done nothing - "It is the will of the gods, and the just punishment for some sin committed in a previous existence." He

He/recently brought his daughter aged II, an early cutaneous case with a fairly good prognosis, but will not allow her to take treatment and sends her to school with other healthy children.

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(III). Climate and Rainfall.

A comparison of the rainfall and humidity of the Presidency with the occurrence of leprosy shows some connection between the two. The West Coast, with its high yearly rainfall and warm moist climate, has the highest incidence of the disease. The east coast districts have a moderate rainfall, but humidity is most marked in the delta regions of the Godaveri, Kistna, and Kaveri rivers, and here again the incidence of leprosy is high. In contrast are the dry and almost rainless inland districts adjoining the Deccan and Mysore plateaux, and here we find the lowest incidence of leprosy. This apparent connection between leprosy and climate was first pointed out by the Indian Leprosy Commission in 1891 and later by Rogers (I) who attempted to explain it. To persons living in a moist hot climate with a fertile soil life is easy and calls for no vigour or robustness. In other areas excessive rain impoverishes the soil by washing away the surface layer. The crops are poor and the inhabitants live in a state of semi-starvation. Consequently their resistance to disease is low and they are easy victims to infection. The humid atmosphere is favourable for the growth of insects and bacteria, as seen in the prevalence of malaria and filariasis and other infections in such regions, so that human

human/resistance is further weakened. It may also be that the frequent skin wounds caused by insect bites are portals of infection for leprosy. On the other hand, in the hot dry regions of the inland districts famine conditions are frequent and the standard of living is low, and yet leprosy is infrequent. It may be that a hot humid atmosphere is favourable to the growth and propagation of the leprosy bacillus itself.

(IV) Diet:

The inadequacy of the average South Indian diet has already been discussed. I consider that this is the most important factor determining the occurrence and spread of leprosy in the individual and the community. "It must be realised that normal nutrition and health cannot be maintained on many of the diets now used by millions of the Indian people", says McCarrison, <sup>(2)</sup>. Muir <sup>(3)</sup> states that the most outstanding determinant in the incidence of leprosy is dietetic. There are three main faults in the diet -

1. Starvation from insufficient quantity.
2. Starvation from insufficient quality and lack of certain food essentials.
3. Intoxication due to decomposing food.

In the poor classes all three faults are present. Among the more well-to-do quantity is

is/usually excessive, but the quality is poor. Three meals are usually taken in the day, and the basis of these meals for all classes is rice. In the morning cold rice left over from the night before is usual. At noon it may be either cold rice again or curry and rice freshly cooked. The evening meal is curry and rice. The poor Adi-Dravida will eat ragi in the morning and noon and keep the rice for the evening meal. Among the more well-to-do coffee and rice-cake make the morning meal. In those districts of the West Coast where leprosy is commonest, the basis of the diet is tapioca, which is wholly carbohydrate and contains no vitamins. Vegetables are included in the curry but the method of cooking and the spices added effectively destroy most of their vitamin content. Milk is drunk as an extra by those who can afford it, but such milk as can be obtained is of poor quality and often watered. A striking contrast is seen in comparing the South Indian diet with that of North India. The people of the Punjab and North Western Frontier, who have whole wheat as their chief article of diet, are much superior in physique and general health to the South Indian. The chief fault in the South is lack of vitamins. Wheat is a greater source of

of these essentials than rice, and even the much despised ragi is richer in vitamins than is rice.

I am convinced that the basal factor in leprosy certainly as it occurs in South India, is faulty nutrition of one kind or another, and that the correction of these nutritional deficiencies is the most effective means we have of combating the disease.

(V). Communications.

The distribution of leprosy is undoubtedly affected by the modern development of communications. There is an enormous shifting population and the old isolation of communities and districts is rapidly breaking down. Even the remotest villages can now be reached by motor bus. There is every opportunity for leprosy to be introduced into areas previously free from the disease, and there is evidence of this actually occurring. A certain small town in South Arcot has for long been known to have a small number of lepers. A few years ago the railway was extended and this town became a junction centre. A recent survey has shown a great increase in the number of lepers and it is not unreasonable to attribute this to the advent of the railway and the consequent increase in population. Religious pilgrimages are probably the main

main/attractions for travelling and in all religious centres the number of lepers is greatly augmented. Twenty miles from Chingleput is Conjeeveram which is one of the sacred cities of India and draws pilgrims from the length and breadth of the country. Lepers come in the hope of propitiating the gods and being cured of their disease. One devotee informed me that after bathing in the sacred tank every day for seven years he was now cured! The sacredness of this city undoubtedly increases its incidence of leprosy.

(VI) Other diseases.

The occurrence of other diseases predisposes the community to the development and spread of leprosy. Malaria is common on the west coast, the delta areas of the great rivers, and the Ganjam plains in the north, and a glance at the map shows these areas to have the heaviest incidence of leprosy. Filariasis occurs in all districts. Nutritional disorders are common. Helminthiasis, and especially hookworm, are universal and the cause of much ill-health. Syphilis and gonorrhoea are very prevalent, especially among the lower classes, but the virulence of both diseases is less severe than in western

western/countries. Syphilis is the commonest accompaniment of leprosy among the patients treated in the Lady Willingdon Leper Settlement. In India leprosy is generally regarded as a venereal disease and associated with immoral living. Other skin diseases play an important part in predisposition to leprosy, and especially ringworm and scabies. Practically every patient who comes to us has one or other or both of these affections.

(VII) Foci of Infection.

A study of the Presidency as a whole and of any one area in particular shows that leprosy occurs in foci, and the incidence falls as one gets further away from these foci. The most heavily infected areas in the Presidency appear to be Ganjam and Vizagapattam in the north and North and South Arcot in the centre. As one gets further away from these centres the incidence gradually decreases. Guntur and the Godaveri districts are adjacent to a highly endemic area of Hyderabad State and the inland parts of these districts show the higher incidence. Similarly, Ganjam is socially undivided from a heavily infected area of Orissa.

Summary.

It is not possible to allot any particular causal factor to the disease in the



the/Presidency. Several factors operate to determine the incidence and distribution and it is often difficult or impossible to say which has most influence in any one area. The basis of the incidence is in mal-nutrition, social customs and the occurrence of other diseases, with general poverty and a poor standard of living. The distribution is largely dependant on population-density, which corresponds with the heaviest foci of infection. Racial factors enter, the primitive tribes and the most civilized elements being the least affected. Climatic and geographical features have their influence, the drier elevated inland areas being less affected than the more moist coastal and delta regions. Lastly, communications and the movement of the population have an obvious influence.

Two other features of the incidence must be considered - the distribution by age and sex.

#### Distribution by age.

The accompanying tables and Graph I are taken from the 1931 Census Report and must be interpreted with certain reservations. As already pointed out, these returns are made by unskilled observers, so that the early stages of the

the/disease in children are frequently overlooked. The tendency is for those suffering from the disease to hide it until gross disfigurements make this impossible. Consequently the greater number of adults recorded are in the advanced stages, or are 'burnt-out' cases. The figures show the highest incidence between the age of 30 and 45, with the peak between 35 and 40, These ages are obviously too high and are not a true indication of the most affected periods of life. The true age incidence is seen in Graph II and the accompanying table of figures. These figures give the age of onset of the disease in 3391 patients treated at the Lady Willingdon Leper Settlement, both as out-patients and in-patients, and show that the onset of the disease is usually below the age of 30. In this series no fewer than 76% showed the first signs before 30. The peak is reached in the 20 - 25 age period, but it is more important to note the high incidence during childhood and adolescence - no less than 48% of this series. After the age of 30 the incidence of onset of the disease is seen to fall rapidly with each succeeding age period. The oldest case of active leprosy met by myself was a man of 83 in whom the disease had first appeared eight years previously; but such a case is very exceptional.

The great majority of cases are infected during childhood and adolescence. In 34% of our cases the incubation period was of such a length as to allow the first signs to be observed before the age of 15, in 48% before 20, and in 76% before 30. After that age it is probably unusual for an individual to be infected. Nearly all of those who show the first signs after 30 have been infected in their youth and have had long incubation periods.

The above data show that children and young adults are most susceptible to the infection of leprosy, and among them the disease shows its greatest incidence.

#### Distribution by Sex.

The 1931 Census figures show that male lepers exceed female in the ratio of 3 : 1. This disproportion between the sexes can be partly accounted for by the greater tendency to concealment of the disease among women. The sex ratio appears to be equal in children up to age of 10, but thereafter it is greatly diminished in females and becomes more so as the ages rise, until the age period of 35 - 45 gives a disparity of 3.7 : 1. Anything that is likely to spoil a girl's chances of marriage will naturally be concealed. Women lead a more secluded life and their afflictions are not often revealed. These factors, however,

however, do not explain entirely the lower incidence among females and it is probable that even a true table of figures would show a difference between the sexes, after the attainment of adult life, making due allowance for the slightly higher male element in the population as a whole. The rise of incidence after the 10 - 15 age period is more marked in males. This period corresponds to the leaving behind of childhood and entry into the world of business and contacts. A sex more exposed to casual and frequent contacts should show a high incidence of a contact disease. Indian customs make the movements of females very much less than those of males. They wear more clothing and, apart from actual movement from place to place, they avoid contact more sedulously and regularly. Males are more exposed to the effects of other diseases, especially venereal disease, and suffer more from the wear and tear of life. These circumstances must contribute strongly to producing a different incidence for the sexes, even though women have to bear the strain of child-bearing and lactation.

It is impossible to prove or disprove that there is any inherent factor in the female sex that may make them more resistant to the disease, In my experience it occurs just as severely in

women as in men, although other observers in this and other countries think that women are not so liable to the severe forms of the disease. Stally-Brass<sup>(4)</sup> gives an interesting discussion concerning the sex incidence of disease in general, and his opinion may be summarised as follows:-

'Greater susceptibility in males may possibly be caused by sex differences; males are bigger and have a more developed musculature which may throw a greater strain on the circulatory and excretory systems and so reduce chances of recovery when attacked.

'The sex factor may be physiological rather than anatomical. The sex hormones are connected with differences in endocrine activity, as shown by the greater activity of the thyroid in women. The endocrine system is intimately connected with destruction of bacteria and their toxins. It is possible that differences in endocrine function in the two sexes may have an influence on the susceptibility to infectious diseases.

' In addition to anatomical and physiological differences in the sexes there is the cytological difference. Each cell in the female contains a group of chromomeres different from

from the corresponding group present in the male, and it is this group that determines sex and sex differences.

Whether these anatomical, physiological, and cytological differences between the sexes have any effect on the sex incidence of disease is uncertain.'

If we consider a selected area with a high incidence of leprosy we can produce evidence in favour of there being no inherent sex difference. In the municipality of Saidapet, already mentioned, with a population of 33,000 males exceeding females by almost 1000. 75% of this community are employed in the weaving and dyeing trade. This is a "family employment" and the women take as large a part in the work as do the men, as well as carrying on their domestic and reproductive duties. The conditions of life are approximately the same for both sexes and among them we find that the incidence of leprosy is only .1% higher among males. Furthermore, the sex incidence among children, as already noted, is the same up to the age of 10.

It appears that the greater incidence of leprosy among males is due to environmental factors and not to differences in sex itself.

This conclusion has been reached by other workers in this and other countries and the whole question is well reviewed by Lowe (5). He considers that while physiological conditions may have an effect on susceptibility and difference in sex incidence, the chief factor is environmental.

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III. LEPROSY IN INDIA.

Leprosy is one of the common major diseases in India and is endemic in all provinces. It is difficult to ascertain how or when the disease was first introduced into the country, whether it existed among the original Dravidian race or was brought by the Aryan and Mongol invasions. We find the Aryans enforcing rigid laws for the isolation of lepers, which even went as far as burning and drowning. The miserable life led by sufferers at all times has induced many to make pilgrimages to holy places with a reputation for curing leprosy. The chief of these has been the deity at Puri, on the east coast, which still to-day attracts many lepers, and accounts for the very high incidence in and around that town.

Such stern measures may have kept the disease in check, but with the Mohammedan invasion the period of Aryan supremacy ended. These latter were driven into the east and south and came into closer social contact with the Dravidians. It is impossible to say how far each race was responsible for the spread of the disease, but it is worth noting that while all Indo-Aryan languages have a word for leprosy, the ancient



ancient/Dravidian languages have no indigenous name for the disease. A long period of ceaseless wars followed the Mohammedan conquest, which doubtless influenced the dissemination of the disease.

After British rule was established in India the country settled down to peaceful conditions. The population began to increase and the rise of industries attracted the superfluous numbers into industrial areas. Sanitation was bad and contact and congestion played their part. Thus the increase of trade, commerce, and communications have caused the disease to spread, infecting areas previously free of the disease. To-day leprosy occurs in all parts of India, but there is a wide variation in its incidence in different areas. These variations have been explained by differences in climate, soil, diet, social habits, industrialisation, and improved communications.

In considering the circumstances contributing to the prevalence of leprosy the report of the Public Health Commissioner for 1929 is significant. He states that a high leprosy rate is associated with a poor soil where vegetables and fodder do not thrive and where cereal crops are apt to fail, with the inadequate consumption of vegetables and milk, and with the consumption of

of/food of bad quality such as spoiled rice and rotten fish.

Whatever influence these factors may have, the fact remains that an infectious case of leprosy living in close contact with others generates the disease, no matter what the environment may be. The importance of preventing such contact cannot be too greatly stressed.

The Census of 1931 returned 147,911 lepers in all India and Burma, giving an incidence of .42 per mille. The accompanying table shows the incidence of the disease in the provinces, according to the Census returns. For reasons already discussed, this figure is far below the real state of affairs. The figures resulting from special leprosy surveys throughout the country are always higher than the Census figures, and the difference seems generally to vary from about 10 times those figures downwards. Workers in India agree that there are at least half a million lepers in the country and probably the true estimate is nearer one million. The same surveys show the highest incidence among semi-aboriginals and the poorer strata of society. Primitive tribes are practically free from infection and the disease has a low incidence among the wealthy classes. A frequent

source of infection among this latter class is the employment of leprous servants.

More than half the total number of lepers recorded by workers throughout the country are of the resistant neural type. The majority of early cases noted are of this type, but many pass on to the cutaneous stage. On the other hand, a very great number of early cases show a spontaneous arrest of the disease, more especially among the neural type. There must also be many people who have been infected and not developed the disease, or in whom the early slight changes have not been recognised.

There is no legislation for the control of lepers in India, and even if there were it would be well-nigh impossible to enforce effective measures on so immense a population. The value of any such measures is very doubtful as voluntary treatment and segregation are far more effective. Public opinion in the country is still apathetic and infectious individuals are to be found in all trades and occupations. Examples of such cases met with personally are as follows: the village barber: several "dhobis" (washermen): (~~washermen~~)/a school-teacher: a milk-man: a baker: a lawyer: a tailor: several clerks. The list could be continued

continued/ indefinitely. Apart from the Leprosy Research Department of the Calcutta School of Tropical Medicine the two most important bodies engaged in anti-leprosy work are the Mission to Lepers and the Indian Council of the British Empire Leprosy Relief Association. During the last ten years this latter body has been the chief organiser of many anti-leprosy campaigns throughout the country. These campaigns are conducted on the "Propaganda-Treatment-Survey" system, and are meeting with a certain amount of success. The provincial governments are now realising the value of such work and are taking steps to consolidate it, and the general public is beginning to take a more intelligent interest in leprosy. Special leprosy clinics have been opened in many places and the facts and dangers of the disease are being made known through lectures and films. All this work is of great value and should be continued and extended, but we should not imagine that by these present methods alone leprosy can be finally eradicated from India.

Leprosy is one of the great problems of India, intimately connected with most of India's other problems. It is a social and economic problem, not merely a medical one. The great

great/ predisposing causes of leprosy in India are poverty, ignorance, bad social and hygienic conditions, mal-nutrition, and debilitating diseases. Leprosy will not finally disappear from the country until these evils are mitigated, but it is to be hoped that, as a result of scientific study and research, methods of prevention and treatment will be evolved which will bring leprosy more easily under control.

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#### IV. WORLD DISTRIBUTION OF LEPROSY.

There are few countries in the world which can claim to have no lepers within their borders, but fortunately the endemic centres of the disease are confined to certain areas of the globe. Maps are on record showing the countries affected by leprosy but they afford little or no information regarding its actual incidence in each. It is only within the last few years that serious attempts to estimate the incidence of the disease have been made, and while the returns for small civilised countries may be correct, those for large countries and populations must necessarily be only approximations. The countries may be arranged according to their latitudes into three zones, the temperate zone above latitude  $40^{\circ}$ , the sub-tropical zone between latitudes  $40^{\circ}$  and  $23\frac{1}{2}^{\circ}$ , and the tropical zone between latitudes  $23\frac{1}{2}^{\circ}$  north and south of the equator.

##### Temperate zone (above latitude $40^{\circ}$ ).

This includes Europe and the northern parts of Asia and America in the Northern Hemisphere, but in the Southern Hemisphere there is only a small part of South America. In no part of this zone is there a high incidence with the exception of Japan. A low incidence occurs in Iceland,

Norway, the Baltic States, and Southern Portugal, and small foci in other parts of southern Europe. Little is known of the disease in northern China and Siberia, except that it does occur. There are a few cases in Canada and Greenland. In considering the temperate zone it is noteworthy that leprosy and heavy rainfall go together, e.g. in Iceland, Norway, and Japan.

Sub-tropical Zone (Latitude  $40^{\circ}$  to latitude  $23\frac{1}{2}^{\circ}$ ).

These regions show a wide infection with leprosy, but, with a few exceptions, there do not appear to be any highly endemic areas. The important exceptions are central China, Korea, and Southern Japan and, to a lesser extent, South Africa and Egypt. The dry extra tropical regions of North West India, the northern African coast, the southern United States of America and most of Australia have a low incidence of the disease. Leprosy is more prevalent in this sub-tropical zone than in the temperate, but in no part does it appear to exceed a rate of 1 per mille. (6).

Tropical Zone.

In this zone are the areas with the greatest number of lepers and with the highest incidence. There seem to be several fairly well defined regions of high incidence.

1. Equatorial Africa.

The meagre data available for the equatorial Africa indicate that this region has the highest leprosy incidence in the world. The peak is reached in the Belgian Congo where it has been estimated that 1 in 5 of the population are lepers. There appears to be a wide belt of highly infected country stretching from Nigeria across to the Sudan and into Abyssinia, but it has not yet been possible to obtain a correct approximation of the true incidence (6)

2. East Indies and Oceania.

This area includes India, Burma and the Malay States, the East Indian islands, southern China, the Philippine Islands, and most of the larger groups of islands in the Pacific, some of which have been recently infected and now have a high incidence. The incidence in China is unknown but it is said that there are "enormous" numbers of lepers in that country. (7) Nowhere, in these regions, however, does there seem to be the tremendously high incidence found in Equatorial Africa.

3. West Indies and North of South America.

Leprosy was apparently introduced into these countries by the European invaders and later



later/by the African slaves. It is unknown among the aboriginals of South America, except where they are in contact with civilisation. Cochrane<sup>(8)</sup> reports a high incidence among some of the West Indian islands but believes the disease is now waning there. The incidence in South America has only recently been estimated and found to be very high in certain of the States. Browning<sup>(9)</sup> found the most severely infected regions to be Paraguay and French Guiana with 10 and 19 per mille respectively. The same observer reports a high degree of infection in Central America and Mexico. The only South American state free from leprosy is Chile, which is ~~now~~ protected naturally by desert and the Andes.

The world distribution of leprosy appears to be dependent on two factors - race and climate. The countries most affected are those having a dense population and a low degree of civilisation with a low standard of living and faulty nutrition. The effect of climate is seen in the prevalence of the disease in those countries with a heavy rainfall and a hot moist atmosphere. The highest incidence occurs where both these conditions are present, as in equatorial Africa and southern Asia.

A third factor that must have its effect on the distribution of leprosy is that of natural selection. Infectious diseases wax and wane in epidemics according to the laws of natural selection. There is no doubt that leprosy occurs as an epidemic which may last over many hundreds of years, if uncontrolled, and eventually dying out as the susceptible individuals in the race are eliminated. There is clinical, experimental, and historical evidence to prove the epidemic nature of the incidence of the disease.

1. Clinical.

It is a commonly observed fact that the manifestations of leprosy vary in the different endemic regions. Some of these variations cannot be accounted for except by racial idiosyncracies. Such are the leprotic alopecia and paralysis of the spinal accessory nerve, found commonly in Japan <sup>(10)</sup> but rarely elsewhere. Other variations are associated with a greater or lesser resistance to the disease. It is now generally accepted that the neural type of the disease indicates a high resistance and the cutaneous type a low resistance of the individual. Muir <sup>(11)</sup> has explained this distinction by the aid of histological findings and the leprolin test. Surveys of endemic regions show that either one or

or/other type may predominate, thus indicating the level of racial resistance to the disease. All workers in India report a greater number of neural cases than cutaneous. Workers in other countries find a majority of cutaneous cases, e.g. Hyashi in Japan (10). Strachen in South Africa (12), and Uruena in Mexico (13).

It is thus justifiable to postulate a higher resistance to the disease in India than in these other countries, assuming that the lepra bacillus is of constant virulence. The reason for this variation in the resistance of different races cannot be satisfactorily explained except along epidemiological lines, and by the elimination of susceptibles.

## 2. Experimental.

The evidence that follows may be called experimental, but the "experiments" are accidental and not deliberate. The effect of introducing leprosy into a previously uninfected race can be studied in the distribution of the disease in Oceania. These groups of islands were infected at different times during the course of last century. In them the rapid spread of the disease was phenomenal, assuming all the characteristics of an epidemic. The striking feature in all these epidemics is that at first the infected individuals were nearly all of the cutaneous

cutaneous/type and that cases of the neural type only became conspicuous later on.

The last stages of an epidemic can be seen in Norway. Lie (14) in 1929 reported only 90 lepers in that country and that no new cases had been observed since 1926. The existing cases were all of long standing and of the highly resistant neural type. Lie states that the epidemic in Norway has lasted for 1,000 years and that its rapid decline in the last 50 years is due to the strict segregation enforced.

### 3, Historical.

Historical evidence of the epidemic course of leprosy is seen in the rise and decline of the disease in Europe, especially in Britain. The disease was probably introduced into England by the Romans about 200 A.D. The first leper house is recorded in 600 A.D. and the peak of the epidemic was apparently between 1100 A.D. and 1300 A.D. Thereafter the disease gradually declined and disappeared altogether between A.D. 1600 and A.D. 1700 . Several reasons for this decline have been suggested, such as the rise in the standard of living and better feeding, but Molesworth (15) has shown that it can only be satisfactorily explained by the influence of natural selection, with the

the/elimination of susceptible stock. The disease has taken the same course in other European countries. These historical and other facts give conclusive evidence of the epidemic nature of the disease in a race or community. They also show that an epidemic of leprosy can be cut short by scientific methods of control with segregation of infected persons. Such methods are now being employed in many countries and communities, with satisfactory results.

## HISTORY OF LEPROSY.

### Ancient History.

Leprosy is one of the oldest known diseases which have affected mankind, and its origin is lost in the mists of antiquity. Descriptions of leprosy have been found in some of the earliest records. It was undoubtedly frequently confused with other skin diseases, but such a terrible and deforming malady must have been recognised by the ancients as an affliction out of the ordinary. The earliest account is found in the Ebers Papyrus, written about 1550 B.C., in which it is called "Chon's swelling" and for which no remedy was known. In India it is described in the Vedas of 1400 B.C., and it is mentioned in ancient Chinese and Japanese writings. Aristotle referred to the disease about 345 B.C., but Hippocrates does not mention it.

### Biblical Leprosy.

There has been much controversy regarding the true nature of Biblical leprosy, for most of the references confuse it with other diseases. The description given in the book of Leviticus resembles that of leprosy in some features but not in others. The disease was recognised as being highly contagious, but the

the/appearance of "white as snow" and being readily curable does not describe leprosy as we know it today. Hydrotherapy was doubtless beneficial to Naaman, but it would not cure leprosy. It is now generally agreed that the Greek translators rendered as "lepra" the Hebrew word "zaraath" which referred to skin diseases in general.

#### The Spread of Leprosy over Europe.

It is probable that leprosy passed from Egypt to Greece by means of the conquests of Darius and later Xerxes, and was carried to Italy in the first century A.D. with the return of Pompey's troops. It was then disseminated through Europe by Roman legions, traders, and later still by the return of the Crusaders. Newman states that the first known leper house in England was established at Nottingham about A.D. 625, and in Ireland in 869. The disease did not reach Scotland until later, for the first recorded leper house north of the Tweed was in 1177. From Scotland it probably spread to Norway, Shetland and Faroe Islands, Iceland and Greenland. The disease increased in Europe to such an extent that by the thirteenth century both Church and State tried to combat its ravages. Stern measures were enforced,

enforced/ and lepers were isolated in Lazarettos outside the towns. The fashionable Edinburgh suburb of Liberton was once the old "leper town". Lepers were compelled to wear a special dress, to use a clapper when passing along the roads, to indicate with a stick the articles which they wished to buy in the market; they were forbidden to drink from public fountains, to touch children, to speak to a healthy person in a loud voice, or to eat with any person other than a leper. The Church performed the Burial Service over a person diagnosed as a leper, and thereafter he was officially dead. These measures, while harsh, were evidently beneficial to some extent as the number of lepers in Europe diminished during the fourteenth and fifteenth centuries, since when the disease has disappeared from most parts of Europe. This decline in Europe has been one of the most remarkable features in the long history of the disease, and regarding its causes there has been much controversy. Newman attributes the decline to "general and extensive social improvement in the life of the people, to a complete change in the poor and insufficient diet, to agricultural advancement, improved sanitation, and land drainage." On the other hand Vandyke Carter declares that "the most patent cause seems to be, not that of a general improvement in the diet



diet/and habits of the people, to which indeed influence must be allowed, but rather the vigorous measures adopted for checking the progress of this scourge". Munro combines both these in saying that "the countries in which the conditions of the people improved most rapidly and in which the strictest segregation and most severe laws against leprosy existed, got rid of it at an earlier period than those labouring under a reverse condition; a marked instance of which is Norway, where the disease lingers to the present day". All these factors have possibly been of influence, but the real cause of the decline appears to be in the process of natural selection, which has been mentioned in the section of this thesis dealing with the world distribution of leprosy. All authorities agree that the disease died down in European countries much in the order in which they were attacked. The improvements in standards of living helped to raise the natural racial resistance, while the harsh anti-leper laws must have diminished susceptible stock by preventing them from breeding.

Leprosy appears to have been introduced into the Western Hemisphere by European invaders and African slaves, as authorities are practically unanimous that the aboriginal inhabitants were free from the disease.

In India, China, and Japan the disease is most ancient. During recent times the Chinese have been moving about the world and are accredited with introducing the disease into Indo-China, Siam, Straits Settlements, Java, Sumatra, Borneo, Philippines, and other East Indian islands. The same race are responsible for carrying the disease to the Hawaii or Sandwich Islands, New Caledonia, Loyalty Islands, Marquesas Islands, and other parts of Oceania: and also to Australia.

Thus the whole history of the spread of leprosy over the globe is one long record of affected persons carrying it to countries previously free, where as a rule it increases slowly and insidiously at first, taking from one to many decades to attract general attention. The countries from which it has disappeared as an indigenous disease, after being firmly established, have been the temperate zone areas of Europe, in which severe repressive measures were enforced, along with a great advance in food, sanitation, and general civilisation, which accelerated the elimination of the disease by natural processes.

In the light of past history and with the aid of modern knowledge and enterprise it is possible to rid the human race of one of its oldest

oldest/and most dreadful afflictions. It is to be hoped that no efforts will be spared to bring that happy day into the not too distant future. Since the beginning of this century several anti-leprosy organisations have come into existence in the most severely affected countries. The first organisations of this kind were those of Missionary Societies, the chief of which was the Mission to Lepers founded in 1875. This body did much to alleviate the sufferings of lepers in eastern countries, and especially in India, but unfortunately confined its activities to the purely philanthropic side of such work. The personnel in charge of the Mission's Leper Homes did little to study the disease or deal with it scientifically, until some fifteen years ago when the policy of the Mission was altered and modern methods of treatment were introduced. The Mission's Homes are now among the most active centres of investigation and treatment. In 1924 there was founded the British Empire Leprosy<sup>Relief</sup> Association, which in the short period of its existence has probably done more to combat the disease than any other organisation. In 1928 a Leprosy Commission was appointed by the League of Nations, to correlate anti-leprosy work all over the world. In January 1931 there was held in Manilla the Leonard

Leonard/Wood Memorial Conference on Leprosy. This drew workers from all over the world, and the report of the conference has been the basis of anti-leprosy work since then.

ETIOLOGY.

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ETIOLOGY.

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Leprosy is a chronic infectious disease due to the presence and growth of the mycobacterium leprae in the body, and the reaction of the tissues to its presence. Though in the minds of some workers there seems to be doubt on this point, leprosy is unquestionably infectious and due to the "leprosy bacillus". This bacillus is found typically in the lesions of leprosy and in no other condition. It is true that Koch's postulates have not been fulfilled; the organism has not certainly been cultivated artificially, and the disease has not been reproduced in lower animals from cultures. To doubt the infectious nature of leprosy, however, or the relation of the bacillus to the disease, would be to deny an overwhelming weight of evidence.

The essentially contagious nature of the disease is no longer seriously doubted. There is no evidence that it can arise from an organism or organisms that are ordinarily harmless, as in the case, for example, of the bacillus coli. On the other hand, there are innumerable definite observations of infection by direct contact with a leper, as occurs with the children of leprous

leprous/parents; and of indirect contact, as in the boy who pierced himself with a pin that a leprous boy had previously used similarly to demonstrate an anaesthetic area, or in the interesting case of an Anglo-Indian patient under my care. While a medical student in Madras he went into lodgings which, unknown to him, had been previously occupied by a leper. He supplied his own furniture except the lavatory commode. Some time later he developed leprosy, the first signs of the disease being macules on the buttocks and backs of the thighs. He was unaware of any other contact with the disease.

Source of Infection.

Leprosy is gotten only from another leper and human leprosy is apparently confined only to man. It occurs in a region only after it is brought there by an infected individual, and its spread may then be spectacular, as has been already described in some of the islands of the Pacific Ocean. No lower animal is known to be infected with this organism and therefore none serve as a reservoir for it, as does the rat for the plague bacillus. It is true that a form of leprosy occurs in certain species of rats, in which an acid-fast bacillus can be found. Although this shows certain analogies to human leprosy it is



is/generally recognised to be due to a different species of the bacillus.

Transmission.

The transference of the bacillus from one person to another is still an unsolved problem. Were there some single way by which this occurred it might be possible to prevent this and so cut short the scourge. Unfortunately no such way is known, and it seems probable that the organism can be transferred in more than one way. The only definite fact known is that there must be contact, either direct or indirect, with an infected person. The leper discharges bacilli by several routes and his surroundings are infected. A healthy person living in intimate contact with him must take in bacilli through the air, food, injured skin, and perhaps otherwise.

Possible transmission by blood-sucking insects has been suggested and observations have been made on many species of such insects without obtaining any evidence that they are of importance as actual carriers. Certain insects such as the mosquito, undoubtedly ingest bacilli through biting infected areas of skin, but there has been no indication of the growth and multiplication of the bacilli in these insects. Biting insects probably play an



an/indirect part, along with stones, thorns, etc., in causing skin abrasions which may be portals of entry for the bacillus from another source.

Conditions determining infection.

It is agreed that the transmission of leprosy is probably due to contact with an infectious leper, either directly or indirectly. However, by no means all healthy persons in such contact are infected or develop the disease. Certain conditions appear to favour the likelihood of infection and render an individual more susceptible. The more important of these conditions are as follows:

1. Number of bacilli discharged.

It will be seen later that leprosy is a disease of low infectivity. It is to be expected, therefore, that the entrance of a comparatively large number of bacilli will be necessary to infect a healthy person. The leper who discharges the greater number of bacilli is thus the greater source of infection. Bacilli may be discharged from the skin lesions - from ulcerating nodules, from reacting macules, and even from intact areas of skin. Muir (16) has shown that unbroken epithelium does not necessarily prevent the escape of bacilli from the surface of the body. The bacilli may be coughed, sneezed and talked into the air from

from/lesions in the nose and throat. They have been found in the sweat, tears, urine, faeces, milk, seminal fluid, and vaginal secretions. It is only when the lesions are very slight or the bacilli are deep seated, as in purely neural cases, that the leper is not a source of dangerous dissemination.

## 2. Portal of entry.

The frequent presence of bacilli in the nasal mucosa led early workers to infer that that was the usual portal of entry. It is true that tuberculosis, which has many analogies to leprosy, commonly enters the body by way of the respiratory tract, and there is no apparent reason why this should not happen in leprosy also. It is possible that a number of persons are infected in this manner, but the available evidence suggests that this is not the most important portal of entry. Most workers now believe that the entrance is usually through the skin and probably through abrasions and wounds. It is generally recognised that the stratified epithelium of skin and mucus surfaces are a natural and effective barrier to the entrance of outside infections. It is not known whether the leprosy bacillus can penetrate this barrier, but it is reasonable to assume that it cannot do so under normal healthy conditions. In the Indian the continuity of the skin is frequently broken, as has been seen, by

by/insect bites, wounds, scabies, etc., thus providing many opportunities for the bacillus to reach the deeper layers of the corium. The lack of vitamins in the South Indian diet has been already discussed. Mellanby and others have demonstrated the connection between vitamins and the resistance of the body to bacterial invasion, and especially the necessity for vitamins A and D for the normal functioning of stratified epithelium. It may well be that the deficiency of these vitamins in the average South Indian diet impairs the protective mechanism of the body surfaces and allows the entrance of the leprosy bacillus. In my opinion this is an important etiological factor in the occurrence of the disease in South India. Support to this hypothesis is given by the recent work of a Japanese worker, Kobashi (17). In dealing with rat leprosy he found susceptibility to be definitely increased by vitamin deficiency. He found that vitamins A and B had the closest relationship, and that vitamin C had no relation at all.

### 3. Nature of contact.

In investigating the source of infection of the patients treated at the Lady Willingdon

Willington/Leper Settlement it was found that only about 25% were able to state with any certainty as to how the disease was contracted. This is largely due to ignorance of the disease and to the long period of time between possible infection and the first signs appearing. Among the more intelligent also, the possible source of infection is often denied, although the patient may be quite aware of it, through fear of incriminating some other person. Among those who were able to state the source, by far the larger proportion were infected by some other member of the family, either father or mother, brother or sister, uncle or aunt. Under the Indian joint-family system many branches of the family live together or are in close association. Rogers (6) collected 700 cases in which the source of infection was known and found that 58% of them were family or house contacts, and that another 40% were due to other close associations with infected persons. There are very few authentic cases on record of infection following only casual contact and such cases usually have other exceptional circumstances to explain them. It thus appears that prolonged and intimate contact is necessary. This is in keeping with the low infectivity of the organism and is now generally accepted as a necessary condition of infection.

4. Individual resistance.

In the discussion on the age distribution of leprosy it has been shown that leprosy is essentially a disease of childhood and early adult life and that it is during these periods that practically all infections occur. The leprolin test shows that children are most susceptible, and that with increasing age the resistance rises. The healthy adult is very resistant to the disease. . Manalang (18) believes that infection occurs only in infants or during the first three years of life. This statement is too sweeping and is not accepted by most leprologists. It is generally agreed, however, that the great majority of infections take place during childhood and adolescence.

The natural resistance of the individual may be lowered by exposure, mal-nutrition, and other diseases. The importance of these has been discussed elsewhere. Cases of infection in adults can usually be accounted for by such causes of debility, and it is the same causes which very often determine the onset of the first signs. Puberty is a critical time in both sexes, but

but/more especially in girls. Sexual over-activity, also is apt to bring out a latent infection or aggravate an existing one. This is a common cause of debility in the over-indulgent Indian and adds to the general belief that the disease is venereal.

It is thus seen that the two chief factors affecting individual resistance are age and debility. The young are most susceptible, and those conditions which debilitate the individual at any period of life increase the possibility of infection and the development of the disease.

#### SUMMARY.

The modern view of the etiology of the disease is that leprosy is not highly contagious and among adults it is quite the reverse. Infection is due to the interaction of various factors; a prolonged and close contact with a leper discharging a considerable number of bacilli; breaches in the protective mechanism of the body's surfaces; and lowered individual resistance, either on account of age or general debility. Those measures which seek to prevent and correct these factors are the most successful means of promoting the prophy-

prophylaxis/and control of the disease.

Incubation period.

In a disease such as leprosy it is difficult to reach any definite conclusions about the period of incubation. It is commonly held to be very long, but probably it is not as long as is suggested by numerous statements in the literature on the subject. Latent periods of 10 to 20 or even 40 years have been recorded but such cases are unusual. It has been already pointed out that the great majority of lepers show the first signs of the disease before the age of 30 and that a large proportion of those are before 20. It is unlikely, therefore, that the average incubation period exceeds 10 years, if as long. Muir and Rogers (6) have analysed data from many sources and conclude that the average incubation period is 2 to 4 years. This estimate is now generally accepted, but it must be recognised that there are many cases which show a considerably longer period.

Other theories of etiology.

Certain other theories of the etiology and causation of leprosy have been put forward by various authorities and must be briefly mentioned.

Theory of Heredity.

