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LEPROSY REVIEW.

VOL. XXVI, No. 2 APRIL, 1955

CONTENTS

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EDITORIAL

LEPROSY AS A Communicable Disease

This subject has been much in the public mind lately, and referred to in the press. The following discussion does not aim at being in any way complete; it merely reflects certain past experience and recent thought, all perhaps rather disconnected, but it does attempt to look at the problem against the background of modern thought on leprosy and of communicable disease in general.

While accepting the general view that in most circumstances the infectiousness of leprosy is of a low order (or perhaps its pathogenicity, for many must get infected without developing the disease) the writer does not subscribe to the view that close contact for long periods is always necessary for transmission; nor does he accept the view advanced by some workers that serious infection is nearly always acquired early in life. Findings in these matters differ widely in different countries, peoples, climates and social conditions. Regional variations in these and in other matters, for example in the incidence, forms and severity of leprosy, are believed to be of importance. It is most unwise to dogmatise about leprosy and anti-leprosy work in one country on the basis of experience in quite different countries.

THE ATTITUDE OF THE LEPROSY WORKER TO LEPROSY

All leprosy workers are faced with the difficulty of attaining and maintaining a rational but human attitude to the disease. A great fear of leprosy seems to be part of the heritage of the human race over most of the world. We all realise that this great fear is largely irrational. We have to try to build up and maintain an attitude to leprosy which is reasonable. To do this is not easy; and even when we think we have done it, we find how easy it is for our thoughts and actions to be influenced by factors operating quite outside the realm of reason.

There have been a few leprosy workers who have reacted so violently against the traditional view of leprosy as highly communicable, that they have ostentatiously discarded most if not all of the ordinary precautionary measures in dealing with patients; but even such people sometimes betray the fact that the deep-rooted fear has only been suppressed and not eradicated. At the other extreme there have been and are still some leprosy workers who have adopted extremely rigid precautions in dealing with

leprosy patients, with rigid segregation, and the use of gowns, masks, gloves, boots and antiseptics, and the avoidance of all direct and also indirect contact. The writer could relate experiences indicating how precautions can be carried to ridiculous extremes.

Most of us have adopted a position somewhere between these two extremes; it would appear most unwise to try to lay down just what precautions are necessary. Each worker must decide for himself, and he will be guided by the experience of others, by his own experience, and also by the circumstances in which he is working; and when he has determined his own policy he must not be surprised if other workers do not share it entirely.

Even so, another matter sometimes operates. Most leprosy workers have taken up their work partly or largely from humanitarian motives; they strive to help those with leprosy in every way, physically, mentally and spiritually. While realising that measures of personal prophylaxis are justified, they nevertheless may sincerely feel that the adoption of certain measures erects a barrier between themselves and their patients, which will make it difficult or impossible to do the work they want to do. Such an attitude commands respect.

The writer will never forget visiting the house of a European patient in a tropical leprosarium and, unprotected, shaking hands with him. The patient was quite overcome, and explained that previous visitors for several years had avoided all contact with him. The untouchability of the patient with leprosy can be a terrible thing; some leprosy workers feel it their duty to mitigate this burden, even at some very slight personal risk.

LEPROSY AND THE PUBLIC AT LARGE

Here again we face the difficulties caused by ignorance and irrational fear. It should be worth while to examine the modern trends in dealing with communicable diseases in general.

A recent book, "Modern Concepts of Communicable Disease," by Greenberg and Matz, of the New York City Department of Health, is reviewed in a recent number of the American Journal of Tropical Medicine.(1) The following paragraphs from this review appear worth quoting in a journal devoted to the study of leprosy, one of the communicable diseases.

"The authors have attempted to illustrate the tendency toward integration and synthesis of modern preventive medicine, curative medicine, social medicine, and public health in the narrow but appropriate field of communicable disease.

" The approach is through a rapid historical summary of concepts: the rise of development of bacteriology and immunology, the accompanying science of sanitary engineering, the discovery of antibiotics and the results of this current emphasis on the last of the epidemiologic triad (host, environment, agent) to receive frontal attack. Changes in control measures to keep pace with newer knowledge are succintly outlined. For example, with reference to the almost obsolete practice of ' placarding ' (of the occurrence of infectious disease) the authors say, ' We have not observed the placard to do more than scare away delivery boys. The discarding of placards by the New York City Department of Health has not arrested the downward trend of communicable disease in the city.' Or this, on nursing: ' Furthermore, the elaborate nursing procedures adopted in former years, the mystic rite of the basin of smelly disinfectant into which the nurse carefully dipped his fingers before leaving the room, the sprinkling of disinfectant solutions on walls and floors, the hanging up of sheets which had been soaked in dilute carbolic solution have all been shown to be elaborate mumbo jumbo. Nursing in communicable diseases is essentially the same as nursing in other diseases.' The movement toward disbanding special hospitals for communicable diseases and opening up general hospitals for their care under certain safeguards is emphasized by devoting a well-written chapter to ' Hospital Management of Communicable Diseases,' in addition to a discussion of home care which brings out the ultimate responsibility of the family for nursing care, and the role of the professional nurse as guide and assistant.'"

What a lot of this " mumbo jumbo," which the authors condemn, has been seen in the past, and is still seen in the handling of patients with leprosy, even occasionally in leprosy institutions which lay claim to a scientific outlook.

On the other hand, it is a great mistake to propagate the idea that the danger of leprosy being communicated is in all circumstances negligible. One point which calls for special emphasis is the infection of children in families.

THE INFECTION OF CHILDREN IN FAMILIES

Workers engaged in attempting to control leprosy in primitive peoples in undeveloped countries often find that people are unable or unwilling to take steps to prevent the infection of even their own children in their own homes. It is often thought that this problem is found only in such peoples and countries. A study of the facts shows, however, that this is not so.

There has recently been published a study of what happened in the first year of life to all the 1,142 infants born in Newcastle during May and June, 1947.[2] There were 44 deaths, 15 of which were considered avoidable. 80 per cent developed an illness during the first year, and of the illnesses 86 per cent was due to infection—general, respiratory, gastro-intestinal, or skin infections.

But the striking report is that on tuberculosis. Between 1 and 2 per cent of children developed tuberculosis infection in the first year; the source was usually a member of the household; the risk of infants exposed to infection in the home contracting the disease in the first year was 1 in 4. The source was usually an infected adult. Two-thirds of the parents of the infected children showed no concern, and had done little or nothing to prevent the spread of infection. No special steps had been taken to make parents aware of the danger to children from cases of tuberculosis in the home. When such things can happen in 1948 in an English city with reasonable prosperity and little unemployment, we must not be surprised if similar things happen with leprosy in people in other countries much less favourably situated.

On the other hand, we should remember that in countries where children are being infected with tuberculosis, as described above, by open cases in families, with little public concern, the mere presence of a single, possibly closed, case of leprosy can cause great public agitation.

LEPROSY IN HOUSES

The leprosy worker's opinion is sometimes asked about the danger of leprous infection in buidings. The *British Medical Journal* in its column " Any Questions? " recently published the following question and answer which may be of some guidance to those of us who have to deal with these matters; for tuberculous infection is perhaps the closest parallel we have to leprous infection:—

T.B. IN HOUSE DUST

Q.—I have heard of several instances of tuberculosis occurring in families occupying houses previously lived in by tuberculous patients. Is the explanation of this that the bacilli persist in the dust and infect the new arrivals? If so, what disinfection should be carried out to make a house safe after a case of open tuberculosis?

A.—Dried tubercle bacilli can survive in the dark up to four or five months, but in unfiltered north room light only for a matter of days. [3] Dust from room surfaces has been said to be an important source of infection [4], but Cruickshank[5] has been

unsuccessful in isolating tubercle bacilli from the dust in two sanatoria and from tuberculosis wards in a general hospital. He estimates that under conditions of desiccation only 1 to 5 per cent of bacilli remain alive after one to three days. It seems improbable that, with ordinary household standards of cleanliness and hygiene, the occupation of a house previously lived in by tuberculosis patients would carry any important risk of contracting the disease. Between 60 and 75 per cent of the population have been infected with tubercle bacillus by the age of 20. A daily bus or tube journey in the rush hours is probably more dangerous than the circumstances mentioned; the latter may well be pure coincidence. To make a house safe after occupation by an infectious case, the floors and flat surfaces can be damp dusted with 5 per cent phenol (which kills tubercle bacilli in five minutes), all windows being left widely open to let in as much air and light as possible. This ventilation may be repeated daily for a week and the rooms then cleaned with a vacuum cleaner. Thereafter there should be very little chance of infection of subsequent occupants.

CONCLUSIONS

To conclude this rather rambling discussion, the writer would re-emphasise the following points. Leprosy is not a disease apart; it is a disease showing resemblances with other communicable diseases, and is influenced by similar factors. In considering leprosy as a communicable disease, it should be viewed in the light of modern concepts of communicable diseases and public health in general. Only in this way can be built up a rational attitude to leprosy which is essential to sound planning and carrying out of anti-leprosy measures, which nevertheless will vary widely with marked variations of the leprosy problem.

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DAPSONE IN DERMATITIS HERPETIFORMIS

In a recent editorial note we discussed the place of diaminodiphenylsulphone (dapsone) in medicine. Since then our attention has been drawn in the fact that it has been widely used for the control of dermatitis herpetiformis following reports on the matter by Esteves and Brandao in 1950 (Trab. Soc. Port. Derm. Vener. 1950, **8**, 209), and Cornbleet in 1951 (Arch. Derm. Syph. 1951, **64**, 684). This information is given in a letter to the *British Medical Journal* by Dr. R. G. Howell (Br. Med. Jour. 1955, **1**, 542).

OBITUARIES

We have with regret to record the death of three Scottish doctors who in the past have been active in anti-leprosy work.

Dr. J. A. Macdonald Smith has recently died in Scotland at the age of 82. As a young man, with very limited educational and other resources, he determined to be a medical missionary and worked hard to that end. He qualified in Edinburgh at the age of 28 and went to India, first under the Presbyterian Church of England and later under the Church of Scotland. He married a woman doctor, became F.R.C.S.(Edin.), and, apart from a period of seven years in England, spent most of his active life as a medical missionary in Bengal. In addition to general medical and surgical work he established a leprosy hospital in Kalimpong, which attracted many patients from long distances in the Himalayan area in which it was situated. He continued to work there until 1939 and then, until 1944, worked in South India. He then retired.

His wife, **Dr. Elizabeth G. Macdonald Smith,** shared his life work and died 18 days later than her husband.

Dr. Donald Dow received his medical training in Glasgow, and from 1933 he was medical superintendent of the Leprosy Hospital, Dichpalli, Hyderabad, Deccan, India, till 1944 when he returned to Scotland for health reasons. He took up a country practice in Angus, and was soon widely known and respected.

He made several contributions to the literature of leprosy; he was a keen student of psychology and theology, and was active as a lay preacher.

He had, it is believed, been considering returning to leprosy work. His death occurred suddenly, while he was travelling, at the age of 49.

LEPROSY IN GAMBIA. WEST AFRICA

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National Institute for Medical Research, London,
and
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Medical Officer of Health, Gambia.

From the Medical Research Council Laboratories and the Medical Department, Gambia.

This paper gives the results of a survey of leprosy in Gambia which was conducted at the same time as a survey of the forms of treponematoses occurring in the country.

Gambia lies between 13′ and 14′ North, and is a narrow strip of territory approximately 10 miles wide on either side of the river Gambia, and extending inland to the East for some 300 miles. The greater part of the country is a British Protectorate which is divided into four approximately equal Divisions, with a total population of 261,564 (Protectorate Census, 1953). There are five main tribes in Gambia, namely the Mandinkos, the Wollofs, the Fulas, the Serahulis, and the Jolas. One village of each of the predominant tribes in each Division of the Protectorate was surveyed. In three of the Divisions, there were four important tribes, and in the fourth Division there were three, i.e. a total of fifteen villages was surveyed. An attempt was made to obtain villages of approximately 400-500 inhabitants (a large village by Gambia standards), but where this was not possible, small neighbouring villages were grouped together. Villages were chosen where at least 90 per cent of the inhabitants belonged to the same tribe, to see if there was any difference in the incidence of leprosy among the tribes. The total number of people examined was 5,890.

