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LEPROSY REVIEW

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CONTENTS

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EDITORIAL

1. The Vellore Conference on Rehabilitation of Leprosy Patients

We are very glad to give a news item on this important conference, which we hope will whet the appetite for the full reports which no doubt the sponsors will make available in due course. This conference seems to have been one of those ideal symposia where the membership is kept low and each man is an expert in some relevant field. The sponsors are greatly to be congratulated on this conference. Dr. E. W. Price, F.R.C.S., has kindly provided the following brief information:

The success of modern leprosy treatment has brought a new optimism, which is reflected in the scope and the conclusions of the Scientific Conference on Rehabilitation in Leprosy, held in November 1960 in Vellore, Madras State, S. India.

The meeting was sponsored jointly by the World Health Organisation, the Leonard Wood Memorial, and the International Society for Rehabilitation of the Disabled; and was indebted to the Christian Medical College, Vellore for clinical and clerical facilities and generous hospitality. The sponsoring organisations were represented by Dr. J. GAY PRIETO (Chief of the Leprosy Section, W.H.O.), Mr. D. V. WILSON (Secretary-General of the International Society for the Disabled), and Dr. J. A. DOULL (Medical Director of the Leonard Wood Memorial) who was elected Chairman of the Scientific Meeting.

The participants in the Conference were Prof. Paul W. Brand (Orthopaedic Surgery), Dr. Margaret Brand (Eye Surgery), Dr. N. H. Antia (Plastic Surgery), Dr. J. A. Doull (Leonard Wood Memorial), Dr. E. Fritschi (Clinical Tutor in Orthopaedics), Prof. H. H. Gass (Dermatology), Dr. R. S. Guinto (Epidemiology), Dr. M. Itchi (Physical, Medicine and Rehabilitation), Dr. C. K. Job (Pathology and Leprosy Research), Dr. R. W. Mackie (Neurological Surgery), Dr. D. E. Paterson (Radiology), Dr. R. G. Pulvertaft (Orthopaedic Surgery), Dr. D. G. Riordan (Clinical Orthopaedic Surgery), Dr. R. V. Wardekar (Leprosy Control), Dr. G. Weddell (Anatomy), Dr. L. Zamudio (Orthopaedic Surgery), Dr. R. H. Bland (WHO, India), Dr. J. Gay Prieto (WHO Leprosy Section, Geneva). The participants included those with experience in leprosy, and also some without previous knowledge of the disease but whose expert knowledge in various scientific fields added greatly to the value of the meeting. It soon became evident that many of the problems discussed had been met in diseases other than leprosy and that experience gained elsewhere could be applied with profit.

The objectives of the Meeting were defined as follows: (1) To state the existing knowledge of the aetiology, prevention, and treat-

ment of disablement as found in lèprosy patients; (2) to advise how present knowledge can best to applied in leprosy control, treatment, and rehabilitation programmes; (3) to recommend what further research studies should be undertaken. The size of the problem, and useful measures of rehabilitation suitable for areas of limited resources, were also considered.

In the discussion on the *extent of the problem*, it was realised that information was incomplete, but it appears that a world total of ten million cases of leprosy may be a conservative estimate, that probably not more than 20% are under treatment, and that as many as 25% of the total may have some physical disability. In view of the importance of having fairly accurate estimations if useful decisions are to be taken, it is urged that all workers should co-operate as far as possible in completing the WHO enquiry form on "Deformity in Leprosy" which was recently circulated.

The discussion on advances in *nerve pathology* drew attention to the recent advances emerging from the use of electron-microscopy:

The site of major damage in nerve lesions is known to be the basement membrane related to the Schwann cells, the melanocytes, and the basal layer made up of epidermal cells. As the pathology seems limited to the cell surface, it is suggested that some antibody-antigen reaction is damaging the cell, and that research should be directed to elucidating the character of this complex.

It has been possible to show that in leprosy patients with no loss of cutaneous sensibility, as many as 25% of nerve fibres to the skin may be damaged.

Attention was drawn to reports of benefit resulting from the use of an enzyme (chymo trypsine) during the course of a reaction in leprosy, and further experience should be gained with this technique. The orthopaedic specialists drew attention to the possibility that the site of the nerve lesions might be the expression of a "compression syndrome" and considered that the operation of nerve decompression might be indicated in such areas as the elbow (by anterior ulnar transposition), at the zygoma (by releasing fibrous bands), and at the carpal tunnel by dividing this structure. However, these manoeuvres should be carried out by those familiar with the problems of nerve compression.

At the session concerned with *physiotherapy and reconstructive surgery*, the meeting was unanimous in its opinion that standard methods of treatment are applicable to leprosy, and that results are at least as good as those following similar treatment for other paralytic diseases.

Because the paralyses of leprosy are well-defined and predictable as to extent, the use of a small repertoire of procedures can combat disability effectively. These will normally be carried out by specialist personnel, and the meeting prepared *a summary of the common*

deformities and the methods of physiotherapy and surgery which prove successful.

In endemic areas where facilities are limited, it is necessary to use medical auxiliary workers, specially trained in a limited number of manoeuvres, and a memorandum was also prepared detailing the various procedures which such an auxiliary should know if he is to give efficient treatment. It is desirable that these auxiliaries act in co-operation with a local orthopedic and plastic surgeon, or professional physiotherapist; but even this is not always possible, and then considerable improvement in the wellbeing of the patient can be achieved by such auxiliary personnel under the direction of the doctor or nursing sister in charge of the treatment.

The *bone lesions* in leprosy were described at length in a further session. The specific lesion of leprosy—the osteitis leprosa of the phalanges—can be healed completely and deformity prevented by immobilisation of the part in a functional position during periods of pain and swelling.

The major bone lesions are due to non-specific causes and occur in any disease with long-standing nerve damage; these include osteoporosis, pathological fracture, secondary infection of bone and joint, and the neuropathic joint of Charcot. The treatment of these lesions follows standard orthopedic methods.

The *deformities of the face* occupied one session. The importance of these lesions was emphasised by two ex-patients who addressed the meeting and who stated that, while they were very grateful for all that was done for their hands and feet, it was the appearance of their face that was their major anxiety.

Apart from the infiltration of skin in lepromatous disease, the deformities include collapse of the nose, loss of eyebrows, and lagophthalmos. It was agreed that collapse of the nose was due to non-specific destruction of the nasal framework by banal infection as a sequel of the lepromatous ulceration of the nasal mucosa. Collapse could be prevented if banal infection were controlled; but if it occurred, reconstruction is possible by standard procedures and is made easier by the fact that there is usually no skin loss. The replacement of eyebrows is an easy procedure and of considerable psychological value. Most important is the lagophthalmos which exposes the insensitive cornea to constant irritation. The surgical procedures to correct this are standard plastic procedures.

The simplest in an emergency is tarsorraphy; the most satisfactory is a temporalis musculo-fascial sling.

A session was given to *plantar ulceration* because of its frequency and the serious damage that may occur to the feet. The theories of causation were reviewed and it was agreed that the major cause appears to be mechanical and related to the strains of walking. The importance of treating the first ulcer was stressed, but it was better

still to prevent the first ulcer occurring. The signs of impending ulceration are obvious enough for auxiliary workers to recognise them, and it was noted that these workers could control the occurrence of plantar ulceration by systematic foot inspection and treatment in the pre-ulcerative stage. Simple ulceration is still treatable by auxiliaries, but major complications (including bone and joint infection, and the neuropathic joint of Charcot) are indications for specialised care. It was recognised that there was no problem in achieving the healing of a simple ulcer—the simplest method being rest in bed; but a walking plaster cast was almost as effective and avoided immobilisation of the patient.

