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EDITORIALS

The article by Dr. J. A. K. Brown, abstracted in this issue (p. 87), raises a point of great interest and importance: can patients with the tuberculoid type of leprosy spread the disease? He writes: "There are parishes of 1,000 people dispersed over 20 square miles without a single lepromatous case, and tuberculoid cases occur five miles or more from the nearest lepromatous patient. It would require the greatest mobility and popularity on the part of the lepromatous subject if all the leprosy in the country could be attributed to them. Open cases could act as the only source of infection in Uganda on the assumption of carriers, an assumption less easy than that tuberculoid cases are infectious."

Put so, this conclusion seems reasonable enough. But what is meant by "a carrier" when applied to leprosy? An "incubatory carrier" is defined as "an individual who is in the incubation period of an infectious disease and will soon manifest the symptoms." Do such cases occur in leprosy? The description of a patient encountered some years ago may help to answer this question. This patient appeared at the Skin Department of the School of Tropical Medicine, Calcutta, where he was treated for three months for seborrhoic dermatitis. It was then noticed that there was a certain amount of anaesthesia of the lower limbs, and he was sent to the Leprosy Department as a possible case of neural leprosy. On inspection the patient appeared strong and healthy, and there was nothing to suggest leprosy, but there was a mild degree of anaesthesia of the ankles. Routine bacteriological examination of skin smears, however, showed massive infection with lepra bacilli extending over almost the whole skin surface. Even epithelial scrapings showed masses of bacilli on the surface of the skin. The skin of this patient was very dark, which probably partly accounted for the absence of visible signs. After a few weeks nodules began to appear, after which the diagnosis at sight was easy, but this patient must have been a potent unsuspected spreader of infection for years before he was first admitted for diagnosis and treatment. This was not an exceptional case, the writer has since then seen many like him, though few of them have shown such massive infection.

Should such a patient be called "a carrier"? This depends on the meaning of the word "incubation," which the dictionary defines as "the period between the implanting of an infectious disease and its manifestation." But obviously this definition is inapplicable to lepromatous leprosy as the manifestation required a microscopic examination. "Concealed" leprosy is a more

suitable term, and the existence of this condition has not been sufficiently recognised. There is reason to believe that if lepromatous leprosy became *manifest* as soon as it becomes *infectious*, the solution of the leprosy problem would be rendered much simpler. The only way to close this gap, which often extends for three or more years, is careful and laborious following up of diagnosed patients to their homes, and bacteriological examination of contacts.

Another, though probably much less frequent, source of concealed infection is the border-line form of leprosy, which may closely resemble and be mistaken for the tuberculoid, while still showing many bacilli on examination.

In the writer's own experience in Calcutta a high percentage of tuberculoid type patients denied at first all knowledge of contact with the disease. It was found, however, that careful and prolonged investigation carried on over a considerable time was able in the end to trace a clear connection with the disease in the majority of such cases.

Reacting tuberculoid leprosy may show large numbers of bacilli in the skin, but, apart from this, before accepting the hypothesis that ordinary tuberculoid leprosy is responsible for spreading infection, even to specially susceptible people, it would be well to prosecute a careful follow-up of contacts as mentioned above.

. . . . . .

Much literature has gathered round the controversial subject of classifying leprosy, and perhaps we have sometimes lost sight of the wood because of the trees. It may be well to ask "What are the reasons for wanting a classification?" Without keeping this question and its answers clearly in mind there is a danger of seeking classification just for its own sake, and that may create a vicious circle which leads nowhere.

I suggest that there should be five clear objectives in mind when we set about dividing cases:

(1) *Control of the spread of infection.* We must divide the infectious from the non-infectious, and divide the infectious according to their degree of infectiousness. In assessing this the important points are the number of bacilli and the degree to which they are likely to be shed from ulcers, etc. On the principle that "prevention is better than cure," surely this division should have the first consideration.

(2) *Facilitate treatment.* The standard treatment of leprosy is now the sulphones, and particularly the simplest form of DDS, and this treatment is appropriate for all forms and stages of the

disease. But patients vary in the dose they can tolerate, and particularly in the initial amount and the rate at which it can be increased. A few suffer from anaemia, anorexia and other complications, and these should perhaps be corrected before specific treatment is begun. Another small number appear, at least at first, to be intolerant of sulphones, and may with advantage be changed for a time to a course of thiosemicarbazone.

A special category is also required for those who have developed or are in danger of developing secondary neural lesions of the limbs or face. The future of many patients depends on appropriate early attention to these conditions.

(3) In a dreaded disease like leprosy much depends on a reliable *prognosis*, and patients should be divided according to their chance of recovery, the time required and the possibility of permanent sequelae. Here the clinical phenomena, the lepromin reaction, and the duration and advance of the lesions are the main determining factors.

(4) Patients may also be grouped according to certain *extraneous elements* apart altogether from the disease itself, but which have an important bearing on the danger of spreading the disease, on the effectiveness of treatment and on the chance of recovery. Among these are the patients' social and economic circumstances, whether they allow of sufficient nourishment, and whether there is freedom from anxiety about the family in the case of the breadwinner. There are also the character, mental attitude and intellectual capacity of the patient, upon all of which depend so much his whole-hearted co-operation, so essential during the prolonged period of treatment.

(5) Lastly, there is the division of leprosy from the *research* point of view. This may to a certain extent include all the above divisions, but also takes cognisance of pathological, biochemical, serological and other matters which, though important for the increase of our knowledge of leprosy, are of less direct significance in dealing with the individual patient.

Whether leprologists agree to be content with the Madrid Congress classification, or decide to amend it further, the above practical divisions should not be lost sight of. Particularly they should be kept in view in assessing the value of new drugs in the treatment of leprosy.

CORRECTION

At the foot of page 37 of the last issue, " yield more readily to treatment than " should read: " yield as readily to treatment as."

FIVE YEARS OF MASS DAPSONE (DDS) TREATMENT

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After five years of treatment of large numbers of leprosy patients with oral Dapsone, I feel that a fair assessment of its advantages and disadvantages can be made. Of its success in reducing the total incidence of leprosy little will be said as Dr. T. F. Davey with the help of others, including myself, is preparing a paper about this.

Suffice it to say that total numbers reached, in Onitsha Province, were 10,600 in 1951 when the use of Dapsone treatment had been fully launched (about a year after it began). Since then a steady decrease has taken place in total numbers to 7,800 at present. This has been due to a continued higher rate of discharge than new and relapsed cases added together. In addition the more severe types are seldom seen except in areas opened up recently.

Progress through Treatment of Lepromatous Cases

These have responded well bacteriologically. Out of over a thousand in various stages, there has been no exception unless some complication such a dermatitis has interfered with treatment. Nodules and infiltrations have become small, leaving skin wrinkled. Ears have sometimes remained thickened or misshapen, but signs of activity have gone.

The severest nodular lepromas, started on treatment in 1950, are now mostly reaching the stage of negative smears. All have much improved. In most the bacilli are much fragmented or have been reduced to acid-fast dust. The milder lepromas responded more quickly.

In 1952, 17 of the more obstinate lepromas were given isoniazid in addition to dapsone. Progress was not much accelerated, but reaction seemed less. These and a few other patients had had sulphetrone since 1949.

Complications

After five years a better assessment can be made of complications than was made in the two preliminary articles in LEPROSY REVIEW, July 1951 and July 1952. The incidence and importance

of different complications seems to have changed, and certain original misconceptions have been proved false.

Dermatitis, with associated hepatitis, is by far the most severe and common of the complications caused by taking dapsone (as distinct from reactions of leprosy during treatment). The incidence of dermatitis continues to be low—about 2 per cent. Nearly all are fairly easily desensitised by a course of sulphetrone mixture starting with 1/80 gram. of sulphetrone. There remain a few who have recurrences. These, at first, were put on thiacetazone as an alternative method of treatment. As, however, it is now established that nearly all acquire a resistance to thiacetazone in about two years, we feel that this is not an adequate alternative.

We now give thiacetazone, but at the same time start a very slow and cautious desensitisation course, completing it in about six months instead of ten weeks with the normal course. This has proved successful.

Occasional cases of *mental derangement* continue to occur, but they are much rarer on twice-weekly treatment. Two mild cases have occurred in 680 settlement patients during the last year. This compares with 24 in the first year out of 1,000 patients on daily treatment with dapsone. A few patients complain of sleeplessness or queer feelings in the head on treatment days. These cases are brought under control by reduction of dapsone dosage. The early recognition of such cases may, in part, be responsible for the low total numbers.

When dapsone was first used on a wide scale, we feared *liver damage, jaundice, anaemia, ascites and oedema* as complications of dapsone treatment. Dermatitis has, as part of its manifestation, a hepatitis which can be very severe, and if repeated can lead on to cirrhosis. Anaemia occurred in some cases and ascites and oedema are, of course, terminal events in both cirrhosis and anaemia of any cause. As a consequence great caution was at first used in the presence of either anaemia or enlarged liver. Extra iron was given as ferrous sulphate to all patients and any with signs of these diseases were given only very small doses of dapsone.

After five years of observation, I am convinced that this early caution was rather excessive. It is true that dermatitis, particularly if it is recurrent, causes severe hepatitis leading to cirrhosis, but in those who never show sign of dermatitis I have seen no evidence of liver damage. On the other hand, I have seen dozens (literally) of patients coming with large hard livers, obvious signs of undernourishment, anaemia and in some cases early oedema and ascites, who have greatly improved under treatment with dapsone. The liver has remained large, though in some cases a slight reduction in size has occurred. The other signs have improved and in some cases very greatly. Mild anaemia may occur in the first three or four months in a few cases, but soon disappears.