METHODS

In each village visited, an examination tent was set up, or a roofless enclosure built for us by the villagers. Every effort was made to see all the inhabitants of the village. The entire skin of the body of each person was examined, and the major nerves

palpated. Cases of leprosy and suspected cases were examined jointly. Owing to time and transport difficulties, skin smears were not made, and the classification of cases rested purely on clinical grounds. The classification employed was the simplest, and consisted of lepromatous cases, tuberculoid cases and cases of doubtful classification. In the absence of skin smears, errors must have arisen here, but an overall picture of the disease in Gambia has been obtained.

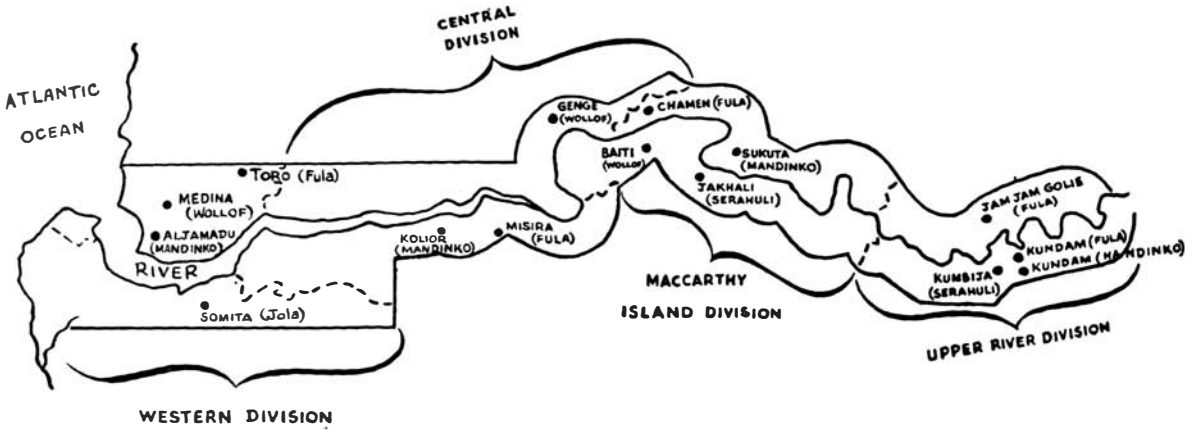
In some villages, the people were afraid that we were going to remove the cases of leprosy from the village, and it sometimes took a lot of explaining before they agreed to come to the examination tent. In other villages, we apparently made a greater impression on the local populace, as cases of leprosy were brought to us from the surrounding villages, but every attempt was made to exclude these. In one village we met the local witch-doctor who was very friendly and regarded us as colleagues. He had three people in his compound with leprosy who were undergoing treatment, but they were not included in the survey figures as they had come to the village during the last year from some considerable distance away. In Upper River Division, we were greatly assisted by an anthropologist who knew the people in the villages intimately, but in the other Divisions some of the villagers may have eluded us. There is no claim to 100 per cent accuracy in the results obtained, and the incidence of leprosy which we have recorded is, if anything, lower than the true figures.

RESULTS

The map shows the villages surveyed with the predominant tribe for each village in brackets. The villages are fairly well distributed over the Protectorate.

The incidences of leprosy found are shown in Table 1. The incidence in the different villages varied from 1% to 3.9%, and the incidence in the different Divisions from 1.4% to 3.1%. The overall figure for the Protectorate was 2.4%. This means that there are approximately 6,000 people in the Protectorate who have leprosy.

The incidence of the different clinical types of leprosy is recorded in Table 2. This shows that 26.6% of the cases were clinically infectious, i.e. there are approximately 1,500 cases of infectious leprosy in the Protectorate.



Showing the villages surveyed with the name of the tribe in brackets

The incidence of leprosy found among the different tribes was as follows:—

Wollof	2.8%
Serahuli	2.5%
Fula	2.4%
Jola	2.1%
Mandinko	1.9%

Analysis of the above figures showed no statistically significant differences in the tribal incidence of the disease.

The incidence in males was 2.5% and the incidence in females 2.2%. There is no statistically significant difference between these two figures.

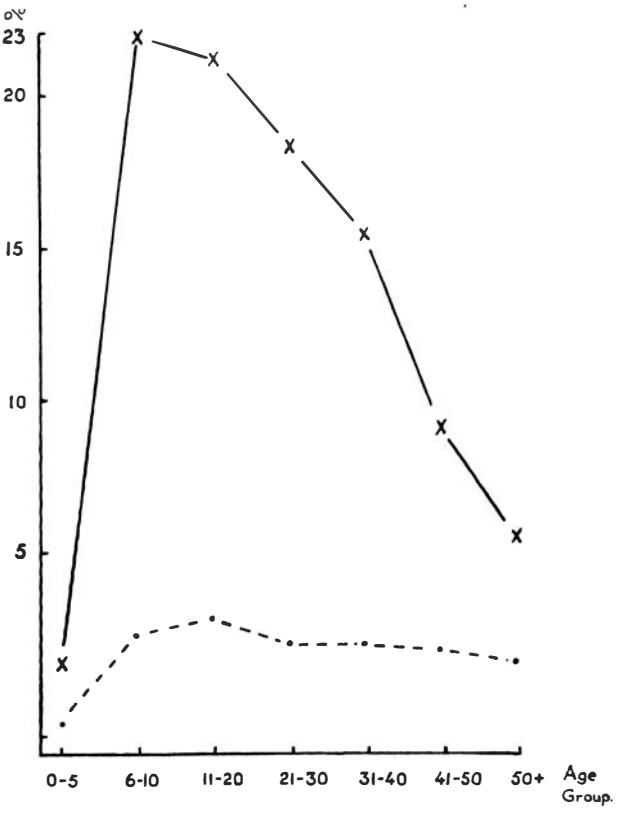
The graph shows the distribution in age groups of the cases of leprosy seen. It also shows the percentage of each age group who were found to have leprosy. Most of the cases of leprosy were between the ages of 6 and 30 years, but the percentage incidence in each age group was remarkably consistent after the first five years of life.

A number of people were seen who have enlargement of one or more of the major nerves without skin signs of leprosy. These were not included in the results as cases of leprosy, but it is likely that these people did in fact have the disease. Ross (1947) stated that in Gambia he found a number of cases of leprosy where the main clinical signs were nerve enlargement with only vague visible cutaneous signs. Lowe (personal communication) has also seen cases in India where nerve enlargement was the only obvious clinical manifestation of the disease.

DISCUSSION

There is very little stigma attached to leprosy in Gambia. Occasionally the Health Department in the main town of Bathurst receives a request for the removal of a person with leprosy from a compound, and leprosy is also used in Gambia as grounds for divorce under Muslim law. There is little attempt at segregation among the people themselves. Occasionally two or three people with leprosy live together, but they are not isolated from village activities. More often, however, the people with leprosy continue to lead a normal life until they are grossly mutilated by the disease. The people are aware of the infectious nature of certain diseases including leprosy, but they show no fear of living in association with leprosy. This is in sharp contrast to Eastern Nigeria where the people are very leprosy conscious and at the first sign of the disease the patient is sent off for examination and treatment.

Ross (1947) surveyed three out of the four Divisions of the Protectorate of Gambia. He reported the incidence of leprosy to be 2.5%. Our figure of 2.4% for spot surveys in the four



Showing the distribution in age groups of the cases of leprosy seen and the percentage incidence of leprosy in each age group.

Divisions is very close to this indeed. Ross recorded that the further up river one went, the higher was the incidence of leprosy. We found this to be the case in the three upper river Divisions, but recorded the second highest incidence in the most Westerly Division.

The different incidences recorded among the different tribes were not statistically significant. It is possible that larger samples might have revealed significant differences.

The incidence of leprosy in Gambia is high, and warrants urgent attention. Until recently, the Gambians did not believe that there was any cure for the disease. However, in the past months a number of cases have been receiving treatment with Dapsone, and owing to the rapid response of tuberculoid cases

the attendance figures for twice weekly treatment have been good. A difficulty which will be encountered in the control of leprosy in Gambia will be the isolation of infectious cases. Voluntary isolation if introduced at present will meet with little success, and only by education will the people realise the value and necessity of this measure. Compulsory isolation is of course out of the question.

The possibility of trying B.C.G. in the control of leprosy in Gambia should be borne in mind. Gambia is a small country, where few measures have been taken against leprosy, where there is a high incidence of the disease, and where isolation will meet with difficulties for many years to come. It is possible that an accurate assessment of the value of B.C.G. in leprosy might be made in Gambia. It is also noteworthy that the incidence of tuberculosis is increasing in Gambia, and B.C.G. introduced for leprosy control might also be of value in the control of tuberculosis.

SUMMARY

1. A spot survey for leprosy was conducted in the Protectorate of Gambia.

2. Fifteen villages of the predominant tribes in the country were surveyed and the incidence of leprosy was found to vary between 1% and 3.9%.

3. The overall incidence in the Protectorate was 2.4%.

4. The differences in the incidence of leprosy among the different tribes were not statistically significant.

5. It is suggested that Gambia might be a suitable place to assess the value of B.C.G. in the control of leprosy as:—

(a) Gambia is a small manageable country.

(b) So far there have been few measures taken against leprosy.

(c) There is a high incidence of the disease.

(d) Isolation of infectious cases will meet with considerable opposition.

(e) The incidence of tuberculosis is increasing in Gambia, and B.C.G. measures may also be of value in the control of this disease.

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ACKNOWLEDGMENTS

We are grateful to the Director of Medical Services, Gambia, who encouraged this investigation; to the Director, Medical Research Council Laboratories, Gambia, for providing facilities; to the Gambia Oil Seeds Marketing Board for kindly providing a launch; to the Senior Commissioner and the Commissioners for help and co-operation; and to Mr. D. P. Gamble for his assistance in the villages.

TABLE 1

THE INCIDENCE OF LEPROSY IN GAMBIA

Name of Village	*Tribe*	*Population*	*Cases of leprosy* No.	%
UPPER RIVER DIVISION				
Kumbija	Serahuli ...	401	14	3.5
Kundam group ...	Fula	439	17	3.9
Kundam Mandinka ...	Mandinko ...	371	9	2.4
Jam Jam Golie ...	Fula	276	6	2.2
Total number examined		1,487	46	3.1
MACCARTHY ISLAND DIVISION				
Jakhali	Serahuli ...	324	4	1.2
Baiti Momadu Fana ...	Wollof ...	608	16	2.6
Sukuta	Mandinko ...	421	4	1.0
Chamen	Fula	411	13	3.2
Total number examined		1,764	37	2.1
CENTRAL DIVISION				
Genge Wollof	Wollof ...	331	7	2.1
Misira	Fula	402	5	1.2
Kolior	Mandinko ...	496	5	1.0
Total number examined		1,229	17	1.4
WESTERN DIVISION				
Somita	Jola	292	6	2.1
Medina	Wollof ...	400	15	3.8
Aljamadu	Mandinko ...	422	15	3.6
Toro	Fula	296	3	1.0
Total number examined		1,410	39	2.8
OVERALL FIGURES FOR PROTECTORATE		5,890	139	2.4

TABLE 2

ANALYSIS OF CASES OF LEPROSY ON CLINICAL GROUNDS

UPPER RIVER DIVISION		
Number of cases of leprosy examined	46	
Number of tuberculoid cases	26	56.5%
Number of lepromatous cases	15	32.6%
Number of doubtful classification	5	10.9%
MACCARTHY ISLAND DIVISION		
Number of cases of leprosy examined	37	
Number of tuberculoid cases	22	59.5%
Number of lepromatous cases	14	37.8%
Number of doubtful classification	1	2.7%
CENTRAL DIVISION		
Number of cases of leprosy examined	17	
Number of tuberculoid cases	14	82.4%
Number of lepromatous cases	2	11.8%
Number of doubtful classification	1	5.8%
WESTERN DIVISION		
Number of cases of leprosy examined	39	
Number of tuberculoid cases	27	69.2%
Number of lepromatous cases	6	15.4%
Number of doubtful classification	6	15.4%
OVERALL FIGURES FOR PROTECTORATE		
Number of cases of leprosy examined	139	
Number of tuberculoid cases	89	64.0%
Number of lepromatous cases	37	26.6%
Number of doubtful classification	13	9.4%

THE EFFECT OF TREATING LEPROMIN WITH LEPROMATOUS SERUM

T. F. DAVEY, O.B.E., M.D., M.SC.

Leprosy Settlement Uzuakoli, East Africa

In an interesting experiment, Ridley[1] found that serum from two patients suffering from lepromatous leprosy, when added to lepromin, tended to inhibit the normal response to the lepromin test in two individuals suffering from tuberculoid leprosy.