For many centuries leprosy was regarded as infectious, until during the nineteenth century opinion changed to the hereditary explanation of the disease. This was upheld by the Norwegian workers, Daniellsen and Boeck, in their monumental treatise on leprosy published in 1848, and was subscribed to by a British commission in 1862. Daniellsen and Boeck based their conclusions on the occurrence of the disease in families, ignoring the possibility of household infection, but admitted that the disease occasionally arose spontaneously from some unknown cause. In their opinion the nature of the disease consisted of an unfavourable blood mixture which was characterised by an accumulation of albumin. The blood tried to free itself of this albumin and deposited it in the skin, wherefrom nodular leprosy resulted, or in the nervous system, which caused the manifestations of nervous or anaesthetic leprosy. So great was the authority of Daniellsen and Boeck that practically all workers shared their opinion, and measures for the segregation of lepers were abandoned in many countries. In 1871 Hansen discovered the



the/leprosy bacillus, ~~and his bacillus~~ and his subsequent work reaffirmed the infectious nature of the disease. A second British commission in 1875 declared unanimously for the infectivity of leprosy. This was upheld by the first international leprosy conference in Berlin, in 1897, which finally dismissed the theory of Daniellsen and Boeck. To-day the theory of heredity is no longer held by leprologists of repute, and there is abundant evidence to disprove it. It is interesting to note that in eastern countries leprosy has for many centuries been considered an hereditary disease.

The possibility of an hereditary predisposition to leprosy cannot be ignored in view of the opinion that there is an hereditary predisposition to tuberculosis. It is not yet possible, however, to prove or disprove this, and nothing definite can be said about it.

#### Fish-eating theory.

Another belief of the prebacterial days was that leprosy was gotten through the eating of certain foods, more especially fish in a badly-preserved or decomposed state. This theory received the persistent and able advocacy of Sir

Sir/Jonathon Hutchinson who declared leprosy to be "fish-eater's gout" . At the international conference on leprosy at Bergen in 1909 Hutchinson found himself in a minority of one and his views are now only of historic interest. Leprosy commonly occurs among people who never eat fish and is absent from many regions where fish is an important part of the diet; nor has the bacillus ever been found in fish. It has already been shown that the eating of decomposed fish is a frequent occurrence in certain parts of India and that this may have some influence on the incidence of leprosy. There is nothing specific in this influence, and the eating of bad fish is only a contributing cause in the lowering of an individual's general resistance.

#### Venereal theory.

The belief that leprosy is a venereal disease and associated with sexual irregularities has long been held, and is still common among lay people of many countries. No leprologist now believes that the disease is venereal, and there is abundant evidence to prove it otherwise. A remarkable feature of the disease is the rarity

rarity/with which a leprous husband or wife infects the other partner, in spite of the prolonged and intimate contact between them. Muir and Rogers (6) found not more than 5% of conjugal infections in a large series of cases. The explanation is that most married persons have passed the susceptible age. On the other hand, there have been authentic records of leprosy following promiscuous intercourse and there is no doubt that this is a not infrequent means of infection. In India the leprous woman has no possibility of marriage and usually prostitutes herself to earn a living. Many males attribute their disease to contact with such women and probably a small number of infections are due to such contacts. The transmission of the disease, however, follows on the general intimate contact and is not due to the sexual intercourse, as are syphilis and gonorrhoea. Genital ulcers of course, may provide suitable portals of entry for the bacillus, but the disease cannot be classified as venereal.

BACTERIOLOGY.

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### BACTERIOLOGY.

That the acid-fast rod-shaped organism commonly and persistently present in leprous lesions is responsible for the disease is almost universally accepted. Apart from certain morphological characteristics, nothing definite is known about the organism, nor is there even a consensus of agreement in explanation of the apparent variety of forms exhibited by the organism. The most remarkable feature of the organism is its apparent proliferation in the human body. One is impressed by the incalculable numbers that are borne by the leper, the amazing adaptation between parasite and host with so little disturbance to each other, and the all but hopeless task that nature is set to overcome a well-established infection.

### MORPHOLOGY.

The organism appears to vary in appearance according to the phase of the disease through which the patient is passing. The appearance during a quiescent phase is considered as the normal vegetative form. Sections or smears from lesions at that period show typically acid-fast rods from 1 to 7 microns in length and 0.2 to 0.3 microns in width, straight or slightly curved, and having

having/rounded ends. They occur singly but tend to adhere closely in masses described as "cigar bundles", or in spheroidal clumps called "globi". These globi are probably masses of bacilli formed inside the cytoplasm of infected cells, for the bacilli are both intracellular and extra-cellular. Denney (19) considers them to represent a phase in the life cycle of the organism, and that they are colonies growing within an as yet unidentified restraining membrane. Branching forms of the bacillus are met with, which classify it among the mycobacteria, hence the correct nomenclature of "mycobacterium leprae" and not "bacillus leprae," as it is so often called.

An important characteristic of the organism is a granular appearance often found, the significance of which is not yet known. These granules or beadings in the bacilli vary in size and number. In the branching forms the offshoot is usually attached to a bead. Two hypotheses have been formulated concerning the nature of the granules. Some workers believe that they represent degeneration and disintegration of the organism, that is, the last stage of cellular

cellular/extinction. Granules are usually found in quiescent cases of leprosy and in those cases that appear to be responding to treatment, and are often regarded as a favourable sign. While they probably are of importance in prognosis and assessing the value of treatment, their appearance is not an established criterion of improvement. Hoffmann (20) and other workers believe that the granules are analagous to spore-formation and represent active proliferating organisms. Manalang (18) thinks that from these granules or spores there develops a non-acid-fast or virus stage of the life cycle of mycobacterium leprae, which is the etiology of the disease, the acid-fast bacillus being an inactive stage. There is much to be said for both hypotheses, and it may be that two forms of granules exist.

The bacillus has little affinity for ordinary stains, requiring a powerful mordant stain such as carbol-fuchsin to colour it deeply. When once stained, however, it is not easily decolorized either by acids or alcohol. The bacillus can be positively stained by Gram's method. Much's modification of Gram's stain is very effective in showing up the granular forms.

No evidence of motility has ever been

been/detected. It is a matter of speculation as to whether the acid-fast bacilli seen in material freshly obtained from leprosy tissues are living or are dead organisms resisting disintegration.

The leprosy bacillus is morphologically similar to the tubercle bacillus, but can be distinguished from it by the following features. The leprosy bacillus is rather shorter and wider and less curved; it is found in far greater numbers and has the typical bunch-like grouping; the sites in which they are found differ; the leprosy bacillus can be neither cultivated nor transmitted to animals. The leprosy bacillus can be similarly distinguished from other acid-fast organisms, such as the smegma bacillus and Moeller's grass bacilli.

#### CULTIVATION.

Although more than sixty years have passed since the discovery of the bacillus by Hansen, there is yet no certain proof that it has ever been cultivated in vitro. No other organism has resisted the efforts of bacteriologists for so long. All ordinary media have failed, as have media modified by the presence of other organisms, and aerobic



aerobic/ and anaerobic methods of culture. Recent methods of tissue and embryonic tissue culture have proved encouraging. Many workers have reported success with this or that method and media, but their results have not stood the test of repetition. The consensus of opinion is that Hansen's bacillus has not yet been cultivated outside the human body.

Among the recent attempts to cultivate the organism, mention should be made of the work of the Japanese workers, Ota and Sato (21). In 1931 they inoculated several varieties of egg media with blood from 65 advanced cases of nodular leprosy. They obtained twelve strains of acid-fast bacilli which gave two types of colonies, one white and the other orange colour. Previous cultures by them from leprosy nodules had given tubercle bacilli, but they believed that the new strains were leprosy bacilli, which they called *Mycobacterium leprae album* and *Mycobacterium leprae auranticum*. They claim to have subcultured both types.

In 1935 Lowenstein (22) of Vienna claims to have successfully accomplished the culture of leprosy bacilli by means of his sulphuric acid method on an egg medium to which fish broth has been added. The organisms were obtained from the blood of lepers in the Philippine Islands. Lowenstein states that the blood

blood/reached Vienna "in good condition and only slightly contaminated"! Like the Japanese workers, he obtained white and orange-yellow colonies. From the white colonies he subcultured "organisms with all the characteristics of true mammalian tubercle bacilli". From the orange-yellow colonies subcultures gave deeply staining acid-fast organisms which he believes are leprosy bacilli. He has yet to report on his attempts to inoculate animals with these latter.

Attempts to apply tissue culture methods to the investigation of the leprosy bacillus have been made by a number of workers. The most important is that of Salle (23) of California in 1934. He investigated both the human and rat leprosy bacillus, using cultures of chick tissue in guinea-pig plasma, Tyrode solution, and chick embryonic extract. This was planted with material from human nodules and rat granulomata, and from both sources he isolated an acid-fast organism and a non-acid fast diphtheroid. Transfers to fresh tissue culture were made every seven days and resulted in a gradual disappearance of the acid-fast organisms and increase of the diphtheroids. This was repeated for twelve transfers, before the growth was added to a medium of mixed

mixed/chick embryo. The acid-fast organisms re-appeared in a profusion, then were gradually replaced by diphtheroids as before. When transfers were made to artificial media only the diphtheroids grew. Salle's conclusions are that the acid-fast rods and the diphtheroids are difference growth phases of the same organism, and that he has successfully isolated the leprosy bacillus. He also believes that human and rat leprosy was caused by one and the same organism, but reports no attempt to reproduce leprosy in rats by the inoculation of this pleomorphic organism. In the absence of such a report, it is very doubtful whether his organism is the leprosy bacillus.

McKinley and Verder (24) report that with the young chick embryo tissue medium they are able to cultivate mycobacterium laprae indefinitely. This work is open to the same criticism as is Salle's. Holt (25) and Lowe (26) have independently repeated, McKinley and Verder's experiments and failed to verify their results.

Transmission to animals and man.

Many attempts have been made to cause

cause/leprotic material to produce lesions in animals. Several investigators have obtained experimental lesions in such animals as guinea-pigs, rats, the Japanese dancing mouse and other mice, and monkeys. None of these have been definite enough to permit their acceptance as evidence of experimental leprosy in these animals. Lesions at the points of inoculation have been obtained. These lesions have progressed for a time, retrogressed, and disappeared spontaneously. In autopsied animals the acid-fast bacilli have been found in the lymphatics and internal organs, but there has been no proof that these bacilli are alive and multiplying. Leprosy, the progressive systemic infection, has never been reproduced. McKinley and Soule (27) claim to have grown the leprosy bacillus on an artificial medium, inoculated the growth into monkeys, and at the sites of inoculation obtained granulomatous lesions suggestive of early lesions of leprosy. They admit, however, to finding no evidence that the bacilli inoculated into the monkeys remained alive and multiplied in the animals' tissue.

Several attempts to infect healthy persons by experimentally inoculating them with

with/ material containing fresh lepra bacilli have completely failed, with one doubtful exception. This is the classical case of an Hawaiian convict who was inoculated by Arning. Two years later this man developed leprosy and subsequently died in an advanced stage of the disease. The value of this experiment is annulled by the fact that the man came of a leprous family and had been in close contact with infected relatives. This negative evidence, however, loses much of its worth on account of all the experiments having been carried out on adults who had passed the susceptible age. Of greater significance are the authentic cases recorded of children being infected by the old arm-to-arm method of vaccination practised in the nineteenth century.

#### RAT LEPROSY.

The existence of this disease was first discovered by Stefansky. In 1903, while searching among rats for those carrying the bacillus pestis, he discovered a certain number of them which were distinguished by enlarged lymph nodes,

nodes, the hypertrophy being due not to the plague organism but to an acid-fast bacillus which was present in large numbers. The disease manifests itself in two forms. One is limited to the superficial lymph nodes, which are enlarged and hard, The other spreads throughout the skin and muscles and invades the whole animal, causing areas of alopecia and extensive ulceration. The cause of this disease is an acid-fast bacillus analagous to that found in human leprosy. All attempts to cultivate this organism have been followed with no more success than have the attempts to cultivate that of Hansen. Innoculation into healthy rats is easy and may be done by merely scarifying the skin. Infection through healthy skin is impossible, even in young rats. Rat leprosy has not been transmitted to any other species of animal. The disease appears to be very infectious among rats in the wild state. Marchoux (28) found 5% of rats captured in the Paris sewers to be infected. The same authority found that secondary infections favour the development of the disease, while good nutrition and good hygiene eliminate a mild infection.

The similarity to human leprosy is obvious, but the two diseases do not seem to be due to the same organism. Salle's view that they are

are/due to the same organism has been mentioned. On the other hand, it has not been possible to infect rats with material from human lesions, or vice versa. An interesting investigation in this connection was recently made by Soule (29) in the Philippine Islands.

During the last thirty years many thousands of infectious lepers have been segregated on one island, in the Culion Leper Colony. Throughout this period the local rats have been intimately exposed to human infection. Soule examined 212 rats caught in the colony and in none of them could he find any evidence of infection with either Hansen's or Stefansky's bacillus, indicating that rats are not subject to infection with human leprosy.

#### Toxicity of the leprosy bacillus.

The study of toxin production by an organism is carried out chiefly with cultures. Since the leprosy bacillus has never been cultivated little definite is known about its toxin production, if any. If toxins exist the leper shows little evidence of it. There is comparatively little general disturbance in the uncomplicated case, in spite of the enormous numbers of bacilli present and the large numbers that are probably

probably/being destroyed all the time, and particularly in the case improving under treatment. There is no suggestion that the bacillus produces an exotoxin, but less definite is the question of an endotoxin. The chief evidence for the presence of a toxin is in the phenomenon of lepra reaction, which will be discussed later. It follows that the leprosy bacillus is an organism of extremely low toxicity, which is in marked contrast to the tubercle bacillus.

#### Immunity.

Knowledge of the immunology of leprosy is very incomplete and specific serological tests have so far proved inconclusive in indicating an immunity in leprosy. Several workers have evolved serological tests which they claim as specific for leprosy, but the results of these tests have varied widely. Rodriguez and Plantilla (30) believe that the histamine test is a fairly reliable clinical test in differentiating the patches of early leprosy from non-leprotic macules. They found the test positive, i.e. the typical "flare" absent, in the majority of the bacteriologically negative leprotic macules tested. Chiyuto (31) repeated their experiments and found the test was not



not/dependable in the earliest stages of leprosy.

The most important of the complement fixation reactions has been that evolved by Gomes (32) of Brazil. He used an antigen prepared from the streptothrix of Deycke, a micro-organism cultivated from leprous nodules, which were defatted by McJunkin's olive oil and acetone method. He claims to have obtained 96% of positive results in established lepers, and also positive results in a proportion of healthy persons in contact with lepers, many of whom have subsequently shown signs of leprosy. He believes his test is reliable in detecting latent cases.

The problem is a complicated one. The serological response of the acid-fast group of organisms is not well marked. Even in tuberculosis, complement-fixation reactions are of doubtful value in determining a latent infection before the appearance of clinical signs. It is probable that the serum of leprous patients possesses the power of fixing complement in the presence of suitable antigens. The problem is to find antigens to discriminate between the different kinds of acid-fast organisms, and a high-value antigen for the diagnosis of leprosy. There would seem to be good hope for the finding of a

a/suitable antigen, and the discordant results recorded by different investigators are largely due to the varying techniques employed.

Apart from any serological test, however, there appears to be clinical evidence of an acquired immunity in leprosy. If this were not so, why should many early and moderately advanced cases subside spontaneously? It is often observed that series of mild lepra reactions is followed by the gradual arrest of the disease, which must be due to an induced immunity. The possibility of a natural immunity in a race or community has been discussed elsewhere.

The available evidence suggests that leprosy does induce a degree of immunity.

#### Summary of bacteriology.

The causation of leprosy is probably the acid-fast bacillus found typically in leprosy lesions. Nothing is known of the life cycle of this organism as it has not been cultivated with any certainty, nor has it been possible to transmit it to animals and reproduce the disease. It appears to be an organism of very low toxicity, and is probably capable of inducing an immunity in infected persons. This is the meagre extent of our knowledge of the bacillus.

PATHOLOGY.

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## PATHOLOGY.

It is not intended to present a detailed account of the pathology of leprosy, but rather to point out certain basic facts essential to the understanding of the principal features of the disease. The subject will, therefore, be discussed somewhat informally.

### Primary Lesion.

The first question that arises in considering the pathology of an infective disease is whether there is a primary lesion to mark the point of entrance into, and infection of, the body. The probable portals of entry of the bacillus have been discussed in the section dealing with etiology, and the conclusion reached that entrance probably occurs through breaches in the continuity of the skin and mucous surfaces of the body. In only a few cases, however, can it be said that the first sign of the disease has appeared at the probable site of inoculation. In more cases the first lesion noticed by the patient is assumed to be primary. When the first manifestation is an area of numbness, or an outbreak of multiple lesions, one is

is/at a loss to know how the organism entered the body.

#### Latent infection.

The time between infection and the outbreak of signs of the disease is notoriously variable and often very long. Even granting a slow incubation period for the bacillus, there is probably in most, if not all, cases, a variable latent period as well. Where this latent infection exists, whether at the site of inoculation or elsewhere in the body, is not known. Some workers believe that the organism lies latent in the superficial lymph nodes, basing this conclusion on their findings in rat leprosy. There is yet no evidence that this occurs in human leprosy. Presumably, in some persons such a latent infection may never progress to clinical leprosy, being overcome before dissemination can occur. This would parallel what happens in tuberculosis, and might explain the development of a relative immunity in people of long-infected regions.

#### METHODS OF SPREAD OF THE BACILLUS.

There are four paths by which the bacillus spreads in the body.

1. Direct continuity.

The bacilli, when present in large numbers, may have a limited spread by direct continuity in the tissues.

2. Lymphatics.

The bacilli, as might be expected, probably enter the lymphatic system at an early stage. Bacilli have been found in the superficial lymphatics and lymph nodes when it has not been possible to find them elsewhere, and the lymphatic system is probably the chief means of dissemination. A characteristic feature of leprous lesions is the radial spread of the erythematous margins. This strongly suggests a lymphatic spread, although in many cases careful bacteriological examination may show no organisms to be present.

3. Blood stream.

The appearance of multiple isolated lesions scattered all over the body, and the infection of the large nerve trunks, can only be caused by a metastatic dissemination through the blood stream. How the bacilli enter the blood-stream will be discussed later.

4. Auto-inoculation.

It is probable that many patients re-infect themselves in healthy areas of skin by scratching lesions of the skin or nasal mucosa.

It has also been suggested that bacilli are disseminated by migratory cells, but there is no evidence in proof of this theory.

#### DISTRIBUTION OF BACILLI IN THE BODY.

Leprosy bacilli have been found in most organs and tissues of the body, but the organism has a greater affinity for certain tissues than others. Some parts seem practically exempt, such as the intestines, pancreas, voluntary muscle, and the central nervous system. The kidneys and liver are sometimes invaded but no lesions of importance are caused in them. The tissues of predilection will be briefly considered in order of importance.

##### 1. Peripheral nervous system.

Affinity for the nervous tissue is such that it is almost always more or less affected, and in many cases it alone. It is only rarely, if ever, that leprosy lesions of the central nervous system occur. The reason for this is probably the absence of connective tissue, in which the bacilli are generally found. The peripheral nerves are involved in practically all cases and often a cutaneous case has neural symptoms before the skin lesions arise. The nerves are affected in either or both of two

two/ways, by an ascending infection or a metastatic infection.

(a) Ascending infection.

Bacilli have never been demonstrated in the sensory nerve endings but the distribution of anaesthesia and other sensory disturbances are sufficient proof that the infection ascends the nerves. In some manner the bacilli invade the sheaths of the nerve-endings and gradually spread up the nerve. There is a capillary engorgement with perivascular infiltration, proliferation of the connective tissue cells of the epineurium, perineurium, and endoneurium, and the formation of fibrous tissue. The nerve fibres and myelin sheath are only indirectly affected by the pressure of the engorgement and later by the fibrous contraction. As the infection spreads higher up the nerve-trunk more and more branches are involved and sensory disturbances appear over a wider area. There may be great swelling of the nerve-trunk which may even proceed to caseation and abscess formation.

(b) Metastatic infection.

The large nerve trunks, such as the ulner<sup>a</sup> and peroneal, frequently show marked enlargement and leprotic involvement at a considerable distance from their terminal fibres. This must be



be/due to bacilli in the blood-stream having been carried to them by their vasae nervorum. The same changes occur as in the terminal nerves and the degeneration of the nerve fibres causes sensory disturbances of the acroteric type.

The astonishing feature of the infection of nervous tissue is the paucity, or even complete absence, of bacilli in the lesions. There may be a profound cellular reaction with no apparent cause. The possible significance of this will be discussed later.

## 2. Skin.

So conspicuous are the skin lesions that the general impression is that the bacillus has a greater affinity for this organ than for the nerves. From cutaneous lesions the bacilli are discharged and transmitted to others. The bacilli lie in the corium of the skin and it is this part that shows the essential changes. The epithelium is also affected, but only secondarily to the corium. The skin lesions may be divided into three sub-types, according to the depth of the bacillary invasion.

### (a) Papillary sub-type.

In this the papillary layer of the corium is infected, with congestion, cellular proliferation, and oedema. The papillae are flattened

flattened/and, consequently, the epithelial inter-papillary spaces. When resolution occurs a very thin epithelial surface is left.

(b) Interfollicular sub-type.

The bacilli lie in the corium between the hair follicles. The cellular reaction and oedema causes an exxageration of the natural creases of the skin as the epithelium is pushed up against the resistance of the follicles.

(c) Subfollicular sub-type.

In this sub-type the bacilli are in the deeper layers of the corium, below the follicles, and may even invade the subcutaneous tissue. The hair follicles and sebaceous glands are destroyed. The oedema causes the skin surface to be raised in a smooth glossy macule. When this lesion resolves the skin is left with a crushed tissue paper appearance.

The three sub-types vary in clinical appearance but tend to merge into one another so that the different stages may be recognised in the one lesion.

The characteristic leprotic nodule is due to an intense cellular reaction round a bacillary embolism in the corium. Frequently the nodule breaks down and ulcerates and discharges the

the/product of the tissue reaction. Ulceration may also occur in the subfollicular lesions.

There is no area of skin which escapes leprous involvement. Muir and Rogers (6) state that the scalp is practically never invaded by lepra bacilli. I have frequently found leprous lesions and bacilli in the scalp of cutaneous cases. Other authorities declare the palms of the hands, soles of the feet, penis and scrotum to be exempt. I have found lesions and bacilli in all these places.

### 3. Lymphatic system.

The superficial lymph glands are affected in all cases of skin leprosy and in many cases of nerve leprosy. The inguinal group, and to a lesser extent the axillary and epitrochlear groups are those most affected. The enlargement of the inguinal glands is sometimes very prominent, but the degree of involvement seems not at all dependent on the extent of affected skin in the area drained. The glands of the face and neck rarely show much enlargement even when the face and ears are grossly nodular. Among the deep lymph glands bacilli have been found in the retroperitoneal groups and in the glands in the hila of the liver and the kidneys. They do not appear in the glands draining the alimentary tract,

tract/, which contrasts with the findings in tuberculosis. On sectioning a gland the structures show up clearly and the ampullae and medullary cords are a characteristic yellow or yellowish-brown colour. The glands are permeable but penetration is evidently more difficult, for the efferent lymph vessels are dilated. Suppurating glands are found not infrequently in skin leprosy, but it is difficult to say whether or not such suppuration takes place apart from a mixed infection.

#### 4. Circulatory system.

The occurrence of multiple lesions in various parts of the body leaves no doubt that the bacilli enter the blood-stream. The possible means by which the bacilli enter the blood are (a) by the lymphatic duct, (b) by erosion of a leproma into a blood vessel, and (c) by infected wandering histiocytes. Which is the most important route it is impossible to say. The bacilli have been found free in the blood serum, in leucocytes, and in large mononuclear wandering cells. Bacillaemia is commonly found in cutaneous cases, especially in the reaction stage, and rarely in neural cases. No marked change in the blood cells is found, except a slight eosinophilia.

Atheromatous changes have been found in the blood vessels of lepers. These are not so

so/much in the aorta as in the smaller vessels, chiefly as a medial degeneration. The most marked lesions are found in the veins of extremities, leading from affected skin areas. There is a leprotic infiltration of the vessel walls. The thickening and diminution of the lumen may be so great as to disturb the circulation of the extremity, and oedema of the limb follows.

#### 5. Mucous membranes.

The upper respiratory tract is commonly invaded and is an important source of bacillary discharge. The nasal mucosa is infiltrated and ulcerated, chiefly over the septum and inferior turbinate. The tonsils are of little importance clinically, although bacilli have been found in them. Lesions of the larynx are common in advanced cutaneous cases. The scarring impedes the action of the vocal chords, causing hoarseness and even loss of the voice. An acute swelling imposed on a scarred and contracted larynx causes severe difficulty in breathing, which may require a tracheotomy to give relief. Bacilli have been found in the mucous membrane of the mouth and in the saliva.

## 6. Testicles.

The testes are affected in the majority of cutaneous cases, often extensively so, and bacilli may be numerous in the seminal fluid. The bacilli are intertubular and intratubular, causing fibrosis and atrophy, which frequently results in sterility. Often these changes are more extensive than one would expect from the degree of leprotic involvement. Acute orchitis is common, especially in lepra reactions. The internal secretion of the testicle is lost and female characteristics develop, such as enlargement of the breasts, feminine distribution of hair, and a high-pitched voice.

The ovaries are not affected to anything like the same extent, and there is no loss of fertility in the female leper.

## 7. Eyes.

Leprosy affects the eye in all its structures, and in severe cases causes complete destruction of the eye. The commonest lesion is a chronic iritis or irido-cyclitis. The cornea may be involved, becoming scarred and opaque. Nodules may form in the conjunctive and around the limbus. The retina and optic nerve are sometimes involved. Bacilli have been found in some leprotic eyes and not in others. The real nature of the lesions is unknown, and it seems to be analagous to

to/tuberculous eye conditions. Certainly it is a most intractable complaint, progressing insidiously to blindness.

#### 8. Lungs.

There has been a variety of opinion regarding pulmonary leprosy. Hansen and Looft (33) and others denied that this condition exists. Wade (34), who has probably conducted more leprosy autopsies than any other pathologist states that he "has never seen a gross leprotic lesion of the lung, intestine, kidney, or central nervous system". On the other hand, Muir (35) from a careful study of clinical cases, believes that leprosy of the lungs does occur. I, personally, have never met a definite case of pulmonary leprosy. All the cases seen with acid-fast bacilli in the sputum has either an obvious tuberculous infection or had gross leprotic lesions of the larynx or pharynx, from which bacilli were being discharged. I find it impossible to come to a definite conclusion in this matter, but am inclined to agree with Muir's findings.

#### 9. Bones.

Bacilli can be found in the bone marrow of cutaneous cases, but they produce no important

important/pathological changes themselves. The changes so common in bones are trophic, and due to loss of nourishment to the periosteum. There follows an osteoporosis, with rarification, and absorption. When this occurs in the hands and feet the process may proceed without ulceration and the whole digit, losing its boney framework, shrinks and is absorbed until the nail is situated on the end of the metacarpal or metatarsal. The process may be complicated by the entrance of septic organisms, causing a chronic osteitis or osteomyelitis and necrosis. It is thus that the metacarpals and metatarsals and larger bones are lost. These bone changes are commonest in neural leprosy.

#### HISTOLOGY.

The leprosy bacilli lie chiefly in the connective tissues, and the earliest microscopic change is a perivascular infiltration of small round epitheloid-like cells. As the lesion progresses there is a generalised proliferation of the connective tissue cells and increase of the capillaries. In the neural macules this



this/proliferation takes the form of dense cellular cords in longitudinal and transverse section with clear cut margins. In the deeper layers of the corium these cords are continuous with similar dense cellular masses in the subcutaneous nerves. In the cutaneous macules the cells are similar in type and abundant bacilli are seen, both inside the cells and in the intercellular spaces, lying chiefly in and around the blood vessels and in the lymph spaces. In the neural lesions the cells are chiefly of the epithelioid type, but plasma and mast cells are also seen, and sometimes multinucleated giant cells. Bacilli are rarely found, and the few seen are lying in the nerve sheaths.

#### Lepra cells.

Characteristic of leprous lesions are the lepra cells. These are the wandering endothelial phagocytes, variously called macrophages or histiocytes, which become crammed with the bacilli. In course of time these lepra cells become vacuolated, paler staining, and larger, until the typical foamy cells of Virchow are produced, often multinucleated. It seems as if these cells, which are essentially removers of foreign bodies and have little bactericidal action of their own,

own,/hardly do more than contain the organisms, as if they were foreign bodies. Certainly, the bacilli find the location satisfactory, for they multiply in the lepra cell to form the rounded masses or globi already described. One gets the impression that they are actually protected from antagonistic influences, either natural or therapeutic. As the lepra cell, however, assumes the foamy appearance the bacilli decrease in number, and stain less deeply, until there remain few or none that retain the stain. The foamy cells seem to be endowed with long life and in old lesions may be seen lying singly, isolated by walls of fibrous tissue. It is an interesting speculation as to when these phagocytic cells are a guest-house and when a lethal chamber, and whether the same cell is capable of being both.

#### Giant cells.

The presence of giant cells has been mentioned. They are very similar to those found in tuberculous lesions and are sometimes associated with caseation and necrosis. This phenomenon is rare in leprosy, but occurs in lesions of nerve trunks, causing nerve

nerve/abscesses, which appear to be a special feature of the disease in India. The origin of the giant cells and their significance is still in doubt. Henderson (36) suggests that they are derived by a fusion of lepra cells and represent a defence mechanism on the part of such cells against impending destruction. There is no real evidence in support of this and it seems more likely that giant cells are associated with a high resistance of the tissues to the invading organism. They are found in neural lesions, and occasionally in early skin lesions. They are chiefly present in the tuberculoid lesion, described by Wade (37). This occurs fairly commonly in India and appears to be associated with a high resistance to the disease.

This histological picture, though classifiable among the infectious granulomata, is very different from that of tuberculosis. There is not the central caseous, necrosis, the peripheral zone of epithelioid cells, and the tendency to encircling fibrosis. Tuberculosis tends to ulcerate, leprosy ordinarily does not. The leproma is more vascular than the tubercle, which probably accounts for the absence of caseation and necrosis. The lepra bacilli and the

the/cells in which they lie are in symbiosis, and a leper may carry his lesions intact for many years. However, the lepra cell and the tuberculous epithelioid cell are probably of the same origin, and in certain leprosy lesions one may find areas of cells in the typical epithelioid arrangement around one or more central giant cells. This gives rise to the tubercloid lesion of leprosy, (37) , which is sometimes microscopically indistinguishable from mild, non-caseating tuberculosis.

#### DISCUSSION.

The most striking contrast between the lesions of the two types of leprosy is the absence or great scarcity of bacilli in the neural lesions. Yet, in spite of fewer or no bacilli, there is a greater cellular reaction in the neural than in the cutaneous macule. In association with this must go the observation that the bacillary concentration is greater in the nerves than in the corium, this being most noticeable in the neural type, and that the cellular response of the corium is greater than that of the nerves.

The absence of bacilli from nerve lesions is difficult to understand and several suggestions have been made to account for it. One theory is that bacilli are present in the larger nerves and the skin changes are vasculotropic, but it is hard to believe that the intense cellular reaction is due to a trophic change. Another theory is that the lesions are caused by toxins set free by bacilli in some distant focus, as seems to occur in the case of tuberculides, but this is not applicable to the gradually spreading lesions of leprosy. An attractive theory is that of Muir (38), who suggests that a neurotropic virus form of *M. leprae* is the cause of nerve lesions. The existence of such a virus is extremely hypothetical and in a later publication Muir (II) has refuted this theory, and states that the absence of bacilli is due to the higher resistance in such lesions. The higher resistance is indicated by the active cellular response, accompanied by phagocytosis and destruction of bacilli.

The reason for the greater bacillary concentration in the nerves, with a lower cellular reaction than in the corium now becomes evident. For some reason, the connective tissue

tissue/cells in the nerves have a less sensitive defence mechanism, perhaps because they are less exposed to infections in general. In the nerves, therefore, the bacilli find a refuge where there is little opposition to their presence, and where they can increase and spread. The presence of a high degree of infection in the nerve does not necessarily produce nerve leprosy. This is produced only when, in addition, to the presence of bacilli, there is a high enough resistance to induce a cellular reaction. In the corium this cellular reaction is sufficient to destroy the bacilli, but not in the nerves, at least not to the same extent. If the corium cellular reaction is not so strong, the bacilli can withstand it and even multiply, and the result is the cutaneous macule or lesion in which bacilli are found.

The hypothesis is, therefore, that the nature of leprous lesions is chiefly determined by the degree of resistance to the disease, and by the degree, duration, and frequency of lowered resistance caused by one or other, or a combination of, the following three factors: tender age, debility from any cause, and hyperinfection. The greater the resistance the more

more/conspicuous are the neural lesions; the lower the resistance the less prominent are the neural manifestations as compared with the cutaneous ones. I have seen cases of leprosy with no clinical signs of the disease, but whose skin was teeming with bacilli. In such cases there is practically no cellular response at all on account of an extremely low resistance.

#### The Leprolin Test.

Mitsuda's leprolin test throws much light on the nature of leprosy lesions and tends to confirm the above interpretation of the phenomena of leprosy lesions. Leprolin consists of an autoclaved suspension of ground-up leprosy tissue containing large numbers of Hansen's bacilli. If 0.2 c.c. of leprolin is injected intradermally into a healthy area of the skin of a leper, a local lesion is produced having clinical and histological resemblances to his existing lesions. If the patient's lesions are of the highly resistant nerve type, with dense cellular proliferation, giant cells, and no bacilli, then in three to four weeks a similar lesion appears at the site of inoculation and the test is said to be positive. If the patient has a low resistance with lesions of the cutaneous type, then

then/there is no reaction at the site of inoculation and the test is negative.

The leprolin test is positive in most healthy adults; it is diminished or negative in children, in debilitated persons, and in those with a hyperinfection of leprosy. It is increased in leprosy persons who are otherwise healthy and are only slightly infected, confirming the suggestion made elsewhere that mild infections induce an immunity.

The value of the leprolin test is enhanced by using as a control a similarly prepared suspension of Stefansky's rat leprosy bacillus. Like Hansen's leprolin, Stefansky's leprolin gives only slight or negative results in children and debilitated adults, but gives positive results in non-debilitated adult leprosy of the cutaneous or non-resistant type.

My own results with the leprolin test, using both Hansen's and Stefansky's leprolin, are in agreement with those obtained by Hyashi (39), Muir (40), and Chiyuto (41).

#### Secondary Pathology.

Only the most important of secondary changes will be mentioned. Tuberculosis is a common accompaniment of leprosy. Nephritis occurs



occurs/ frequently. It is usually a chronic parenchymatous nephritis with acute exacerbations, and is often very intractable. Amyloid changes occur in the liver, spleen and kidneys, but it is not certain what they are due to, as there is not necessarily any chronic suppuration. Arteriosclerosis has already been mentioned.

Causes of death.

Fortunately, or unfortunately, leprosy/<sup>seldom</sup>causes death. Except for occasional cases of suffocation by oedema of the larynx, deaths directly due to leprosy are from severe attacks of lepra reaction~~s~~ or from cachexia from prolonged or frequently repeated reactions. The commonest causes of death in the Lady Willingdon Leper Settlement are toxaemia from septic limbs following trophic ulceration, nephritis, and prolonged lepra reaction. Other causes are those that end the lives of mankind in general and are not peculiar to leprosy. We have had a few deaths from tuberculosis, but do not find it as often as other workers have reported.

SUMMARY OF PATHOLOGY.

It is difficult to associate the site of infection with the primary lesion, as there is usually a long latent period during which the bacilli lie in an unknown focus. The infection spreads in the body by the lymphatics and blood-stream, and also by direct continuity and auto-innoculation.

While the bacilli can be found in most organs and tissues of the body, they have an affinity for certain structures, notably the peripheral nerves, the skin, and the reticulo-endothelial system. The changes produced in these are described. The effects on certain other tissues are mentioned. The histological changes are described broadly, and the significance of the lepra cell and giant cell discussed. The lesions of leprosy are compared and contrasted with those of tuberculosis. The connection between the pathological changes and the *M. Leprae* is discussed and the hypothesis put forward is that the nature of leprosy lesions is determined by the degree of resistance to the disease. The leprolin test is briefly described and its significance pointed out. Leprosy is seldom fatal, death being usually due to secondary complications.

MANIFESTATIONS OF LEPROSY.  
DIAGNOSIS and PROGNOSIS.  
CLASSIFICATION.

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MANIFESTATIONS OF LEPROSY.

It can truly be said that the manifestations of leprosy are legion, almost rivalling in variety the lesions of syphilis. The early signs of the disease in children are very different from those of the advanced leprous adult, and in between these extremes is a wide range of lesions. The disease simulates many other affections of the nerves and ~~cells~~<sup>skin</sup>, but there are nearly always certain characteristic features which make a diagnosis easy to one who is familiar with the disease. The manifestations also vary in the different regions of the earth and among the different races of mankind. The disease will be described as it occurs in the brown or black-brown skin of the South Indian. No attempt will be made to include every variety of manifestation, but only the commonest which I have met with, and which appear to constitute the disease as it occurs in South India. For simplicity the signs of nerve and skin leprosy will be described separately, but it must be emphasized that the two types frequently occur together in the same person. Among our patients the majority of skin cases also have one or more nerve lesions, that is, are mixed cases.