Ulceration could be prevented in the pre-ulcerative stage by rigid-sole footwear, a soft insole, and an artificial means of providing the walking roll such as a rocker or a shaped sole. Similar treatment will forestall recurrence of a healed ulcer.

Ocular damage was discussed by ophthalmologists who emphasised that blindness as a complication of leprosy is largely avoidable. The conditions most likely to lead to blindness are severe lagophthalmos with resultant damage to the cornea, and the irido-kerato-scleral condition resulting from direct lepromatous infiltration or allergy or both. Iritis is the commonest single cause of blindness in leprosy and the importance of atropine instillation was underlined. The value of preventive treatment and the recognition of such early signs as reduced vision was stressed and auxiliary workers should be trained in this.

An important session was given to the *means to prevent deformities*, and the educational problems involved. Most patients should be diagnosed and their disability treated without any help other than is available locally, and without admission to any institution. All workers in leprosy should be trained to look for early signs of damage to limbs, nose, and eye in the knowledge that, with early diagnosis, prevention of deformity is made easy and fully successful treatment is made likely.

In several sessions of the Conference the statement was repeated that the care needed by patients recovering from leprosy was similar to that of patients recovering from other chronic nerve lesions. It is both convenient and desirable that such treatment should be undertaken alongside that of other patients in the departments of general hospitals. The prejudice against leprosy patients in some areas was recognised, and that this may hinder the desired integration. There is no scientific foundation for this fear in non-bacilliferous leprosy patients, but the fear exists among doctors as well as among the public. Enterprising and widespread propaganda is needed to combat this mistaken belief, and efforts made to encourage the integration of leprosy rehabilitation into the general medical rehabilitation service. Nevertheless, it is clear that because of the size of the prob-

lem and of special local conditions, this ideal may not be attainable immediately. Steps should be taken to encourage reconstructive surgeons and professional physiotherapists, to be aware of the large and satisfying opportunities that exist in helping to restore these patients to their place in society.

The *general conclusion of the Conference* was that although some deformities formed still an unsolved problem (notably those resulting from nerve damage during acute reaction) most of the disabilities of leprosy were preventable or, when they occurred, treatable. Statements accepted by the Meeting included the following:

"Facial deformities are to a large extent preventable. All lend themselves readily to reconstructive surgery"; "It can be stated that blindness from leprosy should be a thing of the past"; "It is emphasised that if our present knowledge is properly applied, plantar ulceration should not occur"; "The use of a small number of procedures can restore severely disabled hands to normal appearance and to activity".

The above findings should bring a message of hope and encouragement to all leprosy workers and their patients; there is still the task of spreading this knowledge to the vast areas in which the disease exists and to the millions of people who are affected. This problem is now being tackled by the organisers of the Conference.

2. Increase in Price of Leprosy Review

For some time we have been aware that the previous current price of the REVIEW (3s. 6d. per copy and 15s. 0d. per annum) has been too tiny a proportion of the cost of the REVIEW, and many subscribers have even told us so. The constantly rising costs have at last impelled us to action, and from now on we beg to inform all our subscribers that the price will be 5s. 0d. per copy plus postage and £1 per annum post free. We trust that this very modest increase will not cause too much alarm and despondency but will be accepted as a necessary step in view of the heavy modern costs.

3. The Classification of Leprosy

This subject is a hardy perennial, for the simple reason that full agreement has not yet been reached. We direct attention to the sensible paper on p. 74 by Dr. R. Chaussinaud of Paris.

4. The New Etisul Liquid Formula

A new step forward with this drug has been the issue of a liquid preparation, and Dr. S. G. Browne reports on an acceptability trial of it on pp. 83—84. As regards the practical usefulness of Etisul, and of DPT (Ciba—1906) we draw attention to comments on them in the Research Reports (in this issue, pp. 121—123) of the Colonial

Medical Research Committee and the Annual Report of the East African Leprosy Research Centre.

5. Correction

Dr. D. A. Baird, O.B.E., of Kuching, kindly points out that there is an error in the population figure for Sarawak given on page 6 of the January *Leprosy Review*. The correct figure should be 750,000.

CLASSIFICATION OF LEPROSY

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Since 1931, that is to say since we have specialised in leprosy, much ink has flowed on the problem of the classification of leprosy and without much success, for leprologists are not yet able or willing to agree on one classification that might at last be adopted by all.

I. Primary Classification

At the present moment there are four primary classifications in existence, which are more or less widely accepted. They are: the classifications of the 1st WHO Expert Committee on leprosy and of Madrid which only differ in a few details; the Indian classification; the classification worked out by the Japanese leprologists; and finally Cochrane's classification. Needless to say, we have no intention of proposing a fifth.

We are of the opinion, with ROSS INNES[5] that the WHO and Madrid classifications are acceptable, in spite of several imperfections. They seem to us to be markedly clearer and more practical than the others. What are the criticisms that are most frequently levelled at them?

First of all, the nomenclature used in the primary classification is not unanimously accepted. Thus although the expression "tuberculoid leprosy" is used by the vast majority of leprologists, DAVISON and his co-workers[3] have just recently proposed its suppression, on the ground that the histological structure characteristic of this form is transient. This objection does not appear to us to be valid. The exact classification of a patient ought to be made on his admission to antileprosy treatment and it is not permissible to modify this classification "a posteriori", solely because histological changes have intervened in regressive lesions.

It has been fully established that the histopathology of the cutaneous lesions of tuberculoid and lepromatous patients is gradually modified, and before the cure is complete it is possible to detect the picture of an ordinary non-specific chronic inflammation. It would be a grave error to try at this stage to classify these patients as indeterminate leprosy (as we saw certain leprosy services doing), making the claim that the histology of their lesions is analogous with that of the pathological changes that take place in indeterminate leprosy.

It is obvious that it is not possible to reclassify a tuberculoid or lepromatous patient as indeterminate if the only reason for doing so is that the histology of the regressive skin lesions shows the picture of ordinary chronic inflammation.

While the term "lepromatous" is universally accepted, the word "indeterminate" has been strongly criticised. We cannot understand why it should be considered useless in leprosy classification. Since the descriptions "tuberculoid leprosy" and "lepromatous leprosy" are terms based on histological data, the expression "indeterminate leprosy" seems to us to be correct and intelligible, for it is based just as much on histological observations. A case of indeterminate leprosy is a patient presenting the indisputable clinical signs of leprosy, but whose lesions show the histological picture of an ordinary chronic inflammation. This picture may be called "indeterminate" if one takes into account the more distinctive "determinate" histology of tuberculoid lesions and, more markedly, of lepromatous lesions. Furthermore the definition "indeterminate" implies that we are dealing with a frequently unstable form. *On the other hand we feel there is no profit in describing indeterminate leprosy as a "group" (Madrid classification). It is in fact a clinically defined initial "form" of the disease which may either remain unchanged or evolve in the end into one of the other two forms.*

It would be unfortunate to use, as the Indian leprologists wish to do, histological definitions for the tuberculoid and lepromatous forms and the clinical definition of maculo-anaesthetic leprosy for the indeterminate form. And the more so since certain skin lesions of tuberculoid leprosy, and sometimes even lepromatous ones, may equally well be described clinically as maculo-anaesthetic.

We feel that the terms "tuberculoid", "indeterminate", and "lepromatous" ought to be retained in the primary classification of leprosy. They are already known and accepted by the majority of leprologists and it seems unlikely to us that simple and easily understood clinical definitions could be found to replace successfully the present histologically based terms. *One might all the same wonder if we ought to reserve a place for borderline leprosy in the primary classification.* Personally we consider borderline leprosy to be an unstable variety of the tuberculoid form capable either of regressing to the major tuberculoid variety or of evolving into the lepromatous form. To us it seems hardly necessary to include it in the primary classification. RAMOS E SILVA[4] tries to resolve the difficulty by dividing borderline leprosy into two groups, one predominantly tuberculoid and the other predominantly lepromatous. It seems to us that it is rather difficult to make this distinction in a primary classification. We think it would be preferable to consider borderline leprosy, as long as it remains really "borderline", as an unstable variety of tuberculoid leprosy and so being logically placed in the secondary classification.