If found to apply generally, this observation would have implications which might considerably modify accepted ideas regarding the immunology of leprosy, and Ridley suggested the desirability of confirming and extending his experiment. This paper reports the findings of one such experiment in Nigeria.

LEPROMIN

The lepromin was part of a batch of purified lepromin prepared by a modification of Dharmendra's method,[2] and in this case actually prepared under the personal supervision of Dr. Lowe.* It was in use for routine purposes before, during and after the experiment to be described, and was of proved activity. All the lepromin used in the experiment came from one single batch.

LEPROMATOUS SERUM

Samples of serum from 12 cases of typical lepromatous leprosy were used. It was thought desirable to specify the reaction of the individuals concerned to tuberculin as well as to lepromin, and patients were selected as follows:

Cases 1-3. Patients lepromin-negative and tuberculin-negative, who had had considerable sulphone treatment.

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* (It should be stated that this lepromin was prepared by the method (short treatment with chloroform) designed to give a lepromin with a good late (Mitsuda) reaction, rather than a good early (Fernandez) reaction.
Ridley's work referred particularly to the early reaction.—J. Lowe.)

Cases 4-6. Patients lepromin-negative and tuberculin-negative, who were in the early stages of sulphone treatment.

Cases 7-9. Patients lepromin-negative but tuberculin-positive.

Cases 10-12. Patients formerly lepromin-negative and tuberculin-negative, but who had shown conversion to positive after B.C.G. inoculation.

RECIPIENTS

Each of these 12 samples of serum, when added to lepromin, was injected into 10 individuals whose reaction to lepromin was known. In practice it was found convenient to test two samples simultaneously in the same patient. Sixty recipients were thus sufficient for the whole series of tests. All were leprosy patients, of whom 55 were of tuberculoid type (24 Major, 31 Minor), 3 were indeterminate, 1 was borderline and 1 was lepromatous in type.

CONTROL TESTS

Three control tests were considered to be the minimum acceptable. They were as follows:

1. Lepromin diluted with normal saline in place of serum.

2. Lepromin diluted with serum from a healthy individual who was lepromin negative.

3. Lepromin diluted with serum from a healthy individual who was lepromin positive.

These three control tests were made in all 60 recipients, using the same batch of each for the entire series.

METHOD

Whether the lepromin used in the experiment was being diluted with saline, control serum, or the lepromatous sera being tested, the same technique was followed, the required volume of lepromin being diluted with an equal volume of diluent.

In its subsequent preparation, Ridley's method was followed closely. The samples of diluted lepromin were incubated simultaneously for 1½ hours at 37 C., kept overnight in a refrigerator, and used the following day.

All injections were administered on the same occasion, 0.1 c.c. being injected intradermally on the inner side of the upper arm. Each of the 60 recipients received 5 injections, suitably spaced, as follows, from above downwards.

1. Control: Lepromin plus saline.

2. Lepromin plus a test serum.

3. Lepromin plus another test serum.

4. Control: Lepromin plus lepromin negative serum of a healthy person.

5. Control: Lepromin plus lepromin positive serum of a healthy person.

Arranged in this way, comparison between the test sera and controls presented no difficulty.

The early lepromin reaction was read after 24 and 48 hours.

The late reaction was recorded after 7, 14, 21 and 28 days.

To aid objectivity in assessing the degree of response, a minimum of three qualified observers was used on each occasion, the recorded result being their agreed judgment.

In each recipient, the response to the lepromin-saline mixture indicated the normal reaction of the individual at that time to lepromin in a dosage half that usually employed. This response was the standard with which the other four responses had to be compared.

The results may be summarised as follows:

[In the original manuscript the results are given in detailed tables covering four pages. These are here omitted.—Editor.]

RESPONSE TO LEPROMIN TEST

	Early Reaction			*Late Reaction*		
	Enhanced	Normal	Diminished	Enhanced	Normal	Diminished
1st control (lepromin-saline) (60 persons)	—	60	—	—	60	—
1st lepromatous serum (lepromin and tuberculin negative; much treatmt.) (10 persons)	5	5	nil	nil	10	nil
2nd lepromatous serum (lepromin and tuberculin negative; much treatmt.) (10 persons)	4	6	nil	nil	10	nil
3rd lepromatous serum (lepromin and tuberculin negative; much treatmt.) (10 persons)	3	4	3	1	9	nil
4th lepromatous serum (lepromin and tuberculin negative; little treatmt.) (10 persons)	2	6	2	1	9	nil
5th lepromatous serum (lepromin and tuberculin negative; little treatmt.) (10 persons)	3	6	1	1	9	nil
6th lepromatous serum (lepromin and tuberculin negative; little treatmt.) (10 persons)	3	5	2	1	9	nil
7th lepromatous serum (lepromin negative and tuberculin positive) (10 persons) ...	3	7	nil	nil	9	1
8th lepromatous serum (lepromin negative and tuberculin positive) (10 persons) ...	4	5	1	nil	9	1
9th lepromatous serum (lepromin negative and tuberculin positive) (10 persons) ...	1	8	1	2	8	nil
10th lepromatous serum (lepromin positive and tuberculin positive) (10 persons) ...	7	3	nil	nil	10	nil
11th lepromatous serum (lepromin positive and tuberculin positive) (10 persons) ...	5	4	1	nil	9	1
12th lepromatous serum (lepromin positive and tuberculin positive) (10 persons) ...	3	7	nil	nil	10	nil
2nd control (lepromin neg. normal serum) (60 persons)	25	33	2	7	51	2
3rd control (lepromin pos. normal serum) (60 persons)	25	32	3	15	45	nil

COMMENTS

The results of both early and late lepromin reactions follow the same general pattern, though there are differences in detail. The early reaction is not easy to read in dark-skinned individuals, and in Nigeria the late reaction has proved to be the more reliable.

In this experiment the late reaction yielded results which are quite unequivocal, and can be stated as follows:

1. Out of 120 lepromin tests in which the antigen used was lepromin diluted with an equal volume of lepromatous serum, 111 showed a normal reaction and 9 showed minor degrees of deviation. Out of 120 controls undertaken simultaneously in the same patients, and in which lepromatous serum was replaced by normal serum, 96 showed a normal reaction and 24 showed minor degrees of deviation.

2. Of the 9 abnormal reactions in the test series, 6 showed enhancement of the normal reaction, and 3 showed diminution. Of the 24 abnormal reactions in the control group, 22 showed enhancement and 2 showed diminution.

3. The 9 deviations in the test series were not exhibited by a single lepromatous serum, or by a group of sera, but were distributed through 8 of the 12 sera tested. Duration of treatment, reaction to tuberculin, and even reaction to lepromin itself on the part of the donors thus did not appear to influence the effect of their serum on the lepromin test.

4. With a diminution in response appearing in only 3 out of 120 tests with lepromatous sera, as against two in the same number of control tests, it cannot be considered that any of the 12 lepromatous sera tested had an inactivating action on lepromin.

Similar observations can be made in respect of the early lepromin reaction. Although here deviations were more numerous, they were always of minor degree.

1. Out of 120 test reactions, 66 were normal, 43 showed enhancement and 11 showed diminution. Out of 120 control reactions, 65 were normal, 50 showed enhancement and 5 showed diminution. Thus 54 deviations in the test series compared with 55 in the control.

2. Deviations among the test series were distributed throughout the 12 test groups with no concentration in respect of any single serum or group or sera.

3. No relationship could be detected in the test series between deviations in the early reaction and deviations in the late reaction. No case either of enhancement or diminution in the early reaction reappeared as such in the late reaction.

4. These observations strongly suggest that deviations were non-specific in character.

5. The relatively large number of enhanced early reactions both in the test and control groups is noticeable. It is not surprising. The addition of serum to lepromin inevitably introduces a factor capable of stimulating a non-specific early response.

6. One curious finding was that 6 of the 25 lepromin-positive serum controls exhibiting an enhanced early reaction also exhibited an enhanced late reaction. It is probably without significance.

CONCLUSION

This experiment yielded no evidence of a specific inactivating action on lepromin on the part of 12 samples of serum taken from 12 cases of lepromatous leprosy.

SUMMARY

In order to test the suggestion that the serum of patients suffering from lepromatous leprosy may inactivate lepromin, samples of serum from 12 such patients were added to lepromin, and each tested in 10 individuals. The 12 donors were selected in relation to duration of treatment, reaction to tuberculin, and reaction to lepromin itself. Controls tested in each recipient consisted of lepromin diluted in the same proportion with normal saline, with serum from a lepromin-negative healthy individual, and with serum from a lepromin-positive healthy individual.

Both early and late lepromin reactions yielded similar findings, but as usual in dark skinned individuals, the late reaction gave a clearer picture. Using the reaction to the lepromin-saline mixture as a basis of comparison, out of 120 tests with lepromatous serum, 111 conformed to the normal, and of the 9 deviating results, all of which were small in degree, only 3 exhibited diminution in response. Of 120 control tests with normal serum, 96 gave normal results, 22 showed enhancement and 2 diminution.

All the evidence suggests that deviations were non-specific in character. It cannot be considered that any of the 12 lepromatous sera tested had an inactivating action on lepromin. The duration of treatment, the reaction to tuberculin, and the reaction to lepromin on the part of the donors had no detectable influence on this finding.

ACKNOWLEDGMENTS

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LEPROSY CONTROL IN UGANDA*

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The modern era in leprosy treatment and control dates back thirty years to the preparation of Alepol, a solid compounded from hydnocarpus oil, by Sir Leonard Rogers. That discovery, and Sir Leonard's work with Dr. E. Muir, resulted in an expansion of leprosy services both within and without the British Commonwealth, an expansion which might otherwise have been considerably delayed. The fact that Alepol did not eventually prove superior to the oil and its ester is of little moment. It provided a drug which could be sent to inaccessible places, and overcame what had been the very formidable difficulty of getting bulk supplies from the place of extraction to other countries and continents.

At the same time, public opinion was changing about the advisability or practicability of compulsory segregation. Isolation of all recognisable patients had been the world-wide traditional approach to the prevention of the disease. Nations differed only in the vigour with which they applied it. Apart from the inhumanity of the method, the results achieved did not justify its continuation; for it was only successful where every patient was strictly isolated or every suspect, infected or not, ruthlessly exterminated. The compulsory element drove the disease underground, and only those were caught who were obviously affected or who could no longer hide its signs. The early cases remained at large, spreading the infection among the community.

Voluntary settlements promised to achieve far more. In the hands of Missions and of those who were not easily discouraged by slow or disappointing results of treatment, such settlements were extremely popular. Knowing that they could come and go almost as they wished and that during their residence they would not be treated as criminals but allowed to enjoy reasonably normal lives, patients travelled long distances to obtain treatment. The difficulty of tracing patients under a compulsory scheme was reversed; the new problem was to accommodate all who came.

Before examining the position in Uganda, it may be of comparative interest to take a glance at the other side of Africa. The first settlement of any size in West Africa was built at Itu, on the

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Cross River in Nigeria. It developed from an out-patient clinic at the Church of Scotland Mission Hospital. The patients came in canoes from up and down the river and its creeks. Unable to make the journey every week, or to return to their villages because their homes had been burned, they settled on a sandbank. When the rains came, the river rose, submerging their temporary shacks and compelling the patients to move across to the shore, much to the resentment of the local population. The Government intervened when the situation was becoming tense, provided the necessary assistance, and enabled Dr. A. B. MacDonald to direct this motley and forlorn crowd while they laid the foundations of what ultimately became the largest settlement in the whole of Africa.