There are two explanations which I suggest for this. Dapsone, in many people, produces a much greater appetite. This may have a good tonic effect in undernourishment. It may, however, be noted that in this part of the country undernourishment is of quality rather than quantity of food, cassava taking a much greater place in the diet than it should. The other explanation may be that dapsone is a general bacteriostat and that some infection which is the hidden cause of the trouble may be overcome by it. Even many healthy patients have said that they are stronger and

less easily tired when taking dapsone, though some complain of weakness on the day of treatment, particularly in the early months.

In fact, I believe that dapsone has a tonic action, but that the occasional sensitisation in which severe damage is done to the liver has led to it being regarded as a liver poison. Of course, as a general tonic, its occasional severe complications rule it out. Jaundice has practically never occurred since the early days. As there was an epidemic at that time affecting many without leprosy, I consider that this had no significance in relation to dapsone.

Reactions

Here it is important to state that we started with many severe lepromatous patients, some of whom had resisted hydnocarpus treatment for ten or more years. The new patients coming in now are more and more early cases of leprosy and therefore not subject to reactions in the same degree.

Lepra reaction (erythema nodosum) occurs mainly in the severest lepromatous patients. As these cases are becoming rare, lepra reaction is met much less frequently than before. Treatment with Stibophen injections and reduction of dapsone normally control them within a few days. A few unfortunate patients have frequently repeated reactions, though most are now mild.

Eye reactions have become so rare that they need no special mention. Again they occurred in the most severe types of leproma in the early years of dapsone treatment.

Lepromatous nerve reactions are probably the most distressing complications of dapsone treatment for us now. They occur mostly at the time when bacteriological smears are becoming negative. They give rise in some cases to sometimes intractable pain and thickened tender nerves. I say "in some cases' advisedly. I have been surprised that many have had tender ulnar nerves as thick as a finger. They have had repeated acute pain in them. They have in some cases refused operation or had an operation on one arm but not on the other, equally affected. Yet a surprising number of them gradually improve with no loss of muscle power or feeling. This is at present a mystery. Others develop paralysis and wasting.

Injection of procaine gives temporary relief in early cases, but after a time the nerve is too hard to have anything injected into it. Incision with or without stripping of the sheath, relieves pain in most cases, but by no means all. At operation, it is often noted that the sheath is exceptionally hard and adherent even in those with little or no paralysis or wasting. After trial of early and late operation, injection with procaine, reduction or stoppage of dapsone, alternative treatment with thiacetazone and use of antihistamines, ACTH or sedatives, I think the best treatment is as follows:—

Reduction of dose temporarily (2-4 weeks to ½ dose) relieves the reaction in many cases and often there is no serious recurrence, or if it occurs, it may be dealt with in the same way. In some cases, reactions occur with increasing severity and reduction of dose does not relieve the situation unless it is prolonged on a very low dosage level. In these cases

it is often worth transferring to thiacetazone therapy which gives rise to fewer nerve reactions. Thiacetazone, however, is not always successful and at any rate the drug leads to resistance after about two years of use. Usually, however, this period gives a long enough respite and the reactions seldom recur when dapsone is restarted.

Sedatives such as Tab. Codeine Co. are very useful. Occasionally morphine or pethidine may be needed in severe cases. Operation with stripping or incision of the sheath would appear to be logical in a condition with such great swelling and tenderness. But the fact that many show none of the symptoms of pressure on the nerve fibres—paralysis and anaesthesia—even after repeated reactions, makes one wonder whether it is necessary unless one or other of these signs are appearing. The results are by no means consistently successful and pain may continue after the operation. If practised on early cases, the results are open to question, as many get better after one or a few reactions without paralysis or anaesthesia. My own practice is to operate on fewer lepromatous nerves than previously.

ACTH has been used and it reduces the pain temporarily, but with its adverse effect on the general course of the disease, it is a type of treatment only very rarely to be considered. Exercises, reduction of dapsone and patience on the part of staff and patient seem to be the most important methods of overcoming this, the most distressing trouble arising during dapsone treatment of lepromas.

* An experiment with injection of hyalase and procaine has been started and gives good early promise. I hope to report more fully when I have had time to assess the results.

Tuberculoid nerve reactions do not occur frequently, but due to the caseation, they can cause severe and permanent damage in a short time. Early operation is the only remedy for this.

In the borderline and in the atypical tuberculoid leprosy, particularly if the lesions are much raised and situated on hands, feet or face, severe reactions with paralysis often occur early in treatment. This is particularly true if the dosage is rapidly raised. In these cases I now start treatment on a low dosage and increase more slowly, instructing the Leprosy Inspector administering the drug to observe carefully for nerve reactions and reduce or stop Dapsone at the first sign, referring the patient to the doctor.

Our normal induction of treatment is:—

100 mg. Dapsone twice weekly for 3 weeks
200 mg. " " " " " "
300 mg. " " " " " "
400 mg. maximum.

For these cases, I usually advise a maximum of 200 mg. for at least three months. When reactions occur in this type, they are usually very different from those seen in leproma. Pain is not a marked feature, but severe paralysis and anaesthesia may occur early in the reaction. Stoppage of Dapsone does not lead to a rapid reduction of reaction or to recovery from paralysis. But with patience, exercises and careful raising of dapsone dosage most of these patients gradually recover the use of their limbs.

Nerve stripping may be useful, but I have found many with such a length of nerve thickened that operation would be impracticable. An example of this is in hospital now with ulnars, medians and medial antebrachial cutaneous nerves greatly thickened from the axilla down to the lowest branches. The radials are also affected, but cannot be so readily felt. Paralysis appears almost complete, but I have seen such cases recover a considerable amount of movement.

* See the next article.

About a quarter of the tuberculoid and indeterminate cases at some time during their treatment have crops of new macules, but unless they are accompanied by nerve signs it seems better to continue them on full dosage of Dapsone.

Residual Hypopigmentation

This is distressing to the patient who has, after all, come for treatment of the unsightly patches on his skin which make his friends and relatives shun his company. If he returns home after treatment with much hypopigmentation it is difficult for his home people to feel that the leprosy is properly cured.

Hypopigmentation also poses a problem to the doctor responsible for discharging him as free from active leprosy and perhaps still more for the person re-examining discharged patients. An over-anxious patient, or one whose relatives are worried, will often claim as new a patch which has been present for years. Many times even birthmarks have been produced as new patches of leprosy to prove the necessity to continue or restart treatment.

We have found it useful to estimate the percentage hypopigmentation and not to regard it as inactive until it remains constant for two or three examinations. This is obviously only a rough guide, as different observers, different light and perhaps different opinion by the same person all have their effect.

In inactive patches it is often found that the hypopigmentation is irregular, with greater loss of colour in the wrinkles of the skin than in the raised parts. In some cases there is apparent thickening of the skin, but on palpation, stretching and pinching, it is found that it is only due to course wrinkling from loss of elasticity.

When hypopigmentation has become stationary and there is no sign of erythema or thickening of the macule, trichloracetic acid 25 per cent, seems to be as satisfactory as any. That or any other caustic tends to form a dark scar, sometimes mottled, but it satisfies the patient and his relatives and is therefore justified. Overcautious application is practically useless.

Drug Resistance

No definite case of Dapsone resistance has yet been shown by us but we have a few cases which lead us to suspect its development. One lepromatous patient has shown slow but steady improvement over five years of Sulphetrone and Dapsone treatment, but in the last two smear results there is a slight rise again. No clinical deterioration is shown and the bacteriological index is still well below that at the start of treatment. A few tuberculoid patients remain with active-looking lesions for four or more years. These cases must be watched and if the drug-resistance is confirmed it will be reported.

Relapses

During the past three and a half years we have been averaging nearly 3,000 discharged per annum. Few of these have been lepromatous except in recent times.

The average relapse rate is about 7 per cent.

This, however, does not give a true picture. Relapses have occurred mainly in three types of patient:—

(a) In those previously treated with hydnocarpus oil and apparently inactive, many were given a course of dapsone of one year or less.

(b) In clinically tuberculoid cases, not completely typical, either with not very clearly defined edges or with lack of healing centre, response to treatment is usually dramatic. Lesions disappear in a few months, but lacking an initial positive smear, they were given a relatively short course of Dapsone, usually 18 months.

(c) Those not attending regularly for treatment due to laziness or personal difficulties.

Criteria for Discharge

In all cases a minimum of 24 months' treatment is now observed. In nearly all cases 30 or more months' treatment are given. Typical tuberculoid cases with few lesions and strongly healing centre are the least likely to relapse. Extensive lesions, poor central healing or poor definition call for at least 2½ to 3 years' treatment. When the smear has been positive, at least 2 years' treatment is given after the first negative smear. In cases where the patient is content to stay on, this is prolonged.

Organisation

We have had two doctors most of the time—sometimes only one—and two Leprosy Control Officers, laymen with teaching in leprosy who are responsible for clinical supervision, supplies, sanitation and the many problems which arise in district work. The actual administration of Dapsone and dealing with the complications in the first instance, are in the hands of the Leprosy Inspectors, some with primary and some with secondary education plus six months to a year of tuition by us. There are 56 clinics and about 7,800 patients at present.

This organisation is quite adequate for the simple cases. The more difficult patients are brought in to the Settlement or to the hospital, which has a trained nursing staff plus ward attendants who are themselves patients. This enables a closer watch to be kept on those needing most attention.

Safety of Mass Dapsone as Against Alternatives

At the commencement of treatment by this method the obvious dangers of Dapsone—dermatitis, psychosis, severe reactions and occasional death arising from the first two were pointed out. Now an assessment of the alternatives can be made. With the adoption of twice-weekly treatment, and with experience in treatment of complication, the dangers are much less than they seemed at first.

Hydnocarpus oil was much less successful in treatment, but had less dramatic and obvious complications. Cases did, however, occur of tetanus, and I believe death from that cause was greater than death from Dapsone, even in the beginning.