However the WHO and Madrid classifications and also those recommended by the Indian leprologists and by COCHRANE include borderline leprosy in the primary classification. We feel that this is

an illogical procedure but strictly speaking it is admissible, since it does not cause any confusion when classifying patients. *On the other hand we cannot allow borderline leprosy to be included in the different classifications under completely different names.* Thus both the Latin-American leprologists and Cochrane prefer the terms "dimorfo" or "dimorphous", while the Indian and Japanese leprologists use "intermediate" and "atypical". This would not matter much if all the terms had exactly the same meaning, but unfortunately this is not the case.

Borderline leprosy is described by WADE as an unstable intermediate stage between major tuberculoid leprosy and lepromatous leprosy, and capable of regressing towards major tuberculoid leprosy, from which it derives, or of evolving towards the lepromatous form. Now although the Madrid classification admits this definition and gives eaxctly the same meaning to the word "dimorfo", Cochrane groups under the heading "dimorphous" not only Wade's "borderline" cases, but also patients in the intermediate phase between the clinical beginning of leprosy, which is always, according to this author, potentially lepromatous (we certainly do not share this opinion) and tuberculoid leprosy In the Indian and Japanese classifications the borderline cases are put together with cases of indeterminate leprosy in a group called respectively "intermediate" and "atypical".

It is evident that a unique word is necessary for an international classification and the most appropriate term, one which avoids confusions during the classification is Wade's term "borderline" unless the word "dimorphous" be henceforth used only as a synonym of the word "borderline".

Certain authors describe borderline leprosy as "bipolar", basing their description on RABELLO who considers the tuberculoid and lepromatous forms as the "polar" types of the disease. But in geography the north pole never changes into the south pole, and equally in electricity the positive and negative poles are not interchangeable. Thus the description "polar types" which Rabello gives to the tuberculoid and lepromatous forms of leprosy seems to us to be very questionable since poles are immutable. Now it is no longer possible to claim that tuberculoid leprosy is an immutable form which never evolves towards lepromatous leprosy. The polar conception of leprosy and, therefore, the expression "bipolar", ought to be abandoned.* It would be more logical to substitute the word "extreme" for "polar", the tuberculoid and lepromatous forms of leprosy being thus defined as the two extreme types of the disease *But we do not approve of the inclusion, proposed by Wade and by the Indian leprologists, of a pure polyneuritic form in the primary classifi-*

* Certain Brazilian authors even use the adjective "infrapolar" to describe indeterminate leprosy.

cation. We would then have in the same group patients with tuberculoid or indeterminate leprosy, as well as lepromatous cases who only show polyneuritic lesions since their cutaneous lesions have disappeared. It is inconceivable this group should be given a place in the primary classification since this classification has the precise object of defining the principal forms of the disease with a view to an orderly scientific classification of patients. And for the rest, this procedure is hardly to be recommended from a clinical point of view since the prognosis and the necessary duration of treatment differ greatly for tuberculoid, indeterminate and lepromatous patients.

We know that it is sometimes difficult to classify correctly patients who have pure polyneuritic leprosy, but this is a rare occurrence. A positive Mitsuda reaction permits us to exclude the lepromatous form, and if it is strongly positive allows us to assert that we are dealing with a tuberculoid leprosy. A weakly positive lepromin reaction, however, indicates rather an indeterminate leprosy, especially in patients with a moderate and even hypertrophy of nerve trunks. As for subjects insensitive to lepromin, indeterminate leprosy is probably what exists, unless the cutaneous stigmata or alopecia of the eyelashes indicate that we have a lepromatous patient whose cutaneous lesions have disappeared. In fact pure nerve leprosy in lepromatous cases probably does not exist, or, if it does, remains purely neuritic only for a short time since the skin is rapidly invaded by *M. leprae* in this form of the disease.

In very rare cases which cannot be classified by a result of clinical methods and the result of the lepromin reaction, the classification is helped by the histological examination of a small biopsy taken of a swollen nerve. In this way we were able to establish a diagnosis of tuberculoid leprosy in three lepromin-positive patients who showed only a single unilateral facial paralysis with a mild hypertrophy of one or of several cervical nerves. These biopsies had absolutely no harmful consequences. In two of these patients treatment with diamino-diphenylsulphone brought only a slight improvement, but in the third the facial paralysis had practically disappeared after 11 months of treatment.

We think that patients with polyneuritic leprosy, whether pure or secondary, ought to be classified under one of the three forms of leprosy—tuberculoid, indeterminate, or lepromatous. In case of doubt the patient could be placed provisionally in the group that seems the most likely one, but with a question mark until the classification has been confirmed or rejected by a histological examination.

The adoption of *a binary classification* which covers the primary classification could be achieved by using, in their biological sense, the terms "benign" and "malignant". In our opinion this binary

classification has above all the advantage of avoiding the continual repetition of the words "tuberculoid", "indeterminate", and "lepromatous" in the literature. However, this division might not fit exactly in the case of borderline leprosy, though in fact this unstable variety cannot be called biologically malignant until it has definitely evolved towards the lepromatous form. The terms benign and malignant seem to us to be preferable to lepromatous and non-lepromatous, proposed by certain authors.

On the other hand we do not advocate the use of the terms "open" and "closed" for the classification of leprosy patients. These terms would be grammatically acceptable if they were used as follows: "open" to mean that the nasal mucosa is positive or that the cutaneous lesion is ulcerated, and "closed" to mean that the nasal mucosa is negative and the cutaneous lesion is non-ulcerated. However, at present we find in the "open" group patients with only very few bacilli in non-ulcerated cutaneous lesions and also patients with strongly bacilliferous nasal mucosa and cutaneous lesions, and this seems to us undesirable.

The majority of leprologists consider that patients with few bacilli and negative nasal mucosa can to all intents and purposes be described as non-contagious. All such cases would thus be classified, under the present system, as "open" and so are subject to the sometimes irritating administrative consequences of this designation.

One could perhaps use for the Administration *in place of the terms "open" and "closed" the following expressions*, which would be more easily understood by the non-medical: (in French, "contagieux") *contagious* (with positive nasal mucosa or highly bacilliferous cutaneous lesions, above all when ulcerated); (French, "présumé non-contagieux") *presumed non-contagious* (with negative nasal mucosa, few bacilli in non-ulcerated cutaneous lesions); (French, "non-contagieux") *non-contagious* (negative to bacterial examination).

II. Binary Classification

In order that it might be universally accepted the binary classification should be simple and based principally on clinical observation. The most elementary classification would thus be to subdivide each of the three forms of leprosy into "cutaneous", "neuritic", and "cutaneous-neuritic". But the usefulness of a more detailed classification is undeniable. And thus it is necessary to attempt to define the different varieties of the forms of leprosy.

But it should always be borne in mind that there are certain intermediate and transitory stages that exist between different forms and even between certain varieties of leprosy, and which can sometimes be detected only by histological examination. In our opinion these intermediate stages cannot be considered as varieties as we

describe them, and they ought not, except for borderline leprosy, to be taken into account in the binary classification. Similarly the reactional states, whether of long or short duration, which alter, for good or for ill, the normal course of the disease cannot be classified as different varieties. The use of the terms "pretuberculoid", "tuberculoid reaction", "tuberculoid reactional transformation", "prelepromatous", "lepromatous reaction" and "nodular erythema" will permit us to describe these transitory stages of the disease.

The distinction between the different varieties of leprosy is essentially grounded on the clinical aspect of the cutaneous lesions, except of course for the purely neuritic cases.