The success of Itu encouraged further ventures, one of which was Uzuakoli, in the Owerri Province. It was not, like Itu, an accidental development. It was planned from the beginning, but the experience at Itu was repeated and quotas of patients had to be allotted to the various administrations according to their financial contributions. Patients were admitted through their political and medical officers, but there were always more applicants than vacancies. To increase the capacity of the settlement, additional patients were accepted if they were able to support themselves; but even here, the number of these had to be regulated. It soon became apparent that with the best of intentions only the fringe of the problem could be touched unless there was some modification of general policy. Voluntary settlements alone could have little effect on the incidence of the disease in areas of high density. The annual cost of Uzuakoli was between two and three thousands pounds. There was accommodation for one thousand patients. The Owerri Province was but a small part of Nigeria, yet it alone would have required more than twenty settlements with the necessary staff to make any appreciable impact on the disease. This was a financial and practicable impossibility, and in 1935 the author published the outlines of a scheme of control for the Southern Provinces.

Patients were beginning to create their own compounds or villages. Marriage between a patient and a non-patient was forbidden. The appearance of leprosy in a husband or wife automatically created a divorce. Intermarriage between patients, many of whom were closely related, was the logical sequence, and for this reason the incidence in small, heavy infected compounds increased. Those who were not infected moved out, leaving behind

a " Leper Village." In other places, either because they were ostracized or driven from their homes, patients settled together, petitioning for treatment to be taken to them. However they began, small leper communities were springing up. It appeared reasonable to weave this natural thread into an organised scheme of control based on provincial settlements, using volunteers and ex-patients to survey outlying parts and to encourage the formation of similar communities under the guidance of the local chiefs.

Uganda is quite unlike Nigeria; it has a different social pattern. The people do not live in villages. Their houses are widely scattered, a natural barrier to the spread of epidemics but a disadvantage to the provision of rural medical service. It is probably responsible for the fact that the incidence of leprosy is everywhere less in Uganda than in the villages of Southern Nigeria. Surveys are more difficult to organise, and the creation of treatment facilities is less easily arranged. With few exceptions, the incidence is higher where the population is more dense, and it is in these areas of greater need that less land is available for larger settlements.

Uganda has a leper population in the region of 80,000 spread over a general population of more than 5,000,000 and an area of 93,000 square miles. There are five voluntary settlements, four of them between twenty and twenty-five years old. Together they accommodate rather less than 2,500 patients. It is possible that the older ones may have reduced the incidence in their immediate vicinity. In some cases, however, the long distances have led to extensive squatting by patients, and this has altered the picture. It appeared logical to take advantage of this immigration into the environment of a curative centre and to link it to a community effort throughout the country to establish nationwide treatment and control.

During the last two and a half years more than sixty leprosy surveys have been carried out. Such surveys provide the essential groundwork on which a rational control scheme can be based. They have involved considerable preparation and planning in order that the results should be significant. These examinations would not have been possible without the co-operation of the administrative and medical staff of the country and the goodwill of the peope. An integral part of the surveys has been conferences with the County Councils and the District Teams. At these meetings the local incidence has been discussed and plans suggested which have taken into account particular circumstances or difficulties.

The main argument has been that even if the large staff necessary were available, which it most definitely was not, it would

still cost the whole of the money spent on the medical services of the Protectorate to control this one disease by a series of large-scale settlements. On the other hand, the establishment of small treatment villages within a reasonable distance of rural medical units is economically possible by community effort especially if assisted by community and general funds. If patients are willing to submit to some limitation of their private lives to obtain treatment and to give some protection to the community, the community in return should accept the responsibility of providing the necessary simple accommodation.

Patients cannot travel long distances every week, especially if sick or if the weather is severe. Small treatment villages make continuity possible and secure some measure of segregation. One hundred per cent segregation is the ideal. This is pressed in grossly infectious cases, but it is not suggested that it should be applied too rigorously to the less infectious lest the whole object be defeated. Allowing the patients to visit their homes enables them to obtain food and keep in touch with their families. If eighty per cent segregation results, that and treatment by the sulphone drugs should effectively interrupt the normal spread of the disease. The main problem is to get the right number of tablets into the right mouths at correct intervals. The solution is not easy, even in more highly-developed societies. The man who has obtained benefit from one medicine for one condition does not hesitate to recommend it, but often for something entirely different. Nor is it certain that every dose of medicine is taken as prescribed. It has been known to be thrown away. In less developed communities, the abuse or indiscriminate use of potent drugs may be highly dangerous. Much of the organisation necessary for a leprosy control system is due to the necessity for safeguarding people from their own folly or ignorance, through which they may omit to take the drug regularly, or take overdoses, or give or sell it to their friends.

The community response in Uganda has so far been encouraging. Early in 1952 in the Northern Province three large units were established by the District Councils in Lango, Acholi and West Nile. A fourth, rather smaller, was built in the Madi sub-district in 1953. In the Western Province in Bunyora, the District Council provided a similar village, whilst in Tora quite an amazing effort was seen. In a matter of weeks the local population cleared a site, made a road two miles long, and provided accommodation for a large number of patients. In three weeks from its opening four hundred were accommodated and treatment

was begun. A second such centre, in the same district, is under construction.

The Eastern Province of Uganda is more densely populated and has problems peculiar to itself. Two of the major voluntary settlements are in this Province. A small unit has been provided by the District Council of Busoga near the Buluba settlement, and two others in the north-westerly part of Busoga built by the local population show great promise. In Teso, a similar centre is being built and a scheme linking community effort with the expansion of the settlement at Ongino is under discussion. This will include the provision of a separate village within the settlement by each district in the area.

Very satisfactory progress has also taken place in Buganda, the largest province in the Protectorate. Recent happenings have brought this part of the country very much in the limelight, but not every movement in Buganda is political, either in its origin or its general trend. Four small villages have been built in the district of Mubende, and patients are receiving treatment. A fifth has been completed in the district of Mengo at Mityano and will be opened by the Katikiro, the Prime Minister of the country. Two villages are growing rapidly in more remote areas, and others are on the drawing board. All this work has been done by "Bulungi Bwansi," a form of communal labour whereby each male adult is required to work certain days on community projects when called upon by his Chief.

By some standards, and when measured against what it is hoped to achieve, progress might be considered slow. However, a large machine takes time to gather momentum, and what has been acomplished has taken a comparatively short time. It is early yet to speak of results. There is every reason, however, to believe that this community work begun in so many parts of Uganda will be multiplied, and that by means of it, a disease which has defied treatment for centuries may in a few years become an incident of history.

REVIEWS

B.C.G. and Vole Vaccination, by K. Neville Irvine, M.A., D.M., B.Ch., M.R.C.S., L.R.C.P. Foreword by F. Heaf, M.A., M.D., F.R.C.P. (96 pages, illustrated, 12/6.) National Association for the Prevention of Tuberculosis, London.

This booklet is exactly what many have been wanting, a readable informative account of B.C.G., now very widely used, and of the vole bacillus vaccine now being used on a small scale experimentally.

The seven chapters with their main contents are as follows: chapter one deals with the history of these vaccines; chapter two with the theory of vaccination, including infection, resistance natural and acquired, allergy, vaccination and tuberculin testing, and the phenomena associated with them; chapter three deals with the different kinds of vaccine and the influence of various factors on them, heat, light, freeze drying, etc.; chapter four deals with the safety and effectiveness of vaccination; chapter five deals with tuberculin testing in its different forms, with a description of each test, of the technique, of the readings, with critical comments; chapter six deals similarly with the different vaccination procedures; chapter seven deals with the complications of vaccination; chapter eight deals with the organisation of vaccination measures. Each chapter has its own references. There are ten colour plates, all reproductions of colour photographs, and text figures.

This booklet is strongly recommended as a small practical handbook of the subject.

Leprosy in India. Vol. 26, No. 3, July, 1954.

Dharmendra and Chatterji (K. R.) present a study of the treatment of leprosy with thiosemicarbazone (T.B.1) in 112 cases covering a period of 38 months. Their own summary is as follows:

' 1. An analysis is presented of findings made during three years' treatment of 112 cases of leprosy with thiosemicarbazone.

" 2. Of the 112 cases, 87 were lepromatous and 25 non-lepromatous (15 tuberculoid and 10 simple maculo-anaesthetic). The duration of treatment was below 1 year in 39 cases, 1 to 2 years in 23 cases, and 2 years or above in 50 cases.

" 3. The initial adult daily dose was 25 mg., which was gradually increased up to a maximum of 200 mg. according to tolerance; in some cases the maximum dose had to be kept low (100-150 mg.), and in a few cases it could not be raised beyond 50 mg. About 10 per cent of the cases were found to be sensitive and intolerant to the drug even in very small doses (6 mg.), in such cases the treatment had to be discontinued.

" 4. Of the non-lepromatous cases, all except 3 were previously untreated cases. Of the lepromatous cases half (43) were previously untreated and the other half (44) had been previously treated with other drugs, mostly sulphones. In 27 of these cases thiosemicarbazone replaced sulphones which were discontinued, and in the other 17 it was added to sulphones which were also continued. In these 44 cases the change from, or addition to, sulphones was made from one or more of the following reasons: (i) sensitiveness to the drugs, (ii) lack of improvement, (iii) initial improvement later becoming stationary, (iv) persistence of sensory loss and deformities in cases who had otherwise improved under sulphones.

" 5. In the non-lepromatous cases the results of treatment were in general of the same order, as with the sulphones. However, because of its additional beneficial effects on neurological symptoms, thiosemicarbazone appears to be better than the sulphones. As in the case of sulphones, the results in ' tuberculoid ' cases are better than in the ' simple ' maculo-anaesthetic cases, in which the improvement is slow, any marked change being not seen usually before the end of one year.

" 6. Of the lepromatous cases there was little or no improvement in 19 cases, 9 of which were sensitive to the drug, and the other 10 could not tolerate more than 50 mg. per day. In the remaining 68 cases there was definite improvement (in the group on thiosemicarbazone from the start) or further improvement (in the two groups in which thiosemicarbazone replaced or supplemented sulphones). In 63 of these cases there was both clinical and bacteriological improvement, while in 5 only clinical. Restoration of sensation was seen in some, but the long standing and extensive sensory loss which was present in some of the cases of the last two groups did not respond to the change in treatment.

" The clinical improvement was assessed as moderate (definite subsidence of lesions) in 23 cases, and as marked (almost complete subsidence) in 45 cases. In 6 of the cases with moderate improvement the progress later came to a standstill.

" The bacteriological improvement was assessed as slight (B.I. to 1.5) in 15 cases; moderate (B.I. to 1.0) in 15 cases; and marked (B.I. to 0.5 and below) in 33 cases, 18 of which had become negative. In 7 cases with slight improvement the progress later came to a standstill; and in 8 cases with moderate and 2 cases with marked improvement, there was set back in the bacteriological status during later part of treatment.

" Of the 48 cases with anaesthesia of varying extents there was no restoration of sensation in 21, partial restoration in 20, and complete restoration in 7 cases. It can be concluded that (i) if the loss of sensation is very extensive and of long standing (over 10 years), it is not likely to be favourably affected by treatment with thiosemicarbazone (and of course not with the other drugs in use at present); (ii) if it is of moderate extent and not very long standing (below 10 years), it is likely to improve, but complete restoration is not to be expected; (iii) if it is limited to the patches and/or to distal parts of one or two extremities, and is of recent origin (below 5 years) is very likely to be restored, maybe completely.

" 7. As indicated above, of the 68 lepromatous cases which showed initial improvement, in 23 it was not maintained later. In 6 of these cases there had been only clinical and not much bacteriological improvement, while in the remaining 17 there had been both clinical and bacteriological improvement, 2 of them having become bacteriologically negative. Of these 17 cases, in 7 the improvement later became stationary, while in the other 10 there was actual deterioration (including the 2 cases which had become bacteriologically negative, but which later again became positive). Usually the stasis was first observed after 12 to 18 months' treatment, and deterioration after another 6 to 12 months.