Injections of Dapsone in oil or Sulphetrone carry this danger when administered by relatively untrained staff. They also involve greater organisational difficulties. Provision of a fully responsible trained staff with all facilities is impossible owing to lack of qualified people and of funds.

The only real alternatives, therefore, are to provide sulphone treatment in some way similar to that described, or not to provide anything for the majority of sufferers. This would, and does, from actual experience, result in black market sale of Dapsone with all the dangers inherent in the system described, plus others such as great overdose by enthusiastic salesmen or persistent underdose and irregular treatment for those who cannot afford it.

The dangers and advantages of injections of Dapsone in oil or sulphetrone as against tablets might be weighed up according to the local conditions of population density, roads, leprosy incidence and the staff available.

Abuses. I think it necessary to mention some abuses to which this drug is put, the cure of which is a moral and social rather than a medical problem. There is a wide illicit trade in dapsone as in all successful medicines in this country. Precautions, as much as we are able, are taken by us to avoid theft. Import restrictions are made, but still the trade goes on.

The knowledge that such trade exists makes us speak hesitantly about real statistics, though the fact that an ever-decreasing number of severe cases present themselves shows that the trend towards extinction of leprosy is really present.

The real danger to the whole campaign, I believe, lies in the early lepromatous patient who can easily conceal his disease by treatment which is insufficient to make him uninfective. Will this produce a drug-resistant strain? Will the hidden infecting agents be sufficient to keep leprosy control always in the future. Time alone will tell.

Meanwhile propaganda is a vital weapon, by written and spoken word and we hope a recently produced film will be really helpful.

Summary

Five years of experience in widespread oral Dapsone treatment has shown its practicability with a small qualified staff and a larger locally trained staff.

The difficulties arising from drug sensitivity and reactions of the disease, together with their treatment are discussed. So also are the organisational difficulties.

HYALASE (HYALUNONIDASE) INJECTION FOR LEPROMATOUS NERVE REACTIONS

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While visiting Oji River early in 1955, Dr. Gordon Currie suggested the use of hyalase to diminish the pain and disability of those with severe nerve reactions. He, himself, was on the move and has not had opportunity to test his idea. I have had that opportunity and with his permission I write about these cases.

At first I decided to choose my cases among those with severe reactions in two nerves, using the worst nerve to try the treatment and keeping the other for comparison. I also decided to use nerves which had had severe and frequently repeated reactions. Some nerve reactions are of short duration and repeated only once or twice so that success in these cases would not be significant. My first resolution was only kept partially, as the worse nerve almost invariably became the better nerve and with such intractable pain I could not leave the patient without effective treatment of the other nerve for weeks on end. Several of these patients had previously had procaine injections, nerve-stripping and plenty of Tabs. Codeine Co.

Hyalase was first given by dissolving one ampoule (3 mg.) in 20 ml. of sterile water. This was injected into the affected nerves. In some cases it was so painful that I decided to dissolve it in 2 per cent procaine instead. This, though still rather painful at first, as any intra-neural injection would be, was satisfactory. About 5 to 6 ml. were injected into each affected nerve, though account was taken of the size and length of nerve affected. Injections were given at weekly intervals and a course of five injections per nerve was used as the standard. Both these decisions were empirical.

All injections were attempted intraneurally, starting from the upper end of the nerve. Some of the worst cases, however, had such hard nerves that this was impossible. A perineural injection was then given.

When several nerves were injected at the same time, one ampoule of hyalase was dissolved per 20 to 30 ml. of solvent, e.g. when 75 ml. were needed, 3 ampoules were used.

Abbreviations.—L.U. and R.U.: Left and Right Ulner nerve. L.E.P. and R.E.P.: Left and Right External Popliteal nerve. L.M.C. and R.M.C.: and Right Musculocutaneous branch of E.P.

Case Reports

N.N. Female. Age. 26. Z/5121. Leproma 10 years standing. **May 1951,** started dapsone treatment. **September 1953,** first negative smear. Started nerve reactions shortly before smears became negative. Progressive increase in pain, but only slight paralysis and anaesthesia. **May 1954,** R. and L.U. nerves stripped, sheath very adherent to nerve and surrounding tissues. **July 1954,** continued nerve reactions in ulnars. **January 1955,** R. Radial and L. Median at wrist stripped. These were fairly successful, but ulnars continued painful, and R. and L.M.C. started reaction. **July 1955,** L.U. very painful, R.U. less so. Hyalase started in L.U. and dramatic improvement. R.U. started next week and R. and L.M.C. started next month. R. Radial started 6 weeks later.. She had 10 injections in L.U., 5 in R.U., 2 in R.M.C. and R Radial, and 4 in L.M.C. All except L.M.C. became painless. The latter was stripped and found to have a very thick sheath.

November 1955, she has never, since nerve reactions started, had continued freedom from pain for three months until now. She is brighter and happier. The nerves feel small and not so hard. She says she can feel better with her hands.

E.E. Male. Age 27. Z/2238. 1950, severe nodular leproma with large U.s and E.P.S., started dapsone. **July, 1952,** first severe nerve reaction. **December 1954,** first negative smear. Had frequent nerve and lepra reactions starting from **1952** onwards. **June 1955,** L.U. injected with hyalase with success (6 injections), 6 weeks later R.U. had 5 injections. **October 1955,** he had mild recurrence in L.U. and given 3 more injections. **November 1955,** greatly improved. Nerves smaller and not very hard and he is much brighter in himself.

C.O. Male. Age 35. Z/2446. June 1954, admitted with severe nodular leproma, with large U.s and E.P.S. **July 1955,** much better but R.U. very painful and very large. Hyalase given 5 times. Pain all gone. **November 1955,** no further trouble.

E.A. Male. Age 18. Z/2425. April 1954, admitted with very severe crippling. He had slightly active minor tuberculoid leprosy. His hands have felt very cold, in addition to being paralysed and rather painful in the ulnar area. **September 1955,** L.U. and R.U., 5 injections of hyalase given. **November 1955,** says his hands are a bit stronger and he feels better and has no pain. The only obvious objective sign is that his hands are no longer cold as they have been for the past year or more.

There are 24 such cases and nearly all show the same uniform improvement:—

(a) lessening of pain,
(b) reduction in size of nerves,
(c) claims of increased strength and ability to feel heat and touch better.

I wish, however, to report all those in which there has been failure of any kind, though in most of these success has been at least partial.

N.N. Female. Age 26. Z/5121. As reported above, the L.M.C. did not improve until a nerve stripping had been done. All other nerves improved dramatically.

O.J. Male. Age 38. Z/2009. Leproma over 13 years. **1950,** started dapsone. **April 1955,** first negative smear. Nerve reactions started about same time in R. and L.U. **July 1955,** R.U. injected 11 times. L.U. 5 times. **21st November, 1955** (1 week after last injection in R.U.), both nerves much smaller and free from pain and tenderness. Patient says anaesthesia is less and hands are stronger. But R.U. has paraesthesia near wrist, which was not present before.

M.O. Female. Age 40. Z/1797. September 1950, nodula leproma, thighs and buttocks ulcerated. **1954,** nerve reactions started. **September 1955,** L.U., R.U. and R.M.C. injected 5 times each. **November 1955,** all better, but R.U. has had a mild reaction since then.

V.D. Male. Age 35. Z/1740. His nerve reactions subsided, but the hyalase gave him generalised pain and weakness for a day after each injection. He continued his course at his own request because of improvement in the nerves. **November 1955,** they have remained without pain for 5 months.

O.E. Male. Age 27. Z/2008. August 1951, severe infiltrated leproma U.s and E.P.s. +. **1954,** started ulnar reactions. **April 1955,** had one hyalase injection in each ulnar. **September 1955,** returned for two more, but owing to pain did not bother to come aagin.

A.N. Male. Age 22. Z/2256. January 1953, extensive borderline macules with enlarged U.s and E.P.s. **January 1955,** reported tender L.U. just behind epicondyle. **August 1955,** 5 injections of hyalase. **September 1955,** pain reported improved. **November 1955,** thinks there is no real change for better or worse since the start of hyalase.

Conclusion

Though this is only a short trial, I am of the opinion that this treatment holds out better hope for those suffering from nerve reactions than any treatment so far used. Of course, it is not used in those cases in which caseation is suspected, as the probable result would be a spread of the area destroyed by caseation.

THE BLIND INFECTED WITH LEPROSY IN JAPAN

It is calculated that there are about 10,000 patients with leprosy in 15 leprosaria in Japan, and that of these about 1,000 are blind. However, both the number of those with leprosy and the proportion of those who are blind are diminishing. The leprous blind are doubly unfortunate, as in addition to being unable to read ordinary type, the anaesthesia of their fingers makes it impossible to read braille. However, a way out has been found by which they are able to read braille with their tongues or lips. Already (April, 1955) there are 108 braille typists, 45 tongue readers and 5 lip-readers. Also 73 are able to read braille with their fingers. This new movement has brought a fresh incentive to live to many of the patients. There is reported to be more blindness among those with leprosy in the north of Japan than in the south, and this is considered to be because the greater cold in the north encourages the more severe (lepromatous) form of leprosy, the form which causes blindness. Two reasons are given for the fact that blindness among those with leprosy is diminishing: (1) treatment with Promin, and (2) many of those already blind perished in the war.

LEPROSY CONTROL IN NORTHERN NIGERIA

C. M. ROSS, M.B., B.CH., D.T.M.
Senior Leprosy Officer, Kaduna, N. Nigeria

In 1952 experiments were made in the Katsina and Zaria Provinces of the Northern Region in acquiring necessary information for leprosy control policy suitable to the region. In the Igabi district of the Zaria Province, a pilot scheme of out-patient clinics attached to the Sleeping Sickness Dispensary, Riga Chickun, was arranged to determine certain facts:

1. The response of the general population to treatment made available in their own district, and within easy reach of the villages.