A. Nerve Leprosy.

I. The hypopigmented macule.

Three varieties of hypopigmented neural macules are seen. The type most commonly met with in young children is the pale café-au-lait coloured patch, regular in outline, not raised, with the skin a little roughened, and no sensory disturbances. These patches may occur anywhere on the body, but are usually found on the cheeks, buttocks, over the shoulder-blades, and on the thighs. In the absence of any other signs it is often very difficult to be certain that a solitary patch of this nature is leprotic.

In older children and adults the commonest type of macule is definitely raised above the level of the surrounding skin. It is regular in contour, although several patches may coalesce to form a large irregular area. The surface is rough, with keratosis and loss of hairs, and dryer than normal skin. It is a light copper colour, but in the state of lepra reaction it becomes definitely red and congested. Nearly all such patches show some inability to distinguish between heat and cold and analgesia to pain. Not infrequently there is superficial anaesthesia to light touch, but in the majority of such lesions this is not present.

I cannot agree with the classical description of the neural macule being always anaesthetic, as in South India at least, the neural macule usually is not anaesthetic. When anaesthesia is present it has nearly always been preceded by a period of paraesthesia. The older macule often shows a characteristic ring-like appearance. The centre becomes flattened and scar-like and the pigment may return. The circumference of the lesion is raised and indurated and even erythematous. It is by the radial spread of the active circumference that the lesion increases, while the centre heals. These macules may occur anywhere on the body, but are usually found on the extensor surfaces of the limbs, backs of the shoulders, buttocks, and cheeks, that is, on the areas most exposed to trauma and pressure.

The third variety of neural macule is the tuberculoid lesion recently described by Wade (37). Some workers are doubtful whether this type of lesion occurs in India, but I have found it not infrequently and think it is associated with a strong resistance to the disease. The lesion is raised and indurated, often markedly so. The surface is usually rough, pebbled, and papular, but

but/sometimes the induration is so great as to make the surface smooth and tense. The edges are regular and rise abruptly from the surrounding skin, which often shows a margin of erythema round the lesion. In the larger macules it is the circumference which shows the signs of activity while resolution occurs in the centre. In the quiescent state the macule is hypopigmented or a copper colour, but in the reaction stage it becomes red and congested. Superficial anaesthesia is nearly always present, also analgesia and loss of thermal discrimination. These tuberculoid lesions are very common on the cheeks, and occur also on the extensor surfaces of the limbs and on the back. Usually they are large isolated macules, but not infrequently numerous small macules are scattered all over the body, as if sprinkled from a pepper castor. Tuberculoid lesions respond more rapidly to treatment than any other manifestation of the disease, leaving a scar-like area of thinned epithelium. Sensation usually returns, but in the large macules it may not do so entirely.

While these three types of neural macule can be recognised, intermediate lesions occur commonly. It is often possible to see in

in/one individual several varieties of neural macules, some anaesthetic and some not, some in the stage of reaction and others quiescent. The macules may vary in size from pin-heads to lesions covering a large area of the body's surface. Sometimes they are more of a linear nature, outlining the area supplied by a particular superficial nerve.

## 2. Sensory disturbances.

Disturbances of superficial sensation are the commonest manifestations of leprosy and in many cases they may be the first and only symptom noticed by the patient for months or even years. The various elements of cutaneous sensibility are not always affected simultaneously and equally. In general the first change is in thermal sensibility and the patient is unable to distinguish between heat and cold. The next is a loss of pain, and finally there is anaesthesia to light touch. This last is preceded by a short period of hyperaesthesia and paraesthesia, which often go unnoticed unless carefully tested for in early lesions. The deep or muscle sense is not affected in leprosy. In time the superficial anaesthesia becomes so complete that the area



area/affected may be burned or scalded or cut with no pain whatever being felt by the patient. I have frequently removed fingers, toes, and even metatarsals, without the use of any artificial anaesthetic. This completeness of anaesthesia is a striking characteristic of well-established leprosy but it must be remembered that it is not present in the early stages.

The anaesthesia occurs in two sites. It is often found in the visible lesions of the skin, and the anaesthetic macule is the classical sign of neural leprosy. As already stated, however, most neural macules seen in South India are not anaesthetic, although they may be analgesic and have loss of thermal sensibility. I have found that the small macules, about the size of a shilling or half-crown, are more often anaesthetic than the large macules. Usually the sensory disturbances have an acroteric distribution, occurring on the extremities, buttocks, face and ears. The distribution of the ulnar and peroneal nerves are most commonly affected, and the anaesthesia seldom extends above the elbows and knees. I have not found the great auricular and trigeminal distributions as frequently involved as workers in other parts of India report, but they are not uncommonly affected.

affected./ Anaesthesia occurs on the buttocks and occasionally I have found it in the area supplied by the lateral cutaneous nerve of thigh. Apart from macules, anaesthesia is uncommon on the trunk and neck.

On the upper extremity the earliest anaesthetic changes are usually along the ulnar side of the back of the hand, the little finger and inner half of the ring finger. Gradually the anaesthesia extends upwards and sideways over the back of the hand and forearm, and then on to the palm and ventral surface, until the whole forearm and elbow are affected. Occasionally it spreads up the arm. On the leg the earliest changes are along the outer side of the dorsum of the foot and over the external malleolus. From there the disturbance gradually creeps up and around the leg to just above the knee. In only two cases have I seen the anaesthesia continuous from the toes to above the iliac crests.

### 3. Nerve enlargement.

Even in the early stages of leprosy there may be thickening and enlargement of one or more of the main nerve trunks. Those that are

are/usually found to be enlarged are the ulnar, behind the elbow and lower arm, the peroneal as it curves round the upper end of the fibula, and also the great auricular, and the supra-orbital nerves. It frequently occurs that the cutaneous nerve supplying an area of skin on which there is a macule, is thickened and can be easily palpated. When a nerve trunk is thus affected, anaesthesia is always found somewhere in its distribution.

The nerve enlargement may be so gross as to be visible, and is often associated with a severe and sometimes intractable neuritis. Frequently the enlargement is accompanied by tenderness of the nerve when palpated, and the patient complains of tingling or a burning sensation in the area supplied by it.

In two cases under my care the lesion of the nerve proceeded to actual abscess formation, which had to be evacuated. The abscess is of a subacute type, often causing pain but may be painless and resembles the tuberculous cold abscess. Nerve abscess appears to be one of the characteristic features of leprosy in India, evidently occurring much more frequently in this country than elsewhere. The condition was first reported by Muir (42) and again by Lowe (43). Wade (44) reports that such lesions never occur in the Philippines.

4. Trophic changes.

As a result of the lesions in the nerves and consequent destruction of the nerve fibres, a variety of trophic changes may occur in the tissues supplied by the affected nerves.

(1). Muscular paralysis and wasting.

Muscular paralysis and wasting most commonly occurs in the small muscles of the hand and foot. In the hand the change is first seen in the small muscles of the hypothenar eminence, then gradually extends to the interossei and lumbricals, and finally the short muscles of the thumb. Sometimes the larger muscles of the fore-arm are also affected, as in one case under my care who had a bilateral ulnar deviation of the hands due to paralysis of the brachioradialis muscles. The paralysis of the small muscles of the hand causes bending of the fingers and the characteristic main-  
en-  
griffe. In the lower limbs there occurs flat-foot and drop-foot and often inversion of the foot.

When the facial nerve is involved, as occurs not infrequently, there is a paresis of one or more muscles of the face. This leads to a characteristic loss of expression in the face. Paralysis of the orbicularis palpebrarum is common and the patient is unable to close the eye

eye/completely. Corneal ulceration may then occur, especially if there is also trigeminal anaesthesia of the eye. Ectropion is not infrequent.

(II). Bone changes.

As already described in the section dealing with pathology, there is an osteoporosis and gradual absorption of the bones, following the trophic changes in the periosteum. The digits shrink until eventually the nails may come to be at the end of the metacarpals or metatarsals. This process is frequently accompanied by trophic ulceration, and leads to the popular belief that in leprosy the fingers and toes drop off. In extreme cases the long bones of the forearm and leg may be similarly affected. In several patients requiring amputation I have found the tibia and fibula like thin shells which splintered under the saw. These bone changes are well seen in X-rays, and have been described in an investigation by Murdock and Hutter (45).

(III). Trophic ulceration.

Trophic ulceration is the commonest sequel of neural leprosy and is probably the most

most/crippling of all lesions. It is usually the presence of one or more such ulcers that brings the patient to a leprosy institution, and the healing of them is his chief concern. They occur commonly on the hands and feet and are associated with areas of anaesthesia. On the hands they are caused by a burn, cut or other injury. On the feet they occur practically always on the soles, and are due either to trauma or pressure. The commonest sites are those areas that bear the weight of the body, namely, the ball of the big toe, the outer side of the foot, and the heel. Owing to the Indian habit of sitting cross-legged, ulcers not infrequently develop over the external malleolus. The ulcers readily become infected, and increase in size and depth until the underlying bone or bones are involved. In this way true perforating ulcers are formed which will not heal until the necrosed bone is evacuated. The trophic ulcers of leprosy are extremely difficult to heal and may continue for years, alternately healing and breaking down. Fortunately they are painless, unless an acute septic infection is superimposed. Lepra bacilli are never found in trophic ulcers, nor are they an indication of active leprosy.

Minor trophic changes of nerve leprosy are

are/anhidrosis, loss of hair, and ichthyosis. These occur in the neural macules and in areas of anaesthesia.

B. Skin Leprosy.

I. Erythematous macules.

The erythematous macule may begin in several ways. A hypopigmented neural macule may suddenly become red, raised, and congested, especially around its circumference, and skin scrapings reveal the presence of numerous bacilli where previously none could be found. In this way the neural case develops into a cutaneous case, and is due to some factor which has lowered the patient's resistance, such as an attack of malaria or typhoid.

In other cases one or more small pale pink patches appear, slightly if at all raised, with a smooth surface and regular outline. As they gradually enlarge the borders become raised and distinctly red, while the centre tends to heal. Bacilli can be found in these macules from the beginning, but there are no sensory disturbances of note. As has been already described in the section on pathology, there are three sub-types of

of/cutaneous lesions, - papillary, interfollicular, and subfollicular. Each of these may be recognised clinically.

In yet other cases the first indication of a lesion is a faint blush which appears in an area of skin and can only be seen by careful examination. Skin scrapings from such an area will reveal bacilli. As the lesion progresses the macule assumes an outline and the usual characteristics of a skin lesion.

The lesions of cutaneous leprosy may occur anywhere on the body but, like the neural lesions, show a predilection for areas exposed to trauma and pressure, such as the extensor surfaces of the limbs, the buttocks and backs of the shoulders, the cheeks and ears. The lower abdomen is the part of the body least affected by lesions, possibly because it is protected from external contact by the loin cloth.

## 2. Infiltrations.

Leprotic infiltration is a comparatively early skin manifestation. Because of the changes in the corium the skin is thickened, the natural lines are obliterated, and it appears smooth and tense. There is no definite outline to an area of infiltration and the only colour change is



is/a reddening of the skin involved. If the skin is picked up between finger and thumb the thickening is obvious. As the infiltration advances elevations are formed. These may be entirely focal, with a few rounded projections on a large infiltration, or they may throw the skin into rounded or elongated folds separated by lines conforming to the natural ones of the skin.

While infiltrations commonly occur anywhere on the body, certain situations should be especially mentioned. Not infrequently the first manifestation of leprosy is a slight blush on the cheeks or eyebrows and a suggestion of thickening of the skin of those areas. The same changes occur in the ear lobes. If carefully examined bacilli can usually be found even at this early stage. As the infiltration increases it becomes more obvious, spreads over the cheeks and across the nose, to the lips and chin, and over the forehead. The ears become markedly enlarged and pendulous. There is a coarsening of the features, with loss of expression. In advanced cases the typical leonine facies is seen.

Infiltration of the skin of the hands and feet is common, giving the fingers and toes a coarse thick appearance, as if chilblains were present.

### 3. Nodules.

The erythematous macule and infiltrations are diffuse lesions, but the nodule is a focal lesion due to a bacillary embolism in the corium and an intense cellular reaction around it. A nodule may be only temporary or may be permanent. It may be soft or hard according to the amount of fibrous tissue in it. It usually occurs in the skin but not infrequently is subcutaneous. A recent nodule appears red, congested, tense, and glistening. Often they break down and ulcerate, discharging purulent material teeming with bacilli, and eventually heal with scar formation. The patient may have only one or two isolated nodules, or there may be many scattered over the body. There is no difficulty in recognising a nodular case of leprosy.

### 4. Papules.

Less frequent than the other skin lesions is a papular eruption sometimes found. The papules appear on the chest, abdomen, back, thighs, and upper arms. They are small, red, and raised, varying in size from a pin-head to a farthing. They may be scattered diffusely or gathered in groups. Abundant bacilli are found

found/in them. Sometimes the papules become vesicular and not unlike the lesions of chickenpox in appearance.

5. Lymphatic glands and oedema.

There is some degree of enlargement of superficial lymph glands detectable in practically all cutaneous cases, even in the early stages. The enlargement is non-inflammatory and painless, except during a lepra reaction, when the glands may be very tender and painful and may even suppurate. The individual glands remain intact and freely movable, unless there is a secondary infection. Occasionally the glands break down and discharge through the skin, as occurs in a tuberculous infection, but probably such cases all have a secondary infection. The inguinal glands are most often infected, and then the axillary, epitrochlear, and occasionally the cervical groups.

Associated with the glandular involvement, and probably resulting from it, is a chronic oedema of the hands and feet.

6. Nasal ulceration.

Bacilli can be found in scrapings from the nasal mucosa of many cutaneous cases. In such

such/persons there is a leprotic infiltration of the mucosa, more especially over the septum and inferior turbinate. Both sides of the nose may be affected. In the early stage of infection there is reddening and congestion of the mucous membrane, but this soon gives place to a dryness and crusting and the membrane is lighter than normal in colour. Such patients sometimes state that they never suffer from 'colds'. At a later stage ulceration appears from which abundant bacilli are discharged. Epistaxis is common and in some cases repeated bleeding has been the first indication of the disease. The ulceration may perforate the septum or erode the turbinate. The nasal cartilage is destroyed and the nose collapses. This is different from the sunken nose of syphilis, as in leprosy the bone is not destroyed. Nodules may form in the nasal mucosa.

#### 7. Subsidiary signs.

Affections of the larynx occur in advanced cases and have been already described elsewhere, as also have the eye lesions. Enlargement of the male breasts, known as Powell's sign, is common and causes much embarrassment to the patient. Trophic changes in the skin occur and give the integument of the leper a characteristic appearance

appearance/which is one of the popular signs of the disease. The skin is thin, dry, and hairless, and shining. In cutaneous leprosy the eyebrows and eyelashes are lost early, and the beard often goes if there is much infiltration. I have not seen a leprotic alopecia of the scalp, even when it has been extensively involved. The inability to sweat causes great distress in the hot weather.

The earliest signs.

The difficulty of observing the earliest clinical manifestations in a disease such as leprosy is obvious. The first changes are either unnoticed by the patient, or the passage of time has erased them from his memory. What he states to be the first evidence of the disease is usually the sign of a well established infection. It is only by the careful observation over a period of years ~~of years~~ of the children<sup>of</sup> lepers and those in contact with infective persons that the progress of the disease can be seen from its initial stages. My own experiences and opportunities for observing early cases have been very limited, but certain definite observations will be mentioned. Similar findings have been made by Chiyuto in the Philippine Islands (46) which

which/confirm my own impressions.

The first changes in children are more often cutaneous than neural. Careful examination reveals a delicate flushing, perhaps of the cheeks or ear lobes, or a flushing, glistening, and tenseness over the skins or wrists. In others hazy ill-defined hypopigmented areas with a pinkish tinge appear and give the skin a mottled appearance. These are more easily seen at a certain distance and angle of light than at close range, and must be distinguished from other acromias, such as parasitic, post-inflammatory, solare, and anaemic, that cause slight disturbances of colour. A frequent precursor of the more obvious neural macule is a collection of minute pale papules like goose-flesh.

In older children and adults there are early sensory disturbances such as areas of numbness, tingling, formication, burning sensation, vague joint and nerve pains. Areas of flushing and mottling may be noticed, or repeated attacks of epistaxis. Neuritis and nerve tenderness may be the first indication. The toxic prodromata described by Manson - Bahr (47) and other authors, with fever, malaise,

malaise/dyspepsia, headache, etc. are not an early manifestation of leprosy, but an indication of a generalised lepra reaction.

### Diagnosis of Leprosy.

The diagnosis of an established case of leprosy is usually easy, and yet it is surprising how often it is missed by physicians in the tropics. The protean manifestations of the disease are probably responsible for many of the errors made, and also the fact that most standard text-books describe only the advanced lesions. Diagnosis from the early signs described above is admittedly often difficult, even to one familiar with the disease in all its aspects.

There are three cardinal signs on which a certain diagnosis can be based.

1. The finding of lepra bacilli.
2. Superficial anaesthesia to light touch.
3. Nerve enlargement.

The finding of any one of these is sufficient evidence of the disease, for they occur in no other condition. A warning must be given

given/on diagnosing leprosy solely on the finding of one or two acid-fast bacilli from nasal or skin scrapings. It must be remembered that bacilli of this type, such as *M. smegmatis*, occur naturally on certain body surfaces, and also free-living in water, dung, etc. Therefore an occasional one or more may be found in the nasal mucosa, skin surface, ulcers, etc. There was sent to me for consultation a patient from the Mental Hospital, Madras, who had been treated for leprosy for eighteen months on the strength of rhinitis and a few acid-fast bacilli from nasal scrapings. A careful examination showed no other evidence of leprosy and the bacilli appeared atypical. I found that the patient had a chronic antrum infection and when this was dealt with the bacilli disappeared from the nose.

In the absence of any of these cardinal signs the diagnosis rests on finding several subsidiary signs, and to one familiar with the disease there is usually no difficulty in distinguishing leprotic from non-leprotic lesions. Every depigmented patch in a dark-skinned person is not necessarily leprosy and the scar of an old non-leprotic ulcer may be anaesthetic.



### Differential Diagnosis.

There are several diseases not infrequently confused with leprosy and they will be briefly mentioned.

#### 1. Syphilis.

Syphilis is the commonest accompaniment of leprosy in South India, apart from the universal scabies and ringworm. The secondary and tertiary lesions of syphilis can be readily distinguished by the absence of any of the cardinal signs of leprosy and by their response to arsenical treatment. A positive Wassermann or Kahn reaction is strong evidence of syphilis, but does not necessarily exclude leprosy as the two diseases are so often associated, and there is some evidence to suggest that leprosy itself may affect these tests. Yaws is very rare in South India.

#### 2. Skin affections.

The circinate lesions of ring-worm may simulate macules with spreading margins and healed centres. Psoriasis may be similarly confused. Scabies often forms large plaques. The eruptions of seborrhoea, impetigo, and pemphigus

pemphigus/have to be remembered. Lupus vulgaris is often met with. Ordinary urticaria may be confused with early cutaneous eruptions, or the rashes of lepra reaction. The lesions of pityriasis versicolor are more irregular than those of leprosy, have a greyish colour, and are covered with fine dry scales. Leucoderma is a complete depigmentation, which never occurs in leprosy. It is popularly known as 'white leprosy' but has nothing to do with the disease. Scleroderma may be confused with leprotic infiltration. All these affections can be distinguished from leprosy by the absence of any of the cardinal signs or several other subsidiary signs, and each of them usually has its own characteristic appearance. It is important to remember that a leprotic lesion is not irritating, and an itchy lesion cannot be leprosy.

### 3. Lesions of the spinal cord.

The claw-hand, wasting, and sensory disturbances are typical of syringomyelia, and may be confused with advanced neural leprosy. The anaesthesia of syringomyelia is to temperature and pain, and not to touch, which easily distinguishes it from leprosy. Of other diseases of the spinal cord the one most likely to cause confusion is amyotrophic lateral sclerosis with

with/gradually increasing weakness and wasting of the upper limbs and paraesthesia, but no anaesthesia. In leprosy the motor reflexes are not affected.

#### 4. Beri-beri (dry).

Dry beri - beri causes paraesthetic symptoms similar to those experienced in early leprosy, and if no other signs are present it may be very difficult to be certain of the diagnosis. Vague epigastric discomfort or pain, tenderness of the calves of the legs, paraesthesia around the mouth, and decreased knee and elbow jerks are in favour of beri - beri. Anaesthesia of leprosy usually starts on the ulnar side of the hand or forearm, while in beri-beri it starts on the radial side and is only partial.

#### 5. Dermal Lishmaniasis.

This is often mistaken for nodular leprosy. Bacteriological examination of the nodules reveals no lepra bacilli but Lishman-Donovan bodies.

#### 6. Raynaud's Disease.

This condition is not uncommon in India and must be remembered in diagnosing an atypical case of leprosy. Other signs of leprosy should be looked for.

7. Ainhum.

This is a peculiar disease occasionally met with in which the little toe is slowly lost by a fibrous constriction around its base. Ulceration may occur, but there is no anaesthesia.

8. Anaemic patches.

Pale areas on the cheeks or body are very common in children and are due to anaemia, usually associated with intestinal parasites. They readily disappear if the child is given iron and cod-liver oil, and are in no way leprotic. Birthmarks and other innocent skin markings must be recognised.

There are many other diseases from which leprosy has to be diagnosed from time to time, and not infrequently one meets a case where a diagnosis cannot be clearly made and judgment has to be reserved. All such cases should be kept under observation until the development of further lesions establishes the diagnosis one way or the other.

Lepa Reaction.

Lepa reaction is perhaps the most interesting and puzzling phenomenon of the disease, and

and its true nature and significance are still a mystery. It is seen in both treated and untreated cases, but rather more frequently in the former. The sudden onset of a reaction may be the first indication of the disease. The reaction subsides spontaneously in the course of time, and this feature is responsible for the reputation of the quack remedies freely advertised in this and other countries.

Clinically, lepra reaction appears to be an acute exacerbation of the disease with an exaggeration of the existing lesions and development of new ones. In its simplest form it is characterised by a swelling and congestion of one or more of the existing lesions or by a sudden outbreak of papular eruptions in apparently normal skin. In the more severe forms this is accompanied by malaise, headache, fever of remittent type, prostration, and all the symptoms of an acute toxæmia. The reaction foci are by no means confined to the skin. Frequently there is an acute neuritis, with severe pain and tenderness of one or more nerve trunks and hyperaesthesia and burning sensation in their cutaneous distribution, or acute orchitis, or iritis. Acute lymphadenitis, especially of the inguinal region,

region/, is not uncommon, and the glands may break down. Rheumatoid pains and actual arthritis sometimes occur. The face, ears, hands, and feet are markedly swollen, as if from severe cellulitis. In fact, an acute inflammatory reaction can take place wherever there is a leprous lesion.

After a variable period, usually from four to ten days and according to the severity of the reaction, the condition subsides. The swelling and congestion disappear, fresh eruptions resolve, fever drops, and the patient returns to his normal condition. The skin over the lesions becomes wrinkled, hyperpigmented and flakes or peels off. Severe reactions may drag on for weeks, or successive attacks may follow one after another so frequently that the patient becomes emaciated, cachectic, and bed-ridden.

The after-effects vary. The milder attacks are beneficial and existing lesions may subside or disappear altogether after a brief period of reaction. The patient who improves most rapidly and responds best to treatment is the one who has a series of short mild attacks. Therefore the most successful line of treatment

treatment/is that which will induce such a sequence of controlled reactions. However, when severe reactions are prolonged or successive the patient becomes debilitated and the lesions worse, anaemia becomes marked and a cachectic condition develops which often leads to death. If there is pulmonary tuberculosis this is very apt to be activated. As this progresses one sees the curious phenomenon/<sup>of</sup> simultaneous retrogression of the leprotic lesions. Nephritis is another serious sequel to severe reactions.

Explanation of Lepra Reaction.

Lepra reactions result from various causes and often come on spontaneously from apparently no cause whatever. They occur in both neural and cutaneous leprosy but are commoner in the latter. They occur with equal frequency in both sexes, but are less common in children than in adults. Conditions to which reactions have been ascribed include psychic stress, excessive use of alcohol, change of weather, onset of menstruation, certain articles of diet, an acute secondary infection, and sexual indulgence. Treatment often brings on a reaction and certain drugs

drugs/have the power of inducing it, especially potassium iodide. Stein of Leningrad (48) believes they are due essentially to changes in the atmospheric conditions.

To the older leprologists, lepra reaction was easily and simply explained as an acute, exaggerated stage of the leprous process. In view of further study of the phenomenon and the modern understanding of the complicated interplay of infection and resistance, general and local, this facile explanation is no longer tenable. It assigns the essential factors entirely to the bacillus and its toxins, and not at all to the host's tissues, and ignores many qualitative peculiarities. The remarkably low toxicity of the bacillus has been commented on already, and it is difficult to conceive that it can suddenly and sporadically begin to produce real toxins in important amounts. Another objection is that pus production is not a feature of ordinary leprotic lesions, while it not uncommonly occurs in severe reactions.

Microscopically, reaction lesions show, depending on their severity and duration, acute and subacute changes, with congestion, fluid exudation, and invasion by ordinary inflammatory cells, particularly polymorphonuclear leucocytes which are foreign to the ordinary lesions. It has therefore



therefore/been suggested that a lepra reaction is due to a rise of resistance, either general or local, to the invading organism. The raised resistance causes a more acute tissue reaction, and the break-down products of the bacilli are responsible for the fever and general toxic manifestations. The debility that follows lowers the resistance again and so the reaction subsides. There is considerable evidence in support of such a theory. It has been already stated that the greatest improvement is seen in cases which progress by a series of mild controlled reactions. It is a well-known fact that during an illness such as typhoid or pneumonia leprous lesions usually diminish or even disappear. During this time the bacilli are presumably multiplying unchecked. When the patient recovers and his resistance rises again it is common for a reaction to occur. At the same time this theory does not explain all cases, nor certain features of the condition. In reacting lesions bacilli are found in far greater numbers and often appear where they had been previously absent. It does not explain the long continued reactions in which the patient becomes more and more debilitated and cachectic, nor does it explain why it is possible to induce

induce/and control reactions with certain drugs.

The view of lepra reaction that I have arrived at, as have other workers within the last few years, is that it is a manifestation of allergy. Bacteriologists are not yet certain as to the nature of the processes that go to make up the phenomena of allergy and too often the term is used to cover a multitude of doubts. I confess to this being true in the case of leprosy but at the same time it gives a more satisfactory explanation of lepra reactions and leprotic manifestations in general than any other theory. The difficulties in studying the condition in leprosy are obvious, but a parallel can be drawn to tuberculosis and the familiar tuberculin reactions. Tuberculin, which is made from cultures of the tubercle bacillus, is not toxic and causes no reaction when injected into the skin of a healthy person. If the person has been previously infected then an acute inflammatory reaction occurs at the site of injection. If an excessive dose of tuberculin is given the patient has a general febrile reaction with an inflammatory reaction in the tuberculous lesions and an apparent clinical exacerbation of the disease. Evidently the tuberculous infection has sensitised the tissue cells, so that when the

the/bacillary extract is brought into contact with them the cells are poisoned and react with the signs of inflammation. This is a complicated phenomenon, which, like the skin reaction, is recognised to be primarily allergic.

It is probable that lepra reaction is essentially of the same nature. There is experimental evidence that, as in tuberculosis, the tissue cells are sensitised in leprotic infection. Several workers, notably Stein and Steperin (49), Tisseuil (50), and Ambrogio (51), have injected lepromatous extracts into the skin of leprous persons and obtained apparently specific reactions. The leprolin test already described may be of the same nature. For some reason unknown there is a failure of those elements of the tissue fluids (anti-anaphylactins) that ordinarily protect the sensitised cells from the foreign non-toxic proteins derived from the masses of bacilli present in the body. These come in contact with the cells in one or more foci and an allergic reaction follows, probably with the secondary formation of toxic protein split-products. Hoffman (52) postulates a pre-bacillary virus stage of the organism as being responsible for sensitising the cells. Whatever may be the sensitising agent it does not seem to be very specific as

as/substances other than lepromatous extracts can induce a similar reaction, for example tuberculin, typhoid vaccine, and gonococcus vaccine. Thus it would appear as if the reaction were one merely to a foreign protein and casts considerable doubt on the value of the leprolin test. Granting the presence of an anti-substance or receptor in the cells or the serum, what is the antigen that combines with it to produce the allergic reaction? Is the antigen introduced from outside or does some condition arise which liberates it from a source within the body, or are both possible? These and many other questions arise which cannot yet be answered. Until we have more precise knowledge of the life-history of the lepra bacillus we shall not be able to explain satisfactorily the nature of these apparent allergic reactions.

Muir and Ritchie (53) state that "there is a good deal in favour of the view that anaphylaxis corresponds to an 'acute infection' whereas ordinary infection is of the nature of a gradual and protracted anaphylaxis. . . . . The phenomena of anaphylaxis may thus, in part, explain the symptoms of a disease, and may, on the other hand, be an accidental result of the process of immunity". This view is supported to some extent

extent/in the study of leprosy, and certainly by it many of the apparently anomalous features of the disease are more easily understood. Lepra reaction can only be explained as allergic phenomenon, possibly associated with the process of acquiring a tissue immunity to the disease. No satisfactory evidence has yet been produced that there is any serological immunity in leprosy. A series of mild reactions, do no~~s~~ harm and may even be beneficial by stimulating the production of further tissue resistance. In prolonged reactions the tissue resistance is so reduced that the bacilli become disseminated throughout the body, and especially in the reticulo-endothelial system. This massive invasion is responsible for the cachexia which eventually kills the patient and explains the great difficulty in treating such persons. The natural defensive mechanism of the reticulo-endothelial system is not stimulated for, as has been pointed out elsewhere, the bacilli exist in the cells in a state of commensalism. This theory is based on the hypothesis that the lepra bacillus is a parasitic rather than a pathogenic organism. Such being the case too close a parallel cannot be drawn to the view of Muir and Ritchie quoted above.

There are great possibilities in further investigation along these lines, but the

the/difficulties are serious. At present one can only draw analogies to other diseases, especially tuberculosis, and attempt to correlate them with the clinical findings in leprosy. It is not justifiable to push the similarity too close for we must regard the leprosy bacillus essentially as a parasite in the human host rather than a pathogenic organism.

P R O G N O S I S.

Until the advent of modern treatment methods, leprosy was generally considered as an incurable disease. This was not strictly true for leprosy is a self-limiting disease, dying out spontaneously if the patient lives long enough. Most neural cases cure themselves in a few years, often without having produced any gross lesions or deformities. Cutaneous cases, on the other hand continue for many years, and although a few become naturally cured, the majority die from a secondary disease or from prolonged lepra reaction, while still active lepers. Granting, however, this tendency to self-limitation, the individual is too often left a maimed, deformed, and crippled wreck whose state is as much to be pitied as any misfortune which can inflict a human being. A vivid description of such a person is given by Hansen and Looft (33) as follows. "Lepers usually die before the disease has run its course, but in the maculo-anaesthetic form the cure of leprosy is almost invariably the result. What remains, however, after the cure is very different. We have occasionally a complete subject with vigour and good health, but usually only a miserable rudiment of a human being,

being/, with more or less paralysed and deformed hands and feet; with unclosable eyes, of which the lower part of the cornea is opaque, and from which tears run down over the cheeks; and with paralysed facial muscles unable to close the mouth so that saliva constantly dribbles from it. Such cases may, however, live long and reach a great age, if under such circumstances this can be looked upon as any advantage". In a disease so greatly feared and dreaded as leprosy the prognosis becomes of great importance and is often a valuable asset in helping towards recovery. Considerable experience is necessary before making a confident prognosis, and at the best one can never guarantee the arrest of the disease until the passage of many years has proved it. At the same time it must be emphasised that every individual with one or more signs of leprosy does not face the above gloomy outlook, nor is active treatment always called for.

In making a prognosis there are many factors to be taken into consideration. First there is the stage of the disease at which the patient presents himself for treatment. In the early stage the outlook is most hopeful, and there is a reasonable chance of the patient recovering without any



any/marked blemishes or stigmata. In the second stage, when the disease has become a systemic infection with the manifestations of generalised cutaneous leprosy, the outlook is definitely poor in the majority of cases. In the third stage, when the patient's immunity has reached a high level and the disease is naturally abating, the outlook for arrest is good, but not without scars and deformities. This last type of case can usually be assured that there is little possibility of the disease increasing further, hence the importance of recognising the appearance of resolved lesions.

Further factors to be considered in assessing the outlook for the individual are age, general health, degree of natural resistance, and hyperinfection or bacillary concentration in the body. Of these, the two last are the most important. It has already been pointed out that leprosy is a disease of childhood and adolescence, and at that period of life the resistance is lowest. The child who shows multiple lesions, either neural or cutaneous, has a hyperinfection and a low resistance, and the prognosis is poor, especially in the cutaneous case. The earlier skin leprosy develops, the more serious is the condition. The child with

with/only one or two neural signs has a good outlook, provided he or she lives a healthy life under good conditions of hygiene and feeding, and often such cases require no special treatment. Indeed, anti-leprosy treatment may be actually harmful to such children, and I have seen not a few tragedies follow the indiscriminate giving of treatment. In adults, the later in life that the disease develops the less serious it is, on the whole. Again, the cutaneous case has a worse prognosis than the neural. In those few cases of extreme age who first develop leprosy, the disease runs a rapid course, and I have formed the opinion that in them the outlook is hopeless and that treatment is of no avail. The importance of the general health is very great at all ages.

The prognosis in leprosy, therefore, needs careful thought, for it differs in the various stages and types of the disease and in each individual. In skin leprosy, especially of the severe type, the prognosis must be very guarded. However, the outlook for the cutaneous case is very much more hopeful than it was several years ago, because of the increase of our knowledge of the disease and the advances in treatment. Naturally, the later the patient comes under treatment

treatment/the greater is the likelihood of deformities. While the outlook to-day is much more hopeful, and is increasingly so, yet one must ever keep in mind that leprosy is one of the most deceptive of diseases, and one must not make the mistake of being over optimistic. The introduction of modern treatment has caused much undue optimism, and the frequent failure of treatment is now tending to bring it into disrepute with patients and physicians alike. On the other hand, if there are no grounds for it, one should not be too pessimistic, as the maintenance of the morale of the patient is an important factor in combatting the disease.

My own view of the outlook for the leper is frankly pessimistic in all but a few selected cases. We cannot cure the disease. At the most, we can put the patient under such conditions as will be most likely to effect a natural arrest, and hope for the best. We can do much to relieve suffering and bring some comfort to mind and body, but all too often we fail to do even that. The effect of modern treatment is to turn the weak and sickly leper into a robust and healthy leper, and prolong life. The patient can often be greatly improved clinically and the disease temporarily arrested, but we cannot guarantee a cure. That does not mean that apparent cures do not occur,

occur, both in treated and untreated cases, but too often the old dictum that 'once a leper always a leper' is true.

#### CLASSIFICATION OF LEPROSY.

The classification of leprosy is an important but difficult matter. Leprosy is a general disease and in no type are the lesions confined to a single tissue. All diagnosable cases are in a sense mixed, and in consequence, any classification should be based on the predominating clinical findings. At the same time the clinical findings are not always a true indication of the extent and progress of the disease. The essential factors are the bacillary concentration in the body, and the degree of resistance. Any classification should take these into account, but the difficulties of estimating both these factors are great. Some idea of the resistance can be got by taking into consideration age, general health, nature of the leprotic lesions, rate of erythrocyte sedimentation, and the response to the leprolin test.

test./There is no method of knowing the bacillary concentration except by roughly estimating the numbers of bacilli seen on the slide from a skin scraping.

The classification now in general use is that adopted by the Leonard Wood Memorial Conference on Leprosy at Manilla in 1931. This is based on clinical findings and from many points of view is unsatisfactory. It depends on the arbitrary opinion of each observer, so that what one would call a C-1 case another might consider as C-2. However, it is probably the best method available just now and will be briefly described.

It defines two main types of the disease, the neural (N), and the cutaneous (C), according to whether bacilli are found or not in scrapings from the skin or nasal mucosa. All cases which show any bacilli are regarded as cutaneous even though neural signs may predominate. It must be remembered that practically every case of leprosy has some degree of nerve involvement even though it be so slight as to be undetected clinically.

Neural - All cases that show evidence of **actual** or previous nerve involvement, i.e. alterations of sensation with or without changes in pigmentation and circulation,

circulation, /trophic disturbances or paralyses and their consequent results - atrophies, contractures, ulcerations. These are not accompanied by leprotic changes in the skin.

Cutaneous - All cases showing leprotic lesions in the skin. Such cases may or may not show at any given time, clinical manifestations of nerve involvement.

A leprotic lesion is defined as one which presents clinical or microscopic evidence of inflammatory processes, typically of a granulomatous nature, which are apparently caused by *Mycobacterium leprae* in them. In such lesions the organism can usually be demonstrated by the ordinary methods of examination.

The neural and cutaneous types are subdivided, according to their degree of severity, as follows:

N-I - Slight neural cases with one or a few small areas of disturbed sensation, which may or may not show alterations of circulation or pigmentation, paralyses or trophic disturbances of minor degree.

N-2 - Moderately advanced neural cases with extensive or numerous areas of disturbed sensation, not confined to any one part of the body with paralyses or/and visible evidence of trophic changes - marked depigmentation, moderate atrophy, keratosis, etc.

N-3 - Advanced neural. Cases with more or less extensive areas of anaesthesia and marked motor and trophic disturbances, and mutilations.

C-1 - Slight cutaneous. Cases with one to a few leprotic macules, or a few small areas of infiltration, or one or two nodules.