"Further experience has confirmed the opinion previously expressed that with the doses now in use serious toxic manifestations are not very common. In a majority of cases there is seen a fall in the total W.B.C. and R.B.C. counts and in haemoglobin values in the early stages of treatment, with recovery to varying extent in the later stages. Allergic dermatitis is sometimes seen; it is usually mild and readily responds to antihistaminic drugs, but may occasionally be severe and necessitate the discontinuation of treatment. The serious toxic effects seen were sensitively to the drug, resulting in intolerance to even minute doses in about 10 per cent cases, and obvious signs of liver damage in 3 cases. No case was seen of agranulocytosis—a very serious toxic effect, reported by Lowe, resulting from thiosemicarbazone treatment.

"9. Apart from the drug sensitiveness manifested by some cases, an important limitation of the method of treatment is the loss of efficacy seen in a proportion of cases after first year's treatment. Both these limitations have been encountered so far only in the lepromatous cases.

"10. It may be concluded that in spite of the above limitations, thiosemicarbazone has a definite place in the treatment of leprosy. In cases who can tolerate adequate doses it produces satisfactory clinical nd bacteriological improvement. However, in view of the loss of efficacy seen in a number of lepromatous cases later during treatment, it may be necessary to change over to sulphones after treatment with thiosemicarbazone for a year or so. Because of the comparatively short duration of treatment in the tuberculoid cases, this consideration is not likely to apply to such cases."

Dharmendra and Jagadisan each contribute an article on Social Aspects of Leprosy, which reflect conditions in India, where beggars with leprosy are so numerous, and where return to normal life of discharged patients is often difficult.

The article on B.C.G. in the prophylaxis of leprosy by N. de Souza Campos, is reprinted from the *International Journal of Leprosy*, previously reviewed in our Volume 25 (page 160). The rest of this issue is devoted to abstracts of literature and reports.

Leprosy in India, Vol. 26, No. 4 (Oct. 1954).

This number contains an article by Dharmendra and K. R. Chatterjee on a clinical trial of Cepharanthin, an alkaloid recommended by certain Japanese workers in the treatment of leprosy and tuberculosis. The authors' own summary is as follows:

"Fifteen previously untreated cases (7 lepromatous and 8 tuberculoid) were treated with Cepharanthin for an average period of 41 weeks for the lepromatous, and 52 weeks for the tuberculoid cases. The doses originally used by the Japanese workers were found to be too high, and the maximum weekly dose had to be kept at 1.2 mg. for the tuberculoid cases, and 1 mg. for the lepromatous cases.

"Of the 7 lepromatous cases, there was no improvement in 3, the disease progressively increased in 2, and there was definite improvement in 2. (In the last 2 cases discontinuation of treatment was followed by a setback and progressive increase in the disease.) Of the 8 tuberculoid cases, 1 showed definite and lasting improvement, 4 showed initial improvement later followed by setback, and the remaining 3 showed no improvement.

" It can therefore be concluded that our experience with Cepharanthin has not confirmed the previous favourable reports about its use in the treatment of leprosy."

J. D. Kanakaraj writes on " Surgical Trends in Leprosy," discussing plastic surgery, including excision of redundant leprous tissue, correction of nasal deformities by cartilage graft, operations to correct gynaecomastia, tendon transplantation for the relief of hand deformities.

Dharmendra and N. R. Sen report on a study of the treatment of tuberculoid reaction with Vitamin C, as recommended by certain French workers. No striking results were reported.

The rest of this issue is devoted to abstracts of literature and reports.

International Journal of Leprosy, Vol. 22, No. 1 (Jan.-Mar., 1954).

Emanuel Suter writes on " Some Aspects of Intracelluar Parasitism of Pathogenic Microorganisms."

In this important review Suter, of Massachusetts, states that, in his studies of phagocytosis, Metchnikoff over-estimates the destructive effect of the phagocytes on pathogens. While his interpretation applies to acute infections it does not to the chronic ones where an intracellular parasitism lasting for a long time, often for the lifespan of the host, is apt to take place. In 1916 Rouse and Jones showed that typhoid bacilli when once phagocytised escaped the influence of antisera and antibacterial agents to which they are susceptible when not within the cells. Such infections in which the infective agents are able to survive, and even to multiply within the cells as well as extracellulary, are termed facultative intracellular parasitisms. Typical examples are brucellosis and tuberculosis. The study of this host-parasite relationship is particularly important in leprosy owing to the almost purely intracellular habits of human and murine leprosy bacilli.

Suter reviews the work that has been done on the intracellular parasitism of the tubercle bacilli. He says that it was found that streptomycin was unable to destroy all the tubercle bacilli in the body owing to this intracellular parasitism, and immediately treatment ceased, the bacilli began to multiply again. However, in animals that have been vaccinated with B.C.G. the macrophages have somehow been rendered inhospitable to the bacilli, and the bacilli become extracellular and susceptible to streptomycin. The latter restricts extracellular multiplication while the acquired state of the phagocytes limits intracellular multiplication. Isoniazid seems to retain its full activity against intracellular bacilli, so that in combination with streptomycin the bacilli within and without the cells gradually lose their vitality.

In order to study the action of drugs on the intracellular forms of the tubercle bacillus, Suter was able to prepare slides of cultivated macrophages to which streptomycin had been added so as to destroy the extracellular forms. He found that the virulence of the bacilli depended on their ability to multiply intracellularly, and their capacity to destroy the host cells. In normal animals, they multiplied freely within the macrophages, but when macrophages from B.C.G. vaccinated animals were used, bacillary proliferation was completely suppressed. That this inhibitory power resides in the macrophages and not in the serum was shown by adding serum from vaccinated animals. It was seen to have

no effect. Macrophages are therefore in a key position in regard to acquired immunity to tuberculosis. The possible application of these facts to the understanding of the problem of infection and treatment of leprosy is stressed.

John H. Hanks writes on "The Implications of Suter's Review of Intracellular Parasitism with respect to the Problem of Leprosy." Commenting on the above paper, Hanks writes:—

"Suter's demonstration that mild degrees of extracellular inhibition suffice to convert a cultivable mycobacterium into an intracellular parasite is an observation of prime importance to our clearer understanding of the pathogenesis of leprosy." "In our present views a notable combination of metabolic limitations and of inhibitions of extracellular fluids are main factors which force the fastidious and non-cultivated species toward seclusion in intracellular environment."

Hanks refers to his own work in Culion before the war and which unfortunately had to be given up because of it. In 1947 he had described how actively growing fibrocytes from tuberculoid skin lesions caused rapid reduction of M. leprae to acid-fast debris, whereas fibrocytes from lepromatous lesions grew normally when containing much higher numbers of bacilli, and were unable to bring about their prompt destruction. Thus the behaviour of cells from the two kinds of cases, even after prolonged cultivation in vitro, reflects certain of the well-known differences between the two polar types of leprosy. Later, cultures of blood macrophages were found to be more destructive to leprosy bacilli than fibrocytes. "We must be grateful to Dr. Suter for having again drawn our attention to cellular mechanisms which inhibit the intracellular growth of mycobacteria, and to the existence of physiological states which encompass their destruction. It is to this type of action that the mycobacteria are ultimately vulnerable."

Ng. Ph. Buu-Hoi writes on "The Selection of Drugs for Chemotherapy research in Leprosy."

In this paper the writer suggests certain empirical rules for the choice of drugs for the treatment of leprosy. They must be tuberculostatic and fungistatic. They must be relatively non-toxic for long term use and must be cheap and easily manufactured. He suggests that lipid solubility may increase activity against the leprosy bacillus. He suggests certain drugs for clinical assay, particularly D.D.S.O. (diaminodiphenyl sulfoxide).

Linda Nahas and Hans Rzeppa and Lauro de Souza Lima write on "Blood Picture in Sulfone Treatment of Leprosy."

Four groups of five patients were given: (1) Diasone 0.66 gms. daily (=D.D.S. 0.333 gm.); (2) Diasone 0.90 gms. daily (=D.D.S. 0.555 gm.); (3) D.D.S. 0.2 gm. three times weekly, and (4) 0.4 gm. daily; and the haemologic changes studied. The results showed that blood concentrations of over 0.6 mgm.% induced a moderate progressive anaemia, but that concentrations under that amount produced no anaemia. Daily doses of 0.333 gm. D.D.S. and 0.555 gm. D.D.S. in the form of Dapsone gave the same blood level, and so the larger dose presented no advantage. All patients receiving 0.4 gm. of pure D.D.S. daily showed a blood concentration of about 1 mgm., and showed toxic reactions and anaemia, but those receiving 0.555 gm. of D.D.S. daily as Dapsone showed no toxic reactions or anaemia. The detection of anaemia by haemogloblin determinations is held to be a safe index of the optimal individual dose to be given.

H. Gass and M. Balasubrahmanyan write on "Changes in the Cutaneous Nerves in Leprosy."

The authors made a study of the cutaneous nerves in different types of leprosy and attempted to correlate the clinical observations with the histological findings. In estimating tactile sensation they found that hairs played an important part in the reception of tactile stimuli, and shaving the skin reduced sensitivity very markedly. After shaving they found that maculo-anaesthetic, tuberculoid and lepromatous lesions were all completely insensitve to light touch.

Sections 20-30 microns thick were made from 30 cases of leprosy and were fixed and stained by a silver impregnation method for nerve fibres and then counterstained. It was found that the damage to the nerves in different kinds of lesions was of the same kind, but of different degrees, and was influenced by the nature and age of the lesions. They found fusiform swellings and "bubbles" along the course of the axons, and twisting, flattening and fragmentation of axis cylingers which could be accounted for by Wallerian degeneration consequent to damage by pressure in the deeper nerve fibres.

Seitaro Okada writes on "Studies on Tuberculoid Visceral Leprosy. Tuberculoid Granuloma in the Liver revealed by puncture biopsy."

In order to determine whether tuberculoid granuloma occurred in the liver in cases of tuberculoid leprosy, the author examined specimens obtained by liver puncture from 5 patients. In one case several well defined tuberculoid granuloma were found, and in three of the others incomplete tuberculoid lesions were seen.

S. Miguel, A. Roldan, J. Guillen, J. Terencio and J. Ponciani write on "Plasma proteins in Leprosy." A translation of the authors' own summary is as follows:—

"In our study of the serum proteins of leprosy patients by electrophoresis, the examinations were indiscriminately made by the cell method (Kern apparatus) and the paper technique (Macheboeuf-Rebeyorette apparatus), ascertaining first in both instances the mean value in normal subjects for a point of reference. The findings in the patient were as follows: Total proteins were usually about normal in values, although they were increased in more cases than decreased. The albumin-globulin ratio was generally below unity. The globulin fractions were increased, especially the gamma fraction, there being a decrease of the alpha globulin in the cases where the gamma showed the most marked increase. These changes were most pronounced in the more advanced lepromatous patients, especially those with manifest visceral amyloidosis. In the phases of lepra reaction the disturbances of the globulins were pronounced, but they partly subsided when the lepra reaction disappeared.

"For the evaluation of the Weltman band reaction, the cadmium reaction, the Takata-Ara reaction, and the erythrocyte sedimentation, these tests were made at the same time that the electrophoresis studies were performed. The sedimentation rate was found to be the most sensitive, and to be more in accord with the albumin-globulin ratio and with the gamma globulin increase than the others. In second ranks are the cadmium and the Weltman band tests. We found the Weltman band abnormal (either dimininshed or prolonged) in 78 per cent of the patients, indicating especially the protein disturbances in lepra reactions, in which the band was constantly shortened. In toxic disturbances of the liver caused by the medication, the band was always prolonged, while the Takata-Ara reaction was positive in all cases."