2. The high incidence of leprosy in the district.

3. A scheme of dosage suitable for out-patient treatment that would enable a dispensary attendant to dispense routine treatment under minimum supervision from a Medical Officer.

There was evidence that leprosy was highly endemic in the Northern Region; the majority of leprosy patients segregated in Settlements and Segregation Villages were of a severe lepromatous type, and each village had its own quota of burnt-out cases. Problems relating to treatment were observed in several settlements, e.g. patients suffering from progressive leprosy fever, who did not seem to tolerate DDS well. Most of the Settlements had adopted a standard scheme of treatment suggested by a meeting arranged by the British Empire Leprosy Relief Association of leprosy workers in London on 17th September, 1951. In these schemes twice weekly treatment was recommended as routine treatment, and there was little distinction made in the treatment of mild tuberculoid and severe lepromatous cases.

The district of Igabi had a population of approximately 30,000 people, and could be kept under close medical supervision during the experiment. The District Head was first approached and the details of the scheme explained to him, he was most co-operative and invited the patients to attend the Riga Chukin Dispensary for examination and treatment. The response was slow at first, and then quickly hundreds of patients appeared; many of them had walked ten miles or more from different parts of the district. New clinics were therefore opened throughout the district, and in a short time six clinics were established.

In less than one year's time it was found that in five of the

largest villages at which clinics were held patients attended as follows:

Village	Total population	Leprosy patients attending clinics	Response incidence
Riga Chukin ...	2,449	113	4.6
Rikoko	928	71	7.6
T. Sabuwa	773	53	6.8
Igabi	2,769	134	4.8
T. Safuwa	814	43	4.9

During the first six months very few lepromatous cases were seen, and some concern was felt at their absence; as the clinics became popular they came forward and it was most interesting to notice their relationship to the tuberculoid cases, and especially to compounds and families in which were several leprosy children.

Treatment was given by mouth once weekly. Tablets of 100 mg. DDS were used. As there had been no complication in the treatment of tuberculoid cases by DDS, the dosage was given as follows: one tablet weekly for six weeks, followed by an increase of one tablet every four weeks until four tablets had been given. Tuberculoid cases who were fit and responded well were after a period given five tablets and then six tablets weekly as a maximum dose. Children under 12 years were given half this dosage.

Lepromatous cases, especially L3 with throat and eye involment, were carefully treated; they were given an initial dose of half a tablet for six weeks, and then if there was no sign of reaction or leprosy fever they were increased to one tablet and kept on this dose for a further six weeks. The majority of lepromatous cases were then increased to two tablets for a further six weeks, and after that period their dose was increased by one tablet every six weeks until a maximum dose of four tablets was given. Several lepromatous cases could not tolerate more than one tablet, and one very severe lepromatous boy had to be reduced to half a tablet. Cases such as these responded well to small doses of half a tablet of DDS and their dosage was not increased until they showed signs of improvement and felt better.

It was found in the early stages of treatment of these severe lepromatous cases that half a tablet was effective and that a rapid increase of dosage gave rise to erythema nodosum, noisy breathing, swollen hands and feet, a general toxic feverish appearance and possibly some eye complications. However it was also found that after 18 months of careful treatment L3 cases could tolerate doses of four tablets weekly, and in two years' time doses compared to those given to tuberculoid cases.

During 1953 and 1954 three areas with a total population of 5,704 were surveyed and 390 cases of leprosy were found. These areas included three large villages and their surrounding districts of scattered hamlets.

Interesting features of the survey were:—

Leprosy children aged 1-14 years found	168
Young adults aged 15-14 years found	86
Adults, 25 years and over found	126
Lepromatous cases found by survey	42

An encouraging feature was that no new highly infective lepromatous cases were found who had not registered for treatment at the clinic.

In 1955 approximately 540 patients were discharged after two years 9 months treatment. Forty per cent of these were children who had been admitted with one or two tuberculoid patches which had completely resolved before discharge. No lepromatous cases were discharged.

It was demonstrated by this experiment that patients in the Northern Region will attend for treament regularly if treatment is made available to them in their own districts. An accurate incidence of 68.4 per thousand population was discovered. It was found that all cases of leprosy could be treated successfully by a careful use of DDS, and that weekly doses of 50 mg. could be given with good results in leprosy cases showing signs of persistent leprosy fever.

My thanks for permission to publish this note are due to the Medical Adviser, Federal Government, Nigeria, and to the Director of Medical Services, Northern Region, Nigeria.

NOTE ON SULPHONE ACTIVITY IN MALARIA INFECTION

DR. D. L. LEIKER

Chief of the Leprosy Control Division, Department of Health, Netherlands New Guinea

The Editor of this periodical* has quoted that sulfone drugs are active against at least one protozoon, mentioning the activity against toxoplasmosis only.

Some years ago I noticed that twelve lepers, treated with DDS in a public hospital and twenty-five patients treated policlinically, were free from attacks of malaria for more than one year, although they were living in a holoendemic area and larvae

* Leprosy Review, Vol. 27, No. 1, p. 4.

and adults of *Anopheles punctulatus* were often found in the hospital zone.

Only one attack of malarial fever was diagnosed among 164 inmates of the leprosarium at Miei during one year. This occurred shortly after admission of the patient, who had taken only a small initial dose of DDS. Thick drops of all patients were examined, but no positive one was found.

Malaria is highly endemic in this area and on several occasions full grown larvae and adults of anopheline mosquitoes were found in the leprosarium.

The difference between lepers treated with DDS and the general population is striking. The conclusion that DDS has some suppressive activity against malaria, seems permissible.

This finding has some practical importance in countries where both leprosy and malaria are endemic, especially in remote places where lepers are often treated at the policlinic and proper laboratory facilities are not available. In malarious areas, every sudden rise in temperature first arouses the suspicion of malaria. However, it should be borne in mind that in reaction of leprosy, skin eruptions are not always conspicuous and there may be pains in the bones and joints, which do not differ much from malarial disturbances in partly immune adults.

Reports that sulfones are also active against filariasis are not supported by our experience. Thick smears from 133 inmates of the leprosarium showed noctural microfilariasis in 23 per cent of the patients treated with DDS.

THE MAKOGAI SANDWICH*

The following is the procedure in Fiji regarding the distribution of maintenance doses of sulphone tablets to patients discharged from Makogai Leprosy Hospital as arrested, and their review.

Patients who have been discharged from the Leprosy Hospital, and are resident in Fiji, come under the provisions of the Leper (conditional discharge) Regulations which provide for their periodical examination and imposes on them a duty to report to the medical authorities at stated times for examination.

For the first three years after the date of their discharge from hospital they are seen every three months. For the next three years they are seen every six months, and after that they are examined annually as long as they remain in the Colony.

At each examination, in addition to the usual clinical scrutiny, a " slit smear " is taken on a microscope slide after each twelve

* Extract from letter to Colonial Office from the Director of Medical Services, Suva, Fiji, dated 2.11.55.

months, and the slide is forwarded to the pathologist in the Central Laboratory in Suva for staining and examination. A copy of the report goes to the medical authority making the examination, and a copy is sent to the Central Leprosy Registry in Suva.

The Central Leprosy Registry maintains a full record of each discharged patient, and assumes the duty of tracing patients wherever they may be, and bringing them to review. In a population scattered over more than 100 islands, this is a task of some difficulty, but the success of the scheme is indicated by the fact that out of 511 patients discharged from hospital and assumed to be still living, only thirteen have become untraceable. And even these " untraceable " patients are not regarded as being wholly lost because continuous searching eventually finds them or establishes that they have died.

The treatment of discharged patients is now standardised at the exhibition of two tablets of " Avlosulfon " (DDS) weekly, giving a weekly dose of 0.2 grams. The tablets are issued in batches of 8 (one month's supply), and on starting this scheme it became at once apparent that one could not simply hand out to a patient 8 small tablets and expect him to take them home and swallow two a week. The question of packaging was important so as to secure that the tablets were ready for consumption on the recommended dates. Also, it was considered important to keep an unequivocal record both of the issue to the patient of a small quantity of sulphone, and of the issue to junior medical personnel of larger stocks of this drug. It was thought advisable to take steps to secure that junior medical staff should not have available to them, under conditions insusceptible of control, large stocks of drugs which might be used in the private illicit treatment of undisclosed leprosy.

The " Makogai Sandwich " was therefore devised and is manufactured in quantity by the junior staff of the Central Leprosy Registry. The Sandwiches are issued to medical staff in packages of 10 Sandwiches. Each Sandwich is serially numbered and a record is made of the issue of these numbers to a particular medical station. When medical staff see a discharged leprosy patient (and patients are instructed to report each month to their appropriate medical station), they issue that patient with one Sandwich. At the same time the medical station fills in the printed label which forms part of the Sandwich cover. This states the name, address and serial number of the patient to whom the drug is given, and also the answers to four questions aimed at revealing any toxic reaction to the exhibition of the drug. The patient is told to take the

Sandwich away, and poke a stick through one hole on Sunday and swallow the tablet which comes out. This process is repeated every Sunday and Wednesday until the Sandwich is finished, when the patient returns to the medical station for re-examination and the issue of a new Sandwich. This process is continued for three years from the date of discharge, and the exhibition of sulphone is then to be discontinued. (This system is now in its third year).

We propose in the case of each patient who has taken sulphone in this way for three years, to leave a period of at least one year when no sulphones will be taken, so that an estimate can be made of the risk (if any) of recurrence of the disease if the maintenance dose of sulphone is stopped after three years.

The label from the "Makogai Sandwich" is returned by medical staff to the Registry and the information is incorporated into records.

(1) A card is kept of each particular patient so as to see with what regularity each patient attends to receive his Sandwich. Continual scrutiny of these cards makes it possible to note any lapses, and to send out reminders to medical staff to get the patient in for re-issue of the drug.