C-2 - Moderately advanced cutaneous. Cases with numerous leprotic lesions.

C-3 - Advanced cutaneous. Cases with gross leprotic lesions, especially nodules.

As already stated, the majority of cutaneous cases are mixed. In such the neural

neural/signs are taken into account and the case described as C-I N-I, or G-2 N-I, etc.

There remain two types of cases that cannot be included in the above classification. One is the neural case that was formerly cutaneous, but from which active leprotic lesions have disappeared. This type is described as secondary neural. Finally there is the maimed and deformed individual in whom the disease is no longer active. This is the 'leper mutilans' or "burnt out". Strictly speaking such a person no longer has leprosy, any more than the pock-marked individual has small-pox, but he is still regarded by the general public as a leper.

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T R E A T M E N T .

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TREATMENT.

Introduction.

From time immemorial leprosy has been regarded as an incurable malady, and there is still no specific remedy for it. The earliest records of a treatment for leprosy are found in the works of Aretaeus (54) in the second century. After the manner of those days, he advised numerous concoctions for dispelling the depraved humors, ranging from "shaving of an elephant's tooth in one dram with wine" to a compound medicine from vipers which "is to be drunk in preference to all others, for it contains together the virtue of all others". In this connection it is interesting to note a recent report on the successful use of crotalus toxin in treating lepra reaction (55). However primitive may have been the potions of Aretaeus, yet the general treatment he recommended could not have been improved upon to-day, for he appreciated the necessity of maintaining the patient's general health. "The food should be pure, wholesome and of easy digestion and plain and the régime in every way, well adjusted as regards sleeping, walking, and place of residence. As to exercise - running, tumbling, and the exercise with the leather ball; all these with well regulated intensity, but

but/not so as to induce lassitude".

From the second century until the present day a vast number of remedies have been tried. That the many reputed cures for leprosy during the last few decades have not been generally recognised as of definite benefit, with one possible exception, gives an indication of their very small value in controlling the course of this chronic and intractable disease. In considering treatment, therefore, I shall first give a review of the more important remedies tried during recent years, and then describe the routine practised by myself in the Lady Willingdon Leper Settlement. Finally, I shall indicate the results of modern treatment and assess its value.

#### Review of Remedies Tried.

##### I. Heavy metals.

###### Antimony.

Preparations of antimony are more extensively used than any of the other metals. The first report on it was by Cawston (56) who found improvement in patients given tartar emetic intravenously. The Philippine workers (57) repeated his method, and also gave it orally, but found no

no/benefit after six months. Other workers have used antimony preparations in conjunction with chaulmoogra oil and found it **only** of limited value. I have used potassium antimony tartrate, 0.02 - 0.04 gm. intravenously, in the routine treatment of lepra reaction and found it to be the most effective means of controlling this condition. I have not found it of any value in the quiescent case. Muir (58) reports the same use and found that in larger doses the drug brought on a reaction.

Arsenic.

Hansen and Looft (33) mention that Fowler's solution, though producing diarrhoea, caused diminution of nodules, but when this subsided the leprosy signs were no better. I have used Fowler's solution, m V t.i.d., in reacting cases and found it of value, but not otherwise.

The pentavalent arsenicals have been used by a number of workers with varying results. Hasson (59) first used eparsenal and reported good results in a number of cases, but admitted that it was not always reliable. Others have found it of little use. Novarsenobenzol has been tried extensively and found to benefit those cases complicated by

by/syphilis. Its action is obviously on the spirochaetes and not on leprosy. I have used novarsenobenzol extensively for treating syphilitic patients, but find it has to be given with care as it often induces a lepra reaction.

### Mercury.

Mercurial preparations have been used in leprosy for many centuries. Hansen and Looft (33) reported that patients did badly under mercury, but other workers have had varying results, the best coming from a combination of mercury and chaulmoogra oil by mouth. Muir (60) found that in patients with syphilis a combined treatment with avenyl, a mercury preparation soluble in chaulmoogra oil and esters, often rendered a positive Wassermann or Kahn test negative, with an improvement in the leprosy not obtained by chaulmoogra alone. I have used avenyl frequently in syphilitic cases but in only three persons did the Wassermann become negative, and whether these were due to the avenyl or not I cannot say. The clinical improvement was not any greater than one would expect from chaulmoogra alone. Avenyl produces no toxic symptoms, and I have reserved its use for those cases in whom arsenicals produce lepra reactions.

The mercury compound of most use is mercurochrome. It is used fairly extensively by Indian workers in controlling lepra reactions, and has been reported on by Muir (61) and others. My own practice has been to give 1 c.c. - 5 c.c. of a 5% solution intravenously, to reaction cases accompanied by any septic foci. I have found the septic conditions have cleared up and the lepra reactions subsided. If given repeatedly, mercurochrome produces a liquefaction and bursting of nodules. Large doses tend to bring on a reaction. The drug, therefore, should not be repeated for more than four or five injections. It has no effect on the non-reacting case, except in clearing up any concomitant sepsis.

#### Copper.

Copper preparations have for long been a favourite remedy for leprosy in the Indian Ayurvedic system of medicine. More recently Japanese workers have reported good results with copper cyanide and cyanocuprol. Rho (62) found cuprocyanide and cupriodase beneficial and Henderson (63) reports relief of neuritis but no effect on

on/the disease. A French cupro-cinnamic compound, called zimbyl-cuivre, has recently attracted much popular attention in South India without any therapeutic justification. It was given a trial by those working in the Cochin State Leper Asylum, and in a personal communication they inform me that it has been of no benefit. Feron (64) of Ethiopia gives a similar report on this preparation. Several Indian workers have reported to me some improvement with preparations of colloidal copper.

#### Gold.

The good effects of gold preparations on tuberculosis led to its trial in leprosy, but the results have been disappointing. Sanocrysin is of no use. Solganol has given hopeful results with some workers but not with others. Paldrock (65) uses solganol in combination with local applications of CO<sub>2</sub> snow, giving courses of such treatment at six monthly intervals. He claims that his method is the only treatment that gives specific results, but stands alone in that opinion. Muir (66) and others report unfavourable results with solganol and solganol-B which tend to induce reactions and eye lesions. I have found the same effects myself ~~and~~ in a few cases to whom I have given solganol. I have also used a protein compound of gold, known as

as/auroprotasin, and found it of some benefit in a number of cases. Its chief effect seemed to be to induce in the patient a sense of well-being and to relieve eye conditions. Other workers, Hoffmann (67) and Kupffer (68), have obtained relief in eye lesions by using krysolgan. Cochrane tells me that he has found small doses of solganol-B oleosum of value in controlling lepra reaction and eye conditions. It would seem that certain gold preparations may be of value if given carefully to selected cases and in small doses. Considerable superiority over other forms of treatment will have to be established before this very expensive drug can be recommended for general use.

#### Action of heavy metals.

A few of the heavy metals have a place in the treatment of leprosy but they must be given with care and only in very small doses, smaller than those usually recommended for other purposes. In large doses they tend to produce lepra reaction, eye lesions, and debilitate the patient. The greatest benefit seems to come from combining a metallic preparation with chaulmoogra treatment.

#### 2. Potassium iodide.

Danielssen (69) was one of the first to



to/use potassium iodide in leprosy. At first he used it extensively in diagnosis and treatment and considered the effects favourable, but later discontinued it except for testing cases for recovery. Since then it has been used extensively and most workers have reported favourably. Aoki (70) recommended its use, regulating the dosage by the erythrocyte sedimentation rate, and controlling resultant reactions with potassium antimony tartrate. Lowe (71) and Cochrane (72) caution against its use except in resistant cases, and only then under strict control.

The effect of potassium iodide is to produce a reaction in most cases, sometimes with a small dose and sometimes not until a large dose has been given. How it does this is not known. If injected locally into a leprous lesion it does not produce a focal reaction so can have no direct action on the lesion or the bacilli. It has been suggested that it acts by stimulating the thyroid, but thyroid extract itself does not produce the same reaction. Possibly the drug liberates from somewhere an antigen that causes an allergic reaction as has been discussed elsewhere. However it may act, the drug has been used in the past to induce a series of therapeutic and beneficial reactions. Beginning with one grain a day the dose is raised by one grain daily to gr. 20. and

and/thereafter by gr.5 to a dose of gr. 60 a day. A further gr. 30 a day are added until a final dose of gr. 240 is reached, which should be continued twice a week for a month. The increase must be according to the tolerance of the patient, and the drug stopped at once if the temperature rises or any indication of a reaction appears. There is a great danger that the reaction induced may be severe and uncontrollable as there is no way of knowing how a patient will respond. As little as one grain has been known to do great harm while repeated doses of gr. 240 may have no effect. The other uses of potassium iodide are to establish a diagnosis in a doubtful case and to test for the complete elimination of the disease in an apparently arrested case.

My own opinion of the drug is that it is extremely dangerous, often does more harm than good, and that its use is seldom justifiable. I have seen many cases made worse by it, and not a few tragedies. In the quiescent or arrested case the natural resistance of the body is overcoming or has overcome the infection. It cannot be wise to break down the body's protective mechanism and risk a flare-up of the disease. If a case has become arrested the general resistance of the body

body/should be entrusted to keep the disease in check. A negative reaction to iodides in a doubtful case of leprosy does not mean that the case is not leprosy. If it is leprosy then the doubtfulness of the signs indicates a fair degree of resistance which we are not justified in breaking down. Many such cases never advance further, if left alone. I strongly condemn the giving of potassium iodide, and with the exception of a very few selected cases, never use the drug myself. Fortunately it has fallen into disrepute among most leprologists and this double-edged sword is now seldom used. Care must be taken to remove potassium iodide from all stock cough mixtures, etc. mixtures, /etc. used in a leprosy centre.

3. Other drugs tried.

Carbolic acid.

Carbolic acid in dilute solution by mouth was used by Hansen (33) with no effect. De Raadt (73) believes that the autophenolisation of the body has an injurious effect on both the lepra and tubercle bacillus, and therefore protects the body against these organisms. He thinks that this is achieved by a diet sufficiently rich in

in/vegetable protein. He treated patients with pulmonary tuberculosis by means of daily administration of 250 mgm. of phenol in cod liver oil, and got strikingly favourable results. The effect of such a treatment on leprosy has not been recorded.

#### Creosote.

Creosote itself has no effect on leprosy, either internally or in an ointment. It is largely used in combination with chaulmoogra or hydnocarpus oil and esters (4% strength). It decreases the viscosity of the oil, is antiseptic, antifebrile, tonic, and is said to have an anaesthetic action at the site of injection.

#### Sodium salicylate.

Sodium salicylate is useful in lepra reaction for controlling fever and relieving bone and joint pains.

Of the many other drugs tried at one time or another only a few need be mentioned. An ointment containing resorcin and pyrogallol was recommended by Unna (74), and also an ichthyol ointment. Strychnine and tonics of various sorts have a limited value. Camphor is often included in the creosoted esters.

#### 4. Vaccines and Sera.

Many attempts have been made to treat leprosy with vaccines, sera, bacillary suspensions, lepromatous extracts, etc. Some workers have reported promising results, but these have been obtained from too small a number of cases to be conclusive or have failed on repetition by others.

##### Antogenous Vaccines.

Hasson (75) obtained bacilli from CO<sub>2</sub> blisters on leprotic lesions and added a mixed culture of *B. pyocyaneus*. He reported good results with this suspension, but others failed to get any benefit from the same methods. Devoto (76) separated bacilli by treating triturated nodules with antiformin and reported favourable results in three cases. Many others have obtained suspensions from leprosy lesions by various methods but none of these preparations have so far produced practical results.

##### Tuberculin and tubercle bacilli.

Tuberculin has been used in treating leprosy because of the similarity of the two bacilli. Danielssen (77) was the first to try it, followed by many others since his day.

day./Practically all have reported disappointing results or even definite harm. Row (78) used suspensions of antolysed cultures of tubercle bacilli washed free from fatty substances with petrol ether. He and others reported favourable results with this and apparently the dangerous effects of tuberculin were absent. Others failed to get any lasting improvement with B.C.C.

Other acid-fast organisms.

Various other acid-fast organisms and their products or extracts have been inoculated by various workers. Some of them were under the impression that the organisms they used were true cultures of Hansen's bacillus, and hoped to obtain thereby a specific active immunity. Others aimed rather at producing a group immunity that might affect the leprosy bacillus.

The most widely known preparation of this nature was Deycke's 'nastin' (79). This consisted of a killed suspension of an acid-fast organism cultivated from leprosy nodules. Deycke at first thought it was a culture of Hansen's bacillus, but subsequently he found it to be a

a/non-specific acid-fast streptothrix. A mixture of this with benzylchloride, called nastin-B, was more commonly used as it produced less severe reactions than nastin alone. Deycke and others claimed good results with nastin and nastin-B, but Wise and Minett (80) continued the work begun by Deycke himself and after four years experience concluded that the preparation was inert, and that benzylchloride alone gave the same results.

Rost (90) of the Indian Medical Service prepared a vaccine from an acid-fast culture from leprous material and believed it was a specific 'leprolin'. He and others claimed good results with it. However, it was shown later that Rost's technique was faulty and that his culture was a contaminating organism.

#### Sera and autohemotherapy.

Various attempts have been made to produce an immune serum by injecting into horses and other animals material from leprous lesions or supposed cultures of lepra bacilli. It has been shown that any effect such sera may have has been due to the serum alone and not to any specific quality in it. Some have inoculated lepers with their own blood.

Protein Shock.

Protein shock in the treatment of leprosy was first recommended by Muir and others (81) who injected Kedrowsky's bacillus intravenously with favourable results. Sharp (82) has made an extensive trial with 0.5 c.c. of milkmaid brand tinned milk diluted with nine parts of water and given intravenously. He reports rapid and severe shock followed by decided improvement. He concludes that "desperate remedies are sanctioned by desperate cases" and recommends it for advanced cases. Others have obtained good results with intravenous injections of bacterial vaccines, especially T.A.B. and gonococcal vaccine, sera, milk, and other protein containing substances. It would thus appear that protein shock has a place in the treatment of leprosy, but it must be used with discrimination and care. In my own experience it has been of most use in treating persistent eye conditions, often succeeding where other remedies have failed. Probably the results observed from the various vaccines, sera, and other preparations mentioned above are due to protein shock, and not to any specific action.



5. Aniline dyes and acriflavine.

In 1933 Ryrie (83) first reported on the use of certain aniline and xanthene dyes given intravenously, with encouraging results. He investigated the action of the following dye stuffs - trypan blue, brilliant green, fluorescein and eosin, and also crystal violet, picric acid, malachite green, rhodamine, congo red, iodine green, methylene blue, acriflavine, methyl orange, toluidine blue, acid fuchsin, indigo carmine, crysordine, Giemsa's stain, and auramine. With the first four dyes he found "a definite diminution of the external manifestations of leprosy, accompanied by other signs of clinical improvement". With the other dyes he obtained no improvement. Ryrie later found that the majority of the improved cases relapsed within six months of the cessation of dye treatment, but that the relapse rate with fluorescein appeared to be less than with the others. He therefore investigated fluorescein further and came to the conclusion (84-) that it was of value in early and moderate cases if alternated with courses of chaulmoogra treatment. He found that it had little toxic effect even in large doses, and considered that its essential ingredient was phthallic acid.

Stimulated by Rylie's reports many others have tried the various dyes, some claiming good results with one and some with another. Ryles (85) became enthusiastic over his results with brilliant green and went so far as to state that "brilliant green may furnish almost the whole pharmacopeia of a leprosy clinic" - a rather extravagant claim. Sorley (86) found brilliant green to cause clinical improvement but no bacteriological or erythrocyte sedimentation improvement, and it will be seen later that my own findings are in agreement with Sorley's. Leggate (87) in Rhodesia reports good results with Bonney's Blue given intravenously and locally. Montel (88) advocates methylene blue intravenously and claims with it results far superior to all other methods, but his results have not been repeated by others, including myself. Trypan blue is of little value in the systemic disease, but Muir (89) reports good results in eye lesions by injecting it subconjunctivally. None of the other dyes tried by various workers have produced results of any value. Acriflavine will be discussed later.

My own experience of several of the dyes is as follows:

Fluorescein.

Fluorescein is a xanthene dye formed from the condensation of phthallic anhydride and resorcinol. It is combined with mercury in the familiar mercurochrome soluble 220. Ordinary fluorescein is soluble only in an alkaline solution, but fluorescein-soluble dissolves by itself. Freshly made solutions are non-toxic except in large doses, but a photodynamic action may lead to complications. Both the patient and the dye should be kept from direct sun light, especially in the tropics. A 2% solution is made by adding the appropriate amount of fluorescein to a 2% solution of sodium bicarbonate in distilled water. This solution must be freshly made just before use as it deteriorates with standing in light.

The twelve patients selected were all cutaneous cases, and all except two had been previously treated with esters of hydnocarpus oil. This was stopped during the fluorescein treatment. The 2% fluorescein solution was given intravenously once a week, commencing with 5 c.c. and increasing by 5 c.c. until an average dose of 30 c.c. was reached. Most of the patients tolerated as much as 50 c.c. at a time, but this was not continued. Immediately after the injection each patient was

was/made to lie down in his house for at least one hour, during which time no food was allowed. No patient complained of any discomfort during or after the injection nor a rise of temperature. The fluorescein turned the urine a bright yellow during the following 24 hours, showing that the dye is rapidly excreted. No staining of the tissues was noticed. The treatment was continued for six months, during which time the patients were carefully observed. Once a month they were examined clinically and bacteriologically and the erythrocyte sedimentation rate determined as a guide to the general condition. The leprolin test was done on each patient. The results are recorded in the accompanying table.

In seven <sup>cases</sup> ~~others~~ there was some clinical improvement, in three of whom this was preceded by a mild reaction. In only one, case 8, was there any bacteriological improvement and this was accompanied by a low sedimentation index. Unfortunately this man received less treatment than any of the others as he absconded at the end of four months, so his final result is unknown. Of the remaining eleven patients, only four could be said to have benefited slightly from the treatment, after taking everything into consideration.

consideration./ Strangely enough those four had negative or only weakly positive leprolin reactions.

I also used 2% fluorescein solution in a considerable number of cases of lepra reaction, with more satisfactory results. 10 - 20 c.c. were given intravenously and repeated on alternate days four or five times. It was as effective as mercurochrome, but not so certain as potassium antimony tartrate. It did not cause the rigor that usually follows the last named drug.

It would appear then that fluorescein is of little value in the routine treatment of leprosy, and the same opinion is expressed by Fernandez and Schujman (91) and in a personal communication from Dow of Hyderabad. The drug is of value, however, in controlling lepra reaction and Ryrie (92) now recommends it for this.

#### Bonney's Blue.

The chief constituent of Bonney's Blue is brilliant green. This dye is one of the tri-phenyl methane group and is one of the most powerful disinfectants known. In the presence of organic matter such as serum, however, its action is reduced to 0.3 per cent of its former value

(93). Bonney's blue is made up as follows:

Brilliant green	.....	0.5 gm.
Crystal violet	.....	0.5 gm.
Absolute alcohol	.....	25 c.c.
Aqua dist. ad	...	2,500 c.c.

The crystal violet is first dissolved in the alcohol, added to an aqueous solution of the brilliant green, and the whole made up to 2,500 c.c. The solution keeps indefinitely if stored in the dark.

The eight patients selected were all moderately advanced cutaneous cases. Four of them had been treated with fluorescein some time previously followed by esters. One had had esters for five years and three had had no previous treatment. The dye was given intravenously and the same precautions taken as with fluorescein. Beginning with 1 c.c. the dose was increased by 1 c.c. until 10 c.c. was reached. If more than that was given the patients complained of discomfort, headache, and fever, so the dose was continued at 6 c.c. twice a week. Treatment was given for six months, and the patients regularly examined as before. The results are recorded in the accompanying table. Four cases showed some clinical improvement but in only one of these,

these/ case 7, was there any bacteriological improvement. This was the only case that seemed to be really benefited. The good results obtained by Ryles and Leggate were not seen, and the conclusion that brilliant green is of little value as a means of general treatment has also been recorded by Rao (94) in Bihar, and others.

#### Methylene Blue.

Eleven cases of advanced cutaneous leprosy were given a 1% solution of methylene blue intravenously for four months in the hope of repeating the success claimed by Montel and others. Four had received no previous treatment. The solution was sterilised in an autoclave, and the same precautions with administration were taken as in the other experiments. The most striking feature with this dye was its selective staining of the leprosy lesions in the skin. This was particularly noticeable in the Anglo-Indian patients, and gave them a very peculiar appearance. Beginning with 1 c.c. the dose was increased by 1 c.c. to a maximum of 10 -12 c.c. when they all complained of dizziness, burning pain in the eyes, and fever. The dose was

was/reduced to 5 c.c. twice a week. The dye was given for four months and the results are recorded in the accompanying table. One case became definitely worse, and five showed some clinical improvement. None showed any bacteriological improvement. Three cases developed eye trouble which necessitated stopping the treatment. The final result was no improvement in any, and one patient worse. Other workers report the same disappointing results.

Methylene blue may also be given orally and intramuscularly, but with no better effect.

#### Acriflavine.

Acriflavine is a powerful antiseptic which differs from other similar dyes in that its germicidal activity is increased in the presence of serum. It has the disadvantage of acting very slowly and requiring a strong concentration to produce a rapid disinfectant action (93). It is of fairly low toxicity and is rapidly excreted in the urine, Both acriflavine and the supposedly less toxic trypflavine were used in this experiment. A 1% solution was made with distilled water, and given intravenously.



The three patients chosen were cutaneous cases and had had no previous treatment. The same precautions as before were observed but the treatment had to be stopped in one case after five months on account of vomiting after the injection. Beginning with 1 c.c. the dose was increased by 1 c.c. to a maximum of 10 c.c. once a week, and this continued for six months in two cases. The results are given in the accompanying table. Cases 1 and 3 showed clinical improvement but no bacteriological change, so were not really benefited. Case 2 became worse, even though he also received intradermal injections of the dye. A trial in only three patients is not a fair test of the value of a remedy, but Schwetz (95) reports the same failure in nine cases.

#### Discussion of dye treatment.

The *M. leprae* has a predilection for the cells of the reticulo-endothelial system and in them it dwells in safety, apparently protected from any malign influence that would seek to destroy it. The granules of the aniline and xanthene dyes are also retained by the reticulo-endothelial cells. It was thought that the dyes would exert

exert/their germicidal properties on the lepra bacilli in the cells and kill them. This was the basis for the use of the various dyes, and in theory should give good results. In actual practice this has not been so and the bacilli are apparently unaffected by any germicidal dye that may enter their protective cell. The lepra bacilli appear to be strongly resistant to the usual germicidal influences and it is doubtful whether any clinical substance can be introduced into the body in a sufficiently high concentration to have the slightest effect on them.

Although the results of dye therapy have proved disappointing in the long run, there is a place for a few of the dyes in the treatment of leprosy. They appear to be most helpful if given in short 6-8 week courses alternating with chaulmoogra treatment. Fluorescein is useful in controlling lepra reactions. Trypan blue, injected under the conjunctive is often useful in intractable cases of irido-cyclitis, but how or why it should be is difficult to say. Much benefit must not be expected from the dyes in routine treatment, and they should be reserved preferably for strong healthy cases in the early stages as an adjunct to chaulmoogra treatment.

6. Chaulmoogra Oil.

In India and other eastern countries chaulmoogra or hydnocarpus oil has been known and used as a remedy for leprosy for thousands of years. Ancient Sanskrit writings recommend that it be compounded with other substances and taken by mouth or applied externally. The oil was first introduced to western medicine by Mouart (96) of the Bengal Medical Service, in 1854, as a possible remedy for leprosy, since when it has proved the most useful of all the many remedies tried. The oil was first obtained from the Burma tree, *Taraktogenos kurzii*. Later it was discovered that the oils of *Hydnocarpus wightiana*, grown in South India, and *Hydnocarpus anthelmintica* of Siam and South China had a very similar composition, and these trees now form the chief source of supply. Among related oils is that of *Carpotroche Brasiliensis* of South America. Formerly chaulmoogra oil was used only by mouth or by <sup>un</sup>injection, but during the last twenty or thirty years better results have been obtained by injection. The first to inject the oil seems to have been Tourtoulis Bey in Egypt in 1894. When injections were first used the oil was found to be exceedingly painful, irritating, and slow of absorption. Largely on this account

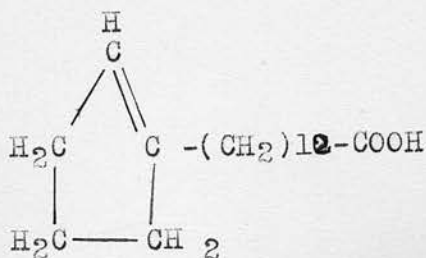
account/various emulsions of other preparations were contrived to overcome these difficulties. The most successful preparation was evolved in 1907 by Engel Bey who got the firm of Bayer & Co. to make for him the ethyl esters of the total fatty acids of chaulmoogra oil. This is still on the market as 'antileprol', and the ethyl esters are extensively used to-day. Of the many other preparations made the only one worthy of special attention was the Mercado-Heiser mixture, consisting of chaulmoogra oil 60 c.c., camphorated olive oil 60 c.c., and resorcin 4 gm. Heiser (97) and others gave this intramuscularly and claimed good results, but it caused so much pain and irritation of the tissues that it was found very difficult to get patients to continue with it, especially in India. On this account the mixture had to be abandoned. Later it was found that if the oil is prepared from fresh ripe seeds the irritating factors are much reduced, so that now the pure oil can be satisfactorily given intramuscularly, subcutaneously, and intradermally. For many years Rogers attempted to obtain the active portions of the oils in a soluble form suitable for

for/injection, and in 1916 (98) he published an account of treatment with sodium gynocardate, having previously found that gynocardic acid was more effective orally than the whole oil. He claimed that sodium gynocardate was effective subcutaneously and intramuscularly although rather painful, but that the effectiveness was increased and the irritation decreased by administering it intravenously. The three preparations in general use now are the pure oil, the ethyl esters of the whole oil, and sodium hydnocarpate. Each of these will be considered further at a later stage.

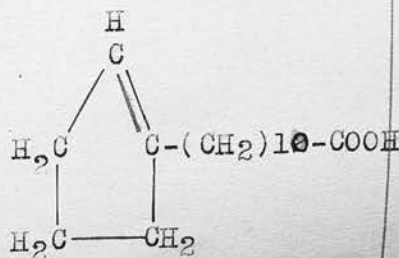
Chemistry of Chaulmoogra Oil.

The crude oil is an evil-smelling irritant substance, and its use in the treatment of leprosy has been made possible by the isolation of its active principles. These are a group of unsaturated fatty acids, the chief of which are chaulmoogric acid and hydnocarpic acid. Power (99) isolated these acids in 1904 and ascribed to them the following formulae:-

Chaulmoogric acid.



Hydnocarpic acid.



These acids are unique amongst fatty acids in possessing a five-chain carbon ring. It is the presence of unsaturation and the five-carbon ring that appear to give the acids their therapeutic efficacy in leprosy. Chopra (100) states that a high optical activity is also necessary. *Hydnocarpus wightiana* should have an index for polarised light of 57.5 to be most effective.

Action of chaulmoogra preparations.

Estimation of the effect of drugs upon the leprosy organism is extremely difficult to attain with any degree of certainty. That the chaulmoogra group have some therapeutic action is generally recognised, but whether this is due to any special bactericidal power, or to a non-specific action through the unsaturated fatty acids, or to their influence on metabolism, or to a local or general tissue reaction, is not certain. It has been suggested that the injection of fatty acids stimulates the formation of lipase, and that the lipase acts on the lipid substance surrounding the lepra bacillus, to make it more vulnerable. In a careful experiment with rats Anderson, Emerson, and Leake (101) have shown that chaulmoogric acid derivatives cause no increase in blood lipase, nor

nor/were they able to find an increase in the lipolytic activity of the tissues. It is not possible to estimate the effect of chaulmoogra on lepra bacilli in vitro, although attempts have been made to do so with both human and rat organism. Muir (102) has suggested the hypothesis that the intradermal injection of chaulmoogra oil causes a break down of lepromatous tissue which liberates an antigen or antigens and encourages the formation of antibodies. In other words there is a process of autovaccination. It seems more likely that the improvement in local lesions after intradermal infiltration is due to a non-specific tissue irritation and not to any action on the bacilli themselves. This has been demonstrated histologically by Nolasco (103). After the administration of chaulmoogra many patients are improved in their general health and say they feel better, so that the drug probably has a general tonic effect on metabolism. On the other hand, some patients are definitely debilitated by the drug. The conclusion at present, then, is that the chaulmoogra derivatives ~~have a general~~ have a general tonic effect and a local irritant action, and it is in virtue of these that the preparations hold <sup>first</sup> place in the treatment of leprosy.

Toxicity of chaulmoogra preparations.

Chaulmoogra or hydnocarpus oil that has been obtained from stale seeds or has been stored exposed to air, heat, moisture, and light, has an extremely irritating action on the tissues. The acids themselves when exposed to day-light gradually deteriorate into sticky varnishes. Aqueous solutions of sodium hydnocarpate not only change colour and become cloudy on standing, but the specific rotation index and the pH both fall steadily. These deteriorations take place more rapidly in the tropics than in temperate zones, and are responsible for the pain and discomfort experienced by the patients. Ethyl esters are no more stable than the oil or free acids, but the pain caused by them may also be due to faulty preparation leaving small amounts of irritating volatile aldehydes or similar impurities. There is an irreducible minimum of irritation caused by even the freshest of pure oils or the most carefully prepared esters but this does not produce any serious discomfort in the patient. Anything more than that is artificial in origin and must be avoided. Much work has been done in attempting to discover the irritant constituent and the fatty acids have



have/been investigated. A careful analysis by Paget and his co-workers (104) at the Wellcome Research Laboratories have shown that the only constituent to exhibit marked irritant properties is a tarry acid fraction consisting essentially of a lactonic acid. This occurs as an oxidation product in old oils. For some time it was thought that the irritation caused by sodium hydncarpate was due to a high pH of the solution used, but Jackson (105) has shown that there is no relationship between the variations of pH and the amount of pain experienced. Read (106) has investigated the toxicity of sodium hydncarpate in rabbits and dogs. He found the drug had a marked cumulative action, and that in high concentrations and large doses given intravenously or subcutaneously, it produced albuminuria, haematuria, and emaciation. He therefore suggests that care should be taken in treating humans, and large doses of high concentrations to saturate the system should be avoided.

To ensure the absence of toxic effects from chaulmoogra oil and its derivatives certain requirements are essential. The oil must be unadulterated and newly prepared from fresh ripe seeds. It must be stored in dark

dark/glass bottles completely filled to exclude air, securely stoppered, and kept in a cool dark place. Esters must be carefully prepared and stored in the same way. Both oil and esters should be sterilised just before use by heating to 120°C for one hour. This can be done in an oil bath or in an autoclave. Injections must be given with all aseptic precautions and the dose adjusted according to the comfort and tolerance of the individual patient. If these precautions are observed there is little pain, and complete absorption takes place in three or four days.

#### Methods of administration.

##### I. Pure oil.

Pure hydrocarpus oil is usually used in preference to chaulmoogra oil, as it is more easily obtained and is cheaper. It may be given orally or by injection.

##### (1) Oral administration.

This is the old method of giving the oil and has the disadvantage of causing nausea and gastric irritation. Many modifications have been devised to overcome this, such as giving it in emulsions with cod liver oil, in salads, with

with/tannic acid, and in capsules, but none have proved satisfactory over long periods or for large doses. Cochrane tells me that he gives 15-30 minims a day in strong gelatine capsules and considers the prognosis best in those who can stand large doses by mouth. The fullest test on record of oral administration is that of Hopkins (107) who in fifteen years experience obtained cure or improvement in 45% of 82 incipient cases and improvement in 21% of 88 advanced cases.

(II) Injection.

The best results with pure oil are obtained with subcutaneous or intramuscular injection. The Mercado-Heiser mixture has been mentioned already, and various other mixtures have been recommended from time to time. The pure oil is now given alone or combined with 4% doubly distilled creosote. It is a fairly thick oil and difficult to inject through the ordinary needle. This can be made easier by heating the oil to about 30° C. before use. Injections are given once or twice a week. Beginning with 1 c.c. the dose is increased by 1 c.c. to a maximum of 8 - 10 c.c. according to the patient. This maximum dose is repeated ten

ten/ times. After a rest of two weeks the same course is gone through, and in this way the treatment is continued for as long as is necessary. Some workers dilute the oil with olive oil which is fatty acid free, using half and half, or three-quarters chaulmoogra with one quarter, olive oil. Pure oil can also be given intradermally if heated to 55° C.

2. Ethyl esters.

Ethyl esters of the total fatty acids of chaulmoogra oil were first used by Engel Bey in 1907. In 1920 McDonald (108) reported improved results with the esters of the whole oil. The esters of the whole oil are commonly used in India, and because of the prevalence of *Hydnocarpus Wightiana* they are prepared from *Hydnocarpus* oil. The methods of preparing esters and testing them are given in the appendix. Esters may be given subcutaneously, intramuscularly, and intradermally with greater ease and no more irritation than pure oil. Attempts have been made to inject it intravenously by many workers, but no one has succeeded in finding a safe method which allowed an effective amount to be given. Recently the Japanese workers, Ota, Sato, and Masuzawa (109) have prepared an emulsion of a very fine suspension of

of/esters in a 40% concentration. Reports on the use of this have not yet been published. In India 4% doubly distilled creosote is added to the esters, but the Philippine workers prefer 0.5% iodised esters. Indian workers have found the iodised esters more irritating than creosoted esters, although this is not the case in the Philippines where it is claimed that the iodine reduces the irritant properties of the esters, as well as having some therapeutic efficacy itself (110). The esters are usually diluted with fatty acid free olive oil in the same manner as described with the pure oil. The method of administration and dosage is the same and courses of the different strengths of esters and olive oil are alternated. A popular mixture in India is esters, creosote 4%, camphor 1%, and olive oil, known as E.C.C.O. This has no better effect than ordinary esters, but the camphor is claimed to act as a stimulant and is a favourite ayurvedic drug.

### 3. Sodium hydnicarpate and Alepol.

A distinct advance was made in anti-leprosy treatment when Rogers introduced the intravenous injection of sodium hydnicarpate. This was

was/a water-soluble preparation given in a 3% solution intramuscularly and a 2% solution intravenously. He later showed that the soaps of hydnocarpic acid were the most effective. These soaps, however, had the disadvantage of being irritating and causing a thrombosis of the vein. Rogers finally overcame these drawbacks when T.A. Henry made for him the sodium salts or soaps of selected lower melting point fatty acids of *Hydnocarpus Wightiana*. This is now used extensively under the name of alepol. A 3% solution of alepol is practically painless, is rapidly absorbed, and is quite efficient either by subcutaneous or intramuscular injection. A 2% solution intravenously causes no irritation and the venous thrombosis can be avoided by the simple expedient devised by Muir (III). This consists of drawing into the syringe containing the dose about an equal quantity of blood from the vein, mixing by gently rotating the syringe, and slowly injecting the mixed blood and alepol solution. Alepol is prepared in a powder form with 0.5% carbolic acid, ready for making into solution. Distilled water or saline can be used, but Dikshit (112) recommends Locke's solution as it diminishes the haemolytic action of the drug. The dose begins

begins with 1 c.c. and rises by 1 c.c. to a maximum of 5 c.c., and may be given once or twice weekly. Many workers have reported good results with alepol, some preferring it to the oil or esters. Its chief advantages are non-irritation and cheapness. Alepol pills by mouth have been recommended as they do not cause gastric irritation.

#### Choice of preparation for use.

Although Rogers and others claim better results with the use of alepol than with esters or pure oil, this is not the general concensus of opinion among leprosy workers of wide experience. It appears rather that no one preparation is therapeutically superior to the others, although one patient may respond best to alepol and another to esters and a third to oil. The choice of preparation to be used is guided by other factors, chiefly mechanical and economic. The pure oil can be obtained in India very cheaply, but its viscosity makes it rather difficult to inject and it seems to be more irritating than esters. The esters are more satisfactory but cost more and unless carefully prepared may give trouble. Alepol is manufactured by Burroughs Wellcome & Co. very cheaply, is of little bulk, and in powder form keeps

keeps/indefinitely. It is non-irritating to the patient, but, as has been pointed out, requires special care and technique in injection to avoid thrombosis of the vein.

In India pure oil and creosoted esters are commonly used. The Calcutta school at present favours the oil. Most leprosy institutions, including the Lady Willingdon Leper Settlement, prefer the esters as it is more easily and rapidly given to large numbers of patients, and gives very little trouble from irritation or non-absorption. In the Philippines the iodised esters are chiefly used and in Japan the oil and esters. In many parts of the British Empire alepol is preferred on account of its small bulk and ease of transport.

#### Other oils tried.

In accordance with the theory that the unsaturated fatty acids of chaulmoogra oil form the chief therapeutic factor, various other similar oils with a high iodine value have been tried. Chief among these have been cod liver oil, linseed oil, and soya bean oil. Rogers treated a number of cases with sodium morrhuate. None of these has proved to be of as much value as chaulmoogra oil. Gurgun oil is an old Indian remedy of



of/little use. Neff (113) reported good results in relieving the nerve pain of lepra reaction from the injection of esters of dilo oil obtained from *Calophyllum bigator*.

7. Local treatment and physical therapy.

Caustics and counter-irritants.