J. Mauzé and G. Arnaud write on "Electrophoresis of Leprosy Serum." The authors' own summary is as follows:—

"The authors hold that electrophoresis, whether by the classical technique or by the paper method, is at present the best and most precise method of investigating sera. They have tested the sera of 100 patients, of various types and grades, most of whom have been under sulphone treatment. The paper method of Machebouef was used in this work.

"It was found that, whatever the clinical form of the case, the albumin fraction is diminished, while the γ globulin, the α globulin, and the β globulin are constantly increased. When the γ fraction reaches $K=2.0$, the patient is in a bad condition and reacts poorly to treatment. The nearer it is to 1.0, the more stable is the case and the more amenable to treatment. Increase of α_2 and β together or separately, to 1.8 or more signifies important intestinal parasitism or microfilaria.

"The authors believe that electrophoresis of the serum is an excellent means of determining the patients' response to treatment, that the γ fraction is the most interesting, and that the sulphones do not cure the disease."

R. D. Azulay writes on "The Protective Role of B.C.G. in Murine Leprosy."

Fifty-seven rats were inoculated with B.C.G. subcutaneously or peritoneally and 115 days later inoculated with M. leprae murium and compared with 20 controls. Clinically the unvaccinated animals showed earlier and larger lesions, and although bacteriologiclly there were no alterations in the bacilli either in shape or in staining, the percentage of positivity in the visceral organs was higher in the unvaccinated than in the vaccinated animals. The writer considers that B.C.G. has a definitely protective effect against leprosy infection in rats, and that this experiment will serve to strengthen the view that B.C.G. may be useful in the prevention of leprosy.

In an editorial in this issue Wade discusses the above papers of Suter and of Hanks, and suggests that macrophage cultures from patients with different forms of leprosy, and patients vaccinated with B.C.G. should be studied, particularly in the matter of their reaction to M. leprae obtained from lepromas.

In this issue is printed Part I of a translation into English by G. L. Fite, of Virchow's chapter on Leprosy from his book Die Frankhaften Geschwülste 1864, said not to have been previously translated into English. This writing of Virchow, of an era before the leprosy bacillus had been discovered, is of considerable interest.

G. O. TEICHMANN.

International Journal of Leprosy, Vol. 22, No. 2 (April-June, 1954).

The following are abstracts (made by Dr. G. O. Teichmann) of the original articles in this issue.

M. Casile, H. Saccharin and P. Destombes write on "An Anatomo-clinical Study. Tuberculoid leprous neuritis, with Caseation, of the posterior tibial nerve, with arteritis."

A patient who had no other signs of leprosy and who had been treated in hospital in French Guiana, and had received many diagnoses, finally had his left leg amputated because of persistent and severe pain. On dissection the posterior tibial nerve was found to be much thickened and irregular, the enlargement extending to the plantar branches; the anterior tibial was slightly larger than normal, but the external peroneal was quite normal. On histological examination tuberculoid caseation and a few bacilli were found. The authors point out how easily a case like this can be missed for a long time when there are no other signs of leprosy.

(The article indicates that there was loss of sensation of the lower leg and foot, and perforating ulcer of the sole.)

J. M. M. Fernandez, B. Appel and E. Dougherty, write on "Influence of hydrocortisone, cortisone, and ACTH on the lepromin reaction."

The object of this study was to ascertain the influence of the hormones especially hydrocortisone on the two responses, early and late, which are induced by the intradermal injection of lepromin in positive reactors. As it is widely believed that the 48 hours Fernandez reaction is of an allergic nature, whereas the 3-week Mitsuda reaction is the expression of a state of resistance or relative immunity, it was particularly desired to ascertain if the hormone has an inhibitory effect only on the former or also affects the latter. Twenty-one adults who had had no contact with leprosy and six who had had household contacts were observed. Intradermal injection of hydrocortisone followed immediately by that of antigen in the same wheal, were given on the left side of the back, while a single injection of antigen alone was given on the right side in a similar position and the results compared. Other cases were tested with hydrocortisone and tuberculin, Frei and Ducrey antigens. It was found that the local injection of hydrocortisone acetate provoked partial or total inhibition of the early reactions of hypersensitivity to lepromin, to tuberculin and to the Frei and Ducrey antigens.

The late (Mitsuda) reaction to lepromin is also inhibited, the drug impeding the formation of the tuberculoid granuloma which characterises it. In two cases in whom the hydrocortisone was inoculated on the 21st day into the positive Mitsuda nodules, the nodules disappeared leaving a slightly atrophic yellowish plaque. In cases receiving general treatment with cortisone or ACTH, the Fernandez reaction occurred with much less frequency than in cases not so treated, and the Mitsuda reaction was positive usually in low degree in only 50% of the cases. The authors state, "The question remains, 'Does this parallelism of the results mean that these phenomena are two stages of one and the same process, or does it simply mean that the hormone inhibits all tissue reactions in situ regardless of their nature?'"

Two articles, one by H. Floch and the other by O. Diniz and H. A. Neto, discuss the use of dilute antigen in the Mitsuda reaction, and an editorial by Wade discusses the same subject.

More and more stress is being laid on the use of the Mitsuda test and yet, because of the success of modern treatment, it is becoming increasingly difficult to get bacilli-rich lepromas with which to make lepromin. For this reason, various attempts have been made to use diluted antigen. Wade writes in the editorial: "Floch is convinced that the 'normal' antigen (which he holds to be 1:30 incidentally, whereas Hayashi's technique makes a 1:20 preparation) is too concentrated. He finds that the lessening of intensity of the response does not parallel the degree of dilution of the

antigen, but occurs more or less stepwise. The results with a 1:50 dilution do not differ much from those with the normal dilution, and he recommends its use. He finds a second zone in the region from 1:300 to 1:750. Further dilution, to 1:1000, again affects the results considerably. In the intermediate zone the positive results, he states, can be correlated with those obtained with the normal dilution by adding one plus (1—) to the reading.."

Diniz and Neto tested a large number of children by giving three injections in the thigh or forearm and comparing the results. Two observations were made. The first was the Fernandez reaction after 48 hours, and the second was the Mitsuda after 21 days. Analysis of the results showed that both of the reactions with dilute antigens were closely comparable to those obtained with the 1:20 control. There was, however, a slight lessening of positivity with increase of the dilution. The findings with the Mitsuda reaction are summarised as follows:

Antigen		*Positive*	*Negative*
1:20	...	78.7%	21.3%
1:750	...	65.6%	34.4%
1:1000	...	49.3%	50.7%

They suggest that to save antigen a preliminary test might be done with dilute antigen. If this is positive the patient will be a lepromin positive individual. If the test be negative the patient can then be re-tested with normal 1:20 concentration.

R. D. Azulay and L. M. C. Andrade write on "Demonstration of M. leprae in sections in 532 cases of leprosy; a comparative study between Ziehl-Klingmuller and the Wade-Fite techniques." Their own summary is as follows:—

"The authors have made a comparative study of two methods of staining M. leprae in paraffin sections of biopsy specimens of the skin, namely the Ziehl-Klingmuller method and the Wade-Fite in which, according to Wade, the bacilli are protected from extraction of their lipids during the deparaffinization. The data of the findings show differences which are statistically significant, and the following conclusions are drawn.

"1. That the Wade-Fite method of staining gives better results in demonstrating M. leprae than does the Ziehl-Klingmuller method.

"2. Repeated examinations of a number of specimens showed that in most cases the results remained the same, thus demonstrating that positivity actually depends on factors inherent in the method itself.

"3. The fact that there were 38 cases found positive (1—) with the Wade-Fite method but negative with the other, of which only 9 were positive in smears made from the biopsy specimens, suggests that the new technique is not exclusively one of protection of the acid-fastness of M. leprae in the lesions, but that it also has the property of restoring acid-fastness which has been lost in the tissues."

Eric Waaler writes on "Leprosy and Cancer." His own summary is as follows:—

"The author gives a short report of a case with basal-cell carcinoma and leprosy in the same lesion, and a review of the older and more recent literature on this subject. The old presumption that leprosy to some degree protects the patient against cancer is not supported in the modern literature. The occurrence of skin cancer in lepromatous granulation tissue

does not appear to be very common, and the combination of the two diseases in the same lesion is mainly of diagnostic interest.''

J. H. Hanks and C. T. Gray write on '' The application of Metabolic Studies to Leprosy Research,'' and J. H. Hanks on '' The Influence of Physical and Chemical Factors on the Hydrogen Transfer Capacity of Murine Leprosy Bacilli.'' These two articles are highly technical and it is impossible to do justice to them in a brief abstract. They report studies of M. leprae murium in vitro, of its hydrogen transfer capacity, and of its oxygen consumption; and of its infectiousness and of the influence of various factors, such as anaerobiasis, environment, pH and blood serum on these findings. Hanks' paper ends:

'' This study provides evidence that metabolic activity, properly measured, affords an index of the infectiousness of murine leprosy bacilli after incubation in vitro.''

Sister Hilary Ross writes on '' The Results of a Modified Middlebrook-Dubos Hemagglutination Test in Leprosy; 261 cases.'' Her own summary is as follows:—

'' The Middlebrook-Dubos hemagglutination test (Scott-Smith modification) was performed on sera obtained from 261 leprosy patients in whom tuberculosis had been excluded. A single test was made in 240 patients; three or more tests were made during a period of one year in 21 other patients who represented different treatment groups—sulphones, thiosemicarbazone, or isoniazid.

'' Of the 261 cases, 231 (88.5%) had hemagglutination titers higher than the highest (i.e. 1:8) found in the control group. Of a group of 169 clinically active lepromatous cases with bacilli, 91.1 per cent had titers above the normal range. Of a group of 52 lepromatous cases which were clinically quiescent and in which bacilli were not found, 75 per cent had titers above normal. Of the 40 tuberculoid cases, 28 (70%) revealed titers above 1:8; the highest reached was 1:256, as compared with 1:4296 in the lepromatous group. The graph shows the marked difference between the lepromatous and tuberculoid cases as regards the distribution of the titers.

'' Serial hemagglutination tests made over a period of one year on 21 cases under therapeusis showed decrease of titer in 6 cases, no change in 7, and increase in 8. The disease progressed in the 8 cases in which an increase in titer was noted. Clinical and bacteriological improvement was noted in six cases in whom the titer decreased.''

Joseph Portnoy and W. F. Edmundson write on '' A Simple Procedure for the Identification of Nonsyphilitic Reactions in Serologic Tests for Syphilis in Leprosy Patients.'' Their own summary reads as follows:—

'' A simple procedure for the differentiation of syphilitic and nonsyphilitic reactions obtained in serologic tests for syphilis with leprosy sera is described. The behaviour of this procedure with sera of normal individuals, syphilitic patients, and patients with leprosy (with or without

evidence of syphilis) is presented. With antigen suspensions containing choline chloride, sera of syphilitic patients (with or without leprosy) show an augmentation of sero-reactivity; non-syphilitic reactive leprosy sera show a diminution of sero-reactivity. On the basis of the clinical and historical evidence, a good correlation was obtained between the differential procedure described and the results of the T.P.I. test in normal persons and in syphilitic, non-leprous individuals. The differential procedure compared favourably with the T.P.I. test in leprosy patients with and without clinical or historical evidence of syphilis. A comparison of reactivity levels of the differential procedure, the VDRL slide test, and the T.P.I. test is presented and discussed."

The second part of the translation by G. L. Fite of Virchow's " Leprosy " from " die Krankhaften Geschwülste," published in Berlin in 1863, is published as a reprinted article.

REPORTS

Report of the Medical and Health Department, Malta, 1953.

The introduction to this report, written by the Chief Government Medical Officer, has a long section dealing with the history of leprosy stating how in 1695 a commission was appointed for the care of leprosy patients, and how in 1900 all male patients were segregated, and in 1912 all known female patients. The Report goes on: " In view of the modern knowledge of leprosy, countries have revised their laws against lepers. The present trend in dealing with leper patients does not seem to favour compulsory isolation. Forcible segregation has been tried in many countries, but it has given poor results. In various countries the laws regarding leprosy are being revised, and this procedure has been followed this year in Malta, and compulsory segregation has been abolished." In the body of the report it is stated that eleven new cases were notified during the year mostly in the 20—40 age group. In the Leprosy Hospital (St. Bartholomew's Hospital) there were 103 patients at the beginning of the year. Six new ones were admitted and 31 were discharged at their own request on the abolition of compulsory segregation, in most of these the disease having been arrested. At the end of the year the number of patients in the hospital was 75, 54 being males and 21 females. Sulphone treatment is being used with good effect, and experiments with other forms of treatment are also being made. Four deaths occurred during the year, two from chronic heart disease and two from chronic nephritis.