Tuberculoid Leprosy

According to the Madrid classification this form of leprosy is divided, from the cutaneous aspect, into the three varieties "macular", "minor" and "major". We would add to this list borderline leprosy.

One may wonder whether there is any profit in considering pure macular tuberculoid leprosy as a true variety. (We would mention that in this article we are using the terms "macule" and "macular" in their strict dermatological sense.) In fact it is rare for an undoubted case of tuberculoid leprosy to show only typical macular changes. A careful clinical examination generally allows us either to detect a very mild infiltration or to recognise previously-infiltrated tuberculoid lesions that are now regressing. Besides, the most of the strictly macular erythematous lesions which are included in this variety exceptionally prove to be purely tuberculoid. They are, more often than not, pretuberculoid or even prelepromatous indeterminate lesions, whose exact nature can often only be determined by bacteriological or histological methods.

As for the terminology, "macular" is a descriptive word, whereas "minor", "major", and "borderline" indicate different degrees of the infection. So if we wish to include this variety in the binary classification it would be preferable to replace the word "macular" by a more appropriate term. The adjective "atypical" might be suitable, since the infiltration, absent from the macule, is one of the principal clinical characteristics of the tuberculoid cutaneous lesions.

Finally we prefer the term "major tuberculoid" to "reactional tuberculoid", for the latter is often confused with the expression "tuberculoid reaction" by doctors unfamiliar with leprology.

We thus have the following list of varieties of tuberculoid leprosy:

Tuberculoid leprosy

atypical	(macular, well-defined) (?)
minor	(micropapular, well-defined)
major	(infiltrated, in a plaque or a ring, well-defined)

borderline (more or less infiltrated, in a plaque or a ring, ill-defined). One may however object to this method of classification which is based principally on the degree of the infection while the terminology at present used to describe the varieties of the lepromatous form is certainly clinically descriptive.

Indeterminate leprosy.

In this form of leprosy there are, from the cutaneous point of view, no varieties, since all the lesions are strictly macular. At most one might make distinctions on the grounds of colour. But these lesions are almost always hypopigmented.

As for erythematous macules, bacteriological and above all histological methods reveal that we are most often dealing with indeterminate pretuberculoid, or even prelepromatous lesions. Finally hyperpigmented macules are extremely rare.

Lepromatous leprosy.

In lepromatous leprosy there are in reality only two cutaneous varieties: lepromatous leprosy with figurate lesions and diffuse lepromatous leprosy.

However, we may find cases, of ordinary recent lepromatous leprosy, with nothing but figurate lesions of the same type. It will therefore be of use for the prognosis and for the assessment of therapeutic results to classify such patients in a more precise way. To do this we might subdivide the variety "figurate" into "papular", "macular", "nodular", and "infiltrated".

But such patients (that is showing skin lesions all of the same type), are relatively rare. Most lepromatous patients have, in varying proportions, skin lesions of widely differing types. And this subdivision could only be applied to them with difficulty. But one could then specify that a certain type of lesion is "predominating".

We may thus list the following binary classification for lepromatous leprosy:

Binary Classification
Lepromatous Leprosy

figurate		*diffuse*
papular macular nodular infiltrated	"pure" or "predominating"	

The essence of this study of leprosy classification is summarised in Table I which is appended. So as not to overload the scheme we have not mentioned the bacteriological, immunological, and histological features of the different varieties and forms of leprosy. Besides, these features are not now in question. Those varieties

which do not seem to be absolutely indispensable have been marked with a question mark.

Conclusion

An acceptable classification of leprosy could be rapidly decided on if leprologists would agree to remove from consideration certain regional or personal preferences, to which it is hard to attach any real importance. And this result could be achieved easily since no doctrinal differences exist in clinical, immunological, or histological aspects. It is high time that we attained such a result for it is hard to believe that only a few years from the 90th Anniversary of the discovery of the bacillus by ARMAUER HANSEN, leprologists are still searching for an acceptable classification of leprosy.

Acknowledgement

We are very grateful to Dr. J. Ross Innes for arranging for the translation into English of this article, which was submitted in French.

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TABLE I

CLASSIFICATION OF LEPROSY

TUBERCULOID	INDETERMINATE	LEPROMATOUS
CUTANEOUS	CUTANEOUS	CUTANEOUS
atypical (macular) (?) *minor* (micropapular) *major* (in a plaque or a ring, infiltrated, well-defined) *borderline* (in a plaque or a ring, more or less infiltrated, ill-defined)	*macular* (?) (hypopigmented, and rarely erythematous or hyperpigmented)	*figurate* papular, macular, nodular, infiltrated } "pure" or "predominating" *diffuse*
NEURITIC	NEURITIC	NEURITIC
pure *secondary*	*pure* *secondary*	*pure* (?) *secondary*
CUTANEOUS-NEURITIC	CUTANEOUS-NEURITIC	CUTANEOUS-NEURITIC

REPORT OF A CASE OF LEPROSY IN A NORFOLK PRACTICE

A. S. GARRETT, M.B., B.S., M.R.C.S.(ENG.)

A man aged 22 years came to my surgery complaining of *a rash on his chest*. For some two months he had noticed a plaque 2 inches by 1 inch in size (2.54 cm. x 5.08 cm.), and many new small raised red lesions had begun to appear a week or two before he came.

The plaque was well-defined, and raised and erythematous, with a slight tendency to central spontaneous healing. The supraclavicular nerve was enlarged leading to the plaque (left internal branch of the nerve). The plaque was anaesthetic. Around the main plaque there were many small raised erythematous lesions with edges less well defined. The left great auricular nerve was enlarged, and the left ear lobe was slightly thicker than the right. Smears were taken from the skin of the ear and of the lesions and showed mild bacterial positivity in 3 out of 5 smears.

Dapsone (DDS) tablets were given at 100 mg. twice weekly by mouth, and during the first 3 weeks new lesions continued to appear over the chest and back. Then the inunction of Etisul was begun, and within 2 weeks the lesions had improved markedly, and within a month the erythema and elevation of the lesions had disappeared, and the nerves returned practically to normal size. The anaesthesia over the area of the original lesion persisted until 2 months, and by that time all smears were negative. The only possible sign left is some hypopigmentation of the skin of the back and chest.

Previous history

The patient had resided 14 months in Cyprus, whence he departed in December 1957. This suggests an incubation period of nearly 3 years from the probable infection.

Summary

A case of leprosy met with in country practice in England is here briefly described. It seems to be a case of borderline leprosy, in which body resistance was in process of breaking down at the time of presentation for diagnosis of a "rash". In this case it was found there was a very rapid response to therapy by Dapsone (DDS) combined with Etisul by inunction, and this therapy has enabled him to return to work within 2 months.

From my previous experience in Africa, Etisul and DDS combined only acted in this very rapid manner in 2 or 3 very early cases of infectious leprosy. DDS alone would probably have taken about 6 months to achieve this effect. Perhaps bringing in Etisul sooner would have prevented the outcrops of new lesions in this case.

AN ACCEPTABILITY TRIAL OF ETISUL LIQUID FORMULA

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Introduction

Favourable reports recently published by DAVY and HOGERZEIL (1959), DAVEY (1959), LECHAT (1959 and 1960), ROSS *et. al.* (1960) on the use of Ditophal in the treatment of leprosy have referred to the persistent objectionable odour of the active principle, ethyl mercaptan. Ditophal is Etisul of ICI, which is diethyl dithiol*iso*-phthalate. Messrs. Imperial Chemical Industries, Pharmaceuticals, Ltd. made early attempts to mask this odour by incorporating various perfumes into the original preparation. The resulting cream as used in the trials quoted above was acceptable to most patients. The manufacturers have made further experiments directed towards producing a bulk liquid preparation, which besides being less costly to produce and pack than a cream which is supplied in individual dose tubes of 5 g., would also have certain practical advantages. A liquid preparation was found very acceptable in a trial, applied twice weekly for 3 months to 17 patients at Uzuakoli Leprosarium. An improved product has since been prepared. This is "Etisul Formulation F-565" which is the subject of this report.