The application of CO<sub>2</sub> snow to leprous lesions is often beneficial. It is an important part of Paldrock's specific remedy mentioned elsewhere. He found that it also caused the disappearance of nodules other than those treated and concluded that it removes the envelopes of the bacilli and produces active immunisation (75). Other workers have used ethyl chloride for freezing nodules.

In India trichloroacetic acid is used extensively for local application and is popular among patients in spite of the temporary burning sensation caused. It is made into solutions of the following strengths, with water - 1 in 1, 1 in 3, and 1 in 5. The solution is applied to the lesions once a week for several weeks, followed

followed/ by a period of rest. Marked improvement generally results. Incidentally, I have found trichloroacetic acid the most effective means of treating ring-worm.

Cauterisation with hot irons or with vegetable juices is a common form of treatment by native physicians in India. This is like cutting off the heads of the daisies and leaving the roots.

#### Ultra-violet radiation.

Ultra-violet rays have no demonstrable effect on leprosy itself, but they are a useful adjunct in maintaining the health and resistance of the patient. They have been of most use when applied to trophic ulcers and seem to encourage healing.

#### Diathermy.

Diathermy must be used with care in treating acutely reacting nerve lesions. Sometimes the symptoms are relieved, and at other times the condition is made worse. The chief value of diathermy is in treating sub-acute and chronic nerve affections, and often brings much improvement.

Other suggested aids to treatment have been continued pressure on nodules, hot mineral baths, X-rays and radium, fulguration, etc.

etc./ Cauterisation with a high frequency current has been found useful in treating nasal lesions.

### Surgery.

Several workers have tried to eradicate the disease when lesions were small and simple by excising them, but apparent primary lesions are usually only the first manifestations of a generalised infection. Trimming of enlarged, thickened, and pendulous ear lobes gives great satisfaction to the patient, as does the removal of enlarged breasts in the male. The chief place of surgery, however, is in treating trophic ulcers by removing necrosed and infected bone and indolent tissue.

### Routine Treatment at Lady Willingdon Leper Settlement.

The therapeutic routine carried out in the Lady Willingdon Leper Settlement embodies the most satisfactory of modern methods of treating leprosy. It includes general and specific measures, of which the former is by far the more important. It must be emphasised that each patient should be studied and treated as an individual, for in leprosy it is essentially true that one treats the patient and not the disease. It has been pointed out that leprosy is a self-limiting

limiting/disease. The aim in treatment is to bring about this limitation and arrest as rapidly as possible and before the development of permanent disfigurements and crippling deformities. How far modern treatment is successful in doing this will be discussed later, but in the absence of any satisfactory specific remedy one has to rely on those measures which do most to assist the natural arrest of the disease. This account of treatment will describe first the general measures, then the more specific remedies, subsidiary aids, and the treatment of complications and special lesions.

#### General Treatment of Leprosy.

As in tuberculosis, the main emphasis in the treatment of leprosy should be laid on improving the general health of the patient. It is of paramount importance to raise and maintain the general resistance. It has yet to be proved that even massive infections can produce leprosy in a healthy individual living under good hygienic conditions. For practical purposes it may be accepted as an axiom that where leprosy has developed there is at the present time, or has been in the past, a lowering of resistance due to some cause or other. The chief factors that lower the

the/resistance have been discussed already, and include age, debilitating diseases, improper diet, unhygienic surroundings and habits, lack of exercise, sexual excess, and physiological conditions such as puberty and pregnancy. These are the predisposing causes of leprosy, and the first essential in treatment is to find out and remove the pre-disposing causes which are lowering the resistance. Childhood, puberty, and pregnancy can only be remedied by time, but every effort should be made to help the patient over these critical periods. It may sometimes be advisable to terminate an early pregnancy. Lactation must be stopped in the interest of both mother and child.

Preparatory to treatment the patient should have a thorough physical examination, including that of the urine, faeces, and blood.

#### I. Debilitating Diseases.

Only the more common diseases met with among our South Indian patients will be mentioned.

Scabies is universal and the easiest and most satisfactory method of eliminating it is as follows. Equal parts of sulphur ointment and crude hydnocarpus oil are rubbed well all over the patient. He is then made to sit in the sun

sun/for two hours before cleaning himself with soap and water. This clears up even the worst cases in a few days. Danish ointment is less irritating to the skin of children and is equally effective.

Ring-worm is treated by painting daily with trichloroacetic acid, in strengths of 1 in 1, or 1 in 3 solution.

Intestinal parasites are common, especially hook-worm. Oil of chenopodium gives satisfactory results and may be repeated at weekly intervals if necessary. Iron should be given for any consequent anaemia.

Filarial infections are common in South India, especially elephantiasis, and are extremely difficult to treat. Often it is impossible to eliminate the infection.

Malaria, and amoebic and bacillary dysenteries require the appropriate treatment.

### Tuberculosis

When tuberculosis and leprosy occur together the former must be treated first and special anti-leprosy measures postponed until it is under control. Fortunately the treatment of tuberculosis is largely that of leprosy. It is important to distinguish between pulmonary

pulmonary/tuberculosis and a possible pulmonary leprosy.

Syphilis in Leprosy.

Every patient should have the Wassermann or Kahn reaction tested. The significance of a positive result in a leper is still a matter of dispute among leprologists, and much work has been done without as yet definitely clearing the issue as to whether leprosy itself affects the Wassermann Reaction or not. The subject was first investigated by Cooke (114) and later by Hasseltine (115), who both concluded that the sera of lepers may give a positive Wassermann Reaction in the absence of syphilis. Subsequent workers in the Philippines have come to the same opinion, notably Pineda and Roxas-Pineda (116), and also Badger of Hawaii (117), and more recently Soule of Michigan (118) who applied the Kolmer- Wassermann and Kahn tests to the sera of 669 Philippine lepers. Certainly there is some clinical evidence to support the suggestion of these workers that leprosy affects the Wassermann and Kahn tests, as these tests give a far higher proportion of positive results among lepers than the incidence of syphilis among the general population would lead one to expect. It has also been suggested that hydnocarpus treatment tends to

to/make the Wassermann positive. Rao (119) has produced evidence that the serum albumin is reduced in leprosy and the serum globulin increased, and still further increased by hydnocarpus treatment. It is known that in syphilis the serum albumin is decreased and the serum globulin increased. This also occurs in kala-azar, typhoid, and malaria, in which diseases evidence has been produced that the Wassermann Reaction may be effected. Lloyd (120) has therefore suggested that the same result may occur in leprosy.

On the other hand, Kolmer and Denny (121), using Kolmer's improved technique, reported negative results in cases known to be uncomplicated by syphilis, as also did Arguelles in Manilla (122). Lloyd, Muir, and Mitra (123) investigated the Kolmer-Wassermann Reaction in 1027 cases of leprosy and noted their response to anti-syphilitic treatment. They concluded that all positive results were due to co-existing syphilis, and that the discrepancies in the results of other workers were due to less satisfactory Wassermann techniques.

In the table in the appendix are given the results of 1045 Wassermann Reactions and 332 Kahn tests done on patients in the Lady



Lady/Willington Leper Settlement during the years 1930 to 1935. The average incidence of positive Wassermanns among all cases is 45%. This includes all results recorded as weakly positive. 25% of neural cases are positive, while the cutaneous cases range from 45% in the early types to 70% in the advanced nodular types. The results in a smaller series of Kahn tests show a similar rise with the more advanced cases of leprosy, although all the results are lower than those from the Wassermann Reaction. As both these tests are thought to be dependent on the same serum changes I am unable to reach any definite conclusion as to the reason for the discrepancy between the results. I am of the opinion, however, that the Wassermann is the more reliable test in lepers, as I found the Kahn test to vary in repeated examinations of the same individuals.

It is to be considered whether this high percentage of positive Wassermann Reactions found in all stages of leprosy can be accounted for by the presence of syphilis. The average incidence of syphilis in South India, both congenital and acquired, is high and has been estimated at about 20%. There is abundant clinical

clinical/evidence of the disastrous effect of associated syphilis on the development of leprosy. In view of these two facts one would expect a high rate of syphilis among lepers, as the presence of syphilis undoubtedly predisposes to the development and progress of leprosy. In cases where syphilis co-exists the leprosy advances rapidly, and early neural cases soon pass on to the more severe cutaneous type. The result is that the Wassermann positive cases tend to accumulate in the advanced skin types, giving the high percentage of positive results found in those cases. If leprosy itself causes a positive Wassermann, especially in the severe skin types as has been suggested by various workers, then why do we find only 70% of positive results in C3 cases? One would expect to find a positive Wassermann in practically all such cases. A further point is that in nearly all cases in which it is possible to give sufficient anti-syphilitic treatment the Wassermann can be rendered negative. Anti-syphilitic treatment in Wassermann positive cases causes considerable clinical improvement, more than is obtained from anti-leprosy treatment alone in such cases. It may cause marked clinical improvement even before special anti-leprosy measures have been given. It has been

been/suggested that the rendering of the Wassermann negative is due to the improvement in the leprosy. It is much more likely that the Wassermann becomes negative on account of the anti-syphilitic treatment, and that the improvement in the leprosy is due to the rise of resistance that follows that.

It seems to me that the available evidence proves that in the vast majority of instances a positive Wassermann Reaction in leprosy is due to co-existing syphilis. It is sometimes observed that the Wassermann becomes positive during or after a lepra reaction. This can be explained by regarding the lepra reaction as a provocative measure which has aroused a latent syphilitic infection. It is therefore, a wise and correct procedure to attempt to treat the syphilis in Wassermann positive lepers as an indispensable preliminary to anti-leprotic treatment. It is not always possible, however, to carry such treatment very far as it often induces a lepra reaction. The effect of treatment in 101 cases is recorded in the appendix. The advanced cutaneous respond least satisfactorily as in them the syphilis has presumably been present for some time and gained a firm footing.

The usual treatment in the Lady

Lady/Willington Leper Settlement is with novarse-nobillon (May and Baker) given as follows:

1st week. . . . .	0 . 15 gm. N.A.B.	
2nd week . . . . .	0.30 gm.	"
3rd. week . . . . .	0.45 gm.	"
4th. week . . . . .	0.60 gm.	"
5th. week . . . . .	0.75 gm.	"
6th. week . . . . .	0.90 gm.	"

Following this course the patient is given one month's rest before testing the Wassermann Reaction again. If it is still positive the course is repeated in the same way, and so on until the Wassermann Reaction becomes negative. A few cases never become negative even after several courses. These are given a course of N.A.B. once in six months during their anti-leprotic treatment. Such cases rarely do well. If the N.A.B. induces a lepra reaction it is stopped and when the reaction subsides the patient is given avenyl in pure hydnocarpus oil.

Avenyl, or 2-myristoxymercuri-3-hydroxybenzaldehyde, and known as Hg 33, is prepared by Burroughs Wellcome & Co. It is a powder easily soluble to the extent of 0.25% in

in/hydnocarpus oil. The solution is given subcutaneously or intramuscularly in the same way as is the pure oil. A course is completed when 100 c.c., or 0.25 gm. of avenyl, have been given. I have not found it to affect the Wassermann Reaction as well as does N.A.B.

Inunctions of mercury ointment are laborious and of little value. Potassium iodide must not be given for reasons already stated. It is often advantageous to administer bismuth in conjunction with the N.A.B.

#### Constipation.

Constipation is a common complaint among lepers and is often very persistent, in spite of the Indian's great concern over the action of his bowels. A constipated leper will not respond to treatment. The frequent use of drastic purges is popular among Indians but should be avoided. A suitable adjustment of diet, exercise, and if necessary a regular laxative such as agarol, are usually sufficient. I have used petrolagar made by ourselves from a modification of the prescription kindly sent me by the manufacturers of that preparation.

2. Diet.

The very great importance of nutrition in the causation and development of leprosy has been already discussed. I am in complete agreement with Sir Robert Mc.Carrison who, in a personal communication on the subject of diet in leprosy, says, 'The more I work on this subject of Nutrition, and its relation to disease in India, the more evidence do I find that 'infection' is the accident, while faulty nutrition is the ever present foundation upon which it erects the structure of disease'. The correction of dietetic faults and deficiencies has the greatest influence in controlling leprosy and it is the most important of all therapeutic measures. Unfortunately the Indian is very conservative about his foodstuffs and looks with suspicion on any attempt to alter the diet on which he has been brought up. The introduction of a more balanced diet into the Lady Willingdon Leper Settlement in 1927 led to a serious riot which was not quelled until over 100 of the patients had been dismissed.

The diet should be a good all round choice with an adequate supply of vitamins.

vitamins./ Fresh fruit and vegetables and fresh milk are essential. Whole cereal grain, and especially wheat and ragi, are preferable to rice, but it is impossible to persuade the South Indian to give up his rice. The rice should be unpolished, that is with the outer coat of the grain still present. No particular article of food need be avoided, except alcohol which must be forbidden. In addition cod liver oil and dried yeast may be given. I usually recommend Ostomalt (Glaxo Laboratories) or Ferradol (Park Davies & Co.).

The general diet in use in the Lady Willington Leper Settlement is given in the appendix, with its analysis. This is not the ideal in many respects. but it has given satisfactory results over a number of years. The carbohydrate content is excessive. All vegetables are grown in the Settlement's gardens and in season more than the minimum 8 oz. is issued. Milk for general consumption is given as 'curd' or sour milk, for which the South Indian has a great liking. Certain cases and especially children are given extra milk. Meat is issued only twice a week as it is an expensive item.

The effect of this diet on the patients is often amazing. The general condition improves and the leprotic manifestations subside. All patients are weighed regularly and a steady increase in weight occurs, which continues in growing children.

### 3. Exercise,

Regular daily exercise is essential. The lazy leper never improves. Exercise should be outside in the fresh air and not confined to physical jerks in the house. Manual labour is the best of all forms of exercise, but caste prejudices and educational pride make all Indians of the higher classes regard manual labour as undignified. Games, walking, and sports should be encouraged.

In the Lady Willingdon Leper Settlement a large number of patients are employed in the gardens and in other tasks connected with the administration of the institution. All those who do not get adequate physical exercise in that way do half-an-hour of Swedish drill, or Yogi exercises, every morning. The younger men and boys have facilities for sports and games such as tennis, hockey, football, etc. as well as various Indian games. Walking and hill climbing around



around/the Settlement are encouraged. The boys are trained in Scouting activities, which benefit them in many ways. The patients have slowly come to realise for themselves the improvement that follows adequate and regular exercise. No one is allowed to persistently overtire himself or herself as this is harmful.

#### 4. Cleanliness.

The skin must be well cared for and kept clean and as active as the nature of the disease permits. An excellent Indian custom is the weekly oil bath. For this purpose crude hydnocarpus oil is issued, not because of any special therapeutic effect but because it is as cheap as the cocoanut or gingelly oil usually used. Mild antiseptic soaps are to be recommended for the daily bath of those who can afford them. Along with bodily cleanliness must go hygienic habits and surroundings. Overcrowding in the house is detrimental to health and favours the spread of infection. The average Indian house is more than overcrowded, not only with humans but also with cows, goats, hens, etc. A clean mind is a great asset, but alas it is all too rare a thing among the Indian people.

5. Sexual activity.

Sexual activity should be avoided and excess is definitely harmful. Many cases of leprosy develop and get rapidly worse after marriage, and in women this is accentuated by pregnancy. In the Settlement the sexes are strictly segregated. Married couples are not allowed to live together for their own sakes and also for the sake of any children that may be born to them. The care of the healthy children of leprosy parents is a very serious problem in a leprosy institution.

6. Occupational therapy.

The individual with a job to do is happier and healthier in mind and body. Occupational therapy is of great importance in leprosy as it affords exercise and helps the patient to persist in the long and tedious period of treatment necessary. For those patients not in a leprosy institution this is a serious difficulty. An employer is naturally inclined to dismiss any individual who is even suspected of having leprosy. The neural case is not regarded as a source of infection and may safely continue his employment while undergoing treatment. In the Government services this is allowed and several of the large commercial and other firms are now doing the same. The cutaneous case must not continue

continue/to work along with healthy people or in public services, and leprosy institutions should be reserved for these cases only.

The general treatment of leprosy consists of the adoption of every measure that will help to raise the patient's general health and well-being to the highest possible level and to maintain that level. This is the essential preliminary to more specific forms of treatment, and indeed during the remainder of the patient's life. A good standard of health and living is the best prophylaxis against leprosy, and it is the neglect of this that is responsible for most of the relapses that occur in arrested cases.

#### Specific Treatment of Leprosy.

##### Hydnocarpus Oil Preparations.

The routine treatment during the first two years of the Lady Willingdon Leper Settlement was with pure hydnocarpus wightiana oil for cutaneous cases and with the ethyl esters of that oil for neural cases, as it was then thought that the esters had a greater tendency to induce lepra reaction in skin cases. This was found not to be the case, and from 1927 all patients were treated with esters alternated with courses of alepol. The alepol did not seem to have any superior effect

effect/to the esters and the difficulty of administering it was a disadvantage when treating large numbers of patients, so it was eventually abandoned as part of the routine treatment. Since 1930 the ethyl esters have been given to almost all patients with ease and satisfactory results. At first these esters were prepared by ourselves, but since 1933 they have been obtained from the Government Medical Stores, Madras, at a saving of cost and labour to ourselves. This depot now supplies nearly all the esters used in leprosy centres in India at a present cost equivalent to 2/6 a pound.

My own practice has been to prescribe the creosoted esters almost exclusively. I have reserved the pure oil for those few individuals who are unable to tolerate the esters, and especially Angle-Indian patients. Alepol I have rarely used, and prescribed it only for those private patients whose physicians could be trusted to administer it correctly. I have not used the oral method of administration.

Three strengths of esters are used according to the following formulae.

E preparation.

Ethyl esters of hydnocarpus oil...48 c.c.  
Olive oil (fatty acid free) .....48 c.c.  
Creosote (doubly distilled)..... 4 c.c.

E1 preparation.

Ethyl esters of hydnocarpus oil.....73 c.c.

Olive oil (fatty acid free)..... 23 c.c.

Creosote (doubly distilled)..... 4 c.c.

E2 preparation.

Ethyl esters of hydnocarpus oil.....96 c.c.

Olive oil (fatty acid free)..... nil.

Creosote (doubly distilled)..... 4 c.c.

The esters supplied by the Madras Medical Stores have the 4% creosote already added and are sterilised. We re-sterilise the above mixtures just before use by heating in an autoclave at 120 C. for one hour.

Method of administration.

As already described, the esters may be given subcutaneously, intramuscularly, or intradermally. As our injections are given by trained patients the subcutaneous route is usually adopted, and certain injectors are also taught the intradermal method. The injections are given with all aseptic precautions.

Subcutaneous injections.

The sites chosen are the outer surfaces of the thighs and arms and not more than 4 c.c. are allowed to be given at any one site. I have found an ordinary 5 cc. record syringe the most satisfac-

satisfac-/tory in the hands of the unskilled injectors. Needles of medium bore are used, about size 12. If finer than that the oil is difficult to force through and if any larger they are unnecessarily painful. After cleaning the skin with spirit the needle is inserted and pushed in up to its hilt. The oil is slowly injected while withdrawing the needle. When the point only is left under the skin the needle is again pushed in to its hilt in another direction and the oil injected in the same way. This is repeated until the syringe is empty and the mixture is thus distributed over a wide circular area. This method is found to be the most comfortable for the patient and makes for more rapid absorption. The patients like to massage the area for a<sup>few</sup> minutes after injection. An important precaution is to withdraw the plunger each time before injecting to ensure that the point of the needle has not entered a vein, as an oily embolus is an unpleasant and even dangerous complication.

#### Intradermal injection.

Leprous lesions subside more rapidly if infiltrated with the esters, but the method is painful and I have not found it popular among our patients. It is however, the most satisfactory method of administration if the patient can be

be/persuaded to persist with it. A special needle is used, not more than a quarter of an inch long and with a short bevelled point. As much as five c.c. can be given in this way to a strong adult, but most patients will not bear more than 2 c.c. I have found the E1 mixture the preparation of choice. The E2 is apt to be too irritating and cause ulceration. The area or lesion to be infiltrated is selected and cleaned with spirit. The needle is inserted at an angle and pushed in up to its hilt. Its shortness will prevent it penetrating further than the deeper layer of the skin. Sufficient oil is injected to raise a weal the size of a threepenny coin. The needle is withdrawn and re-inserted about half-an-inch further on and another weal raised. In this way the lesion is infiltrated by a number of coalescing weals. A certain amount of oil escapes from such superficial injections but most of it remains. All the lesions on the body should be infiltrated in this way, doing a small area at each sitting. The same area should not be infiltrated more often than once a month or ulceration and necrosis may result. The immediate effect is a swelling, congestion, and inflammatory reaction in the area infiltrated. This gradually subsides in four or five days and the

the/lesion becomes flatter and darker in colour. Nodules either subside or break down and discharge their contents before healing.

Intradermal administration gives the best results in the erythematous cutaneous macules and the raised indurated neural macules. It is of no value in the simple hypopigmented macules in children, nor have I found it to have any effect in areas which show only anaesthetic changes.

Dosage and course of treatment.

The hydnocarpus preparations may be administered once or twice a week according to the tolerance of the patient. In children and weakly adults a weekly injection is sufficient but in a strong adult with only moderately advanced disease one should endeavour to push the treatment by giving it twice a week. Most patients in the Lady Willington Leper Settlement are given a weekly injection. The dosage of the esters given is as follows.

E & EI preparations.

1st week .....	1 c.c.
2nd week.....	2 c.c.
3rd week.....	3 c.c.
4th week.....	4 c.c.



5th week..... 5 c.c.  
6th week..... 6 c.c.  
7th week..... 7 c.c.  
8th week.....8 c.c.  
9th week..... 9 c.c.  
10th week..... 10 c.c.

The maximum dose is repeated 10 times before proceeding to the next course.

The patient begins treatment with a course of the E preparation given as above and then goes through the same course with the EI preparation. When this is completed he is given the E2 preparation as follows.

E2 preparation.

1st week ..... 1 c.c.  
2nd week..... 2 c.c.  
3rd week ..... 3 c.c.  
4th week ..... 4 c.c.  
5th week ..... 5 c.c.

The maximum dose of this preparation is not more than 5 c.c. and this is repeated 10 times.

On the completion of this course the EI preparation is again given as before followed by the E2 course again. Courses of EI and E2 are thus alternated throughout the rest of the period of treatment necessary.

The gradual increase of dosage and strength of the preparation is guided by the patient's tolerance to treatment. Should an injection cause fever or signs of a lepra reaction then the following dose must be reduced or not given until the individual returns to his normal state. Any further increase must be given with care. The maximum dose tolerated varies with the individual. Only strong males are able to stand 10 c.c. The average dose is 8 c.c. and with women I never exceed that. Children receive a lower maximum of all preparations according to their age. Should a patient miss an injection for one or two weeks he may continue from the dose at which he stopped. If he is absent for any longer than two weeks it is wiser to begin that particular course again. When treatment is resumed after a lepra reaction the weaker mixture should be given.

It is not necessary to adhere strictly to the above routine in all cases. Each patient should be treated according to his or her requirements, toleration, and response. Many advanced cases of long standing are better treated by small weekly doses, such as 5 c.c. of EI. There is no doubt that the saturation which follows several

several/years of treatment in such cases may do more harm than good. Most benefit from hydno-  
carpus treatment is obtained during the first two or three years, and after that it seems to have no effect if the case is not approaching the arrested stage. Prolonged administration of hydnocarpus preparations causes debility and cachexia, and in the patient whose disease remains stationary after 2 to 3 years of rigorous treatment it is safer to continue with a small weekly dose or only an occasional dose. Young children in the early neural stages should receive no hydnocarpus treatment as they do better with general care alone. There is no evidence that hydnocarpus is of any prophylactic value.

#### Complications of Hydnocarpus treatment.

##### I. General.

Sometimes a patient complains of dizziness, choking, and a tight feeling in the chest immediately after injection. A short rest lying down usually relieves this. Severe chest pain and coughing mean that some of the ester has entered a vein and become a pulmonary embolism. This is rarely serious and the pain passes off in a few hours. Most of the immediate complications

complications/and discomforts are unimportant, but may be taken advantage of by certain patients as an excuse for discontinuing treatment or receiving special favours.

There is often a slight rise of temperature in the evening of the injection day. This should not exceed 99' and should have passed off by the next morning. If it is more than this the patient should be watched for the onset of lepra reaction or other complication, and the subsequent dose of ester reduced.

Hydnocarpus treatment sometimes arouses a latent tuberculosis infection. Frequent complaints of chest pain, with cough, fever, and loss of weight should make one suspect such a possibility.

## 2. Local.

If the injections are given properly there is no local discomfort after the first few minutes. The persistence of an indurated swelling after a few days means that the esters have not been absorbed. Hot fomentations usually relieve this.

If too large a quantity is injected into one area, or the esters have been improperly prepared, an abscess may occur. This is a sterile abscess and care must be taken to prevent it becoming

becoming/ infected. Small ones often subside with hot fomentations. Larger ones should be aspirated rather than incised, and <sup>m</sup>percurochrome or weak tincture of iodine injected after the pus is withdrawn. A septic abscess following faulty injection technique should be incised and drained in the usual manner.

Contra-indications to Hydnocarpus Treatment.

These may be briefly stated as they are discussed elsewhere.

1. General debility.
2. Pulmonary tuberculosis.
3. Nephritis.
4. Leprous eye lesions.
5. Lepra reaction.

Treatment of Complications and Sequelae.

Lepra Reaction.

In treating lepra reaction the first essential is to look for and remove any possible cause, such as constipation, an attack of malaria, a dietetic indiscretion, some special therapeutic drug, etc. Most mild reactions subside spontaneously in two or three days. It has been my custom to give such cases a good purge with Epsom's salts, or Mist. senna co., or the following mixture:

$\mathcal{R}$

Sod. salicyl.	gr vi
Calcii lact.	gr x
Phenazone	gr iii
Sod. bicarb.	3 iss
Mag. sulph.	3 iss
Sp. ammon. aromat.	m x
Aq. chlorof.	ad $\frac{7}{3}$ i

Sig.  $\frac{2}{3}$ i t.i.d., p.c.

If the lepra reaction is more severe or the fever lasts for longer than 48 hours, the following is the procedure I have found most satisfactory.

- I. Put patient to bed and stop all other treatment.

2. Give a saline purge and keep on light diet. Give a diaphoretic mixture or the following mixture:

R  
Vim. antimonali            m x  
Calcii lact.                gr x  
Sod. bicarb.                gr xxx  
Mag. sulph.                ʒ ii  
Aq. chlorof.            ad ʒ i  
Sig. ʒi    t.i.d., p.c.

3. Give potassium antimony tartrate intravenously as follows ----- 0.02 gm. in 5 c.c. sterile water or saline on the first day, and two days later 0.04 gm. in the same way. Repeat 0.04 gm. dose on alternate days until the fever falls or until not more than four doses in all have been given. If the patient does not respond to one such course of potassium antimony tartrate a week should elapse before repeating it or trying one or other of the two following doses.

i.    Mercurochrome, 2% solution, is given intravenously in the following doses

1st day. .... 1 c.c.  
3rd day    ..... 2 c.c.  
5th day    ..... 3 c.c.

7th day ..... 4 c.c.

9th day ..... 5 c.c.

ii. Fluorescein, 2% solution, is given intravenously in doses of from 10 c.c. to 30 c.c. on alternate days.

When the fever and other signs of lepra reaction subside the patient should be encouraged in gradually increasing daily exercise until he returns to his normal condition. It is usually advisable to give a tonic for two or three weeks, such as Easton's Syrup or Mist. ferri et arsenii.

The treatment of protracted and persistent lepra reaction is extremely difficult. Such patients appear to be sensitised to the leprosy bacillus, or so overwhelmed by its dissemination that they do not respond to the usual procedures. It is best to keep them in bed on light diet with the bowels moving regularly. Occasional courses of potassium antimony tartrate, mercurochrome, or fluorescein should be tried and a general tonic added. Calcium is often of value, and the preparation I have used most is Colloidal Calcium and Ostelin Vitamin D. (Glaxo Laboratories). I have sometimes found these cases to respond to small doses of hydnocarpus, using the pure oil



oil/ rather than the esters. Cases of chronic lepra reaction require all the ingenuity, skill, and patience that the physician can command. One thing after another should be tried, in due moderation, but it is general nursing and care that count for most. Very often death is the ultimate result in spite of all efforts,

Leprotic Neuritis and Nerve Abscess.

Neuritis is associated with thickening of the nerve trunks. It may occur in any of the main nerves but is commonest in the ulna and peroneal nerves. It causes severe pain which is often difficult to relieve, and the nerve becomes swollen and tender. The following measures should be tried.

1. Put the affected limb at rest.
2. Apply dressings such as ichthyol, methyl salicylate, lead and opium, antiphlogistine, etc.
3. Analgesics such as aspirin, phenacetin, Dover's powder, combral, novalgin, etc. may be necessary.
4. Adrenalin, 1 in 1000 solution, subcutaneously in mv doses gives immediate but only temporary relief of pain. More lasting is ephedrine sulphate, gr 3/4, given orally or dissolved in

in/sterile saline and injected intramuscularly or along the course of the affected nerve. This may be repeated as often as is necessary.

In severe cases with much enlargement of the nerve surgical treatment is advisable, both to relieve the pain and to prevent subsequent bending of the fingers from muscular atrophy, as it is usually the ulna nerve that is thus involved. The nerve is exposed behind the elbow and its sheath stripped off for  $1\frac{1}{2}$  to 2 inches. It is often a good plan to transplant the nerve to a new bed in the muscles on the front of the medial epicondyle. I have had very satisfactory and permanent results with this simple operation.

Not infrequently an abscess develops in the nerve trunk. This appears to be a feature of the disease in India as it is not reported from other countries. An abscess may occur in any of the nerve trunks or their cutaneous branches. I have seen it in two cases, both of whom were children with the ulna nerve affected. One, a boy of 14 years, had two large abscesses about the size of hens' eggs. They were 4 inches apart and communicated with each other by a tunnel through the intervening portion of nerve. This boy was an N2 case. In the other case, a girl of 10 years, the abscess and slight bending of the little finger were the only signs of leprosy. The abscess

abscess/should be evacuated and scraped out. Iodoform or B.I.P.P. should be rubbed into the cavity and the wound closed around a small drain. In both my cases a small sinus persisted for several weeks, but healing eventually occurred. In neither case has there been any further advance of the disease nor loss of function of the nerve, although there appeared to be little of the nerve structure left at the time of operation.

A type of peripheral neuritis occurs in leprosy which may be very painful and intractable. The patient complains of tingling and burning over wide areas of the body. General measures, sedatives and analgesics should be tried, but in one or two cases I have found morphia the only means of giving relief.

#### Leprotic Eye Lesions.

Leprotic involvement of the eye is always a most serious condition and often leads to blindness. It is probably the most difficult of all complications to treat. It occurs only in cutaneous cases and especially in those in whom the face is extensively involved. Eye trouble is frequently associated with lepra reactions and in most cases appears to be of a similar allergic nature.

nature./Leprotic iritis causes great pain. One woman under my care was nearly demented with the pain which even large doses of morphia failed to alleviate.

At the first suggestion of any eye trouble all anti-leprotic treatment must be stopped at once. The patient should be confined in a shaded room and both eyes put completely at rest. A good purge should be given. The eye is bathed thrice daily with warm saline, or 20% soda bicarbonate solution, or 10% magnesium sulphate solution. The pupil must be kept widely dilated with daily instillations of 1% atropine drops. In many cases I have found 1% atropine ointment more satisfactory and comfortable to the patient. Often this is all that is necessary and the condition clears up in a few days. In severer cases further remedies may be tried. Trypan blue, 0.5% solution, injected under the conjunctive until it is all ballooned up is sometimes very effective and gives permanent relief. Gold preparations in small doses, such as krysolgan, solganol-B oleosum, and auropratasin are often beneficial, and also protein shock with 1 c.c. of sterile milk. The pain should be relieved with analgesics such as aspirin and phenacetin. When the pain is



greatly/improved. If the eye is so destroyed as to be useless it is often a good plan to remove it, especially if it is causing pain or discomfort.

The other type of eye trouble common in leprosy occurs in advanced neural cases and is due to paralysis of the muscles of the eyelids. The upper lid droops and the lower lid is everted, so that the eye cannot be closed. It is unsightly and often leads to corneal ulceration. Drops of liquid paraffin should be put in the eye during the day and cotton wool soaked in liquid paraffin bandaged on at night. Corneal ulcers should be treated with atropine and cauterisation. Permanent relief can be given by doing a lateral canthorrhaphy. The outer eye-lash-bearing 1/4 inch of the lower lid is removed and a corresponding area of the conjunctive under the edge of the lower lid. The two are stitched together and fusion occurs in a few days.

In patients with any suggestion of eye trouble I have found it a good plan to make them wear dark glasses with side-screens, as a protection from dust and the glare of the tropical sun.

#### Ulceration in Leprosy.

Two varieties of ulceration occur in leper patients, true leprotic ulcers and trophic ulcers.

Leprotic ulcers.

These are usually the results of breaking down nodules, either from lepra reaction or in the course of treatment. They may occur anywhere on the body. With due regard to cleanliness and the application of creosoted hydnocarpus oil or esters they usually clear up rapidly.

Trophic ulcers.

Trophic ulcers occur in the more advanced cases and are due to nerve destruction. They occur on the hands, feet, and outer sides of the ankles. Ulcers on the hands and ankles can be persuaded to heal fairly easily. Those on the feet are extremely difficult to heal and are one of the chief problems in the treatment of leprosy. They often persist for years, and the Indian patient will apply anything in his desperation to alleviate them. I have removed cow-dung, leaves, stones, sticks, wads of cloth, etc., from the feet of patients. Why such individuals do not develop tetanus is a mystery. Frequently there is gross sepsis and necrosis and the only remedy is amputation of a foul, stinking limb.

Before beginning the treatment of a trophic ulcer it must be thoroughly examined. A probe must be used to ascertain the depth of the necrosed tissues, the presence of a sinus, and the state of the underlying bone. Thickened overhanging skin edges must be cut away, all necrosed tissue removed, and a sinus laid bare and scraped. Usually the first thing required is the cleaning of the ulcer. I have found this best done by eusol or potassium permanganate baths and dressings, for a few days, As soon as possible wet dressings must be stopped as their continued application makes the skin and tissues sodden. A dry or oily dressing should then be applied. A powder containing 1 part iodoform and 3 parts boric acid is the best dressing for long use. Alternatively, 5% iodoform in eucalyptus or hydnocarpus oil may be used. I have obtained rapid healing in a number of long-standing ulcers with 5% Dettol in crude cod liver oil. An effective and popular dressing introduced by one of our own patients is a mixture of 1 part camphor and 3 parts cocoanut oil. This is extremely cheap, easily made anywhere, and the camphor seems to



to/have a stimulating effect on the tissues. Many and varied are the applications that have been tried on trophic ulcers and include mercuriochrome, acriflavine, brilliant green, basic fuchsin, B.I.P.P., tannic acid, idoine, strapping with elastoplast, etc. Their very number is an indication of the difficulty of treating such ulcers. I have had good results in cleaning dirty septic ulcers by dressing them with 5% dichloramine-T in cod liver oil. Dichloramine-T is soluble only in an oil and liberates its chlorine content slowly over 24 hours.

Operative measures are necessary if necrosed bone is present. Dead bone is present if pressure around the ulcer causes bubbles to escape from its base, and healing will not take place until the dead bone is removed. Phalanges are removed in the usual way by amputating the digit. A necrosed metatarsal should be removed in its entirety through an incision on the dorsum of the foot and not through the ulcer. After removing the metatarsal the ulcer can often be excised and the edges stitched together. The wound on the dorsum of the foot should not be closed but allowed to granulate slowly. The fibrous tissue in some measure compensates for

for/the loss of the bone. If several bones are involved by a large ulcer the foot should be amputated through the tarso-metatarsal joint or the mid-tarsal joint. Necrosis of the calcaneus from a heel ulcer is very difficult to deal with. My practice has been to first try scraping away all the necrosed portion of the calcaneus and allowing the wound to granulate up. If this is unsuccessful a Syme's amputation is the only remedy.

Periarterial sympathectomy causes immediate healing but the ulcer invariably recurs within a few months, so I have abandoned this form of treatment.

The results of treating trophic ulcers on the feet are disappointing and healing is seldom permanent. Pressure from weight bearing is responsible for the recurrence and it is almost impossible to avoid this in the barefooted Indian. Removal of a metatarsal upsets the balance of the foot, so that the pressure bearing area is shifted and an ulcer develops elsewhere. During treatment the foot should be kept at rest by confining the patient to bed or making him use crutches. After healing padded shoes should be recommended, if possible. A curious feature I have observed in

in/long-standing cases is that the constant bandaging distorts and mis-shapes the foot to an extraordinary degree.

### Nephritis.

Acute nephritis as a complication of leprosy calls for no special form of treatment. All anti-leprotic measures must be stopped at once, the patient confined to bed, and the usual details as to diet, etc. attended to. After recovery hydnocarpus treatment must be resumed with care.

Chronic nephritis is not uncommon, especially among cutaneous cases. Treatment is difficult and the outlook poor. Hydnocarpus should be avoided.

### Orchitis.

Leprotic orchitis is treated along the usual lines by putting the patient to bed, supporting the scrotum, applying ichthyol and glycerine, and keeping the bowels well open. In chronic cases that cause the patient pain an orchidectomy should be performed. The testicle is functionless in such cases.

Arthritis.