East African Leprosy Research Centre, Itesio. Short Report for the year 1954.

This report starts as follows: " The East African Leprosy Research Centre is a new project for East Africa initiated by the British Empire Leprosy Relief Association, who gave a large part (18/27th) of the capital funds necessary, as well as a large part of the recurrent cost (half). The Centre is under the administration of the East Africa High Commission, and the East African governments have also contributed to the capital and recurrent costs." The centre is at the Itesio leprosarium, which itself is a new venture founded in 1952 and now growing. Itesio is on the Kenya/Uganda border. Makerere College is 2½ hours by road, Buluba leprosarium 1½ hours, Kumi leprosarium 2½ hours, and the East African Tsetse and Trypanosomiasis Research and Reclamation Organisation has research laboratories at Sukulu, only ten miles away. The initial staff of the centre include the Director, Dr. J. Ross Innes, the laboratory technologist, Mr. E. J. Bishop, the secretary, Mrs. Bishop, the clerk, Mr. A. S. Ferandes, and two drivers.

" The main work of the centre during 1954 was the struggle to come into existence." Building has been delayed by the state of emergency in Kenya, but good progress is reported in recent months. Laboratory equipment has arrived and the laboratory-office building is nearing completion. Proposals for research include studies of the action of new drugs in leprosy, the value of B.C.G. vaccine in leprosy, the control of leprosy, studies of lepromin, etc.

Report for 1954. Ndanda Leprosy Colony, Tanganyika Territory.

This report is detailed and informative. 539 patients remained from 1953, 215 were newly admitted, and discharges were 125, 41 absconded and 7 died, 581 remained at the end of the year. Of the 7 deaths, three were due to pulmonary tuberculosis, which has presented a problem.

Of the 581 patients under treatment, 508 have been treated with sulphones, and a few with T.B.1 and Isoniazid. Old debilitated patients and some very weak newcomers are treated with hydnocreol.

The sulphones used included sulphetrone injections and D.D.S. Good results are reported. The outbreak of new lesions is recorded in a few tuberculoid cases under treatment. Of six lepromatous cases started on sulphetrone in 1949, two have absconded, one was discharged as negative, and three are in very good condition, but smears are still positive. Dimness of vision after sulphetrone injections (two cases) and mental disturbance after D.D.S. (one case) are recorded. T.B.1 has been used in 5 patients with striking response in some. One patient who had become allergic to sulphone has responded well to T.B.1, but a single dose of 2 c.c. of sulphetrone accidentally given caused immediate recurrence of signs of sulphone sensitivity.

Leprous reaction is not uncommon in the treated cases. In a few cases it is severe and persistent and antihistamine and phenacetin and aspirin are found useful.

Of 30 patients readmitted during the year, 16 had previously had sulphone, six of them having been treated for two years before discharge, and the remainder for shorter periods. The relapses appear to have been most common in tuberculoid cases.

The report gives details of farming and social, building and educational activities. The operating theatre provided by a grant from BELRA has been very useful.

The Annual Report of the Medical Department, Tanganyika, for 1953, contains the following statement about leprosy:

Cases of leprosy in Government and mission institutions at the end of the year totalled:

Government	976
Mission	3,792

It is well known that these numbers represent a very small proportion of the total number of cases in the territory, which the Interterritorial Leprologist has estimated as being as high as 100,000 cases of active infection.

During the past year measures were intensified to ensure that the best use is made of the accommodation available for the treatment of leprosy patients. In general, only those cases likely to benefit from institutional treatment were retained in the leprosaria; the burnt out or untreatable cases being discharged to their homes wherever possible.

There are seventeen leprosaria in Tanganyika where specific anti-leprosy treatment is given. Five of these are administered by Government (either central or local), and the other twelve by missions. British Empire Leprosy Relief Association staff work at the two principal Government leprosaria, Makete and Chazi, and at two mission stations, Mngehe and Lulindi. The largest leprosaria are those run by the Benedictine Mission at Peramiho and Ndanda in the Southern Province, the Augustana Lutheran Mission at Mkalama in the Central Province and the Africa Inland Mission at Kolandoto in the Lake Province. Other large settlements are those maintained by Government at Chazi in the Eastern Province, and Makete in the Southern Highlands; by the Universities

Mission to Central Africa in the Southern Province; and by the Church Missionary Society in the Central Province.

Treatment of leprosy with sulphone drugs continued on a large and increasing scale. Results are encouraging, although during the year certain centres have reported a number of relapses among patients who had previously undergone sulphone treatment. Drugs are issued free of charge to all approved centres, including mission centres where treatment can be given by experienced staff under qualified supervision.

The Medical Department employed two medical officers on whole-time leprosy duties during 1953. Since it is impossible to provide in-patient treatment for all cases, increasing emphasis is being given to encouraging the development of out-patient leprosy services.

The most notable progress in the development of out-patient facilities for the treatment of leprosy was in Tanga District. Here, the small Government leprosarium at Mtindiro was the centre of a district-wide system of out-patient treatment posts visited on regular days by the medical officer in charge of the scheme. When treatment was first offered very few patients appeared. Inquiry revealed that they were afraid of being compelled to enter Mtindiro leprosrium. There was also a widely held conviction that leprosy could not be successfully treated. When it became clear that sulphone did favourably affect the course of leprosy there was a dramatic increase in the number of persons offering themselves for treatment, and patients began to appear even in places where, during his preliminary investigations, the medical officer had been assured that no leprosy existed.

In spite of the bad roads and difficult weather conditions the medical officer was able to visit each centre weekly. Apart from treating leprosy, he spent much time advising patients on their diet owing to the widely-held belief that a person suffering from leprosy should eat only such food as decayed meat, porridge made from old grain, and wild vegetables. Fresh corn, salt, sugar and oil are denied him, and this abstinence frequently causes severe malnutrition. The progress of the work was greatly helped by the interest and assistance rendered by the nursing sisters employed by various sisal estates visited. In addition, African dressers from various native authority dispensaries assisted in bringing in new patients. By the end of the year approximtaely 1,000 patients were under regular treatment.

ABSTRACTS

UNGAR, J., TOMICH, E. G., PARKIN, KATHLEEN, R. and MUGGLETON, P. W.

Effect of Pyridoxine on the Action of Isoniazid. Lancet, 2, July, 1954, p. 220.

The toxic effects of isoniazid given for long periods are discussed, including " burning feet syndrome " and pellagra (suggesting vitamin deficiency), agranulocytosis, skin rashes, headache dizziness, pains in hands and feet. A record is quoted that the symptoms are not relieved by giving nicotinamide or vitamin B1. A recent report is made that neuritis occurring in 40% of patients treated with isoniazid is relieved by giving pyridoxine.

The present paper records studies in animals. High doses of isoniazid retard growth and cause involution of thymus and testes and reduce fertility. These effects in animals can be prevented by giving pyridoxine but not nicotinic acid. Pyridoxine did not interfere with the action of isoniazid on tubercle bacilli in cultures or in experimental animals.

It is suggested that patients receiving isoniazid and showing signs of drug intolerance should be given pyridoxine.

FLOCH, H. and RIVIEREZ, M.

Discussion sur le role possible de l'heredite dans la transmission de la lepre. (Discussion of the Possible Role of Heredity in the Transmission of Leprosy.) Bull. Soc. Exot. 1953, v. 46, No. 6, 922-5.

The case is described of a child born of a mother who had suffered from leprosy. This child developed a lesion of the left buttock on the 8th day after birth, and this gradually spread to the hip and to the back. On repeated smears and biopsy no bacilli could be found. The lesion continued till the death of the child at the age of between 2 and 3 months. The biopsy showed diffuse cellular infiltration in the superficial part of the dermis and distension of blood vessels. The question is discussed whether leprosy can be hereditary, and it is concluded that this is not possible, but that very occasionally there may be a congenital infection in the uterus.

ERNEST MUIR.

MONTESTRUC, E.

Vaste leprome bacillifere chez un enfante de trois mois ne de parents sains. (Coexistence d'une tache monoglique.) (Extensive Bacillary-Positive Lepromatous Lesions in a Child of Three Months born of Healthy Parents). Bull Soc. Path. Exot. 1953, v. 46, No. 6, 877-80.

At the time of examination the child was 3 months old. Leprous lesions covered about one-fifth of the body surface and numerous bacilli were found in serum taken from the lumbar region. The dermal lesions were first seen when the child was 2 months old. As far as the authors know this is the earliest age at which lepromatous leprosy has been found. As the parents were healthy it is presumed that infection was obtained from the father's sister who not only had leprosy but had nodules of the elbows rich in bacilli. When leprosy occurs in infants it has been suggested that infection takes place in the uterus, but here there is no question of this as the mother was healthy, and the danger of familial or cohabitational contagion is clearly shown. There was also a small naevus showing through the leprous lesion, but this is not supposed to have any connection with the leprous infection.

ERNEST MUIR.

MONTESTRUC, E.

A propos de la classification de la lepre de R. Chaussinand. (La reaction d'Hemagglutination dans les differentes formes de la lepre.) (The Classification of R. Chaussinand and the Haemagglutination Test in the Different Forms of Leprosy.) Bull. Soc. Path. Exot. 1953, v. 46, No. 6, 985-91.

This is a plea that the simple form of classification advocated by Chaussinand should have added to it the haemagglutination test results (Middlebrook and Dubos) as a means of dividing the three principal forms of leprosy. Results of a number of tests are tabulated in support of the proposition: not only were more positive results obtained in the lepromatous form, but the mean titres were very much higher.

ERNEST MUIR.

FLOCH, H. and SOHIER, R., with the technical collaboration of BUISSIERE.

La reaction d'hemagglutination a la tuberculine (type Middlebrook-Dubos) duns la lepre. (The Haemagglutination reaction to Tuberculin (Type Middlebrook-Dubos) in Leprosy. Bul. Soc. Path. Exot. 1953, v. 46, No. 6, 918-22.

The reaction was tested in the sera of 102 leprous patients. In lepromatous cases positive results were higher (64.5 per cent), than in tuberculoid (25.9 per cent), and indeterminate cases (22.8 per cent). It might be convenient to study this test as additional biological evidence in the diagnosis and prognosis of leprosy.

ERNEST MUIR.

MARKIANOS, J.

Action eventuelle de l'injection de lepromine sur l'apparition de la lèpre et sensibilité tardive a cet antigene provoquée par la vaccination au B.C.G. (Eventual Effect of Lepromin Injection on the Appearance of Leprosy and Delayed Sensitivity to this Antigen Provoked by B.C.G. Vaccination.) Bull. Soc. Path. Exot. 1954, v. 47, No. 1, 30-32.

The following is a translation of the author's summary:—

Leprosy became manifest 21 days after injection of lepromin in a child having a negative Mitsuda reaction, who had been separated from leprous parents for 22 months. The question is posed whether the injection of this antigen had favoured the appearance of a previously latent infection. Later, B.C.G. vaccination resulted in a positive Mitsuda reaction 194 days after this single injection of lepromin.

H. J. O'D. BURKE-GAFFNEY.

BLANC, M., PROST, MARIE T. and MARIE-SUZANNE (Soeur).

Influence de l'injection d'une suspension d'un mycobacterium isolé d'un cas de lepre (souche Chauviré) sur la reaction de Mitsuda. (The influence of the Injection of a Suspension of the Mycobacterium Isolated from a Case of Leprosy (Chauviré Strain) on the Mitsuda Reaction.) Bull. Soc. Path. Exot. 1953, v. 46, No. 6, 1009-14.