(2) A record is made of the issue of packets of Sandwiches to each medical station, and when it is observed, from this record, that a station's stock is exhausted from 50 per cent to 90 per cent, according to the distance from the Central Registry, and the estimated rate of consumption of Sandwiches, a new supply of Sandwiches is automatically sent out by the Registry to that station. Medical staff in the country, therefore, are relieved from the burden of attending to their stock in hand of sulphones.

In our experience with patients on the above *maintenance dose*. it has not been necessary to issue concurrent iron medication against anaemia.

Now that it has been shown, under the pragmatic test over almost three years, that the central control is effective, although known contacts of new cases of leprosy are examined when the case is discovered, we now propose to go on to the next stage in the control of leprosy; the follow-up of all family contacts over an extended period. This, of course, is an undertaking rather larger than that of the original Registry. It remains to be seen how far existing staff and facilities can bring this about. It is felt, however, with Rogers (Lancet, July 9th, 1955, page 80), that the survey of contacts is to be placed high among the desirable methods for the eradication of leprosy.

LETTERS TO THE EDITOR

Nigeria Leprosy Service Research Unit,
Uzuakoli,
E. Nigeria.
17th March, 1956.

The Editor,
Leprosy Review,
London.

Sir,

The continued appearance of new drugs having anti-tuberculous activity makes your editorial in the October 1955 number of the LEPROSY REVIEW on the subject of their testing in leprosy as timely as it is valuable. Some experience in this type of work prompts me to offer a personal opinion on some of the theoretical and practical aspects of it.

It does not follow that because a drug has been used with safety in the short term treatment of tuberculosis that it is equally suitable for leprosy patients. A case has already arisen where dangerous toxic effects appeared in tuberculous patients in the fourth month of treatment, and the long term treatment inevitable in leprosy may involve a situation not covered by the toxicity tests undertaken by the manufacturers before issuing the drug. It follows, (a) that initial trials demand in the interests of the patient volunteers concerned, a very reliable laboratory service making it possible to maintain a close watch on red and white blood cell formation, liver and kidney function, and (b) that several months must elapse before reliable evidence can be forthcoming as to the suitability of a drug on toxicity grounds.

The number of centres suitable for such primary trials is limited. It would appear desirable to initiate trials at two or three of these simultaneously, recognising from the start that if the drug is found active, long term trials are involved in each case. A comparison of findings after six to nine months, if establishing the facts of anti-bacterial activity and low toxicity, could then lead to additional trials at centres less fully equipped.

LEPROSY REVIEW,

Choice of patients. I am not at all sure that the first patients chosen for such trials should be advanced lepromatous cases. Patients of this type who have had no previous treatment are becoming increasingly uncommon, and when found, their physical

condition often renders them unacceptable for trial purposes. Furthermore, at least six months trial may be needed before convincing evidence of drug activity may be forthcoming in such patients. As encountered here they are usually in urgent need of treatment, and deserve the best available, namely sulphones, without delaying for some months while taking a drug which is at best an unknown quantity.

Early lepromatous cases are in a different category, applying the term " early " to mean " of short duration." Such patients are usually able-bodied, suffering as yet very little disability as the result of their infection, yet often harbouring considerable numbers of bacilli in their skin. Their response to sulphone treatment is usually rapid, both clinical and bacteriological improvement being unmistakable in six months or less, and if placed on a new drug would thus not need a longer period than this for a judgment on its activity to be made.

Furthermore, active tuberculoid and indeterminate cases are not to be despised. The disease is a unity, and if a drug has activity against *M. Leprae*, all forms of the disease harbouring living bacilli will respond to it. We have not encountered, nor are we likely to encounter, a drug active in one form of leprosy and inactive in another. Tuberculoid cases can yield rapid information. Under sulphone treatment the vast majority show signs of resolution within three months. Resolution of such cases in the absence of treatment is of course common enough, though it is extremely unlikely that a group would all do this simultaneously. Even if it is conceded that the resolution of such cases is of little statistical value, their failure as a group to show resolution is quite a different matter, and is indeed definite and valuable positive evidence that the drug concerned is of low activity in the dosage tested. If forthcoming at all, such evidence will be obtained within three months of starting the trial.

It is therefore a sound procedure to build up a trial group of patients on a basis of early lepromatous and active tuberculoid cases in the first instance, adding suitable more advanced lepromatous cases as signs of drug activity begin to appear, up to a total of 16 to 20 lepromatous cases and 8 to 10 tuberculoids. With such a group six months suffices for proof of activity, and twelve months for a short term comparison between the drug concerned and DDS. A group of this size is necessary if allowance is to be made for wastage, individual idiosyncrasy, and other incidents, and manufacturers should recognise this.

Such a method of selection is in accord with practical necessity.

Nowadays one rarely encounters an adequate group of previously untreated suitable patients, capable of being placed simultaneously on a new drug. Patients have to be selected as they come, today a lepromatous patient, tomorrow a tuberculoid patient, and, allowing for controls, it inevitably takes time to build up a group of trial patients of adequate size. We therefore very definitely need to include patients of those types which are going to yield an answer as quickly as possible as to the suitability of the drug for wider trials.

It is worth stressing the importance of the word "suitable" where these patients are concerned. The successes of sulphone treatment introduce an important ethical aspect into the matter. Reference has already been made to this where severe lepromatous patients are concerned. It applies in fact to others as well. As a general principle we are not justified in accepting for pilot trials any patient whose deprivation of sulphone treatment for three to six months can be considered detrimental to his subsequent progress. This eliminates all patients with signs of active neuritis of motor nerves, ulceration of the nose or larynx, or involvement of the eyes in any way. Suitability must also depend on the existence of a clear clinical picture of active disease, classification being supported where necessary by biopsy.

Controls. The selection of controls is also not without its difficulties. The adoption of individual controls, patient for patient, is certainly to be advocated, but the difficulties and limitations of this system need recognition. In the first place, the patient and his control must be strictly comparable. In addition to type, degree, and duration of the disease I would add sex, approximate age, and also equality in lepromin reaction. This last item is important, for differences here may influence progress quite considerably. Even though 90% of lepromatous patients may be steadfastly lepromin negative, the remaining unstable 10% may be a source of real difficulty. These additional factors narrow down very considerably the choice of suitable controls, so that a rather large reservoir of patients on sulphone treatment is necessary to provide what is needed.

As a trial proceeds, this system of controls leads to other difficulties. There is first the problem of wastage. If a control patient drops out from observation for one reason or another, the corresponding trial patient may also be wasted. Furthermore, over the long period needed for a full clinical trial, sufficient individual variation in progress remains between one leprosy patient and another to rob individual controls of much of their value. For short term assessments it may be concluded that individual controls are valuable, but in long term studies it is probably more accurate to review the progress of each type of patient as a group, in comparison

with groups of the same type of patient receiving DDS.

Perhaps after all the best yardstick of progress in patients receiving new drugs is that provided by the accumulated experience of DDS treatment at the centre concerned. We have now available, in the records of DDS treatment, ample material for a general statement of progress relating to each type of leprosy during the first and subsequent years, and this, based on large numbers, is probably more accurate than the findings in a small group could possibly be.

I have found the preparation of such a statement by the analysis of records here a salutary experience, reminding me that the achievements of DDS are out of all proportion to its deficiencies. It is right therefore as you say, that the conditions for testing new drugs should be stringent. Only by making them so will trials of new drugs really be to the advantage of present and future patients.

I remain,

Yours faithfully,

T. F. DAVEY, M.Sc., M.D.

[Further comment on this very important subject will be welcomed from those who like Dr. Davey have had practical experience of controlled trials of drugs, especially drugs for the treatment of leprosy.—EDITOR].

Dear Sir,

In perusing the October number of the REVIEW (which has just reached me) I observe that you have inserted a report of mine on leprosy. Although I am gratified that you considered the standard of the work as one meriting publication, there are a number of hiati on which I should ask the indulgence of your readers.

The first is that since having had the benefit of Dr. Cochrane's opinion on what should be done out here, my concepts of leprosy control as is implied in the word " segregation " has been basically altered.

The second point I have to make is that for anyone other than those who have an inside knowledge of the operation out here, the position must be obscure. That is to say, while rehabilitation is being handled by an Agency of the United Nations (United Nations Korean Rehabilitation Agency or in short UNKRA) disease control was at the time that the report was made, the responsibility of the American Army embodied in the Korean Civil Assistance Command (KCAC). The last mentioned was in effect an advisory group using professional staff who were (like myself) mostly on loan from UNKRA, or recruited as Department of the Army Civilians. My role was therefore one of an adviser with a special responsibility for the Prevention of Epidemic Disease. Leprosy

merely came into my field as a study and it was not the subject of an army sponsored programme of control.

I have also mentioned " AFAK," or in clear, Armed Forces Aid to Korea.

The intention of this plan was to supplement what had already been achieved in the reconstruction of the country by the building of churches, orphanages, schools, hospitals, etc., and its secondary objective was to give an interest to the men of the American Army who found themselves in danger of being bored in an eastern country devoid of the ordinary amenities. The men themselves were responsible for the supervision of such work.

Abbreviations used in my report were in common useage out here, but unless the background is understood, they may well be unintelligible!

Yours faithfully,

(Dr.) M. L. SMITH.

U.N.K.R.A.,
Korea.
4th January, 1956.

Dear Sir,

With reference to the second part of my contribution entitled " Leprosy in Korea," which you have kindly published in the January issue of LEPROSY REVIEW, there is an error on page 19, line 16 from the top. The sentence reads " In our study of child leprosy in India we found that 7% of childhood leprosy . . . etc., etc." The figure should be 70%. This was an error which was in the original mimeographed report, and an errata slip was unfortunately omitted.