Leprotic arthritis is treated by rest and the application of ichthyol and glycerine, or antiphlogistine, or Scott's dressing. Pain is usually relieved by ephedrine sulphate given as for neuritis.

Lesions of the Nose and Larynx.

Nasal ulceration is common in cutaneous cases and causes great discomfort to the patient. Crusting should be removed by daily irrigation of the nose with 15% sodium bicarbonate solution. The ulcer should be viewed and cauterised with 5% chromic acid which usually produces healing after a few applications. Alternatively the ulcer may be painted with creosoted hydnocarpus oil or esters, or with the following preparation.

R

Camphor	3 i
Creosote	3 i
Hydnocarpus oil	$\frac{2}{3}$ i
Olive Oil	$\frac{2}{3}$ i

A patient with lesions on the pharynx can be made more comfortable by the daily use of an astringent gargle such as the following.

R  
/

Potassii chlorati            ʒ iss  
Liq. ferri perchlor.       ʒ ii  
Aquae                        ad ʒ vi

The Gargle.

Sig. ʒ ss. in a cup of warm water as a gargle  
night and morning.

Little can be done for lesions of the larynx. When they cause obstruction to the breathing some relief is obtained from menthol or benzoin inhalations, or by spraying with tannic and glycerine. In severe cases a tracheotomy may be necessary.

Enlarged Breasts in the Male.

Removal of enlarged breasts in the male is usually done from the aesthetic point of view to relieve the patient's embarrassment. Sometimes pain in the breasts is complained of. A curved incision is made along the outer side of the breast just beyond the nipple. The breast shells out easily and the nipple can be left.

Enlargement of the Ears.

The enlarged and pendulous ears of the advanced cutaneous leper can be made more sightly

sightly/ by trimming off the redundant tissue. Muir's special curved ear clamps make this procedure easy and the raw edge soon heals without stitching.

The Control of Treatment.

It has been stated that a series of mild and controlled lepra reactions are beneficial. Some physicians press the special treatment until a lepra reaction is induced, but in my opinion this is often a dangerous procedure and should be avoided. The aim in treatment is rather to keep the general health and resistance at the highest possible level all the time, and special measures should stop short at the point just before a lepra reaction is induced. This means that every case must be carefully watched and the treatment controlled. There are several procedures of value for this purpose and for assessing the patient's resistance.

The general appearance and feelings of the patient are useful guides and he should be weighed regularly. Those who have well developed muscles, and not unduly fatigued by exercise, have a good appetite, and sleep well show the best improvement and seldom suffer from lepra reaction. The temperature should be recorded night and morning and any rise at once investigated and dealt with accordingly. A generalised cutaneous case often runs a continuous low

low/fever between 99' and 100' with a small daily swing. Such cases are in a sub-reacting stage and must be treated with care. Hydnocarpus often benefits them considerably if given cautiously and in small doses. The chronic low-grade reacting patient with a temperature continuously above 100' is very difficult to treat, and hydnocarpus should be avoided. Such cases should be confined to bed for most of the day with a light, nourishing diet, and an occasional course of anti-reaction treatment.

I have found two tests of some value in estimating the general resistance and the patient's progress. These are the erythrocyte sedimentation rate and the serum formalin reaction. The combined results are a better guide than either of them alone.

#### Erythrocyte sedimentation rate.

The method of doing this test in leprosy is described in the appendix. The index recorded is the level to which the red cells fall in a fixed time. It must be stated at the outset that the erythrocyte sedimentation rate is an indication of the general health of the individual and has no specific significance in leprosy. The lower the index, that is the less the red cells



cells/fall in the graduated tube, the more satisfactory is the individual's general condition. The normal index in a healthy person is 20 or less. Anything that tends to disturb the normal balance in the body raises the S.I. The delicacy of this test was seen in the higher indices recorded in a group of healthy children during a particularly hot spell in the month of May when the shade temperature rose to 110°F. NI cases and many CI cases have a normal S.I. or slightly above normal. N2 cases are above normal and C2 and C3 cases are definitely raised, sometimes as high as 50 or more. If other complications have been eliminated then the raised index must be due to the leprosy. A lepra reaction causes an immediate rise of the S.I. and I have known it to go up to 85 in severe cases. Indeed, a rise in the S.I. occurs before there is any other indication that a reaction is about to develop, and it thus serves as a valuable warning. As the reaction subsides the S.I. falls to the patient's normal level. The presence of a trophic ulcer in a neural case may be the cause of a persistently high S.I. The individual who maintains a low S.I. progresses well and in him treatment can be pushed, using

using/repeated tests as a guide. If the S.I. keeps high, above 30, treatment must proceed more slowly and possible complications looked for.

Serum formalin reaction.

The technique of performing this test is described in the appendix. The serum formalin reaction, or formol-gel test, has been applied to a number of diseases and found to give positive results in certain of them. These are kala-azar (124), malaria (125), trypanosomiasis (126), and amoebic dysentery, syphilis, tuberculosis, and leprosy (127). Wade (128) found the test to be strongly positive in leprosy and suggested its use to detect incipient cases. While the formol-gel test is not specific for leprosy it is more so than the erythrocyte sedimentation test just described, and especially if the other diseases mentioned can be eliminated. This I have done and found the test to give positive results which vary with the severity of the disease, over a large series of leper patients. The same opinion has been recently reported by McKenzie in East Africa (129). In performing the test in leprosy I have not considered the degree of opacity that may occur to be of any significance.

The greater the dissemination of the bacilli throughout the body the higher is the reading, that is the sooner a gel forms in the serum. In neural cases and in those early cutaneous cases in which the disease appears to be more or less localised, the reading is low, either 0 or I. As the disease progresses and becomes more generalised the reading rises. Similarly, the onset of a lepra reaction causes a higher result. The serum gels rapidly, giving a reading of 5 or 6, in nodular cases, severe reactions, and long-standing chronic reactions. As the disease improves and becomes arrested the reading falls to the normal zero. A persistently low reading suggests a good outlook for the patient. A continually high result, even in the absence of marked clinical signs, is usually associated with a gradual advance of the disease. The test is thus of some prognostic value. I always regard with suspicion an apparently arrested case with a formol-gel index of I or over, and advise careful observation.

The routine practice in the Lady Willingdon Leper Settlement has been to give each patient a thorough clinical and laboratory examination every three months, and to record the results of

of this examination on special progress charts. C2 and C3 patients are examined once in six months only unless there is any special reason for doing it more frequently, as they show little change in a period of three months. At this examination the patient is weighed. The general health is observed and the clinical manifestations of leprosy carefully recorded on special charts. The bacillary concentration is roughly estimated from the scrapings from the nasal mucous membranes, both ear lobes, and any other lesions or areas of skin. The erythrocyte sedimentation rate and the serum formalin reaction are done, and any other test, such as the Wassermann reaction, that may be called for in the individual. The results of this examination are used as a guide to treatment during the ensuing three to six months. In this way a careful check is kept on the progress of each patient.

#### Length of Treatment.

The length of treatment required necessarily varies with the individual and the severity of his disease. The time elapsed between the onset of the first signs and the commencement of treatment is an important factor. In general, the

the/earlier treatment is begun the shorter does it need to be continued. The more rapidly active signs disappear the shorter is the treatment required to effect an arrest. In all cases treatment must continue for at least six months to one year after all active signs have disappeared, and it is often advisable to continue with a modified treatment for longer than that minimum period, if the patient's circumstances allow it. The criteria of the disappearance of active signs are made clear in the rules laid down for the discharge of Government servants from the Lady Willingdon Leper Settlement. These rules are as follows:

"No Government servant may be discharged until he has satisfied the following conditions:

1. No new lesions have appeared for a period of at least six months.
2. Old lesions have shown no change, either increase or decrease, or any other signs of activity over a period of six months.
3. Repeated bacteriological examinations of skin and mucous membranes, and by puncture of lymph glands, have proved negative over a period of six months."

These rules are laid down from a public health point of view and are a satisfactory criterion for the discharge of a patient from an institution, provided the patient returns for periodic examinations. The Government rules also state, "that a patient discharged from the institution under these conditions must report at a recognised leprosy centre for examination every month for the first six months, and thereafter every six months for eighteen months, and again after two years before being finally discharged."

From the therapeutic point of view a period of two years should be substituted for the six months in the above rules. No case can be considered as 'arrested' until he has at repeated examinations over a period of two years shown no signs of activity in any lesions, and in whom no bacilli have been found. Macules must not be raised above the level of the surrounding skin and must have no suggestion of erythema, and there must be no tenderness of the nerves. Unfortunately, the economic circumstances of the patients and their families, and the demands on the capacity of the institution make it impossible to attain this ideal. It has been my practice to discharge on parole a patient who has

has/ fulfilled the above conditions for six months to one year, with instructions to report for periodic examinations during the next two years. Children, and especially those who have been cutaneous cases, are kept in a healthy area of the Settlement for as long as possible after the disease is no longer active, the minimum period being one year.

Among all patients admitted into the Lady Willingdon Leper Settlement during the ten years under review, the average time since obvious onset of the disease has been 5 years. This alone is a severe handicap to treatment. The length of treatment that has been required for 469 patients discharged with 'arrested' certificates since 1925 is recorded in a table in the appendix. The average time for all cases is three years. Neural cases require from 2 to 3 years, and cutaneous cases from 3 to 4 years. It is significant that only 32 C2 and C3 cases have been discharged during the ten years. The longer period of treatment shown for children is due to the longer period of observation they undergo before discharge.

The Results of Treatment.

The clinical changes that occur in those patients who respond to treatment may be briefly described. There is an improvement in the general health and well-being, with an increase of weight. This is particularly noticeable in those who come under institutional care, and is the 'sine qua non' for improvement in the disease itself. The lesions of the skin and nerves diminish first in severity and then in extent. Macules become flattened, normal pigmentation returns to a variable extent, and sensation is restored. Healed macules, both cutaneous and neural, often have a crushed tissue paper appearance which is characteristic. Nodules diminish until only a scar marks their site. Anaesthesia usually diminishes in extent and may disappear altogether, but often there is some permanent change left. Nerve tenderness goes but enlargement of the nerve trunks may be permanent. Trophic changes, such as bending of the fingers, muscular wasting, and tendency to ulceration, are permanent. The bacteriological improvement is marked by a gradual decrease in the numbers of bacilli found and in the positive areas, by a fragmented or beaded appearance of the bacilli, and by the



the/eventual disappearance of bacilli altogether. A few cases are restored to health without blemish, but the majority bear one or more scars of the disease for all time. These vary from one or two areas of slight anaesthesia, or depigmentation, to gross deformities.

From 1925 to 1935, 2130 patients received treatment as in-patients in the Lady Willingdon Leper Settlement. Of these, 1445 had left the institution up to the end of September 1935 and the results of treatment in them are recorded in the appendix. 469, or 32%, were discharged with healthy certificates after having fulfilled the requirements already discussed. Of this group, in 174, or only 12% of the whole, the disease was apparently arrested without leaving any blemish. By far the largest number of these were early neural cases, NI, and 68% were children. It thus appears that early neural leprosy, especially in children, is the most amenable to treatment. The significance of this will be discussed later. 295 patients were discharged as 'arrested with deformity'. Of all those discharged with the disease arrested 76% had been neural cases and only 24% cutaneous, which is another significant feature. Stated in another way, only 18.5% of all cutaneous

cutaneous/cases recovered as against 42% of all neural cases. The length of treatment required to arrest the disease in these patients is recorded in a further table.

Among the remaining patients treated 352, or 24%, were improved but left the institution before the disease was arrested or they had fulfilled the necessary requirements to gain a healthy certificate. 492, or 34%, showed no improvement or got worse, but many of these left before receiving any appreciable amount of treatment. 132, or 9%, died in the institution, but in only a few of these was death due directly to leprosy. The majority of deaths occurring in the Settlement are among patients admitted 'in extremis' from some concurrent disease or grossly septic ulceration.

After the minimum period of six months free from all signs of activity of the disease, patients are discharged with instructions to report at regular intervals for examination. Unfortunately many patients fail to do this, and conditions in India are such that it is almost impossible to adopt any adequate system of checking a patient's further progress. This is one of the great drawbacks to the study of the disease and its treatment,

treatment, and until the social conditions of the country improve little can be done to amend it. Nevertheless a certain number do report regularly or irregularly, and among them a high relapse rate is found. Details of relapsed cases are recorded in the appendix, but it is probable that the actual relapse rate is higher than that given. Among all cases that have been discharged with the disease arrested 14% have returned with a recurrence. Only 9% of neural cases have relapsed as against 32% of cutaneous cases. The average time between discharge and the first signs of the disease re-appearing varied from 4 months to two years, but among cutaneous cases it rarely exceeded one year. Among the 32 relapsed neural cases 3 returned in the cutaneous stage, and among the 35 relapsed cutaneous cases all but 4 returned with the skin type of disease again. I have no doubt that a relapse occurred among all of the 5 C3 cases discharged, although they did not return to us, as in the severe cutaneous types the relapse rate is very high. In investigating the reasons for relapse it was found that nearly all persons returned to bad conditions of living and malnutrition, and developed other diseases. Most adults admitted that after the long period of confinement in the institution they indulged in an orgy of sexual activity and frankly attributed

attributed/their relapse to that. Only a very few had attempted to or been able to resume their employment, and the majority thus lived idle lives. A few cases relapsed in spite of returning to good conditions and careful supervision.

Thus we find that a fairly large proportion of patients discharged as apparently arrested had a relapse of the disease within a comparatively short time. I admit that the conditions of discharge from the Lady Willingdon Leper Settlement are unsatisfactory, as other factors than the therapeutic one have to be considered. Allowing for this, the relapse rate among arrested cases of leprosy is high, and especially among cutaneous cases. The length of treatment given seems to have no bearing on the subsequent tendency to relapse, but rather is it dependent on the severity of the disease and the general health and resistance of the patient.

The Value of Treatment.

The literature on leprosy abounds with contradictory statements on the value of treatment. Even workers of wide experience appear to differ on important questions. The introduction of modern methods of administering chaulmoogra and hydnocarpus oil caused a wave of optimism among physicians and brought a new hope to sufferers. It was claimed by many that at last there was a 'cure' for leprosy. Muir and Rogers conclude their textbook, "Leprosy" (6), with these words: "The improved methods of dealing with leprosy have therefore placed in our hands a simple and effective means of diminishing the disease by providing treatment under attractive conditions,....  
..... only funds and organization being required to bring about a great decrease of the disease in all countries....." Unfortunately this optimism has not been justified by the passage of time, and from my acquaintance with Muir and his recent work I do not think he still supports the above statement. Indeed, no little harm has been done, and is still being done by enthusiastic lay supporters of anti-leprosy campaigns, by extravagant claims that leprosy can be cured and if only patients will submit to treatment the disease can be eliminated from the community.

In evaluating the effect of a drug or line of treatment various fallacies are commonly made by the unexperienced. The subsidence of a lepra reaction is mistaken for the elimination of the disease, and the granulation of bacilli that such a reaction causes is attributed to the effects of the drug. The clearing up of leprosy manifestations is attributed to a treatment when it is really due to the removal of another disease or aggravating factor. A direct or specific effect is ascribed to protein shock, trichloroacetic acid, metallic compounds, proprietary preparations, etc. On the other hand, the failure of drugs to remove permanent trophic lesions has often unjustly led to their discredit. The psychological effect on patients and physicians of the failure of some much advertised preparation is not inconsiderable. In assessing the value of treatment in general it is important to bear in mind the self-limiting nature of the disease and the tendency to spontaneous arrest in many cases.

In considering the value of treatment it is essential to distinguish between neural and cutaneous leprosy. The failure to do this is the cause of much of the contradictory evidence claimed by different workers. It is generally agreed that the early neural case has the best

best/chance of recovery, and our own results already stated show that this is true. Such cases have three possible fates. They may become spontaneously arrest<sup>ed</sup>/without further advance: they may proceed to the more advanced neural stage: or they may pass into the cutaneous type. There is no doubt that a great many early neural cases do become spontaneously arrested without any form of treatment. Such 'abortive' cases are commonly seen in India, and frequently that is as far as the disease ever goes. For them treatment is unnecessary and of no value. All that is required is observation over a number of years. If there is evidence that the disease is progressing to a more advanced neural stage then treatment is of value and usually checks the advance. In the neural case that is becoming cutaneous treatment should be given to its limit in order to prevent the general|dissemination of the disease. Sometimes this is successful. It is in these two latter stages that I have found treatment to be of greatest value and give the most hopeful results. Nevertheless, many such cases continue to advance in spite of treatment. Thus, when the early neural case presents itself one can be hopeful but not always certain of effecting an

an/arrest. It requires considerable experience of the disease to decide when and what treatment should be given to such cases. The age and general health of the patient are the important factors. Treatment must not be given indiscriminately to all who have any sign of the disease, as not unfrequently it is unnecessary and even harmful.

The established cutaneous of leprosy is a more serious problem. Treatment in the early stages often effects an arrest but the permanency of this is always doubtful. It should be recognised that spontaneous arrest does occur in a few such early cases, but all cutaneous cases call for immediate treatment. In the advanced stages treatment usually causes considerable improvement and even arrest in a few cases. In the majority, however, it is only possible to keep the disease more or less under control at a minimum severity, and prolong life, The immediate effect of treatment on such cases is often gratifying and the gross lesions subside considerably, but eventually a stage is reached when improvement stops and the patient's condition remains stationary. At this stage the hydnocarpus



hydnocarpus/treatment should be modified to prevent excessive saturation which may be detrimental to the general health.

In my experience the treatment of children has been more satisfactory than that of adults. In the early neural child the disease can usually be aborted if the child is put under good living conditions, without the need for special treatment. Signs of further advance or passage into the cutaneous type call for very special care and hydnocarpus treatment, modified according to the age of the child. Established skin cases usually respond well to treatment, and I have found a higher percentage of them becoming arrested than among similar adults. The younger the child the more serious is the outlook, and the time of puberty is critical, especially among girls. There is good hope for the child who passes safely through that period without further advance of the disease. I have always found the treatment of children the most satisfactory, hopeful, and attractive aspect of leprosy work, but it must be emphasised that leprosy is a very serious disease in a child, requiring constant care until adult life is reached.

To investigate more fully the value of hydnocarpus preparations in the treatment of leprosy I carried through a small experiment. The first 12 patients admitted into the Settlement in 1934 received no hydnocarpus therapy at all, but only the routine general treatment with an extra pint of milk and  $\frac{1}{2}$  oz. of cod liver oil daily. This was maintained for one year. Of the 12 cases, 4 were neural and 8 cutaneous. At the end of the year all the neural cases were definitely improved and approaching arrest. Of the cutaneous 2 improved so far as to become bacteriologically negative, 4 improved clinically and in their general health, 1 remained stationary, and 1, a nodular case, showed an increase of nodules and appeared to be worse. The cutaneous cases were then given the routine hydnocarpus esters treatment. After a further six months all, including the nodular case, had improved more rapidly than they had when not receiving the esters. In these cases, then, the esters were of definite value in causing more rapid improvement.

My own opinion of the value of anti-leprosy measures is based on these results of the treatment in the Lady Willingdon Leper

Leper/Settlement over a period of ~~the~~<sup>ten</sup> years.  
General treatment, including diet, exercise,  
and freedom from other diseases, is of the great-  
est value for all cases. Hydnocarpus therapy  
is of value in most cases but its limitations  
must be recognised. It is in <sup>no</sup> way a cure for  
leprosy, but is rather an adjunct to general  
measures, and is the least unsatisfactory of  
the many remedies that have been tried. In spite  
of modern advances the treatment of leprosy is  
still uncertain and unsatisfactory. It is true  
that a number of cases are apparently arrested  
and improvement occurs in many, but hydnocarpus  
preparations have small responsibility for this.  
Rather is it the general care, nutrition, and  
the natural resistance of the individual that  
enable us to say that the disease can be impro-  
ved, suffering relieved, and life prolonged, but  
there is yet no cure.

EPIDEMIOLOGY AND PREVENTION.

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EPIDEMIOLOGY AND PREVENTION.

For as long as leprosy has ravaged the human race the cry has been to 'get rid of the leper'. To-day the slogan of anti-leprosy work is to 'get rid of leprosy'. It is easier to prevent a dozen cases of leprosy than to cure one, and it is being increasingly recognised that the methods of combatting leprosy are chiefly preventive. As far as the control of the disease in a community is concerned the provision for treatment, although necessary, is not the primary consideration. The unsatisfactory nature of modern treatment has been already discussed, so that the problem of the control of leprosy is essentially its prevention. Despite the gaps which still exist in our knowledge of the disease it is possible, by applying modern principles of prophylaxis and hygiene, to effectively control leprosy and eliminate it from the community. The problem cannot be solved, however, by any one measure, as the methods of dealing with it must vary with the geographical, social, economic, administrative, and other conditions of the countries where it exists. In South India, with its large mass of

of/people, mostly poor and living in primitive conditions, and with its own peculiar social features, the task of controlling leprosy may well seem impossible. I believe, however, that a great deal can be done and must be done, always remembering that leprosy is only one of the many problems of the health and welfare of the people. Measures for its control must be closely associated with measures for the economic and social improvement of the people and the relief of other diseases, and only as the general standard of living rises will leprosy and other infirmities decrease.

The more specific measures applicable to an anti-leprosy campaign will now be discussed. I do not propose to give a detailed description of such a campaign but rather a broad outline of the principles on which I consider it should be based in South India. These principles are themselves based on such epidemiological features of the disease as are known to us, and these will first be reviewed.

#### EPIDEMIOLOGY.

It is only within the last ten to fifteen years that the epidemiology of leprosy has received serious scientific investigation.

investigation. /Consequently the available knowledge is limited and much of it is based on theory rather than observed facts. The most important work along this line has been done in the Philippine Islands, where for the last thirty years efforts have been made to control leprosy among the population of the islands. It is interesting to note that it is only within the last few years that some decrease of the disease has been obtained, if any, and that the original methods have been considerably modified. Such knowledge of the epidemiology of the disease as we have is based on the following features: (1) the infectious nature of the disease: (2) the infectious type of leper: (3) the susceptibility of persons: (4) the fate of the infected person.

#### I. The infectiousness of leprosy.

That leprosy is infectious there is no doubt, in spite of our scanty information concerning the alleged causal organism. This has already been discussed in the section dealing with the etiology of the disease, where it has been pointed out that although the disease is infectious it is not highly so. The disease enters a community only by the advent of a leper and spreads by the

the/contact of healthy individuals with infected persons, but there is abundant evidence to prove that given good hygienic and healthy conditions such a spread may not occur. Thus leprosy is very much easier to control and check than most infectious diseases.

## 2. The infectious type of leper.

Every case of leprosy must be regarded as a potential source of infection, but in practice it is customary to regard the cutaneous cases as 'open' or infectious, and the neural cases as 'closed' or non-infectious. This is based on the presence of acid-fast bacilli in cutaneous cases and their absence from neural lesions. Few leprologists, however, hold positively for the absolute non-infectiousness of neural leprosy and some even believe that it is infectious from the presence of a hypothetical virus stage in the life-cycle of the organism. There is no evidence that such a virus stage exists but its possibility cannot be denied. Likewise there is no definite evidence that the acid-fast rods found in such profusions in cutaneous lesions are living organisms or that they are the re-infecting agents. Until we obtain more information about the organism, however, it is justifiable to assume that the presence of the



the/acid-fast rods are an indication of the infectiousness of the case. Furthermore, there is abundant clinical evidence that healthy persons are infected by cutaneous cases, while there are very few authentic instances recorded of a healthy person being infected by a purely neural case. For epidemiological purposes the cutaneous case must be regarded as the source of infection and should therefore be segregated from healthy persons. All cutaneous cases are not equally infectious as the advanced nodular leper discharges an infinitely greater number of bacilli than the early case with only one or two skin lesions, but so long as a single bacillus can be found in the lesions that person must be regarded as a source of infection. As far as we know at present pure neural leprosy, for practical purposes, is not infectious, but there is no means of knowing for certain that a neural case will not become cutaneous and discharge bacilli. It is probably safe to allow these individuals to associate with healthy persons so long as they are kept under observation.

### 3. The susceptibility of persons.

All persons are not equally susceptible to leprosy. Differences in racial susceptibility have been pointed out elsewhere, and in

in/the discussion on etiology it has been shown that the chief factors affecting individual susceptibility are age and debility. Children are highly susceptible, adolescents moderately so, and adults are practically immune. Debility at any period of life greatly enhances the liability to the disease. It is therefore essential that in any measures to control leprosy infected persons must be prevented from coming <sup>in</sup> contact with children and adolescents, and the general health and hygiene of the community are the best safeguards against the spread of the disease.

4. Fate of infected persons.

It is a recognised fact that every person who is infected with the tubercle bacillus does not necessarily develop tuberculosis, and there is evidence that the same is true of leprosy. The hypothesis that leprosy is usually acquired in childhood or early adolescence is being more and more generally accepted, and it is during these periods that the disease is most likely to spread and become active. While a large proportion of infected children do develop the disease there are also many cases in which the infection is established but does not go on to an advanced stage of the disease. Early clinical signs appear but

but/remain stationary or disappear in the course of time, without the child having received any treatment. It is also justifiable to assume that foci of infection may be present without any clinical evidence ever appearing, as undoubtedly occurs in tuberculosis. The fate of the infected person and the progress of the disease from its earliest stages are as yet a mystery, and leprosy workers to-day are concentrating more attention on this very important aspect of the disease. There is yet no answer to the simple question of what happens to the early N-I child. Why does one such case progress to the cutaneous stage, another to the N-2 stage, and another remain stationary or even lose all evidence of the disease? Much has been said about resistance and the influence of environmental factors but these terms are a cloak to hide our ignorance of the real factors that control the disease. The truth is that we do not know what happens when an individual is infected with the organism that we assume is the cause of leprosy, nor do we know what factors control the growth and spread of that organism in the body and the consequent clinical signs of the disease. Evidence is slowly accumulating of various external factors which seem to influence the disease in one way or another and it is on these that we must base our knowledge of the epidemiology of the disease and build up anti-leprosy measures.

When a child is infected with the organism of leprosy it appears that one of five things may happen.

1. No evidence of the disease may ever appear and the infection presumably is confined to deep foci. Such cases, if they exist, do not come into this discussion as they are never recognisable.

2. The disease may advance into the active stages and the individual become progressively worse.

3. There may be a stationary or latent period and then, because of some lowering of resistance, the disease may light up many years later.

4. The infection may become stationary and the lesions be naturally arrested though remaining evident.

5. The lesion or lesions may disappear altogether.

Cases of categories 2 and 3 need not be discussed further as they are the established lepers with whom all workers are familiar and are the subject of the main part of this thesis. Types 4 and 5 are not familiar to all and their existence and importance have only recently been recognised. They may be termed the 'abortive' cases. The existence of abortive cases and potentially abortive cases must greatly modify the conclusions drawn from data of the incidence of the disease in

in/a community. A survey of an area may reveal a high incidence of leprosy, and in the past it has been assumed that all cases discovered need active treatment. We now know that this is not necessary.

The abortive case.

That abortive cases of leprosy occur is not surprising when one considers the self-healing nature of the disease. It is important to recognise such cases from the point of view both of the individual patient and of general anti-leprosy measures. In an adult it is easy to be reasonably sure of such lesions from their nature and their history. Recognition in children is more difficult and requires considerable experience of the disease. There is no reason to suppose that the abortive case is a source of infection to healthy people so they need not be debarred from associating with others. Treatment has no beneficial effect on these cases and may even be harmful. There is no evidence that our present anti-leprosy drugs are of any prophylactic value. Good living conditions are the best means of defence. Such children should not be at once branded as lepers but should be closely watched and cared for over a number of years until their fate one way or

or/another is reasonably sure. Proper care probably gives a child a 75% chance of complete recovery. The same is even more true of the adult abortive case.

We may conclude that when evidence of leprotic infection is found it does not necessarily follow that either treatment or isolation should be at once instituted, unless there is definite evidence of activity of the disease and of the infectiousness of the case.

## CONTROL AND PREVENTION OF LEPROSY.

The public health aspect of leprosy is, as a whole, so vast a problem that it is humanly impossible to cope with it completely in a country where the disease is endemic, and especially in a country such as India. An adequate system would engulf the medical resources of any budget, and to concentrate on such a colossal task is perhaps unnecessary when other needs of the country are considered. Leprosy, after all, is only one of the many endemic diseases in the country and the treating of even every case would involve an expenditure of money and absorption of time out of all proportion to its relative importance. Nevertheless, certain principles should be laid down which if adhered to can be expected to go a long way towards controlling the disease in a given area. Theoretically it is possible to eliminate leprosy within the lifetime of a generation, but, as in other spheres, it is almost impossible to put theory into practice. In South India there is lacking among all classes of the population the knowledge and willing co-operation so essential to success.

### I. General health of the community.

It has been already stressed that the control of leprosy is intimately bound up with the

the/general health and welfare of the people, and that not only in relation to other diseases. An inadequate diet, bad social and hygienic customs, ignorance, and poverty -- these are the foundations on which the disease, any disease, flourishes, and their correction is a matter for the Indian people themselves. India, for all her boast of an ancient civilisation, her wealth, and her art, must be ashamed of the conditions under which millions of her people live. Those conditions will improve only with a change in the minds and hearts of her people, with a casting off of the lethargy and apathy of the East, and a realisation that human beings are something more than animals. The future of India lies, not in the rise and growth of her cities and industries, but in the rebuilding of her countless villages and on the welfare and prosperity of her village people.

## 2. Leprosy surveys.

As complete a survey as possible of the leprosy infected area is required. Some workers are not in favour of surveys, believing they are of little value beyond statistical interest. There is no doubt, however, of the practical value of a thorough survey of a district, as the foundation on which to base an anti-leprosy campaign. It is often found that in certain streets of a town or in certain



certain/villages there are a great many lepers while in other streets or villages perhaps adjacent to the former there are very few or no cases at all. These foci of infection are a striking feature of the incidence of leprosy and the factors that cause them are as yet imperfectly understood. There is need for a detailed investigation of such foci as an epidemiological study.

In carrying out a survey the important features to be noted are the type of cases and the ages of the infected persons. From these two facts it is possible to deduce the stage reached by the epidemic, and subsequent anti-leprosy measures can be modified accordingly. Where there is a high proportion of cutaneous cases and a high incidence among children the epidemic curve is on the up grade, the community is most susceptible and can expect a further increase of the disease. If neural cases predominate and the incidence among children is low the epidemic is naturally waning, the community resistance is high and a gradual decrease of the disease can be expected. I have already referred to the survey carried out in the municipality of Saidapet. This survey revealed a high proportion of cutaneous cases and a very high incidence among school children. I was thus able

able/to point out to the authorities concerned that the disease was rapidly spreading in the town and would continue to do so unless vigorous measures to check it were adopted. In India as a whole neural leprosy predominates and Indian workers are agreed that the epidemic curve has passed its peak and is on the down grade, although it may be definitely rising in certain small areas and communities like Saidapet.

A survey is a tedious task involving much time, labour, and tact. Every house must be visited, actual cases ascertained, and all contacts examined. In India there is often opposition to this intrusion on personal privacy and many hide themselves when the survey party approaches. Nevertheless it is an essential part of an anti-leprosy campaign and must be persisted in.

### 3. Propaganda.

In view of the general ignorance of the people and to correct common misconceptions about the disease an important part of a campaign is propaganda. This can be done by all the usual methods such as the distribution of literature, lectures, demonstrations, films, etc. The following points should be emphasized:

1. Leprosy is an infectious disease and not hereditary.

2. It is neither venereal nor a curse of God.

3. Infection occurs through close and prolonged contact, as in home-life.

4. Only certain types of the disease are infectious and children are most susceptible.

5. Every case does not need treatment or segregation.

6. The earlier treatment is begun the better is the chance of recovery.

7. Non-infectious cases need not give up their work.

8. All who have been or are in contact with a leper should submit to a periodical examination.

9. A healthy body is the best defence against disease.

### Segregation.

Colonies and asylums are the ideal method of segregating infectious cases but their expense is considerable and in a large population it is impossible to provide accommodation for all infectious cases. Home segregation is possible among the more intelligent and well-to-do, where the patient can be given a room to himself and all his belongings kept separate from the rest of the household.

household./The disadvantage of this is that the patient develops a sense of inferiority, feels he is an outcast and unwanted, and the psychological effect is a drawback to his recovery.

66           In a village infective persons should be made to live in separate huts a little apart from the others. If able-bodied they may be allowed to do field-work, cultivation, etc., to earn their own living. Those unable to support themselves must be cared for by relatives or the charity of the village. Needless to say it is extremely difficult to introduce such a system into an Indian village but it has been done in some places with considerable success.

          If possible there should be a central colony or settlement in every district with a hospital for the more acutely ill. Little need be said about the nature of the colony beyond referring to the description of the Lady Willingdon Leper Settlement given at the beginning of this thesis. Entrance into colonies must be voluntary as compulsory segregation will defeat its own ends. There is no doubt that patients do far better under institutional treatment than anywhere else. There is no comparison between our in-patient results and those of the out-patient department. Perhaps the most

most/striking difference is in the demeanour of the patients. In a colony the patient recovers his self-respect, lives a normal life, is more hopeful and cheerful, and forgets that he is a social outcast, and this has a great effect on his progress towards health. I am strongly of the opinion that with our present limitations institutions should be reserved for infectious cases only among adults, and for all active cases among children, both cutaneous and neural.

The problem of the burnt-out case is largely the beggar problem and has nothing to do with anti-leprosy measures. Such cases should not be in a leper settlement, but are rather candidates for a beggar's home. The Hindu religion teaches that one acquires merit for one's soul by giving alms to the beggar and so long as that belief lasts begging will be a popular profession in India.

##### 5. Treatment centres.

Apart from the colony this is a question of treating patients at an out-patient clinic. An out-patient clinic must not be a centre for the treatment of all and every person with signs of leprosy, and a large number of such clinics by themselves will do nothing towards controlling and preventing leprosy. Treatment is the part of

of/anti-leprosy work that impresses the general public but it is the least important of all anti-leprosy measures. Out-patient clinics should be used for the spread of propaganda and the treatment of selected cases. The abortive and the burnt-out cases do not need treatment, and advanced skin cases are rarely benefitted by out-patient injections of hydnocarpus preparations. The clinic should be the clearing station between the community and the settlement, passing on such cases as are in need of institutional or hospital treatment, rejecting those who do not need any treatment, treating all active neural cases and early skin cases in good general health, and examining regularly contacts and observation cases. The out-patient clinics at present established throughout the Madras Presidency are of little value as a means of combatting leprosy, but clinics run on the lines suggested above would play a very important part in an anti-leprosy campaign. While treatment should be available for all it must be given with due regard for the value of our present methods, otherwise it will fall into disrepute.

#### 6. Training of Workers.

Mention must be made of this point as I have been amazed at the ignorance about this

this/common disease shown by medical men in India, both European and Indian. Most practitioners are unable to recognise any but the advanced types and their sole idea of treatment is the injection of some hydnocarpus preparation. Along with this ignorance there is a reluctance to treat leprosy for fear the presence of leper patients will turn away others. Another regrettable consideration with many is that treating leprosy is laborious and seldom lucrative. There is much need for propaganda in the medical profession, and in the medical schools a short course should be given on the disease. There should be facilities and encouragement for more men to specialise in the disease. I doubt if there are more than a dozen physicians in South India who are really familiar with leprosy, and yet the Census Reports include it as one of the four chief infirmities of the country.

The control of leprosy is a problem to which there is no easy solution, for it is as much a social and economic problem as a medical one. Leprosy is a disease not only of individuals but of the community, and its control demands measures involving the whole community and not only the sufferers from the disease. Its control means better

better/hygienic conditions, better social customs, better food, better housing, and better education especially in health matters. The most vital need of all is a real social awakening of the people. India will not be free from leprosy until the people of India have an earnest desire to free their country from the disease and are prepared to work for that end.

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SUMMARY OF THESIS.

The thesis submitted is a consideration of the chronic infective# granulomatous disease apparently due to the organism 'mycobacterium leprae', and is an account of the incidence, nature, and treatment of that disease in South India. The geographical, racial, social, and economic features of South India are described and the incidence of leprosy is estimated at not less than 3.19 per mille of the entire population. Among the predisposing factors the most important is the poor diet eaten by the South Indian. A study of the age distribution of leprosy shows that it is essentially a disease of childhood and early adult life. An account of the world distribution and history of the disease completes the introduction to the subject.

The infectious nature of leprosy is well established, but it does not appear to be highly infectious and prolonged and intimate contact is necessary for transmission of the disease. The resistance of the individual is of prime importance and this is influenced by age and debility, the healthy adult living under good conditions being practically immune to

to/infection. Very little is known of the bacteriology of leprosy. The acid-fast rods found in such profusion in cutaneous lesions are assumed to be the causal organism, but they have never been artificially cultured nor has the disease been reproduced experimentally in animals. Rat leprosy is apparently due to a different organism. The bacillus is of low toxicity and probably induces a form of tissue immunity.

The view of the pathology of the disease put forward is that the mycobacterium leprae is a parasitic rather than pathogenic invader of man. The organism apparently finds a home in the reticulo-endothelial system and dwells in the cells of that system in an astonishing state of commensalism, neither host nor parasite seeming to cause much disturbance to the other. The organism may multiply and spread and invade most of the tissues and organs of the body, but it has a particular affinity for the peripheral nervous system and the deeper layers of the skin. The resultant lesions are of a granulomatous nature with certain characteristic features which differ according to the type of disease present. These variations are explained as being due to tissue resistance, which in turn depends on age, debility,

debility, / and degree of infection.