This is a suspension in normal saline of a mycobacterium isolated from a leprous patient, cultivated in Sauton's medium, and killed by heating to 120° C. This antigen is not the mycobacterium of leprosy as it gives a positive reaction when injected intradermally into cases of leprosy of the lepromatous type. It is claimed that of 339 subjects studied, 240 (70.8 per cent) had a negative Mitsuda reaction, that after injection of this antigen in these 240 subjects 155 (64.5 per cent) became Mitsuda-positive, and that of the lepromatous cases (it does not say how many or their general condition) 50.8 per cent. became Mitsuda-positive.

ERNEST MUIR.

LAVIRON, P., LAURET, L. and JARDIN, C.

Treatment de la lèpre par les injections hebdomadaires de suspensions de T.B.1. (Note preliminaire.) (Treatment of Leprosy with Weekly Injections of T.B.1 Suspensions). Bull. Soc. Path. Exot. 1953, v. 46, No. 6, 886-9.

The suspension consists of 60 gm. of crystallized T.B.1 in 460 c.c. of a mixture of equal parts of neutral chaulmoogra oil and chaulmoogra ethyl esters with 4 per cent of guaiacol. Of this the patients received 5 c.c. weekly, equal to 600 mgm. of T.B.1. The

trial had only lasted from 3 to 5 months, but already 70 per cent have shown amelioration. It is hoped by further trials to study the absorption and work out the dosage. In the 25 patients already treated there were no adverse signs apart from slight local pain and occasional slight reactions.

ERNEST MUIR.

LAVIRON, P., LAURET, L. and SCHNEIDER, J.

Etude de l'activite antilepreuse des thiosemicarbazones. (Study of the Antileprous Activity of the Thiosemicarbazones.) Bull Soc. Path. Exot. 1953, v. 46, No. 6, 880-85.

In addition to T.B.1 the authors tried out 3 other allied derivatives (4544, 4545 and 4546 R.P.); in none of these 3 were the results encouraging or comparable to those obtained with T.B.1. With the last (T.B.1) 38 patients were treated. Of 32 lepromatous cases, 20 showed much improvement after periods varying from 12 to 38 months' treatment, and 9 showed less improvement. Of 3 tuberculoid cases 2 showed considerable improvement, and of 3 undifferentiated 2 showed much improvement. The authors consider that clinical improvement with T.B.1 is equal to that with sulphones, but that the bacteriological action is less marked. T.B.1 may be used as a complement to, or a substitute for, sulphones, but it should only be used under hospital conditions or for individual medication.

ERNEST MUIR.

CHAUSSINAND, R., GABBAI, A., DORENLOT, H. and VIETTE, M.

Action de l'hydrazide de l'acide Isonicotinique sur la maladie de Hansen. (The Action of Isoniazid in Leprosy.) Bull. Soc. Path. Exot. 1953, v. 46, No. 6, 905-10.

After treating 44 patients, 31 of whom were lepromatous, for periods varying from 3 to 12 months with isoniazid alone or in association with D.D.S., the authors found that isoniazid was well tolerated in daily doses up to 7 mgm. per kgm. of body weight. There were cutaneous improvements in 13 lepromatous and 1 indeterminate, but there was aggravation of nerve symptoms in some of the tuberculoid cases. Isoniazid is better tolerated but less effective than the sulphones. It cannot be recommended by itself, but may be used with profit along with the sulphones, and more trials should be made of this combination.

ERNEST MUIR.

LAVIRON, P. and LAURET, L.,

Essais de traitment de la lepre par l'hydrazide de l'acide isonicotinique (I.N.H.) seul ou associé a la diamino-diphenylsulfone (D.D.S.) et a la streptomycine. (Treatment Trial of Leprosy with Isoniazid either alone or in Combination with Dapsone (D.D.S.) or Streptomycin.) Bull. Soc. Path. Exot. 1953, v. 46, No. 6, 896-9.

Under the different categories 18, 9, 10 and 10 patients were treated for 5 months, the daily dose of isoniazid rising to as much as 500 mgm. The only improvement was an increase of weight which occurred in 80 per cent of the patients. The only patients who improved as regards the disease of leprosy were those who were getting small amounts of D.D.S.

ERNEST MUIR.

FLOCH, H.

Interet du benzal-isonicotyl-hydrazone-meta-sulphonique en therapeutique antilepreuse. (The Use of Isonicotyl Hydrazone of Metasulphobenzaldehyde in Treatment of Leprosy.) Bull. Soc. Path. Exot. 1954, v. 47, No. 1, 21-5.

The author has already reported on his results with isoniazid. Since then he has treated for 10 months 18 patients, 8 of whom were lepromatous, with the sodium salt of isonicotyl hydrazone of metasulphobenzaldehyde (G.605). With one exception they all benefited, 2 improved very much and 4 became bacteriologically negative. In the author's opinion the risk of drug resistance to G.605 is similar to that with isoniazid, but the former is active and can be used with profit in association with sulphones in the treatment of leprosy. The average supported dose was 3 gm. daily. For details of actual cases, the original should be consulted.

ERNEST MUIR.

FLOCH, H.

Les hydrazides derivés de l'acide isonicotinique. Leur essai (notamment celui du benzal isonicotyl-hydrazone metasulfonique) en therapeutique antilepreuse. (The Hydrazides Derived from Isonicotinic Acid, their Trial in the Treatment of Leprosy, especially that of Isonicotyl Hydrazone of Metasulphobenzaldehyde.) Arch Inst. Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 308, 1953, Dec., 10 pp.

As the consensus of opinion is that isoniazid is of little use in the treatment of leprosy, the author considered certain other kindred substances and chose from among them the sodium salt of isonicotyl hydrazone of metasulphobenzaldehyde (G.605). He found that patients tolerated this drug in about 10 times the dose of isoniazid and that the results were much more favourable. For

adults the most suitable daily amount was 3 gm., larger doses producing gastric disturbances. In 6 lepromatous cases there was bacteriological as well as clinical improvement. A borderline case became bacteriologically negative after 6 months' treatment. As there is a danger of bacilli becoming drug-resistant, the author prefers to use G.605 in combination with sulphones.

ERNEST MUIR.

CHAUSSINAND, R., COLIEZ, R., LEFEBVRE, J. LOISEAU, A. N. and VIETTE, M.

Essai de traitment des griffes cubitales dans la maladie de Hansen par les ultra-sons. (Trials of Treatment of Ulnar Deformity in Leprosy by means of Ultra-Sonic Waves.) Bull. Soc. Path. Exot. 1953, v. 46, No. 6, 899-904.

A quartz electric generator of a frequency of 1 megacycle was used, and the terminal was applied along the course of the ulnar nerve for 8 to 10 cm. above and below the elbow, being the part where the nerve is most superficial. In 2 out of 3 patients with marked claw-hand there was marked improvement, which occurred during the time of the application. The authors suggest that this method should be used on a larger scale.

ERNEST MUIR.

MURAZ.

Note preliminaire sure une organisation rationnelle, en Afrique Equatoriale Francaise de la lutte contre la lepre. (Preliminary Note on a Rational Organisation for the Fight against Leprosy in French Equatorial Africa.) Bull. Ecad. Nat. Med. 1954, v. 138, Nos. 9/10, 155-9.

From recent surveys it is calculated that there are in the French West African territories of Oubangui-Chari, Tchad, Middle Congo and Gabon no fewer than 56,670 sufferers from leprosy. In one district of 14,858 inhabitants, more than 10 per cent suffer from leprosy. At the end of 1953 only about one-fifth of the known cases were under treatment. The scheme proposed is to form villages for leprosy patients, some 78 of these for the whole Federation. Treatment would be given in the form of injections of sulphone (D.D.S.) suspended in chaulmoogra esters twice a month. There would be a large staff of doctors and assistants and, at first, selected treatment centres. Transport would be furnished by 15 motor vehicles and 62 bicycles. In the leprosy villages there would be mass oral vaccination with B.C.G., if its value is confirmed, and arrangements would be made for improved agriculture, horticulture, etc. They would be arranged in a manner similar to the

villages already in existence for the prophylaxis of sleeping sickness. (The author originally advocated such measures nearly 3 years ago.)

ERNEST MUIR.

HOBBY, GLADYS L., HANKS, J. H., DONIKIAN, MARY A. and BACKERMAN, T.

An Evaluation of Chemotherapeutic Agents in the Control of Experimental Infections due to mycobacterium leprae murium. Amer. Rev. Tuberculosis, 1954, Feb., v. 69, No. 2, 173-91, 9 figs. (13 refs.).

This paper describes a laboratory method which may serve to determine the efficacy of drugs in the treatment of leprosy, although the authors acknowledge that argument from murine leprosy to human may not entirely apply and that in any case clinical confirmation is necessary. Mice were inoculated intraperitoneally with a suspension of rat testis infected with the Hawaiian strain of Myco. leprae murium. The spleens from mice killed at intervals were homogenized by an elaborate process and acid-fast bacilli counted in films made by a quantitative method. Various control experiments showed that successive counts made in this way were reproducible and reflected accurately the progress of the disease. Therapeutic tests on this basis showed that isoniazid and a chemical isoniazid-streptomycin combination (streptomycylidene isonicotinyl hydrazide) were the most effective drugs, streptomycin and viomycin being next most effective and more so than Promin. Oxytetracycline (terramycin), actithiazic acid, amithiozone, carbomycin and D.D.S. (dapsone) were ineffective. It is pointed out that clinical evidence of the efficacy of some of these drugs is unsatisfactory or contradictory and implied that further clinical trials based on laboratory evidence such as that described in this paper should be instituted.

L. P. GARROD.

(All the above abstracts are copied from the *Tropical Diseases Bulletin*, Vol. 51, No. 8.)

CORRESPONDENCE

The Editor,
"Leprosy Review."

Dear Sir,

In "Leprosy Review" of October 1954 (Vol. 25, No. 4), Dr. Relvich refers on page 180 to the fact that in 1953 Latapi and his co-workers reported good results with isoniazid in lepromatous leprosy. He does not mention a further report by the same authors in which they record deterioration in all their patients after continuing treatment a few months longer; and, as this report is not generally known, I would like to take this opportunity to draw attention to it. It appears in the "International Journal of Leprosy" (1953), Vol. 21, No. 4, page 569, in the form of a short abstract in Spanish of their paper presented to the Madrid Congress. In a personal communication Dr. Latapi wrote: "Our final results, in fact, were identical to yours. The apparent improvement which we pointed out in our report published by the J. Invest. Dermat. dated July, 1953, was followed later on by a definite deterioration in all cases."

I am, Sir,

Yours faithfully,

W. H. Jopling, M.R.C.P., D.T.M. & H.

Jordan Hospital,
Earlswood, Surrey.
January 19th, 1955.

The Editor,
"Leprosy Review."
Dear Sir,

I have read with great interest your editorial in the October issue of the "Leprosy Review." However, I should like to take up one or two points in that editorial with which I would not quite agree.

In our conditions where in diagnosing the tuberculosis of lungs we have to depend entirely on physical examination by a physician not specialised in the diseases of chest and on examination of sputum we can only hope to pick out cases of patent tuberculosis and my paper has dealt only with these more severe cases of tuberculosis. This is why I wrote at the end of the second paragraph of my paper: " There might have been a decrease in morbidity. . . . There has been no change whatever in case mortality." It seems to me that this statement is on the whole in agreement with what you say on page 173: " Sulphone given alone as a treatment for patent tuberculosis gives disappointing results."

It might interest you that I have noticed recently in our patients what seems to be a downward trend in the morbidity of tuberculosis of lungs. During the last eight months we have diagnosed only four cases of open tuberculosis, out of whom two were new patients. This small number of cases which we find nowadays might mean that sulphone prevents the development of tuberculosis of the lungs or arrests the disease before it becomes obvious enough to be diagnosed by us. There is, of course, no definite proof and other factors might be involved here as well.

To sum up, our differences of opinion as to value of sulphones in tuberculosis does not seem to be as great as you suggest in your editorial.

Yours faithfully,

A. L. Relvich.

Ossiomo Settlement,

Agbor, Nigeria.

February 28th, 1955.