Since the publication of these figures the follow up work at the Children's Clinic at Saidapet has continued, but we have, as yet, no evidence to refute the contention that much child leprosy is benign, and that the lesions disappear before adult life is reached. You yourself, Sir, many years ago, pointed out that leprosy was a self-healing disease. The problem, therefore, is not the amount of leprosy in the community, but what is of importance is the percentage of cases that develop into the more serious forms of leprosy, either from the point of view of becoming open cases or resulting in deformity. In countries where leprosy is an endemic disease it would be well to study its natural evolution, so that our treatment and preventive measures may be applied with more enlightened knowledge.

I am,

Yours truly,

R. G. COCHRANE, M.D.

REVIEWS

Round the World of Leprosy, by **Dr. R. V. Wardekar.** (Gandhi Memorial Leprosy Foundation, Wardha, M.P. (India)).

The author of this book is the secretary of the Gandhi Memorial Leprosy Foundation in India, and this book is an account of a four-month study tour round the world, the principle places visited being the United States, Hawaii, Japan, Hongkong and the Philippines. Much of the book is occupied with accounts of journeys and shrewd observations of the customs of the people; but short as the visits were to each leprosy centre, important information was gathered and the observations made and conclusions reached are worthy of study.

At the large leprosarium in Louisiana he remarks on the propaganda advocating complete disregard of the infectivity of leprosy and the abolition of all restrictions; he notes a staff of 200 healthy workers to look after 400 patients at an annual cost of about $4,000 per patient. "It was the only colony in the world where patients were provided every comfort and even luxury, but still it could not wipe out of their minds the sense of being segregated. The Carville Leprosy Colony was an excellent example to show that nothing could compensate for being taken away from the home family and society." The leprosy problem in the U.S.A. is of a minor nature, but it illustrates how control of other communicable diseases is linked up with leprosy, and control depends not only upon antileprosy measures but also on improvement in the general standard of living. No colony can be ideal if it is meant to be a place of permanent residence for the patients. If not supported by a case-detecting campaign a colony by itself cannot eradicate the disease.

In Hawaii he found that although the population had increased threefold in the last 50 years, leprosy had diminished from 2,000 to 447. This was due to antileprosy measures combined with improved sanitation and raising of the standard of living. But he also learned that many of the new cases detected were Samoans immigrating to Hawaii as labourers.

In Japan the chief stress in leprosy control is placed on segregation and vasectomy. "Dr. Mitsuda himself was a great advocate of sterilisation of the male partner and never permitted a marriage unless the male partner had submitted to the operation. In the other colonies, however, some of the couples were not

sterilised, but out of a total of 1,958 couples in all the colonies taken together, about 71 per cent were sterilised. The main treatment was with Promin and Promizol, and though other sulphones also were used, they did not use DDS." Dr. Wardekar was particularly struck with the frequency of alopecia of the scalp: streaks of hair were still preserved only in that region of the scalp where there was a blood vessel underneath.

In Japan there were 9,659 leprosy patients, 9,427 being in ten government leprosaria, and 232 in three private leprosaria. All types, " open " and " closed," are subject to compulsory segregation. In the official figures there were 30,393 patients (0.64 per 1,000) in 1904, but in 1950 only 12,000 (0.15 per 1,000). Unofficial figures, however, put the 1950 number at 15,000, and the writer considers that " it is quite safe to believe that in 1950 the total cases were 20,000 at least, of whom only 10,000 were in segregation.

In the Philippines the writer found that there were 5,899 patients segregated in nine leprosaria, of which 2,104 were in the Culion Leper Colony, and 1,400 in the Central Luzon Leprosarium. Some of his remarks about the Culion Colony are very disturbing: " Mere isolation without any treatment is not an end in itself. But in Culion I had seen that many of the active cases did not take any anti-leprosy treatment except when they were in reactions or had some other complications. There were a number of reasons for this attitude, but the main cause was the inherent weakness of administrative control, which arose from the very nature of compulsory segregation on isolated islands like these. Even the best administrator could not have been able to enforce compulsory treatment to all active cases." Even more distressing is the account given of the large number of children born on the Colony every year: " this process had gone on for so many years that the relatives and the society outside have been reaching the point of saturation beyond which the children born there cannot possibly be sent out. Thus every year the children born there are accumulating in the colony and being exposed to infection daily. That place has therefore become a breeding ground for adding new cases every year to the previous lot. . . . Removing the cases to far off islands completely out of sight and thought of the society is not conducive to the world-wide effort of changing the outlook of society."

At Hongkong the new colony of Hay Ling Chau " presented quite a pleasant contrast to all the others I had seen—the patients

were actively working for the colony and they seemed to be quite happy about it."

The last chapter of the book is devoted to a description of the leprosy problem in India and the methods adopted by the Gandhi Memorial Foundation. "The main activity of the Foundation is . . . to start control units based on the use of oral DDS, early detection of cases and repeated examination of contacts. Isolation of infectious cases is to be done either at home or in the village whenever it is possible." To begin with units have been started in twelve places. Other activities are training of leprosy workers, and subsidising a few research projects. The importance of protection of children from infection is acknowledged, but "to my mind the only method of protecting children when the anti-leprosy campaign is still in the hands of voluntary agencies is . . . to see they are looked after by some of the patient's relatives or to arrange for their adoption. In addition, BCG vaccination may help in protecting some."

The book is full of useful information and thoughtful reasoning, and is written in an interesting and readable style. It should be read by all who are interested in the solution of the leprosy problem. There are 2 maps and 11 photographic illustrations.

International Journal of Leprosy, Vol. 23, No. 2, April-June, 1955.

The original articles are as follows:

K. P. C. A. Gramberg writes on *Nerve Decapulation in Leprosy.* He recommends the total stripping of the fibrotic epineural sheath in thickened painful nerves. He describes the technique, and states that there is practically no danger of complications. Pain and parethesia disappear in nearly all cases. He performed the operation 169 times, of which 108 were on the ulnar nerve. As regards pain and paresthesia the results even after 12 years are good, but as regards paralysis not so good.

Yukichi Satani *et al.* claim good results by injecting Acidomycin intradermally. This substance is obtained from *Streptomyces acidomyceticus.* Subcutaneous injection has no effect either on tuberculosis or leprosy, but intradermal infiltration of leprous lesions causes fading or disappearance of the infiltrated lesions and improvement of sensation. In some the bacilli become fewer or disappear. In some, lesions at a distance also improved.

R. S. Guinto, J. A. Doull and E. B. Mabalay write *A Note on the Lepromin Reaction in Males and Females.* As reactivity to lepromin is generally interpreted as an indication of resistance to lepromatous leprosy, and lepromatous leprosy is much commoner

in males than in females, a comparison of the results of the lepromin test was made in 776 males and 1,075 females. The early positive reactions in males and females were respectively 3.9 and 6.1. The late positive reactions in males and females below 5 years of age were 17.7 and 14.1, and for those of 20 and over 94.6 and 97.0 respectively. Thus as far as the lepromin test is concerned there is no evidence of higher resistance in females than in males.

The same authors also write on *The Mitsuda Reaction in Persons with and without Household Exposure to Leprosy*. Three groups of persons were examined: (1) those exposed to lepromatous leprosy in the household, (2) those exposed to non-lepromatous leprosy in the household, and (3) those not known to have any household exposure to leprosy. They were all residents of the same town. The reactors in the three groups were respectively 73.4, 68.3 and 68.2 per cent. It is concluded therefore that household exposure does not have any effect on reactivity to lepromin.

J. H. Hale *et al.* describe *The Relationship and Significance of the Mantoux and Lepromin Reaction in Leprosy*. Leprosy patients were found to have a much lower Mantoux rate than the normal population, this being especially so in children, though the adult rate in Singapore approached that of the normal population. Children with leprosy responded to BCG vaccination and gave a Mantoux conversion rate very little lower than that found in normal children. It is considered that leprosy infects a selected population consisting of Mantoux negatives, tuberculosis infection thus giving some protection against leprosy, although there is evidence that tuberculosis is readily superimposed on existing leprosy. The essential feature is conversion to a Mantoux positive state and not the positive lepromin response that may result from BCG vaccination, which response is nonspecific.

E. W. Gault, A. P. Jayaraj and H. H. Gass describe *The Application of Histochemical Methods in the Study of the Skin in Leprosy*. By these methods capillaries and nerves have been found to contain sufficient alkaline and acid phosphatase, respectively, for these structures to be outlined in the skin. Carbol-fuchsin staining combined with these methods has shown the presence of bacilli in the capillaries and in the axons. In the capillaries the bacilli are probably in the endothelial cells. " If they were in the lumen it does not seem very likely that they would have remained massed as we found them." As regards the nerves, acid phosphatase activity in nerves provides an excellent method of showing axons and neurilemmal cells in the tissues. The myelin sheath remains relatively unaffected. " Our findings confirm the presence

of bacilli in swollen and apparently degenerate axons, but we are not able from our material to prove that the bacilli had actually travelled along the axon." This article is well illustrated with 10 photomicrographs.

The title of the next article is *C-Reactive Protein in Serum of Patients with Leprosy.* A. S. Rabson found this abnormal protein (CPR) in 79 per cent of 47 cases of active lepromatous leprosy, in 30 per cent of 41 arrested lepromatous cases, and in 58 per cent of 12 tuberculoid cases. The significance of these findings is doubtful, but further studies are planned.

J. Convit *et al.* write on *The Mantoux and Mitsuda Reactions in Hamsters and Guinea-Pigs before and after Vaccination with BCG.* None of 120 hamsters vaccinated orally, intradermally or intracardially showed a change of these two reactions from negative to positive, and it is concluded that this species (*Cricatus auratus*) is not immunalergically responsive to either PPD tuberculin or to lepromin. Forty-five guinea-pigs were divided into five groups and given BCG orally, intradermally, intracardially, and by a combination of these three routes, the fifth group being a control. Of the nine control animals in the unvaccinated group seven became Mitsuda positive; the two that remained negative became positive later as they approached adult age. All the vaccinated animals became Fernandez and Mitsuda positive. As regards the Mantoux reaction, only those animals that were vaccinated intradermally became positive.