The clinical manifestations of the disease as it occurs in the South Indian are described. A number of clinical features observed by myself, especially among the earliest signs, are recorded. The phenomenon of lepra reaction is described and an attempt is made to explain it by the hypothesis that it is a manifestation of allergy. The prognosis is bad except for early neural cases. The disease has a tendency to spontaneous arrest, but often this occurs only after the patient has been grossly disfigured and deformed.

The treatment of leprosy is unsatisfactory. The best results are got along general lines with good diet, exercise, hygiene, and freedom from other ills. The least unsatisfactory of the numerous drugs recommended are preparations of chaulmoogra or hydnocarpus oils. The most recent therapeutic innovation has been the use of certain of the aniline and xanthine dyes, but they have proved disappointing over a large series of cases. My own experience with some of the dyes is recorded. The treatment carried out in the Lady Willingdon Leper Settlement is described in detail. The results of treatment are uncertain and often disappointing. The

which/will lead to elimination of the foundations  
upon which the disease erects itself.

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The/relapse rate in the apparently arrested cases is high. The chief value obtained from modern treatment is improvement in the general health of the leper and the prolonging of life.

Anti-leprosy work must therefore be essentially preventive. Certain epidemiological features are discussed and the importance of the 'abortive' case is pointed out. The basis of an anti-leprosy campaign in an endemic area is briefly described.

So ends the study and discussion of this most ancient of all diseases. The 'Chon's swellings' of the Egyptians, the 'kusta' of the Indian Vedas, the 'elephantiasis' of the Greeks, and the 'living-death' of Mediaeval Europe are the leprosy of to-day, still claiming millions of victims, and still incurable. Anti-leprosy work may justly be called one of the 'crusades' of our times, a crusade calling for those with medical skill and ability, human sympathy and understanding, courage and fearlessness, and infinite patience. Leprosy will not be conquered by the dramatic effect of some specific drug but by the gradual piecing together of knowledge gained by patient study and observation, which

**APPENDIX.**

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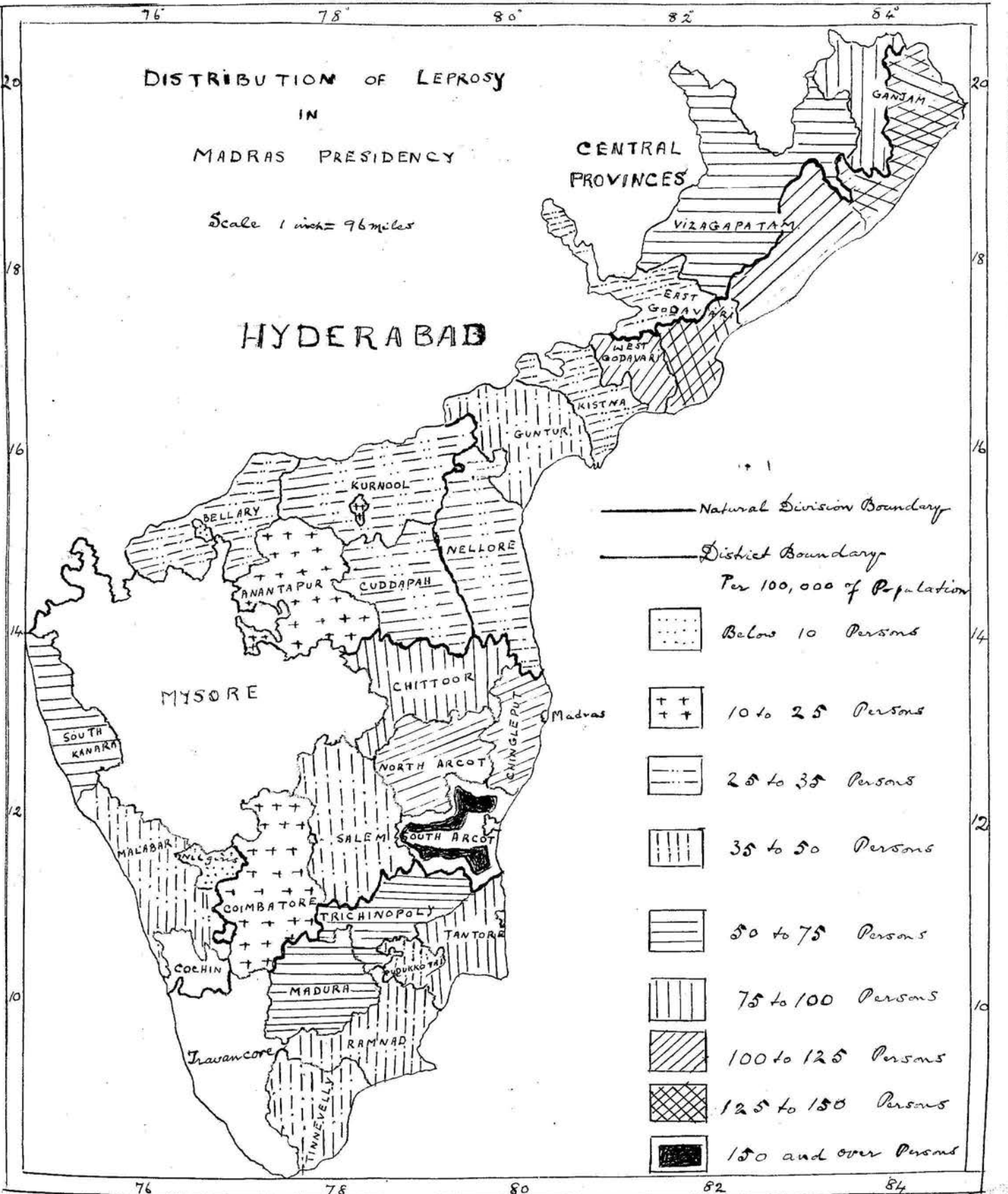
# DISTRIBUTION OF LEPROSY

IN  
MADRAS PRESIDENCY

Scale 1 inch = 96 miles

## HYDERABAD

### CENTRAL PROVINCES



- Natural Division Boundary
  - District Boundary
- Per 100,000 of Population
- Below 10 Persons
  - 10 to 25 Persons
  - 25 to 35 Persons
  - 35 to 50 Persons
  - 50 to 75 Persons
  - 75 to 100 Persons
  - 100 to 125 Persons
  - 125 to 150 Persons
  - 150 and over Persons

CENSUS OF INDIA, 1931.  
MADRAS PRESIDENCY.

DISTRIBUTION OF LEPERS BY AGE AND SEX.

L E P E R S.

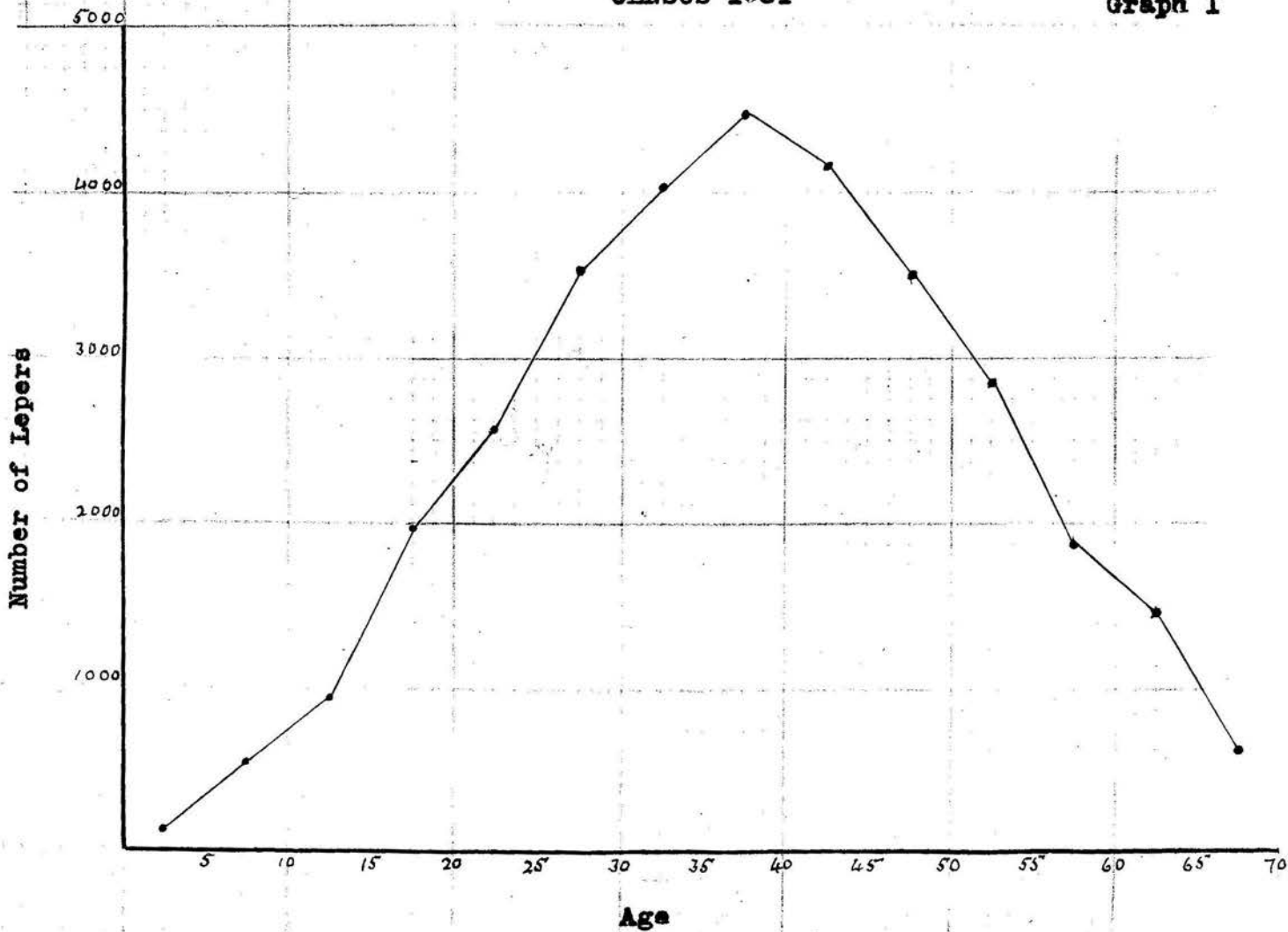
<u>Age.</u>	<u>Males.</u>	<u>Females.</u>	<u>Total.</u>
0 - 5	64	59	123
5 -10	297	234	531
10 -15	597	352	949
15 -20	1,370	601	1,971
20 -25	1,833	737	2,570
25 -30	2,642	874	3,516
30 -35	3,111	906	4,017
35 -40	3,509	948	4,457
40 -45	3,289	908	4,197
45- 50	2,693	810	3,503
50- 55	2,169	700	2,869
55 -60	1,380	494	1,874
60 -65	1,067	382	1,449
65 -70	480	152	632
70 and over	490	173	663
	<hr/> 24,991	8,330	33,321 <hr/>



### DISTRIBUTION OF LEPERS BY AGE

CENSUS 1931

Graph I



AGE OF ONSET OF LEPROSY IN 3391 PATIENTS TREATED

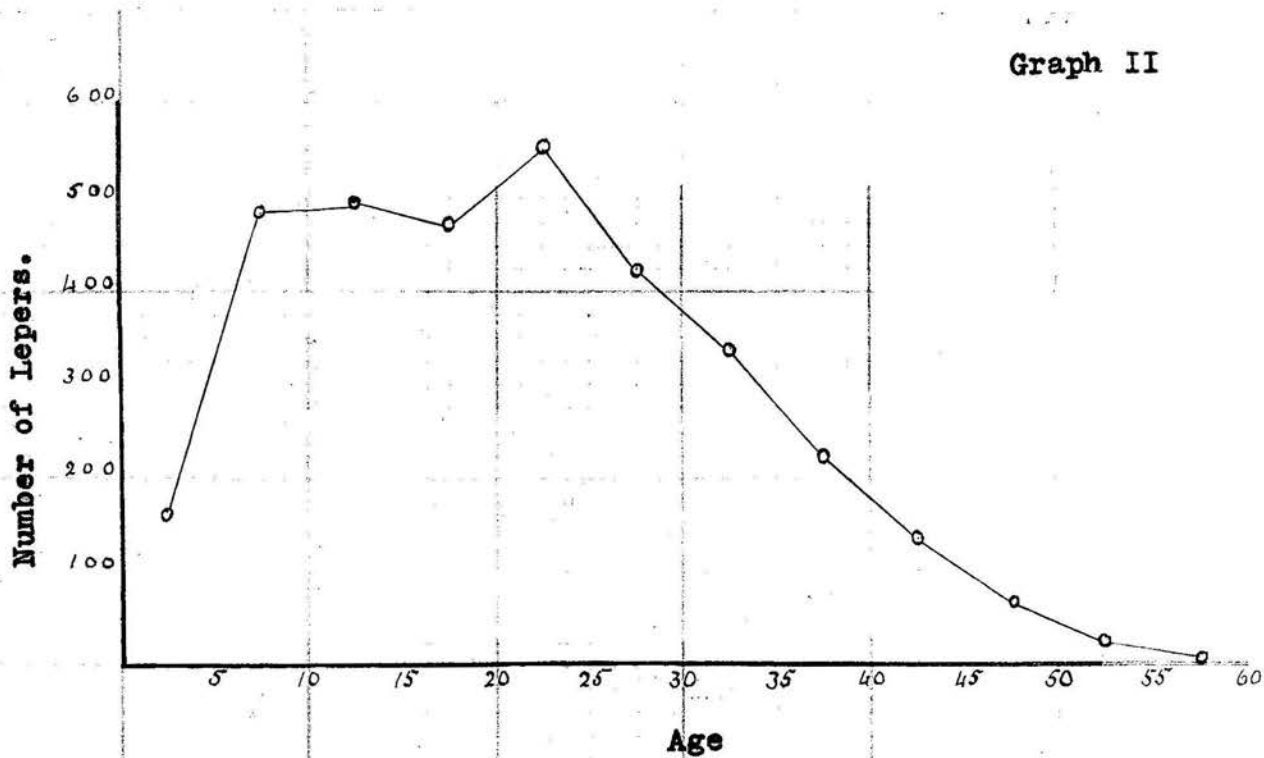
LADY WILLINGDON LEPER SETTLEMENT.

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<u>Age.</u>	<u>In-patient.</u>	<u>Out-patient.</u>	<u>Total.</u>
0 - 5	118	46	164
6 - 10	356	125	481
11- 15	387	110	497
16- 20	293	177	470
21 -25	369	187	556
26 -30	228	193	421
31 -35	169	166	335
36 -40	96	131	227
41 -45	64	70	134
46 -50	32	37	69
51 -55	12	15	27
56 -60	3	4	7
61 -65	1	-	1
66- 70	-	-	-
71 -	2	-	2
	<hr/>	<hr/>	<hr/>
	2130	1261	3391
	<hr/>	<hr/>	<hr/>

AGE OF ONSET OF LEPROSY IN 3391 PATIENTS TREATED AT  
LADY WILLINGTON LEPER SETTLEMENT.

Graph II



## INDIAN CENSUS, 1931.

## FIGURES FOR LEPROSY.

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Total No. 147,911 (Males 107,892.)  
(Females 40,019)

Province, State, or Agency.	Number of lepers per 100,000 of population.
1. India	42
2. Assam	59
3. Baluchistan	6
4. Bengal	42
5. Bihar and Orissa	54
6. Bombay	41
7. Burma	76
8. Central Province and Berar	70
9. Madras	71
10. North West Frontier Province	10
11. Punjab	10
12. United Province	30
13. Baroda	24
14. Central India	16
15. Cochin	62
16. Gwalior.	12
17. Hyderabad.	26
18. Jammu and Kashmir	62
19. Mysore	II
20. Rajputana	5
21. Sikkim	6
22. Travancore	55

## TREATMENT WITH FLUORESCEIN.

No.	Case.	Type.	Previous Treatment.	Treatment.			Results of Treatment.						
				Lgth. in mths.	Dose Range c.c.	Total c.c.	Bacillary concentration.		Sedimentation Index.	Leprolin Test.	Clinical Changes.	General Condition.	Final Opinion.
							Before	After					
1.	Male 24 yrs.	C-1, N-1	Esters, 4 yrs.	6	5-50	545	M/1	M/1	45-22-12-20	Weak Positive	Improved	Slightly Improved.	Slight Improvement
2.	Male 21 yrs.	C-1, N-1	Esters 1 yr.	6	5-45	530	M/1	M/1+	35-35-41-26-30	Negative	Improved	Improved	Slight improvement
3.	Male 21 yrs.	C-1, N-1	Esters 6 mths.	5	5-30	465	1/10	M/1	53-15-19-10	Weak positive	Lepra reaction induced followed by improvement.	Stationary.	Slight improvement
4.	Male 28 yrs.	C-1, N-2	Esters 2½ yrs.	6	5-50	590	1/10	1/25	53-52-53-52-52	Weak positive	Lepra reaction followed by improvement.	Stationary.	Improved

## TREATMENT WITH FLUORESCEIN. (CONTINUED)

5.	Male 20 yrs.	C-1, N-2.	Esters 6 mths.	6	5-45	550	M/1++	M/1+	53-51-50- 48-50	Positive	Station- ary	Station- ary	No Benefit.
6.	Male 21 yrs.	C-1, N-1.	Nil.	5	5-40	370	M/1+	M/1+	7-8-7-17- 8-17	Weak positive	Station- ary	Station- ary. Developed jaundice.	No Benefit.
7.	Male 42 yrs.	C-2, N-1.	Esters 4 mths.	6	5-40	550	M/1+	M/1+	14-39-30- 28-34	Weak positive	Lepra react- ion, followed by im- prove- ment.	Station- ary.	No real benefit.
8.	Male 24 yrs.	C-2, N.1.	Nil.	4	5-30	300	M/1 +++	M/1	10-6-7-11- 2	Weak positive	Much improved	Improved.	Improved. (absconded before end of treat- ment.
9.	Male (A.I.) 28 yrs.	C-2, A-1	Esters 3 yrs.	6	5-30	530	M/1 ++	M/1	27-24-30- 19-34	Negative	Station- ary	Station- ary. Dimness of vision.	No Benefit.

## TREATMENT WITH FLUORESCEIN. (CONTINUED)

10.	Male 27 yrs.	C-2, N-1.	Esters 1 yr.	6	5-50	500	M/1 +++	M/1+	29-31-29- 25-32	Positive	Slightly improved	Station- ary.	No real benefit.
11.	Male 31 yrs.	C-2, N-1.	Esters 5 yrs.	4	5-50	310	M/1	M/1 +++	30-25+19+ 27	Negative	Stat- ion- ary.	Station- ary	No benefit.
12.	Male 35 yrs.	C-2, N-1	Esters 3 yrs.	6	5-50	550	M/1+	M/1+	35-40-30- 20-25	Weak positive	Stat- ion- ary.	Station- ary	No benefit.

Average dose was 20 - 30 c.c. once a week.

## TREATMENT WITH BONNEY'S BLUE.

No.	Case.	Type.	Previous treatment.	Treatment.			Results of Treatment.						
				Lgth in mths.	Dose Range c.c.	Total c.c.	Bacillary concentration.		Sedimentation index.	Serum Formalin Index.	Clinical Changes.	General condition.	Final Opinion.
							Before	After					
1.	Male 22 yrs.	C-1, N-1.	Fluorescein for 6 mths. Esters 4 mths.	5	1-11	192	M/1+	M/1	5-14-14-6	0-1-1-0	Slightly improved	Stationary	No real benefit
2.	Male 25 yrs.	C-1, N-1.	Esters 5 yrs.	6	1-12	261	M/1	M/1+	7-9-9-8	0-0-0-0	Stationary.	Stationary.	No real benefit.
3.	Male 30 yrs.	C-2, N-1.	Nil.	5	1-12	165	M/1+	M/1+	52-49-28	0-5-5-	Improved	Improved.	No real benefit.
4.	Male 32 yrs.	C-2, N-1	Nil.	5	1-12	200	M/1	M/10	45-40-34	2-5-5	Stationary	Improved.	No real benefit
5.	Male 21 yrs.	C-1, N-1.	Fluorescein 4mths. Esters 4 mths.	5	1-12	150	M/1	M/1	44-32-40	1-2-3	Stationary	Worse	No benefit



TREATMENT WITH BONNEY'S BLUE. (CONTINUED)

6.	Male 35 yrs.	C-2, N-1.	Nil.	6	1-12	240	M/1+	M/1	5-33-20-11	0-2-2-1	Stationary	Improved.	No Benefit.
7.	Male 30 yrs.	C-2, N-1.	Fluorescein 5 mths. Esters 2½ yrs.	4	1-12	200	M/1+	1/10	35-45-30	2-2-1	Improved	Stationary.	Slight Benefit.
8.	Male 28 yrs.	C-1, N-1.	Fluorescein 5 mths. Esters 2 yrs.	6	1-10	210	M/1	M/1	30-35-18- 26	1-2-2-1	Improved	Stationary.	No Benefit.

Average dose of 6 c.c. twice weekly well tolerated.

## TREATMENT WITH METHYLENE BLUE.

No.	Case.	Type.	Previous Treatment.	Results of Treatment.									
				Treatment.			Bacillary concentration.		Sedimentation Index.	Serum Formalin Index.	Clinical changes	General Condition	Final Opinion.
				Lgth. in mths.	Dose Range c.c.	Total c.c.	Before	After					
1.	Male (A.I.) 23 yrs.	C - 2.	Nil.	4	1-10	120	M/1+	M/1+	17 - 45	2 - 2	Improved	Improved	Slight benefit
2.	Male (A.I.) 22 yrs.	C-2, N-1.	Esters 1 yr.	4	1-10	100	M/1++	M/1+	29 - 20	1 - 1	Much Improved	Stationary. Eye pain and dim vision	No real benefit.
3.	Male (A.I.) 20 yrs.	C-3	Esters 3 yrs.	2	1-5	52	M/1++	M/1++	15 - 40	3 - 1	Nodules breaking down & throat lesions	Worse iritis.	Worse.
4.	Female 37 yrs.	C-2, N-1.	Esters 2 yrs.	4	1-10	115	M/1+	M/1+	64 - 65	4 - 5	Stationary. Oedema of hands.	Stationary, but says feeling better.	No real benefit.

## TREATMENT WITH METHYLENE BLUE. (CONTINUED.)

5.	Female 41 yrs.	C-2, N-1.	Esters 1½ yrs.	4	1-10	92	M/1	M/1+	54 - 62	4 - 5	Stationary.	Stationary iritis.	No Benefit.
6.	Male 20 yrs.	C-2, N-1.	Nil.	4	1-12	137	M/1	M/1	28-32	0 - 4	Slightly improved	Improved	No real benefit.
7.	Male 35 yrs.	C-2, N-1.	Nil.	4	1-12	182	M/1	M/1+	25 - 36	0 - 4	Stationary	Slightly improved	No benefit.
8.	Male 18 yrs.	C-2, N-1.	Esters 6 mths.	3	1-12	120	M/1+	M/1+	48 - 48	4 - 5	Improved Lepra re- action later	Improved	No real benefit.
9.	Male 20 yrs.	C-2, N-1.	Esters 3 mths.	4	1-10	128	M/1 ++	M/1 ++	29 - 37	0 - 0	Improved	Improved	No real benefit.

TREATMENT WITH METHYLENE BLUE. (CONTINUED)

10.	Male 18 yrs.	C-3, N-1.	Esters 4 mths.	4	1-10	126	M/1 ++	M/1+	48 - 49	4-4	Stationary	Stationary.	No benefit.
11.	Male 20 yrs.	C-3, N-1.	Nil.	4	1-10	125	M/1 ++	M/1+	49 - 55	2-4	Stationary	Stationary.	No benefit.

Notes:- 1. Average dose tolerated was 5 c.c. twice weekly.

With larger doses patients complained of dizziness and burning pain in the eyes and fever.

2. In several cases iritis was induced.
3. The dye showed selective staining of leprosy areas.

TREATMENT WITH ACRIFLAVINE.

Results of treatment.

NO .	Case.	Type.	Previous Treatment.	Treatment.			Bacillary concentration.		Sedimentation Index.	Serum Formalin Index.	Clinical Changes.	General Condition.	Final Opinion.
				Lgth. in mths.	Dose Range c.c.	Total c.c.	Before	After					
1.	Male 20 yrs.	C-1.	Nil.	5	1-10	173	M/1	M/1	6 - 13 - 6	0 - 1-0	Improved	Stationary.	No real benefit.
2.	Male 28 yrs.	C-2, N-1.	Nil.	6	1-10	288	M/1	M/1+	37-33-46-2	0-3-3-3	increase of nodulation & infiltration	Stationary.	Worse.
3.	Female 30 yrs.	C-2, N-1.	Nil.	6	1-10	268	M/1+	M/1+	42-42-46-40	1-3 -5-3	much improved	Stationary.	No real benefit.

Average weekly dose was 5 c.c.

No. 1. had to stop after 5 months on account of vomiting after injection.

Nos. 2 and 3. had no complaints.

## THE PREPARATION OF ETHYL ESTERS.

The ethyl esters may be prepared by either the hot or cold method. The method here described is the hot process.

### Esterification.

Into a 3000 c.c. flask pour 1300 c.c. of 95% alcohol and 75 c.c. of pure sulphuric acid ( S.G. 1.84) and when these are thoroughly mixed add 1090 c.c. of pure hydnocarpus wightiana oil. After mixing the oil falls to the bottom of the flask. Heat on a water-bath with a reflux condenser attached to the flask so that there is just a steady drip of condensed alcohol from the bottom of the condenser. The esters when formed are a light brown oily fluid which rises to the top of the fluid in the flask. They form in about 3 to 4 hours. Having noted the time needed for separation to start, say, 4 hours, allow an equal time of 4 hours for completion of esterification before cooling.

### Test for complete esterification.

Mix 2 c.c. of the esters with 2 c.c. of 95% alcohol. If esterification is complete, complete solution of the esters occurs with a little shaking and without heat.

### Washing esters and neutralising free acid.

Pour the esters into two separating funnels of 2000 c.c. capacity. Run off the lower layer, leaving the esters. About 70% of the fluid thus removed is absolute alcohol which can be recovered by redistillation. Wash the remaining esters with equal quantities of cold water. Next add an equal quantity of hot caustic soda 1% solution (filtered). This forms a very thick emulsion. At once fill up the funnels with boiling water, add to each funnel about 4 drachms of common table salt, place the stopper in the funnel and without shaking rotate the funnel in the horizontal position to bring the salt into contact with the emulsion. Rotate for one minute, then gently replace the funnel in stand and leave until separation is complete. This may take 1 to 2 hours. If separation is slow it can be accelerated by running out what water has separated at the bottom of the flask and refilling with boiling water. After complete separation the esters should be washed three times with boiling water. At the end of this process the esters are light brown and opaque because of a considerable amount of water remaining in emulsion.

### Steaming.

The irritating volatile impurities can be largely removed by steaming, by passing steam through the esters for two hours. This is best done between washing and drying as it introduces water into the esters. Steaming makes the esters lighter in colour and reduces the irritating smell of the esters, and should be continued until this smell has disappeared. The water introduced by steaming can be removed by a separating funnel.

### Drying.

The esters are heated over boiling water, for which a double saucepan is very convenient. After about 1/4 hour's heating the top pan containing the esters is removed and allowed to stand for a few minutes. Nearly all the water settles to the bottom and the esters at the top can be gently poured off. They are again heated in the double saucepan and the process of water removal repeated as often as is necessary. Within half-an-hour of the heating being started the esters can be rendered perfectly free from water, the small amount of water left at the end being driven off as steam. The esters should finally be clear and free from emulsion, though there may be fine particles in suspension.

### Filtration.

The dried esters are now allowed to cool before being filtered. A large funnel and filter paper one foot in diameter greatly accelerates filtration. The resulting esters are light brown in colour and perfectly clear.

By the method here outlined 1150 c.c. of esters are obtained from 1090 c.c. of oil. Of the 1300 c.c. of alcohol used, 60% can be recovered by redistillation and used again.

### Methods of testing esters.

#### I. Test for complete esterification.

The esters should be completely soluble in an equal amount of 95% alcohol, without heating.

#### 2. Test for free acid.

The suitability of esters for injection

depends very largely on the amount of free acid they contain. The amount present can be estimated by titration, the esters being dissolved in absolute alcohol. Since absolute alcohol is itself usually acid in reaction it must first be neutralised. Place 10 c.c. absolute alcohol in a flask and using phenolphthalein as indicator, run in sufficient N/20 sodium hydroxide solution to just neutralise the alcohol. Now dissolve in the alcohol 5 c.c. of esters. Repeat the titration with the N/20 sodium hydroxide until the solution is again just neutralised. The amount of N/20 sodium hydrate required to neutralise 5 c.c. of esters should be less than 0.5 c.c. If more than this is required then further washing and neutralisation of the esters by caustic soda is necessary. If esters are prepared by the above method only 0.2 c.c. of N/20 sodium hydrate is required to neutralise 5 c.c.



RESULTS OF 1045 WASSERMANN REACTIONS

AND 332 KAHN TESTS.

(Percentage Positive).

	N-1	N-2	C-1	C-2	C-3	Average.
W. R.	25%	27%	45%	59%	70%	45%
KAHN	7%	18%	35%	48%	51%	32%

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RESULTS OF ANTI-SYPHILITIC TREATMENT  
IN 101 CASES TREATED WITH NOVARSENOBILLON.

Type.	Number of cases treated.	Number of courses of N.A.B. required to render W.R. negative.	Amount of N.A.B. required to render W.R. negative.	Average. Courses	N.A.B
N-I	12	I	3.15 gms.		
	6	2	6.3 gms.		
	18			2	6.3 gms.
N-2	4	I	3.15 gms.		
	I	2	6.3 gms.		
	5			2	6.3 gms.
C-I	42	I	3.15 gms.		
	II	2	6.3 gms.		
	2	3	9.45 gms.		
	I	4	12.6 gms.		
	I	5	15.75 gms.		
	57			2	6.3 gms.
C-2	15	I	3.15 gms.		
	2	2	6.3 gms.		
	2	3	9.45 gms.		
	19			2	6.3 gms.
C-3	2	2	3.15 gms.	2	6.3 gms.
Total.	101.			2	6.3 gms.

GENERAL DIET GIVEN TO PATIENTS IN THE  
LADY WILLINGDON LEPER SETTLEMENT.

<u>Food.</u>	<u>Amount</u> in oz.	<u>Proteins</u> in gms.	<u>Fats</u> in gms.	<u>Carbohy- drates</u> in gms.	<u>Calories</u>	<u>Vitamins</u>
Rice (unpolished)	18	33.12	3.96	469.98	2052	Bx
Dhall	6	39.0	5.94	97.2	600	Ax Bxx
Vegetables	8	3.68	-	22.0	108	AxxBxxCxx
Ghee (fat)	1/2	-	11.55	-	104	Axxx Dx
Curd (milk)	15	12.75	2.1	20.4	150	Ax Bx Cx
Onion	1/2	0.18	0.01	1.53	7	BxxCx
Tamarind	1/2	0.2	-	4.45	18	Bx Cx
Curry stuff	1/4	-	-	-	-	-
Salt	I	-	-	-	-	-
		88.93	23.56	615.56	3039	
Less 10% waste		8.9	2.35	61.56	304	
<u>Total.</u>		<u>80</u>	<u>21</u>	<u>554</u>	<u>2735</u>	

Glucose fatty-acid ratio

G: F.A. - 10 : 1

PATIENTS TREATED AT LADY WILLINGDON LEPRO SETTLEMENT.

From July 1925 to September 1935.

	Discharged.	At present under treat- ment.	Total.
Men.....	993	354	1347
Women.....	143	104	247
Boys (under 15).	223	179	402
Girls (under 15).	86	48	134

Distribution by caste.

Hindus.....	963	441	1404
Brahmins.....	46	24	70
Muslems.....	124	51	175
Christians.....	174	61	235
Out-casts.....	106	69	175
Anglo-Indians.....	32	39	71

Classification.

N1.....	518	174	692
N2.....	328	89	417
N3.....	...	5	5
C1.....	289	162	451
C2.....	217	186	403
C3.....	93	69	162

Results of Treatment.

Arrested without deformity	174
Arrested with deformity	295
Improved	352
Stationary or worse	492
Died	132

Persons treated	1445	685	2130
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CLASSIFICATION OF 2130 PATIENTS TREATED.

<u>Type.</u>	<u>Discharged.</u>	<u>Remaining.</u>	<u>Total</u>	<u>Percentage.</u>
N-1	518	174	692	32.5%
N-2	328	89	417	19.5%
N-3	. . .	5	5	0.2%
C-1	67	37	104	5.0%
C-2	56	40	96	4.5%
C-3	28	13	41	2.0%
C-1 N-1	180	102	282	13.5%
C-1 N-2	42	23	65	3.0%
C-2 N-1	117	110	227	10.5%
C-2 N-2	44	36	80	4.0%
C-3 N-1	41	40	81	4.0%
C-3 N-2	24	16	40	2.0%
<u>Total</u>	<u>1445</u>	<u>685</u>	<u>2130</u>	

RESULTS OF TREATMENT OF 1445 PATIENTS.

	NI	N2	CI	C2	C3	Total	Percentage.
Arrested with- out deformity.	144	-	25	5	-	174	12%
Arrested with deformity.	129	85	54	22	5	295	20%
Improved.	120	42	94	75	21	352	24%
Stationary or worse.	112	155	106	82	37	492	34%
Died.	13	46	11	41	21	132	9%

Results of Treatment of 2130 Patients.

Disease arrested	22%
Improved	17%
Stationary or worse	23%
Died	6%
Still under treatment	32%

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LENGTH OF TREATMENT REQUIRED BY 469

DISEASE-ARRESTED PATIENTS.

Type.	<u>ADULTS.</u>		<u>CHILDREN.</u>		<u>TOTAL.</u>
	Number arrest- ed.	Average time in months.	Number arrest- ed.	Average time in months.	Average time in months.
N-1	134	22	129	24	23
N-2	76	30	9	41	36
C-1	55	28	24	39	34
C-2	25	37	2	54	46
C-3	4	49	1	36	43
Total	294	33	175	39	36

RELAPSED CASES.

Case No.	Arrested without Deformity.				Arrested with deformity.				Average time between discharge and relapse.		Type on Relapse.	
	Total discharged.	Total relapsed	Percent relapsed.	Average period of treatment. in mths.	Total discharged	Total relapsed	Percent relapsed	Average period of treatment in mths.	Arrested without deform.	Arrested with deform.	Cutaneous.	Neural.
1	144	12	8%	22	129	13	10%	36	22	11	2	23
2	-	-	-	-	85	7	8%	35	-	26	1	6
1	25	7	28%	38	54	18	33%	40	8	12	23	2
2	5	2	40%	49	22	8	36%	54	13	14	8	2
3	-	-	-	-	5	-	-	-	-	-	-	-
	174	21	12%	36	295	46	16%	41	-	-	34	33

Percentage of relapses.

Skin.....32%  
 Nerve..... 9%  
 All cases.....14%



THE ERYTHROCYTE SEDIMENTATION TEST IN LEPROSY.

0.3 c.c. of a 5 per cent solution of sodium citrate in distilled water is drawn into an all-glass 2 c.c. syringe; 1.2 c.c. of blood is drawn from the patient's vein into the same syringe and a small quantity of air having been taken into the syringe barrel, the blood and citrate solution are thoroughly mixed by reversing the syringe several times, and the mixture is evacuated into a clean test tube. Sedimentation is carried out in 300 m.m. pipettes graduated from above downwards from zero to 100, there being a space 3 m.m. between each mark. The content of the pipettes when filled up to zero is approximately 1 c.c., but a variation of 0.05 c.c. makes no appreciable difference in the results. The pipettes are placed upright in a rack with their points inserted in small holes bored in rubber corks.

One of these pipettes is taken and its upper end is attached to a 10 c.c. syringe by means of a rubber tube. The point of the pipette is inserted in one of the test tubes and, suction being applied by pulling on the piston of the syringe, the blood citrate mixture is drawn up into the pipette to the zero mark. The pipette is then placed in the rack, the point being inserted in a rubber cork which prevents the mixture escaping, and the rubber tube is then disconnected from the pipette.

The top level of the erythrocytes is read off after  $1\frac{1}{2}$  hours and again after  $2\frac{1}{2}$  hours and the average of those readings is taken as the sedimentation index ("S.I."). Thus if the level of the top of the blood cells falls to 10 (30 m.m.) after  $1\frac{1}{2}$  hours and to 20 (60 m.m.) after  $2\frac{1}{2}$  hours the S.I. will be the average of 10 and 20, i.e., 15.

SERUM FORMALIN REACTION.

Withdraw 5 - 10 c.c. of blood and allow to stand in a test tube for 24 hours. Take 1 c.c. of this 24 hours' old serum, place in a small test tube and add one drop of commercial formalin. Readings are taken after 1 hour, 4 hours and 24 hours, and recorded in the following manner, (Solid - serum does not fall out on inverting test tube. Half-solid - serum does not flow on violently shaking test tube.)

Solid in 1 hour or less	...	...	...	6
Half solid in 1 hour	...	...	...	5
Solid in 4 hours	...	...	...	4
Half solid in 4 hours	...	...	...	3
Solid in 24 hours	...	...	...	2
Half solid in 24 hours	...	...	...	1
Unchanged in 24 hours	...	...	...	0

PREPARATION OF LEPROLIN.