The Trial

For this trial 14 intelligent adult patients, already under treatment with standard doses of Dapsone or Thiambutosine (which is the diphenyl thiourea, Ciba-1906) were invited to co-operate in this acceptability trial of the Etisul liquid preparation. Of the 14 patients 3 already had experience of the standard Etisul cream and with the earlier Etisul liquid preparation: 3 others had previously used the cream only. The dose was 5 ml. which could be measured conveniently from the multidose pack into a cylindrical container supplied to each patient, this container having been scored to show the 5 ml. level. During the trial there was no absenteeism and all the patients spontaneously continued the treatment for the whole period. There was one exception in a patient who had to cease treatment because of severe recurrence of lepra reaction.

On three occasions the patients were questioned individually and privately (1) after the first four applications twice-weekly; (2) after 3 months; (3) after the end of the trial period of 6 months. The responses were as follows. The 4 patients who had used the Etisul cream previously were unanimous that the Etisul Liquid (Formulation F-565) was much superior to the cream from their point of view. They found that it rubbed in more easily, and disappeared more

rapidly from the skin. They volunteered the view that the rubbing required a less vigorous effort for a shorter period of time than was necessary with the cream. The mercaptan odour emanating from the skin seemed to be less persistent than was the case with the cream, and it disappeared more completely after a warm bath with scented soap, taken 2 hours after inunction. It seems likely that when the cream was used, a proportion of the active principle was adsorbed on to the surface of the particles of inert and unabsorbable excipient (magnesium stearate) used in the preparation. Since a higher proportion of the active product is probably absorbed percutaneously in the case of the liquid preparation, the therapeutic effect should be greater.

As for persistence of the mercaptan odour in the breath, no difference between the cream and the liquid was noted by those who had experience of both. After 3 months of treatment, all but 2 of the patients found the smell of the liquid quite acceptable, even though several of the new patients had begun the trial with some prejudice against the drug derived from hearsay. By the end of the trial, all the patients were quite enthusiastically in favour.

Our conclusion was that Etisul Liquid Preparation (Formulation F-565 ICI) is a very satisfactory preparation of diethyl dithio*iso*-phthalate for percutaneous administration. It proved acceptable to all 13 patients who used it in 5 ml. doses twice weekly for 6 months.

Acknowledgements

Our thanks are due to Messrs. Imperial Chemical Industries (Pharmaceuticals) Ltd. for a generous supply of Etisul Liquid, and especially to Dr. J. Michael Mungavin for his help and advice.

We thank Dr. S. E. Onwu, M.V.O., O.B.E., Chief Medical Officer, Director of Medical Services, and Perm. Sec. to the Ministry of Health, Eastern Region, Nigeria, for permission to publish.

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CHLORAMPHENICOL THERAPY IN REACTIONAL LEPROSY

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In reaction cases in leprosy we previously used intravenous potassium antimony tartrate in a dose of 2 ml. of a 2% solution, in conjunction with 10 ml. of 10% calcium gluconate solution. The course consisted of 6 injections usually and 1 injection of calcium gluconate was given on alternate days. We have also used intravenous mercurochrome, 2 ml. of a 1% solution. Neither of these two therapies gave good results in some cases, and in such cases the reaction could not be arrested. There is also the trouble that if a single drop of potassium antimony tartrate solution escapes into the subcutaneous tissues there is severe pain and swelling. In those cases where the intravenous injections were ineffective, we tried oral capsules of Chloromycetin and the results were good. We then continued with Chloromycetin alone, and the reaction ceased within a few days. Here follow *case reports of our experience with Chloromycetin.*

Case No. 1. LACHI DEBI, F., 25 years. An L_2 case, with smears from ears 2 +. On 9.11.59 she was admitted to the ward with a temperature of 102°F. (39.9°C.), also pain the whole body, headache and slight cough. This was all due to lepra reaction. We gave an injection I.V. of 2 ml. PAT, with 10 ml. of 10% calcium gluconate I.V. On 10.11.59 the temperature was 101.2°F. (38.4°C.). She had body pain and headache, and nodules appeared. On 11.11.59 again PAT and calcium gluconate I.V. injections were given. The temperature rose to 103.8°F. (39.9°C.). On 12.11.59 the temperature reached 104°F. (40°C.). On 13.11.59 we began Chloromycetin 1 capsule twice a day. The temperature was 103°F. (39.4°C.). On 14.11.59 the temperature was 98°F. (36.6°C.). Headache and body pain had gone. We kept on the Chloromycetin for 2 more days, the reaction ceased and the general condition of the patient improved.

Case No. 2. TILESWAR, M., 19 years. An L_2 case, with smears positive 1 + to 4 +. He was admitted on 14.11.59 with a temperature of 100°F. (37.8°C.), pain in the joints, and crops of new patches appearing. PAT and calcium gluconate injections I.V. on 17.11.59 when his temperature was 103°F. (39.4°C.). On 18.11.59 his temperature was 103.8°F. (39.8°C.). On 21.11.59 he was given PAT and calcium gluconate injections once more with no effect. Chloromycetin was given 1 capsule twice daily from 23.11.59 and on the next day, 24th, his temperature descended to 96°F. (36.6°C.). He had no more joint pain. Chloromycetin was continued for 3 days.

Case No. 3. DAUD MUNDA, male, aged 32 years. An L_3 case with bacterial index 3 + to 4 +. He was warded on 28.11.59 with temperature of 101°F. (38.4°C.) with headache, joint pains and new nodules. Chloromycetin was given, 1 capsule twice daily. On 29.11.59 his temperature was 99°F. (37.2°C.), and on 30.11.59 it was 97.4°F. (36.3°C.). Joint pain and headache disappeared and the reaction subsided. We continued Chloromycetin until 2.12.59.

Case No. 4. ROBIRAM DAS, male, aged 45 years, an L_3 case, with bacterial index 2 + to 4 +. He was warded on 15.6.60 with a temperature of 101.6°F. (38.7°C.), headache, body pain, and new nodules. He was given PAT and calcium gluconate injections, but the reaction did not yield, and the temperature kept at 101° to 103°F. (38.3°C. to 39.4°C.). From 29.6.60 Chloromycetin was begun, 1 capsule twice daily, and the next day the temperature fell to 98.6°F. (37.0°C.)

and on 1.7.60 to 97.8°F. (36.6°C.). Headache, bodyache and joint pains ceased and the reaction disappeared. We continued Chloromycetin for 2 more days.

Case No. 5. CHOMA, female, aged 25 years, an L_3 case, with bacterial index 3 + to 4 +. She was warded on 8.7.60 with a temperature of 101°F. (38.3°C.) and was given PAT and calcium gluconate injections, but nodules, headache, and body ache appeared and a state of lepra reaction supervened. On 13.7.60 her temperature was 101.2°F. (38.4°C.) and at that time Chloromycetin was begun, 1 capsule twice daily, and continued thus for 5 days. On 14.7.60 her temperature was 100.4F. (38.0°C.), the next day 98°F. (36.7°C.), and then normal, and the reaction and its symptoms and signs disappeared. A *relapse* occurred on 28.10.60, when new nodules appeared, and the temperature rose to 100°F. (37.8°C.). This relapse yielded when Chloromycetin was given, 1 capsule twice daily for 5 days.