Y. T. Chang writes on *Chemotherapy of Murine Leprosy. The Effects of Amithizone (TB1/698), p-Aminosalicylic Acid (PAS), B283 (a Phenazine Pigment), Five Antibiotics and Three Dipenylthiourea Compounds on Mouse Leprosy.* These substances were administered to mice which had been infected intraperitoneally with rat leprosy, and the effects observed as to retardation of the progress of disease in the pelvic fatty pads and omenta. Amithiozone appeared to cause some stimulation of the infection; the other substances, including the antibiotics: aureomycin, terramycin, penicillin, erythromycin showed no significant activity.

In an editorial on *Properdin and Natural Immunity,* this substance is described. It is an euglobulin with a molecular weight at least eight times that of gamma globulin, is not an antibody, but under certain conditions participates in such varied activities as the destruction of bacteria, the neutralisation of viruses, and the lysis of red cells. The different concentration in the sera of different animals have a highly suggestive parallel with the natural resistance of those animals to infection. " The rat, notoriously resis-

tant, has the highest titer, 25 to 50 units per cc., while the guinea-pig, a susceptible animal, has only 1-2 units. Normal man is in the intermediate zone, with 4-8 units, at the same level as the rabbit but below the hog and cow and above the sheep." It is suggested that leprosy should be explored along this line. " Does the resistant tuberculoid case differ materially from normal in its properdin titer? On the other hand does it differ significantly from the non-resistant lepromatous case? How about cases in various kinds of reactions as compared with non-reaction cases of the same types of leprosy? "

REPORTS

East African Leprosy Research Centre.

The East African Leprosy Research Centre is a concept of the British Empire Leprosy Relief Association and has been largely financed by them with the added backing of the three East African territories, and has come into being through the co-operation of the East Africa High Commission, who also administer the Centre as one of the Non-self-contained Services. The centre is situated on the territorial boundary between Uganda and Kenya, near to Busia and Tororo, and with the agreement of the Kenya Government is sited at the Itesio Leprosarium. This leprosarium is planned to accommodate 1,000 in-patients when all buildings are completed, and from Itesio, the Church Missionary Society Leprosarium at Kumi, and the Roman Catholic Missionary Leprosarium at Buluba, are within easy reach. It is thus well situated as regards wealth of clinical material. The heavy leprosy incidence of 25 to 35 per thousand of Nyanza Province of Kenya and Eastern Province of Uganda should also be noted.

The objects of the Centre are, briefly, to conduct leprosy research of a practical and basic nature in East Africa.

The following draft proposals for research projects have been made:—

(a) *Bacteriological.* The techniques of Hanks and Clarke Gray in the hydrogen transfer capacity of the mycobacteria of rats, should be tested out on human mycobacteria of leprosy, and the special staining methods now being perfected by Hanks be given a thorough test in all types of clinical leprosy of East Africa.

If these methods stand the test, an extensive study of *M. leprae* obtained from all places in East Africa should be undertaken. The methods which claim to ascertain the viability and infectiousness of these mycobacteria should obviously be applied widely in the hope of advancing our study of the specific germ by these relatively simple methods.

(b) *Immunological.* A long-term test of the claimed protective action of BCG against human leprosy should be planned and set going. A mobile laboratory is possessed by the Centre, and the district or districts where such a trial can be carried out lies at the door of the Itesio Leprosarium, wherein the Centre is sited.

(c) *Therapeutic.* No specific project has been as yet chosen, but a suggestion is that investigation be made into retarded absorption therapy, which has a great practical advantage, if proved that the absorption is steady, harmless and efficient, in the control of large numbers in countries of high leprosy prevalence.

It is intended also to conduct carefully controlled therapeutic trials of new drugs which are known to be effective against tuberculosis, for example, or which are equally effective against other mycobacteria.

Annual Report of the Medical Department, Uganda, for 1954.

LEPROSY

The 60th survey of a series begun in 1950 was completed and analysed during the year. The surveys consisted of the examination of every person resident in well defined but widely scattered areas. The incidence range obtained was 0.0%—4%, with an average lepromatous rate of 10% and a child rate of 20%.

The age distribution showed that the heaviest incidence was not in childhood, but after the age of 20. The disease occurred equally among males and females. Climate and population density did not appear to be related to the incidence. The higher values were obtained in the smaller tribal groups such as the Bwamba, Bakonjo, Bachopi, Banyuli and Badama. The evidence suggests that susceptibility is of primary importance and in such people, contact at any age can produce leprosy with the age frequency in a community, depending on the age at which the social pattern makes contact more likely. It was not uncommon to find large areas with many tuberculoid patients, but not a single lepro-

matous case. The surveys suggest that tuberculoid cases are infectious. They may be less infectious than lepromatous cases, but if such cases are mobile they will have greater opportunities of contact with other people.

The survey provided opportunities to discuss local measures to introduce treatment in the simplest manner. The response has been encouraging and at the end of the year 20 treatment villages were in operation and others were projected.

In 1951 treatment was only available on any large scale at five settlements maintained by missionary societies but subsidised by annual grants by Protectorate Government, District Councils and the British Empire Leprosy Relief Association. The average number of patients resident in the settlements at that time was approximately 2,000 and out-patient treatment was being given at the settlements to about 2,000 more. The result of the efforts by the District Councils has been to increase the total number of lepers under in-patient treatment to more than 3,000.

In addition, out-patient clinics have been opened as pilot schemes, so that including the 2,000 attending settlements, the total number of out-patients registered is now in the region of 4,000.

Treatment villages are preferable to out-patient clinics because they help to guarantee continuity of treatment. It has been found that in the course of a year most out-patients put in only half the attendances possible, whether treatment is given weekly, twice weekly, or fortnightly.

The average incidence appears to be higher in the Eastern Province and about half the cases in Uganda are in that province.

The main treatment used has been diamino-diphenyl sulphone by tablet and, in a few cases, sulphetrone. The results have been gratifying but unfortunately patients have a tendency to discharge themselves as soon as they find their lesions disappearing and their general health improving. For this reason the number of those discharged is not mentioned in the report as it would not reflect the value of the treatment given. The major part of the work of leprosy control in Uganda has still to be begun but the outlook is good and progress to date has been reasonably satisfactory.

ABSTRACTS

Tratamiento de las Leprorreacciones con Cortisona, by **Drs. Contreras, Guillen, Miguel, Terencio** and **Tarabini.** Fontilles, 1955, V. 3, No. 8. Treatment of Lepra Reactions with Cortisone.

The authors first review the results obtained by previous workers, many of whom found that there was only temporary relief of reaction, with a return of the condition when cortisone was stopped. Their own trial was in ten patients, all with the lepromatous form. In nine of these the lepra reaction was general, one of them having suffered for a year with reaction which would not yield to any form of treatment. In the remaining patients the reaction was in the form of *erythema nodoso*. The preparation of cortisone used was Altesona, made up in 20 c.c. flasks with 25 mgm. per c.c. for parenteral injection. The history and course of treatment, along with temperature charts, are given for each case. Fever disappeared in from 24 hours to 3 days. The signs of inflammation in the skin and mucosa disappeared more slowly. Neuritis and pain in the bones disappeared yet more slowly. From the very beginning of treatment there was a feeling of physical and mental well-being. In two cases there was a relapse which disappeared on further treatment. The authors consider that the more permanent results they obtained as compared with other workers, were due to the use of smaller doses, 1.5 gm. being the maximum total amount used, as compared with 4 to 8 gm. Tolerance was perfect except for one case in which there was generalised oedema with albuminuria. This patient had had lepra reaction for a whole year. The usual daily dose of cortisone was 100 mgm. given in two injection of 50 mgm. each, continuing for eight days. The same treatment was resumed for a few days if there was any return of symptoms.

The authors continue to treat the majority of lepra reactions with haemotherapy, reserving cortisone treatment for those who do not yield to haemotherapy.

***Trop. Dis. Bulletin, Vol. 52, No. 7, July, 1955**

Ocular Leprosy. Proc. Roy. Soc. Med., 1955, Feb., V. 48, No. 2, 112-117 (Sect. Ophthalm. 6-11), 3 figs. By **E. W. O'G. Kirwan.**

The author draws upon his unrivalled experience of ocular leprosy to provide probably the best description of the clinical manifestations as they affect the eyes which the reviewer has so far had the good fortune to read.

He gives in considerable detail the manner in which the various parts of the eye may be affected. There are several excellent illustrations. He stresses that early diagnosis and early

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treatment of eye lesions are of great importance, but adds that in his experience the benefit to the eyes from sulphone therapy is considerable. The lepra reaction is also indicated as a dangerous ocular complication and he discusses the use of cortisone in its control.

With regard to lesions of the posterior segment, the author's touch is perhaps a little less sure. He states, " lesions of the posterior segment . . . do occasionally occur. . . . The wonder is that they are not more frequently observed." The next paragraph, however, contains the statement that " as lesions of the posterior segment of the eye do not occur or at all events occur rarely . . ." The reader is thus left in some doubt as to the author's real beliefs with regard to this controversial point.

Apart from this minor detail, this paper is one of the most balanced and best written accounts of ocular leprosy to appear in recent years and should be read by all those with an interest in the subject.