(Muir's method.)

Take cuttings from ears and nodules, remove the epithelium, and mince into small portions. Add a small quantity of normal saline and pound well in a mortar. Spread this on a tray and leave to dry for twenty-four hours or more under a fan or in the sun. When as dry as possible the tissue is again thoroughly ground in a mortar so as to form a fine powder. Continue the drying in an incubator for several hours, and then transfer to a dessicator containing calcium chloride, and, if possible, create a vacuum in the dessicator. The fine powder thus obtained must be kept absolutely dry in the dessicator, and will keep indefinitely.

Preparation of the Solution.

Take 0.4 gm. of the powder in a mortar and grind with 10 c.c. normal saline for 15 minutes, adding 2 c.c. saline at a time. Allow this to settle for 5 minutes, and then transfer the supernatant fluid to a test-tube. Add 5 c.c. saline to the residue in the mortar and grind further for 10 minutes. Allow to settle for 5 minutes and again remove the supernatant fluid, adding it to the first. Allow the fluid thus collected to settle for one hour, and then transfer the supernatant fluid to another test-tube. The residue left in the first test-tube is mixed with 10 c.c. saline, stirred, and allowed to settle for 15 minutes and the supernatant fluid removed (A). The residue in the mortar is gradually ground with 15 c.c. saline, allowed to settle for 15 minutes, and the supernatant fluid collected in test-tube (B). After 15 minutes A and B are separated from their respective residues and added to the original fluid collected, and the whole mixture made up to 100 c.c. with saline, and carbolic added to make a concentration of 0.5%. The mixture is well shaken to mix thoroughly and made into  $\frac{1}{2}$  c.c. ampoules. The ampoules are then sterilised by heat and will keep indefinitely.

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Female - aet. 12.

NI case.

Early neural leprosy in a child, showing multiple hypopigmented macules with no sensory changes. This type of case requires very careful watching as such frequently progress to cutaneous leprosy.

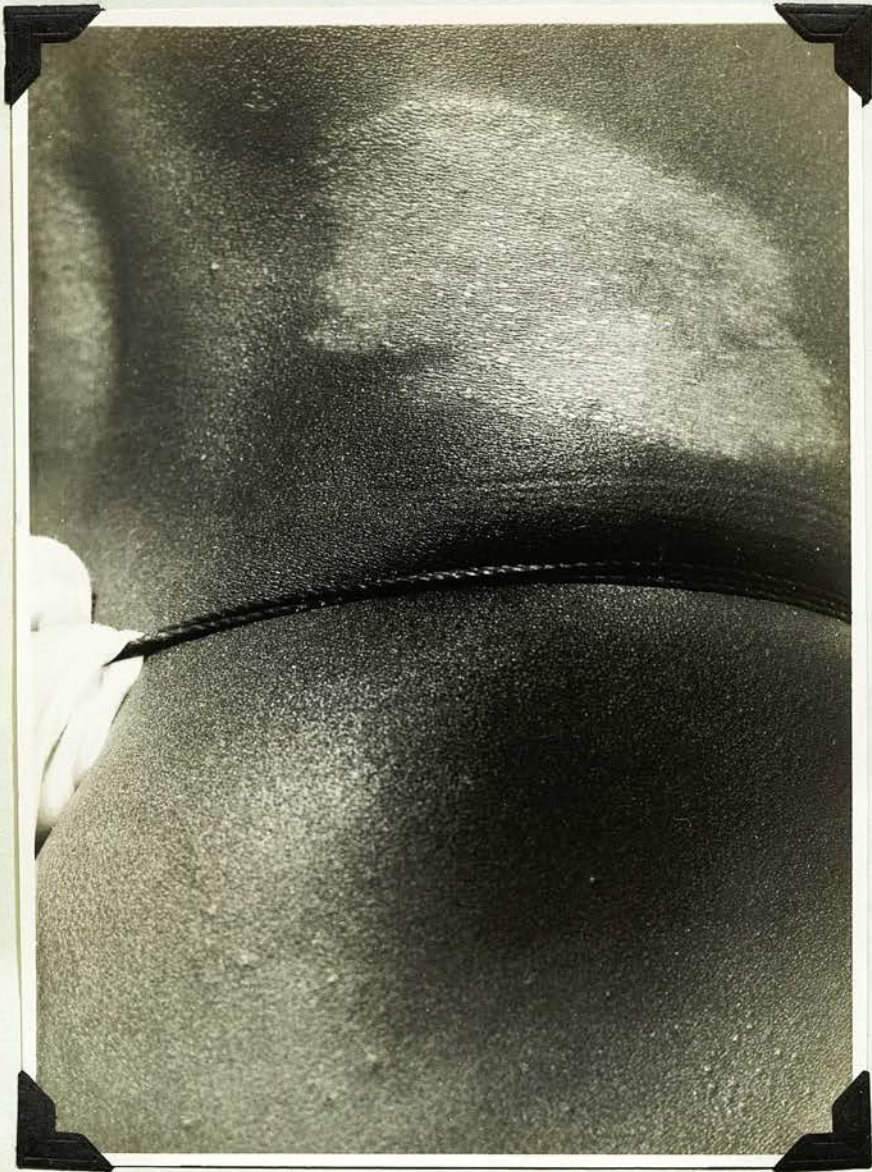
Mother was a cutaneous case.



Male - aet. 12. NI case.

Early neural leprosy in a child. Only signs were the patches of depigmentation on the cheek and chin. These are slightly raised and pinkish but show no sensory changes nor bacilli.

Elder brother has leprosy, and these signs appeared 1 year ago. Prognosis hopeful.



Male - aet. 12. NI case.

Typical neural macule in a child, showing hypopigmentation with rough surface and slightly raised at edges. There are no sensory changes. Macule has been present for 5 years without change but raised upper edge now suggests renewed activity.

Note in bottom right corner an area of goose-flesh appearance. This is often the earliest sign of onset of a neural macule in a child.



Female - aet. 14.      NI case.

Showing a reacting neural macule on back of thigh. Note raised upper edge which is spreading. No anaesthesia present nor nerve enlargement. No bacilli found. This macule has been present for 3 years.



Male - aet. 9. N2 case.

Multiple neural macules in child, been present for 5 years. No sensory changes present. Note healing in centre. Left ulnar nerve was enlarged and tender and ring and little fingers began to contract, so ulnar nerve was stripped of its sheath for two inches. There was no further bending of the fingers and tenderness disappeared.

The disease is at present quiescent but the outlook is not good considering the child's age and the extent of the lesions.



Female - aet 7. N2 case.

Advanced neural leprosy in a young child in the stage of very acute lepra reaction -- unusual in so young a child. Note swollen inflamed macules all over the body. There was no anaesthesia and no bacilli could be found in skin scrapings. A superficial abscess formed under macule on upper left leg. Ulnar nerves were tender.

The first lesion was macule on right cheek 2 years ago.

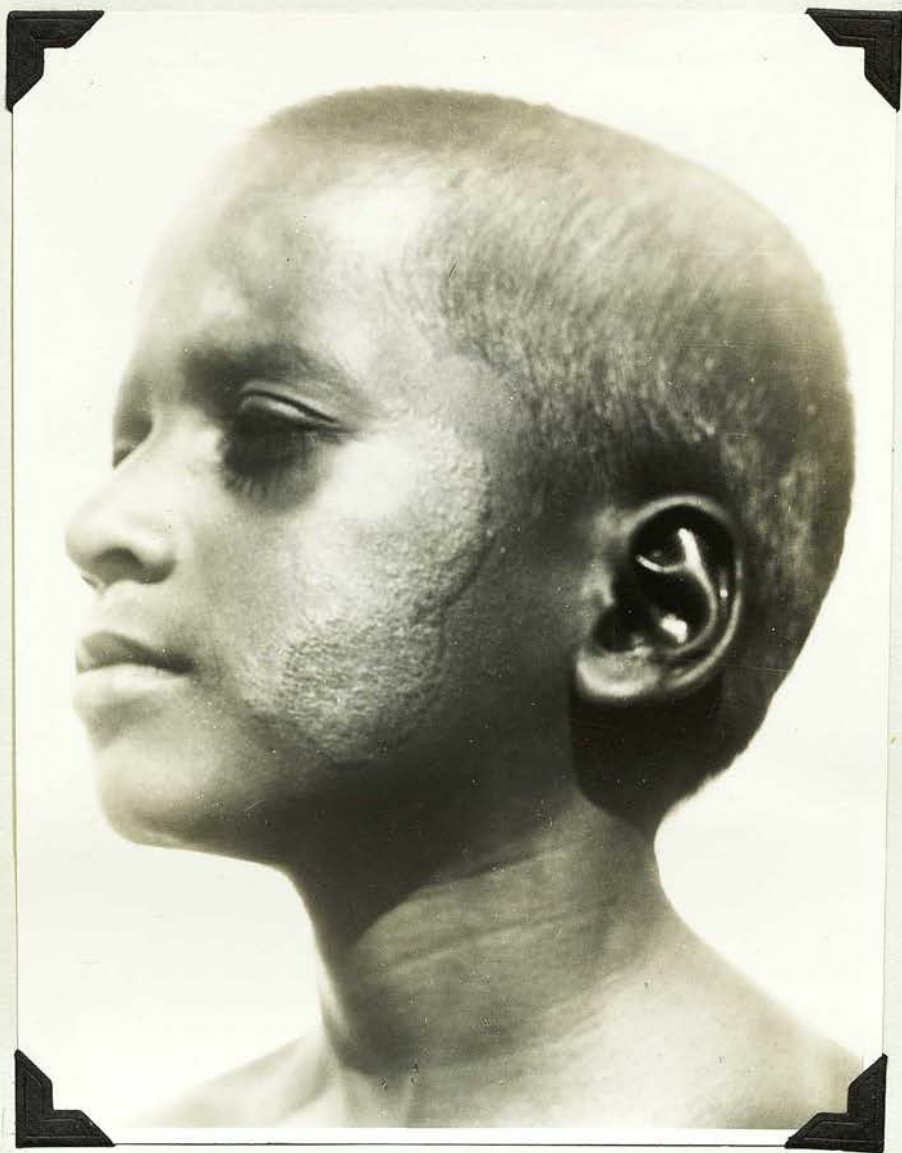




The same case two months later. The reaction has subsided leaving skin over the macules thin, atrophic, and scar-like. The only treatment given was rest in bed with light diet and one course of potassium-antimony-tartrate.

One year later the child showed continued improvement with no further reactions, but the scar like patches will be permanent.





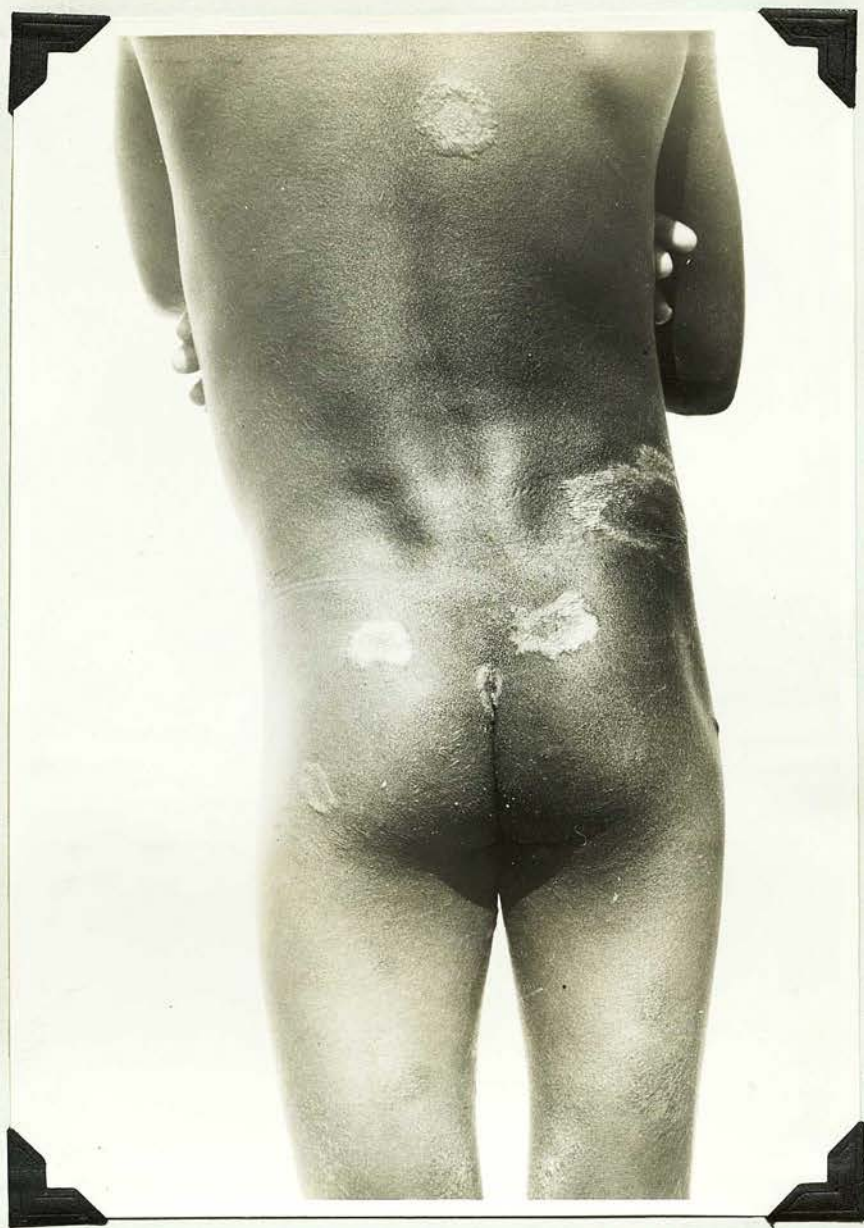
Male - aet. 8.      NI case.

Tuberculoid leprosy.

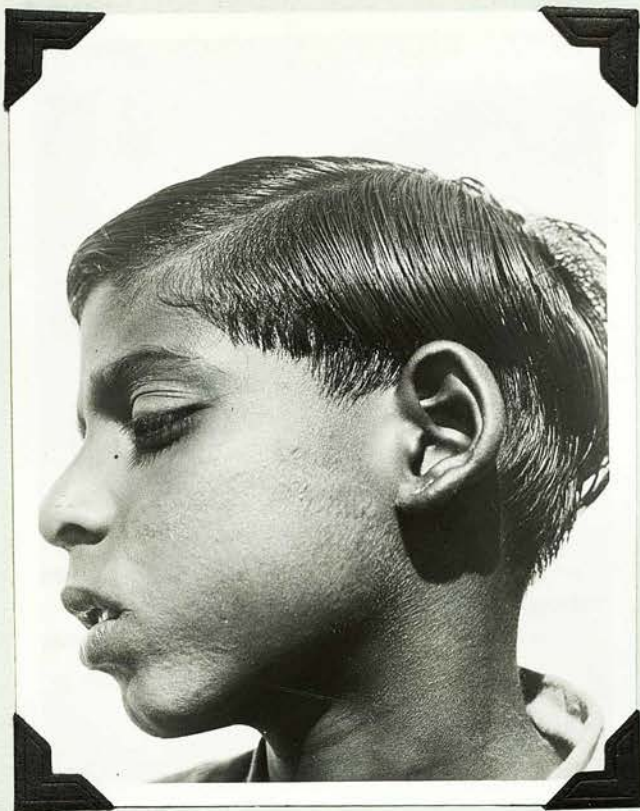
Scattered raised indurated hypopigmented macules, some of which show resolution in their centre. Macule on cheek showed neither analgesia nor anaesthesia but some macules on trunk had superficial anaesthesia. No enlarged nerves found. No bacilli found.

This boy's father had leprosy. The cheek macule appeared first at age of 4 and others gradually since then. He responded well to treatment and after 6 months macules were flattened and pigmentation returning.





Back view of same case, showing raised tuberculoid lesions with healing centres.



Male - aet. 11.      NI case.

Tuberculoid leprosy.

This boy was admitted with a tuberculoid lesion on the cheek similar to that in last case, except that analgesia and anaesthesia of macule were present. He now shows the result of six months treatment, with disappearance of induration and return of sensation in upper half of lesion. Tuberculoid responds well to treatment and usually has a good prognosis. It is probably associated with a high resistance to the disease.



Male - aet. 12. Cl N1 case.

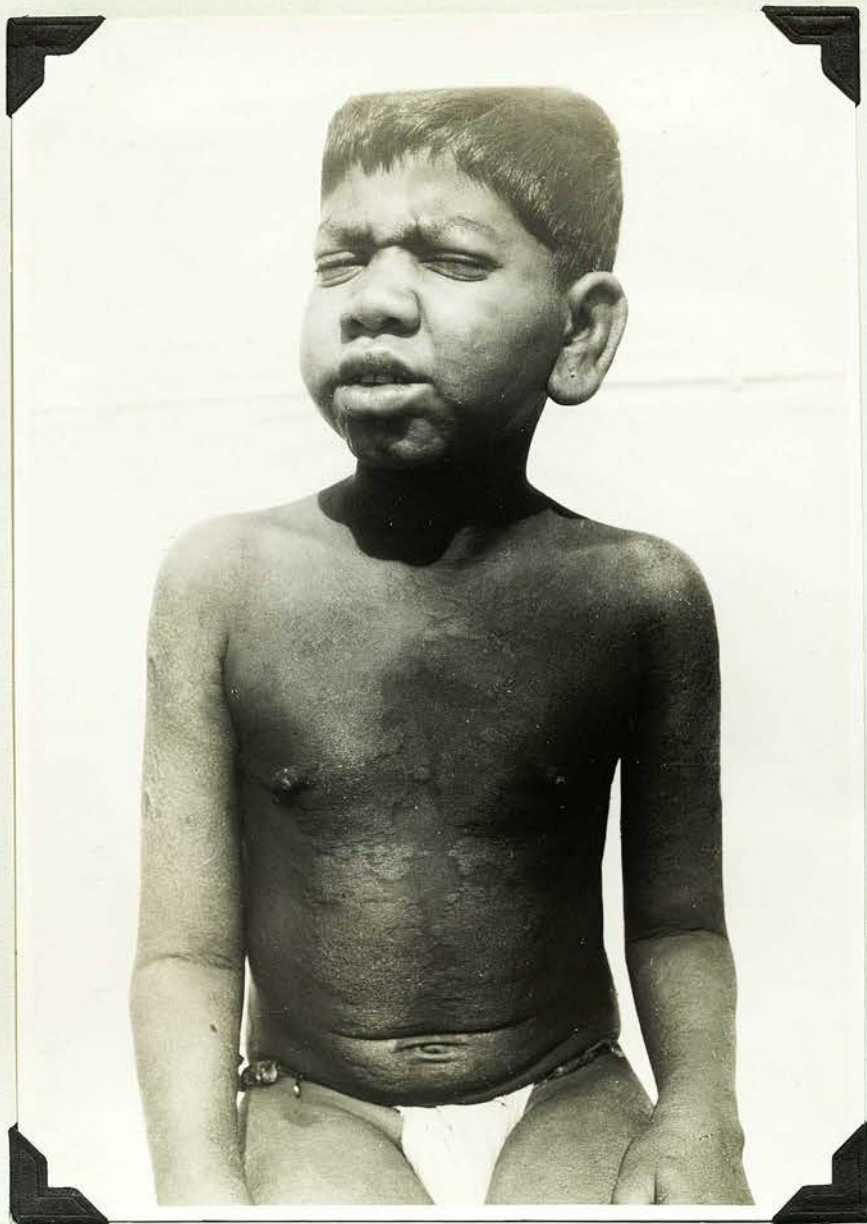
For six years has had multiple hypopigmented macules which showed no sensory changes, and no bacilli found, i.e. neural leprosy. Now macules are becoming erythematous and are spreading and bacilli can be found, illustrating the progress from neural to cutaneous leprosy. Superficial anaesthesia present on hands and feet with enlargement of ulnar nerves. Classified now as Cl,N1. Infection from elder brother.



Male - aet. 11.      C2 case.

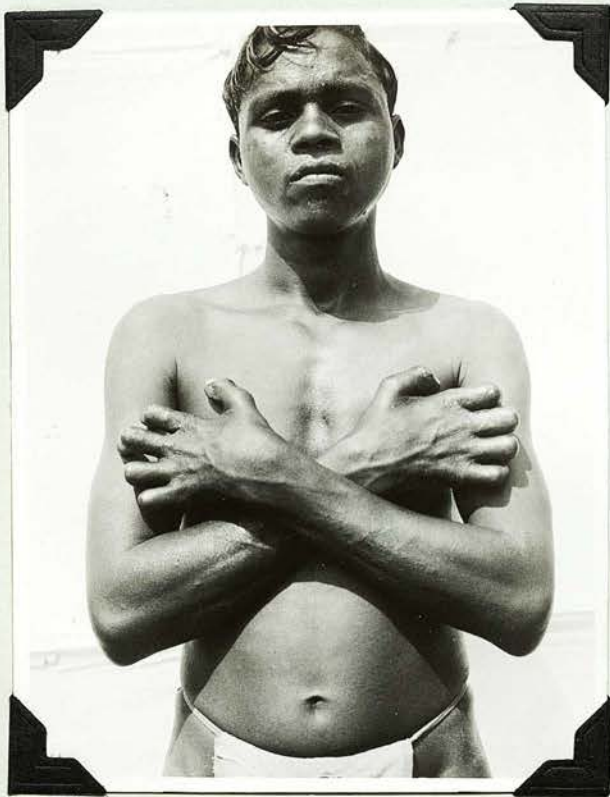
Generalised cutaneous leprosy in a child, of 5 years duration . Note shining appearance of skin of arms and knees, thickening of ears and great enlargement of inguinal glands.

This boy responded well to treatment with Calcium and ostelin vitamin -D, but prognosis is bad.



Male - aet. 8.

First signs noticed 4 years ago. Now has generalised cutaneous leprosy - C2, and is in the stage of an acute lepra reaction with fever. Note thickening and oedema of skin, especially on face and ear, with raised erythematous macules on trunk.



Male - aet. 17.

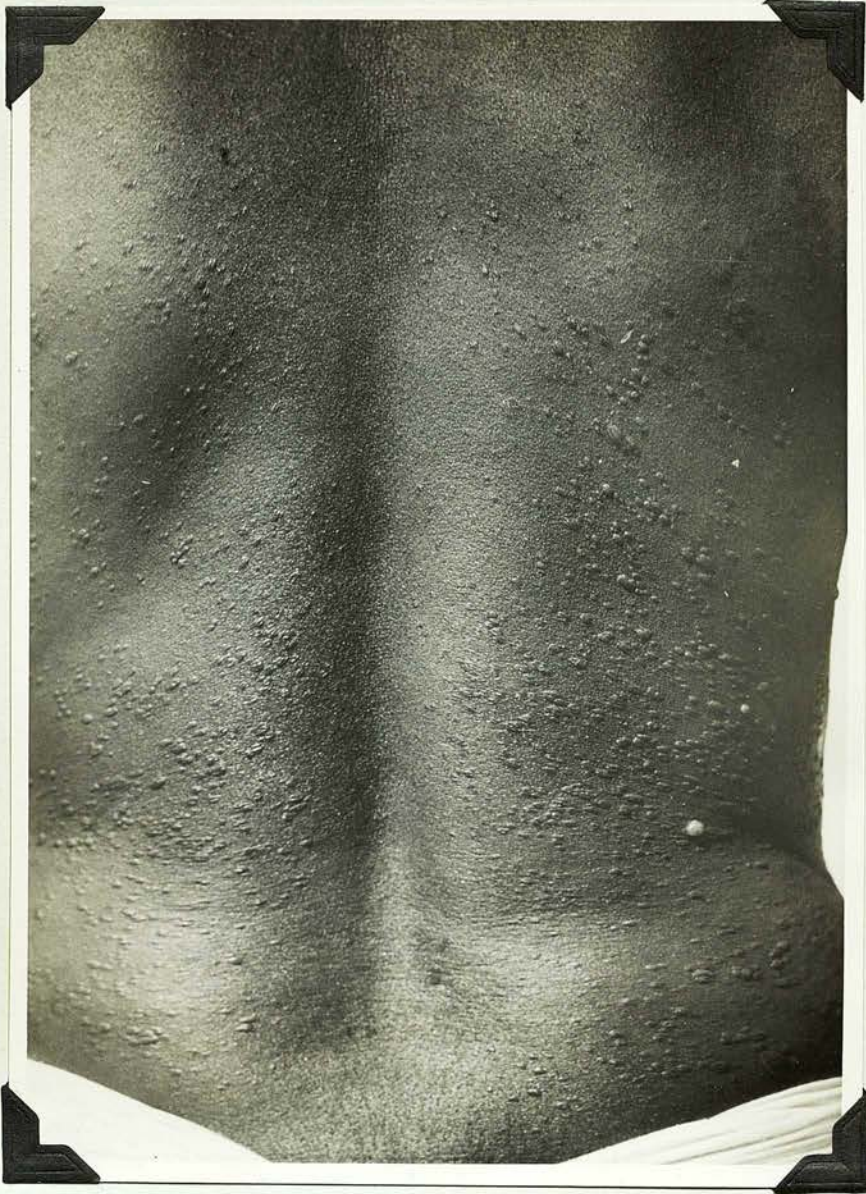
C1, N2 case.

Generalised leprosy of the mixed type with neural signs predominating. Note claw hands, and infiltration of skin of face. Poor response to treatment and outlook bad. First signs appeared 8 years ago, and were anaesthesia and bending of fingers.



Male - aet. 29. C2, N1 case.

Generalised cutaneous leprosy with vesicular lesions, an unusual type. Many bacilli present, and anaesthesia of feet and hands. Has had the disease for 9 years, and response to treatment is slow. Outlook bad.



Back view of same patient.





Male - aet. 40.

C2,N1 case.

Cutaneous leprosy in stage of acute lepra reaction, with swollen, inflamed lesions teeming with bacilli. Note intense activity in the periphery of the lesions while the centres tend to resolution. The large patch over the right shoulder demonstrates well spread by peripheral activity.

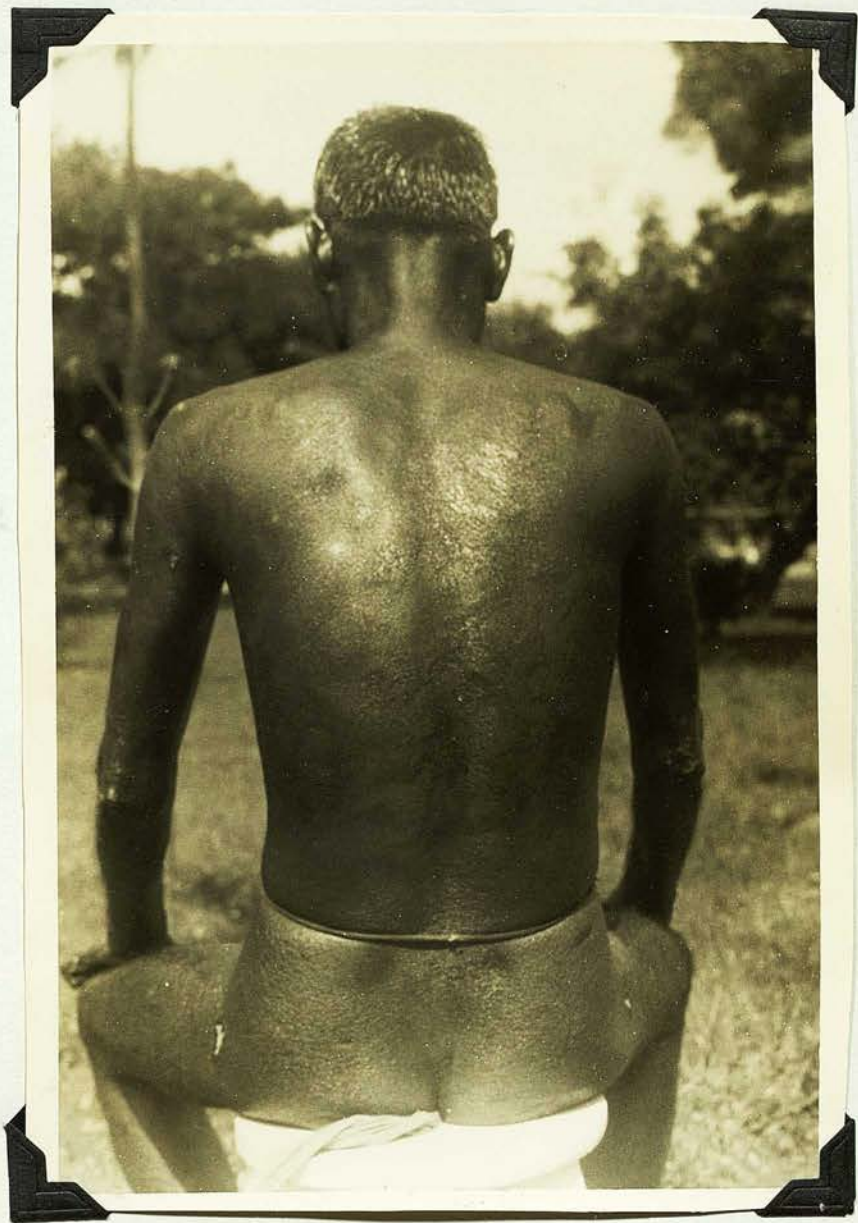
This man has had leprosy for 12 years and the present reaction for one month.



Male - aet. 30.

C2 NI casē.

Generalised cutaneous leprosy with neural lesions also. Patient is having an acute lepra reaction, with fever and intense swelling and inflammation of all the lesions. This state lasted for five months inspite of all efforts to control it and then subsided spontaneously.



Back view of same case five months later,  
when reaction has completely subsided.



Male - aet. 28. C3 case.

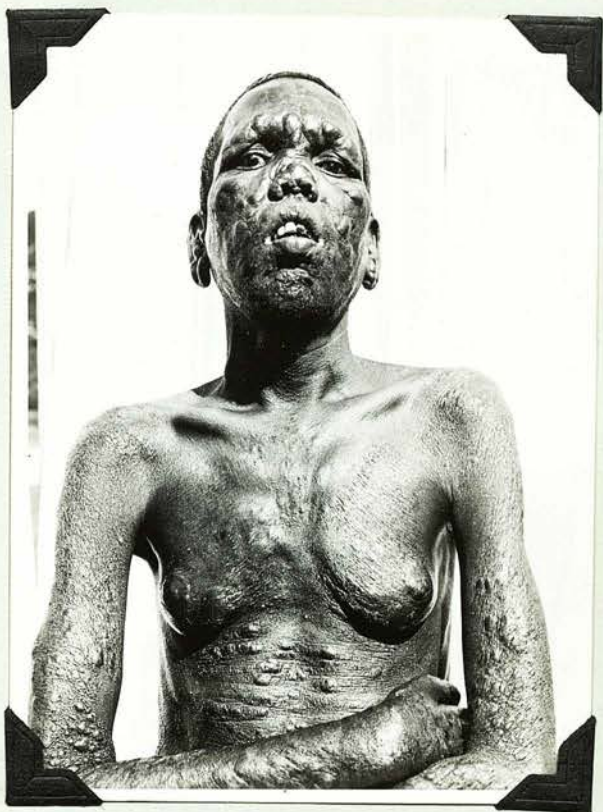
Nodular leprosy.  
Patient has had  
leprosy for 8 years  
but nodules appeared  
only 4 months ago.





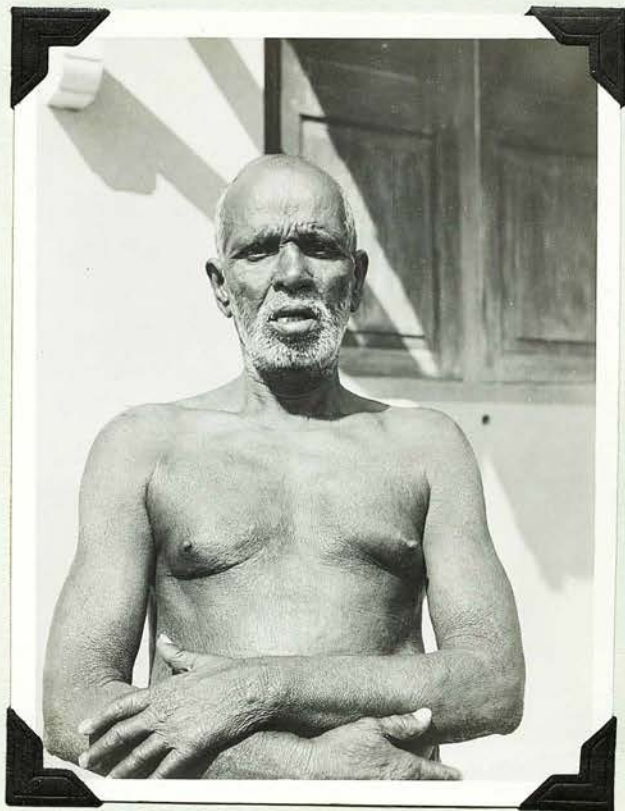
The same patient  
after two years  
treatment. The  
nodules have subsided  
leaving scars, and the  
general improvement  
is considerable.





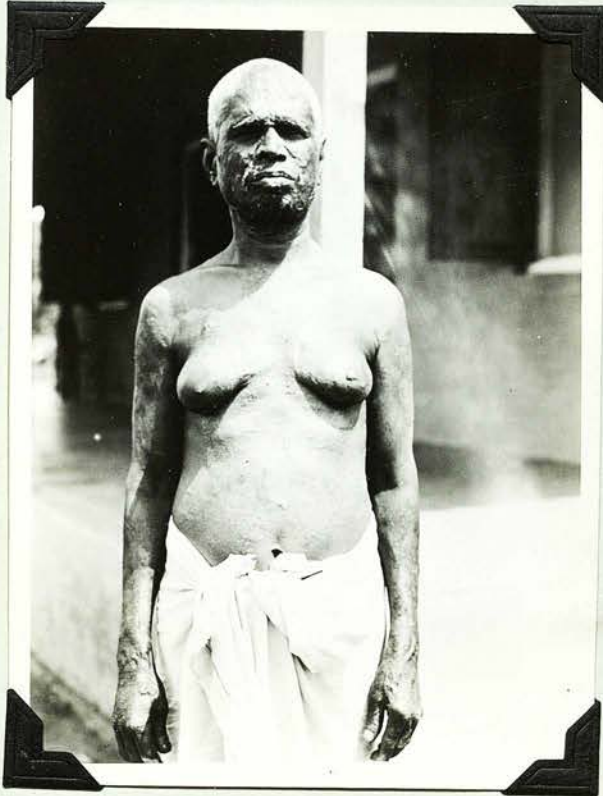
Advanced cutaneous leprosy of many years standing, showing gross disfiguration, nodules, destruction of nasal cartilage, and enlargement of breasts.

C3, N1 case.



Generalised cutaneous leprosy showing  
general infiltration of the skin in which  
numerous bacilli are present everywhere.

C2, N1 case.



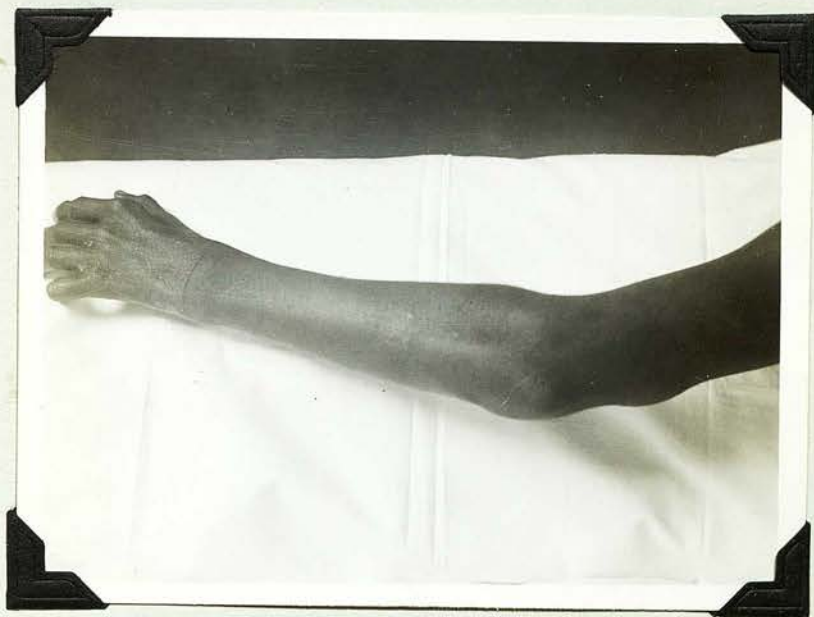
Powell's Sign.

Generalised cutaneous leprosy of many years standing associated with syphilis. Note marked enlargement of the breasts.





Same patient after removal of breasts  
by operation, as described in thesis.



Male - aet. 14. N2 case.

Double abscess of ulnar nerve. Note neural macule on back of hand and bending of little finger, which were associated with anaesthesia.

(Case mentioned in thesis)



Trophic ulceration of the feet in an advanced neural case. Note the sites of the ulcers - the weight-bearing areas.

Incurable & no specific

Earliest record in works Aristotle in 2nd Century -

Crotalus Tom in Lepus siccus (54)

Food & Education (55)

Remedy of Remedies used  
Heavy mineral - antimony, Calcium = (56)

25/ Pegg before [Purley works 57  
orally also]

Charlottesville - more (58)

Qualitative arsenic (38)

Fowler  
Perisulphur. 59