Case No. 6. SIRISH CHANDRA DAS, male, aged 30 years, a borderline case (B_2), with bacterial index 2 +. He was warded with flushed face and swollen hands and legs, and raised smooth shiny red patches, in fact a case of reaction in borderline leprosy. He was given an injection every second day of PAT up to a total of 5 injections, without effect. On 11.8.60 Chloromycetin was begun, 1 capsule twice daily, and kept up for 6 days. The patches and the swelling subsided and the reaction ceased.

Case No. 7. PROBHAT, male, aged 32 years, with bacterial index 3 + to 4 +. He was warded with widespread body ulcers and lepra reaction, and given PAT and calcium gluconate injections, then Panmycin, and lastly Chloromycetin 1 capsule twice daily for 6 days. The temperature became normal and the reaction stopped, but the ulcers were slow in healing.

Case No. 8. GOROK BAHADUR, male, aged 32 years, an L_2 case with bacterial index 1 + to 3 +. He had fever, swelling of ear lobes and pain over the whole body. PAT had no effect, and on 15.10.60 his temperature rose to 102.4°F. (39.1°C.). When Chloromycetin 1 capsule twice daily was given for 5 days, the reaction subsided completely.

Case No. 9. LETHRO SOREN, male, aged 30 years, an L_3 case with bacterial index 2 + to 3 +. He had a reaction without fever and pain, but swelling appeared of ear lobes and legs. From 22.10.60 he was given Chloromycetin 1 capsule twice daily for 5 days, and the swelling and reaction subsided completely.

Case No. 10. DAUD HASDAK, male, of 22 years, a Tuberculoid (T_2) reactional, with bacterial index 1 +, with fever, joint and body pains, swelling in hands and legs, and thickening of the ulnar nerves, so that on 25.10.60 he was warded with temperature of 100.8°F. (38.2°C.). We gave Chloromycetin, 1 capsule twice daily for 5 days. The temperature became normal in 2 days, and pain and swelling subsided in 5 days, and the nerve thickening decreased.

Case No. 11. JANKI, female, aged 30 years, an L_2 case with bacterial index 2 + to 4 +. On 16.11.60 she had a temperature of 100°F. (37.8°C.), with headache, and pain over the whole body and was warded and given Chloromyceti 1 capsule twice daily for 6 days. Her temperature became normal in 4 days and the reaction was gone in 6 days.

Case No. 12. KHAGENDRA, male, aged 32 years, an L_3 case. On 2.11.60 his temperature was 100.8°F. (38.2°C.), nodules appeared on his face and ear lobes, swelling of his legs, headache, body and joint pains. We gave Chloromycetin 1 capsule twice daily for 7 days, and in 5 days his temperature was normal, and the reaction abolished within 5 days.

Case No. 13. GENDRA, male, aged 20 years, an L_2 case, with bacterial index 2 + to 3 +. On 2.11.60 his temperature was 101°F. (38.3°C.). New nodules appeared, he had ulcers in his throat and thickened ulnar nerves, headache, and body pain. We gave Chloromycetin capsules 1 twice daily for 9 days and the temperature became normal in 4 days. The reaction had subsided in 9 days, but the ulnar nerve remained thickened and painful. The throat ulcers healed.

Case No. 14. SUKU CHORON, male, aged 50 years, an L_3 case, with bacterial index 4 +, was warded on 28.10.60 with temperature of 100°F. (37.8°C.), nodules, headache, body pain, and conjunctivitis. We gave Chloromycetin 1 capsule twice daily for 7 days and the temperature became normal in 5 days. In 7 days the reaction ceased. His eye condition improved.

Case No. 15. KHANDRU, male, aged 32 years, an L_2 case, with bacterial index 3 +, nodules, headache, body pain, and conjunctivitis. On 19.11.60 his temperature was 99.6°F. (37.6°C.). We gave Chloromycetin 1 capsule twice daily for 6 days. The reaction ceased and the eye condition improved.

Case No. 16. JONGBIR, male, aged 35 years, a T_3 case. He had double conjunctivitis and corneal ulcer and we gave sulphathiazole, and penicillin injection, with a daily eye lotion of normal saline, and the application of penicillin eye ointment. Protargol 5% also was tried, but his condition did not improve. Then we gave Chloromycetin 1 capsule twice daily for 5 days and the eyes improved.

Case No. 17. GEARA, male, aged 35 years, an L_3 case who also had cavitating pulmonary tuberculosis. He had fever, nodules, joint pains and swellings, and a corneal ulcer. We gave Chloromycetin 1 capsule twice daily for 6 days, and the fever and reaction ceased, nodules and joint pains and swelling decreased, and the eye condition improved.

Conclusions

We found that Chloromycetin acts upon all types of leprosy reaction. It has a definite beneficial effect on nerve pain, thickening of nerves, eye conditions, and ulcers, when these form a part of lepra reactions. Chloromycetin seems to us to be speedier and more effective than injections of potassium antimony tartrate or mercurochrome, and its mode of administration is easy (1 capsule of 250 mg. given by mouth twice daily for 6 days, more or less).

Acknowledgement

I wish to thank REV. G. FOSSLAND, Supt. of Santipara Leprosy Hospital, Miss B. A. JORGENSEN, Miss LUCILE FRICKSON, and hospital staff who were very helpful to me.

TREATMENT OF REACTIONS IN LEPROSY BY AQUEOUS SULPHETRONE INJECTIONS AND ORAL INH IN A RURAL CENTRE

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Introduction

We aim in this paper to present the results of our study of the treatment of reaction states in leprosy using injections of 50% aqueous solution of Sulphetrone and oral INH daily. We also studied a few cases not in reaction who were treated with this therapy.

It is worth while defining Reaction states in leprosy. COCHRANE thinks that reaction in leprosy is a local or systemic response to the release of bacilli or bacillary products into the tissues. NELSON SOUZA CAMPOS and P. RATH DE SOUZA say that the term "lepra reaction" is used in a general way by many authors to describe a class of quite different clinical and pathological processes. They point out that when the term is used in the general sense it comprises 3 main groups: (1) the classical lepra action, which means a syndrome similar to that of erythema nodosum, e. multiforme, e. exudativa, etc., and this e.n. syndrome is peculiar to lepromatous type of leprosy; (2) reactional tuberculoid leprosy, which some authors call "tuberculoid lepra reaction", including the transitional lesions; (3) outbreaks of acute reactivation and exacerbation of the disease, which can occur in any of its clinical forms, and the list of clinical forms of reaction shows how varied they are in their pathogenesis.

They go on to classify lepra reaction of the classical variety into 2 sub-groups, namely *Progressive Lepra Reactions* and *Erythema Nodosum Leprosum* (ENL), which occur in the lepromatous type, and the exact nature of the reaction, whether *allergy* or *para-allergy*, is not yet understood clearly. The ENL type of reaction includes the reactional tuberculoid leprosy and the transitional lesions, of which the Borderline type is the best example. Tuberculoid reaction is of the nature of an acute exacerbation of the disease occurring in any of the clinical forms of leprosy.