Cortisone in the Treatment of Leprous Reactions. Bull. Soc. Path. Exot., 1954, V. 47, No. 6, 848-56, 9 charts. By **E. Montestruc.**

The author treated five patients in whom severe reactions interfered with sulphone or thiosemicarbazone treatment. He began with 200 or 300 mgm. (half by mouth and half by injection) twice on the first day, 150 mgm. on the second day, then 100, 75 and 50 mgm. on the following days. Generally the reaction ceases, but if necessary the amount is increased again to 75 or 100 mgm. He finds that with this it is possible to return to sulphone treatment patients who would otherwise be unable to coninue it.

***Trop. Dis. Bulletin, Vol. 52, No. 8, Aug. 1955**

Specific Tissue Alteration in Leprous Skin, VIII. Inoculation of, " Leishmania tropica " into Leprous Patients. Arch. Dermat., 1955, Apr., V. 71, No. 4, 441-50, 7 figs. By **E. Liban, A. Zuckerman and F. Sagher.**

This paper is in continuation of a series (see this *Bulletin*, 1955, V. 52, 273, 274 *bis*) in which the effects of inoculation of lepromatous patients with BCG and *Leishmania tropica* are studied. Out of the 23 lepromatous patients tested 15 had active lesions with bacilli demonstrated, and 8 failed to show bacilli. All but 3 had negative responses to the leishmanin test. All 23 patients

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were injected intradermally in the deltoid region with a standard dose of a million washed culture lepromonads. All the patients responded clinically to the inoculation in the same way as normal persons, a papule developing after a period of two weeks and increasing from 1 to 4 cm. in diameter, ulcerating within 6 to 7 months and scarring by the 7th to 12th month. In 44 biopsies of inoculation lesions, 20 of the 23 patients showed histological lesions identical with specimens from lepromatous leprosy, including foam cells with sudanophilic vacuoles. In four specimens there were a few giant cells of the Langhans type scattered among the foam cells. In seven specimens the foam cells contained Leishman-Donovan bodies often in large numbers. In five specimens the general picture was that of tuberculoid granulation tissue as seen in relapsing cutaneous leishmaniasis. The isopathic response is similar to that observed in leprous patients following inoculation of living BCG bacilli.

Tuberculin and Lepromin Sensitivity in the South African Bantu. A Pilot Survey. Lancet, 1955, May 14, 996-1001, 3 figs. (17 refs.). **S. W. A. Kuper.**

An investigation was made in three groups of South African Bantus to see if there was any co-ordination between the tuberculin and the lepromin reactions. The three groups consisted of 102 patients with leprosy, 57 patients with pulmonary tuberculosis, and 114 healthy controls. Lepromin was injected into the left arm and tuberculin into the right. The results are shown in graphs. The degree of correlation established between tuberculin and lepromin sensitivities was small, and was found only among the patients with pulmonary tuberculosis, the smallest of the three groups tested. The tuberculous patients showed a greater degree and sensitivity to lepromin than did the controls, though this might only be a consequence of the former correlation. In lepromatous leprosy a small proportion of patients showed an intense degree of sensitivity to tuberculin; but when these were excluded the two main groups of leprosy patients did not show greater tuberculin sensitivity than the controls.

The conclusion is arrived at that there is no simple and direct relationship between tuberculin and lepromin sensitivities, but that observations in patients with tuberculosis and lepromatous leprosy suggest the existence of a relationship of some kind.

Sheet Grafts in Leprosy. Rev. "Fontilles," Valencia, 1955, Jan., V. 3, No. 7, 528-31, 8 figs. on 2 pls. By **D. J. Terencio.**

Owing to the use of sulphones the number of patients at

Fontilles with lepromatous ulcers of the legs has been reduced from 62.6 per cent in 1943 to 14.04 per cent in 1954. However, there are some ulcers of the lower parts of the legs which have continued for a long time and refuse to yield to ordinary treatment. The author has found that these may be successfully treated with sheet grafts, either of the thin (0.2 to 0.25 mm.) Thiersch variety, or of the thicker (0.3 to 0.4 mm.) Blair Brown variety.

For 15 days beforehand all treatment is stopped, the ulcer is washed with normal saline and exposed to the sun daily. Vitamin and other general treatment is given. Anasthesia is produced locally with 1 per cent Novocaine-adrenaline solution, and an ampoule of Escofedal (not described) is given intravenously. The ulcer is scraped thoroughly and all thick fibrous tissue removed, leaving only a vascular base. The raw surface is covered with a compress of normal saline while the graft is removed with a razor from a healthy part of the thigh. The graft is stitched into position with fine silk and covered with sterile vaseline gauze for 10 to 15 days. Penicillin, 400,000 units, is given daily for 4 to 5 days. The results obtained were much superior to those obtained with small skin snip grafts.

Effect of vaccination with BCG on the Evolution of Murine Leprosy: Observation in Rats Inoculated Intraperitoneally with a small dose of "Myco. leprae murium." Rev. Brasileira Leprologia, S. Paulo, 1954, June, V. 22, No. 2, 124-34, 10 figs. and 1 chart (12 refs.). English summary. By **W. A. Hadler** and **L. M. Ziti.**

In this experiment 50 rats were divided into four groups; 13 were given 25 mgm. of BCG orally; 12 were given 5 mgm. similarly; 12 were vaccinated with 5 mgm. of BCG intramuscularly; and 13 were left as controls. All animals were inoculated with 0.03 mgm. *Myco. leprae murium* after 90 days, and were observed for 450 days. Between those vaccinated with BCG and the controls there was no difference in the evolution of the disease. While rats vaccinated with BCG do not show in their macrophages the power to destroy mycobacteria like those of leprosy, rat leprosy and tuberculosis, the macrophages of guinea-pigs vaccinated with BCG do acquire this power.

A Comparative Study of Lesions Provoked by the Intradermal Injections of Suspensions of "Myco. leprae" and "Myco. tuberculosis" in Guinea-pigs previously Vaccinated with BCG. Rev. Brasileria Leprologia, S. Paulo, 1954, June, V. 22, No. 2,

109-23, 10 figs. and 1 graph. English summary. By **W. A. Hadler.**

Ninety-eight guinea pigs were inoculated with BCG intramuscularly and intraperitoneally. Of these, 58 were injected 40 days later intracutaneously with 0.05 ml. of BCG suspension, and another 22 with 0.1 ml. of lepromin, while the remaining 20 were injected on the one side with BCG and on the other with lepromin. (There is a discrepancy of 2 in the numbers.)

It was found that in normal guinea-pigs the cellular reaction was different in the sites of BCG and lepromin injection, only the BCG producing an abscess. But in guinea-pigs previously inoculated with BCG the cytological and histological appearances were similar in nature. It was found, however, that after observation for 50 days the reaction with BCG was stronger than that with lepromin, but disappeared more rapidly. It is concluded that *Myco. tuberculosis* is more easily lysed than *Myco. leprae*, and that this probably depends on their different structures, chemical compositions and physico-chemical properties. Possibly the lipids account for these differences, at least in part.

***Trop. Dis. Bulletin, Vol. 52, No. 9, Sept. 1955**

The Incidence and Epidemiology of Leprosy in Uganda. Trans. Roy. Soc. Trop. Med. & Hyg., 1955, May, V. 49, No. 3, 241-52, 1 chart. By **J. A. K. Brown.**

Uganda, with a population of about 5 million and an area of 93,981 square miles, of which a seventh is open water, is divided into Eastern, Western and Northern Provinces, with the kingdom of Buganda in the centre. These are sub-divided into districts, counties, sub-counties and rural parishes.

As there are no towns or villages, surveys were made at the parish or sub-county level. Help in enumeration and in gathering the people together for examination was given by the chiefs and the local medical and other officials. Sometimes numbers of local populations could be obtained from previous sleeping sickness registers. In tabular form the results of 36 sample surveys are given, divided under the four divisions of the country. The subjects with leprosy are divided according to age, sex and type of disease.

Because of its varying climatic conditions, Uganda is considered a particularly suitable country for studying the effect of climate on the incidence of leprosy. The surveys showed that " atmospheric humidity, temperature and nearness of water did

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not appear to have any relationship to incidence," and there was no correlation between incidence and population density. The proportions between sexes was almost equal. Among 882 subjects, 19 per cent were under 15, 32 per cent between 15 and 30, and 31 per cent between 30 and 45. The surveys showed a series of incidence values from 0.0 to 4.1 per cent.

It is concluded that " the social structure determines the age of onset, the age frequency and the disease pattern. Clinical leprosy develops in susceptible persons after contact with a patient. Susceptibility is inherited and may be transmitted through successive generations without the appearance of clinical leprosy. Variations in incidence are due to those factors which influence the number of susceptibles and their opportunities for contact."

The suggestion that leprosy may be spread by tuberculoid cases is argued as follows: " The infecting patient is usually thought to be the lepromatous case. Where the lepromatous rate is 20 per cent it may be difficult to find a village without at least one. The inference. then may appear legitimate. With a lepromatous rate of 10 per cent, the same incidence and similar living conditions, difficulties arise. A lower lepromatous rate implies a higher general level of resistance. It is not easy to understand why the greater the resistance the greater should be the potentialities of fewer lepromatous cases. The more intimate communal life may be sufficient explanation in a compound or a village but not under the different conditions of East Africa. There are parishes of 1,000 people dispersed over 20 square miles without a single lepromatous case, and tuberculoid cases occur five miles or more from the nearest lepromatous patient. It would require the greatest mobility and popularity on the part of the lepromatous subject if all the leprosy in the country could be attributed to them. Open cases could act as the only source of infection in Uganda on the assumption of carriers, an assumption less easy than that tuberculoid cases are infectious. Admitted that lepromatous cases more easily infect and that intimate contact increases the risk, for susceptible people contact with a tuberculoid patient may be sufficient to decide the issue."

[This would imply that tuberculoid cases could infect considerable numbers of those with fairly high resistance as shown by their tuberculoid type, a very serious implication. This matter is one of importance and requires careful study (see Editorial). The paper is of much interest, and deserves to be studied in the original.]