In our therapeutic study we directed attention mainly to the 2nd and 3rd varieties of lepra reaction as described above. COCH-

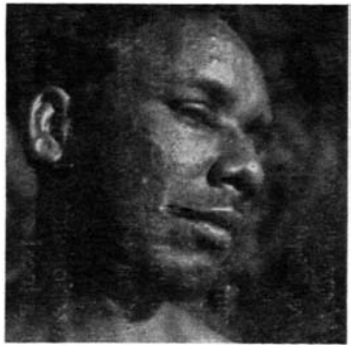
CLINICAL RESULTS OF TREATMENT WITH AQUEOUS SULPHETRONE PARENTERALY AND INH ORALLY

A. *of Patients in a* ***Reactive*** *State*

1. Before Treatment
Date: December 1959

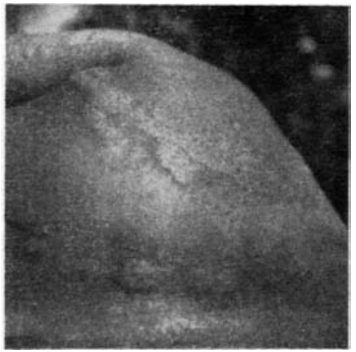
1. After Treatment
Date: 18 - 6 - 60

2. Before Treatment
Date: 3 - 9 - 58

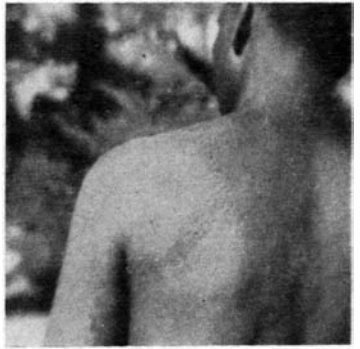


2. After Treatment
Date: 4 - 11 - 58

3. Before Treatment
Date: 3 - 9 - 58



3. After Treatment
Date: 4 - 11 - 58



4. Before Treatment
Date: 17 - 8 - 58

4. After Treatment
Date: 4 - 10 - 58

RANE described tuberculoid reaction as the manifestation of an acute tissue response to prevent the attempt of the bacilli to penetrate the skin and nerve barrier. In reactional tuberculoid he states that every lesion shows an acute reaction phase, whereas in a tuberculoid reaction, if there are several lesions, some of them are quiescent. The borderline type is itself a state of reaction, even though it can react further, with local and constitutional disturbances. To treat reactional states in leprosy has always been a problem, because their nature has not been fully understood. Empirically corticosteroids, antimalarial drugs, and antimony compounds have found to be of use. COCHRANE, writing on the treatment of reaction states in tuberculoid and borderline leprosy states that these are cases of active tissue defence, and that sulphones or other therapy must be stopped immediately, as the reaction in these types of leprosy often results in healing of the condition. He gives worning also of the *danger of nerve damage, with resultant deformity*. Yet the only treatment advised by him is palliative, i.e. drugs such as aspirin and phenacetin to relieve pain.

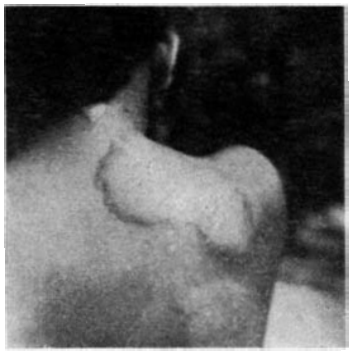
SOUZA CAMPOS and RATH DE SOUZA say also that tuberculoid reaction may lead to severe nerve involvement and consequent trophic changes, and point out that this may be insidious, and without marked change in the size of the nerve. In reactional tuberculoid leprosy and in borderline leprosy there may be similar difficulties. H. J. WHEATE prefers to treat reactional states on thiosemicarbazones, rather than on the sulphones. In our experience we have not got satisfactory results in reaction states in leprosy by treatment on the lines suggested by COCHRANE, or by small doses of sulphones, or on thiosemicarbazones. There is great need for some specific therapy for reactional states which would improve the condition without damage to the nerves, in a short period of time. The aggravated reactional macules do not improve the appearance of the patient, so in addition to the danger to nerves there is this cosmetic factor, which interferes with leprosy campaigns by introducing a factor which militates against free social contacts by the patients and causes time off work, etc.

We have made trial of the sulphetrone - INH drug combination. We had previously found the injection of 50% aqueous sulphetrone safe, effective and cheap. It was suitable for even debilitated patients, and in reactions more suitable than the parent sulphones. DAVISON reported not too favourably on INH, but V. EKAMBARAM studied it during his tour of Thailand as a WHO Fellow and formed a better opinion of it, especially in reacting cases.

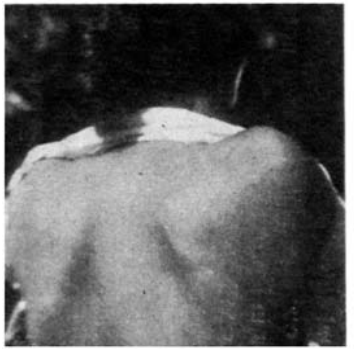
Methods and Dosage

It was decided to give parenteral aqueous Sulphetrone (50%) in a dose of 0.5 ml. daily and add to this orally 150 mg. daily of INH

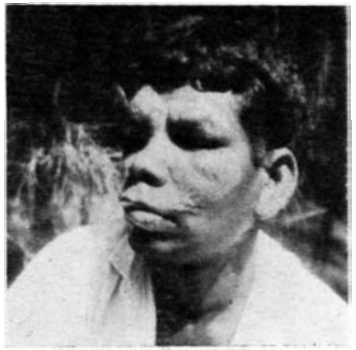
5. Before Treatment
Date: 17 - 8 - 58



5. After Treatment
Date: 6 - 11 - 58



6. Before Treatment
Date: 30 - 7 - 58



6. After Treatment
Date: August 1958

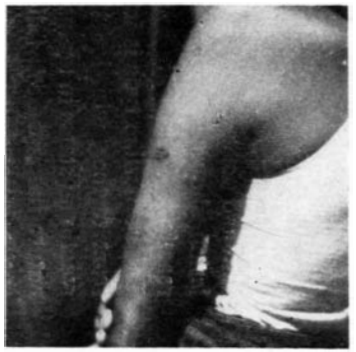
B. *of Patients in a* ***Non-Reactive*** *State*

1. Before Treatment
Date: 28 - 1 - 59

1. After Treatment
Date: 13 - 3 - 60

2. Before Treatment
Date: 28 - 1 - 59

2. After Treatment
Date: 13 - 3 - 60



RESULTS OF TREATMENT (PATIENTS IN REACTING STATE 1958 AND 1959—ANNEXURE—I)

Total number of patients	*L.*	*Types of reactive patients*			*Number improved clinically with reduction of reaction*	*Number not improved*	*Number in whom nerve damage developed during treatment*	*Average number of days required for subsidence of reaction in T.M. and R.T.L.*	*Average number of days for subsidence of lesions of Borderline cases*
		T.M.	*R.T.L.*	*Borderline*					
9	Nil	5	3	1	7	1	Nil	45 days	90 days

ANNEXURE—II

(a) Patients not in a state of reaction in 1958 and 1959—remarks about results of treatment

Total number of cases started	*Type analysis of these cases*		
	Lep.	T.M.	INDT.
6	3	2	1

(in 3 doses of 50 mg.). The therapy was continued even in the face of mild pyrexia, but was stopped for raised pyrexia or signs of nerve involvement. Otherwise it was kept up even after the reactive phase subsided. As regards *choice of cases*, in the beginning of the trial only reactive cases unsuitable for sulphone therapy or those who did not improve with thiosemicarbazone were selected, but as the trial progressed and the results were found satisfactory, we added a few lepromatous and non-lepromatous cases not in a state of reaction. The total number of cases chosen was 20, of whom only 5 discontinued treatment. There were 9 patients in a reactive phase and 6 non-reactive. The duration of treatment was 2, 3, 5, 6, 13 and 24 months in 1958 and 1959.

Results

These were good in reactive cases. The therapy could be described as potent and specific, and the reaction was controlled without any danger to the nerves. The reactive macules subsided within a month or so, and oedema and erythema subsided, and the macules seldom persisted beyond 2 months. Neuritis and pyrexia also cleared up. Days of hospitalization were reduced and the patient became normal and fit for his daily occupation in a relatively short period.

The non-reactive lepromatous cases were not immune from lepra reaction. Patient "M" had 2 reactions during the 4 months of treatment, and "Miss K" had 4 reactions during 18 months.

In non-reactive tuberculoid cases the clinical improvement under this treatment seemed to be quicker than with the ordinary sulphone treatment. The lesions flatten, but further improvement is not satisfactory, the general clinical and bacteriological improvement not really being appreciably better.

In non-reactive lepromatous cases, the clinical and bacteriological is slow and the new treatment is not recommended.

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Our grateful thanks are due to Dr. K. RAMANUJAM, M.B., B.S., Medical Officer, Silver Jubilee Clinic, Saidapet, Madras, for his valuable suggestions and advice in the preparation of this article.

MKUNYA
AN EXPERIMENT IN LEPROSY CONTROL

by J. E. J. HURMAN, M.B., B.S.(LOND.), D.T.M. & H.(ENG.)

"Public expenditure on national health is like expenditure on a life-boat or a fire-engine; even more it is like a long term investment. It yields its interest with absolute certainty, a thousand-fold, but only in the course of years and sometimes in the course of generations. It is money hidden in maternity, in good schools, in pure food, in clean streets, in sanitary houses, in an abundant water supply, in dispensaries, hospitals and sanatoria, and in the vast network of a sanitary and protective cordon in every village and city of the land. Its efforts are unappreciated until they are withdrawn. Yet without this investment the nation is bankrupt".—SIR GEORGE NEWMAN: Annual Report of the Chief Medical Officer of the Ministry of Health, 1921.

Leprosy Incidence in Southern Tanganyika

The Southern Province of Tanganyika stretches across the width of the Territory from the shore of Lake Nyasa to the Indian Ocean, and is adjacent to Portuguese East Africa. It occupies an area of 55,223 square miles (about 143,000 sq. kilom.).

In 1950 the Interterritorial Leprologist to the East African High Commission surveyed 36 samples of the population of the Province, numbering 884,679 persons at that time. (Ross Innes 1950). 1,384 cases of leprosy were found in 52,214 persons examined, giving an incidence of 26.5 per thousand. The incidence was highest in Newala District (35 per thousand) and Masasi District (30.8 per thousand), both of which Districts lie to the eastern end of the Province. It was estimated that 8,900 cases of leprosy existed within these two Districts.

Treatment for the disease was being provided by the medical services of two Missions working in these Districts. The Benedictine Mission at Ndanda in Masasi District was treating 600 patients at its Leprosarium, and the Universities' Mission to Central Africa was running a chain of 15 outpatient clinics centred on the previous work of Miss Edith Shelley at Lulindi, also in Masasi District and treating a total of 2,000 patients. Hydnocarpus injections were the standard treatment at both Missions, although sulphetrone had been tried in 5 cases at Ndanda with good results.

Ross Innes recommended that the leprosarium at Ndanda should be enlarged and that a secnod leprosarium should be opened near the Masasi-Newala border, with initial residential accommodation for 100 patients, but capable of expansion to accommodate 1,000 patients. He thought that such a leprosarium could become self-

supporting on the produce obtained as the result of work by the residents, but in view of the interest shown by the Native Authorities of the Districts, these Authorities should be asked to contribute towards the capital cost of the construction and assist in the maintenance of the colony until such a point had been reached.

The Early Days of Mkunya Leprosarium

A suitable site was found at Mkunya, in the south-western corner of the Makonde Plateau, lying 12 miles (about 19 km.) from the Newala District Headquarters and about 1,000 ft. (304 m.) above the Ruvuma River, which flows 3-4 miles (about 5 km.) to the south. 960 acres of land (about 38,500 sq. decam.) was available, of which 125 acres (about 5,000 sq. decam.) was allocated for the colony. A capital expenditure of £9,000 was estimated. £3,500 would be contributed by the Native Authorities and the remainder by BELRA. BELRA would be responsible for the building operations, including the house for the Supervisor, whom they would supply. A further capital grant of £750 was to be made by the Native Authorities for the purchase of equipment.

In the event, between 1952 and 1955, while the Leprosarium was under construction, £13,000 was spent on capital works and equipment, of which the Native Authorities contributed £5,500 and BELRA the remainder.

Three Native Authorities combined in making contributions—that of Mikandani (Mtwara) District joining the scheme—and all three Authorities were represented by the District Commissioners on the interim Management Committee formed during the construction period. The Supervisor of the U.M.C.A. outpatient scheme and one of the Mission doctors also sat on this committee, as it was envisaged that the Mission could assume clinical charge of the Leprosarium when it was opened to patients.

The main buildings were pre-fabricated, but the residential accommodation for patients was of a semi-permanent nature, built of mud-brick on concrete rafts with corrugated iron roofing. Buildings were in units, holding eight patients each, and consisted of two rooms each housing four patients, with a central verandah.

When construction neared completion, a Board of Visitors was appointed, consisting of:

The District Commissioner from each of the three Districts concerned;

One African representative from each Native Authority contributing;

A representative of the Government Medical Department;

A medical representative of the U.M.C.A.;

A medical representative of the Benedictine Mission.

The Manager of the Leprosarium was to act as Secretary.

The policy of this Board was to co-ordinate anti-leprosy treatment carried on by all agencies in the three Districts around the Leprosarium. All grants in assistance to outpatient treatment centres would be made through the Mkunya Organisation. Each agency operating treatment centres would continue to be responsible for the administration of its own units and the Board would only intervene in cases of dispute.

The estate account and the medical accounts of the Leprosarium would be administered separately. The working of the estate—mainly a cashew-nut plantation—would be the duty of the patients, but outside labour might sometimes be required. Any profit from the estate account would be used for the extension of anti-leprosy units.

The admission of patients from each of the three Districts would be in proportion to the annual maintenance contributions from each. A registration fee of five shillings would be payable by all outpatients receiving treatment under the scheme. Four outpatient centres were planned at this time, including the outpatient clinic at the Leprosarium itself.

The Leprosarium opened in May 1955, with the Manager assuming charge of the day-to-day medical supervision, as well as the running of the estate. It had been found that the Supervisor of the outpatient scheme could not undertake this work, and he remained at Lulindi.

Early in 1956 a memorandum on the future expansion of the scheme was submitted to BELRA. At that time 2,500 outpatients were under treatment in 16 treatment centres, all on sulphone therapy, so that less than a quarter of the 11,058 cases estimated in the three Districts five years before were known to be receiving treatment. The supervision of these outpatient centres was found to be beyond the capacity of one supervisor, so later in the year a second BELRA worker arrived at Mkunya to assume medical charge there, and to assist in the supervision of the outpatient centres.

At the same time it was decided to implement the new general policy with regard to the segregation of patients in leprosaria, consequent upon the proved therapeutic success of the sulphone drugs, and to confine admissions to lepromatous patients, those cases showing a reaction to the sulphone therapy and patients with the tuberculoid form of the disease requiring surgical procedures. Building operations were therefore deferred at a stage when the accommodation was sufficient for 110 residents.

Financial Difficulties

The cashew crop for 1955 was a poor one; by the middle of 1956 the liquid assets of the Leprosarium were exhausted and an overdraft was negotiated to meet recurrent expenditure until such time

as the 1956 crop had been sold. The 1956 crop was no better. However, after a contract had been made with a produce dealer, the 1957 crop realised sufficient to cover the costs of running the estate.

Early in 1958, when a new Manager arrived, the accounting system was found to be other than the Board had advised. It was evident that the farm had been run at a loss and that the main crop was less than could be expected from the cashew trees bearing. For the 1958 crop, a bonus system of harvesting was introduced, whereby patients received payment by result in addition to their daily "wage". The farm showed a considerable profit as a result, but even with this addition to the medical account, expenditure exceeded income.

Maintenance of buildings was becoming increasingly expensive and the scheme was committed to the building of three outside permanent clinics, for which a further grant of £1,100 had been made by BELRA. The Government Agricultural Department reported considerable land erosion on the estate; preventative measures would cost £500 over a period of three years.

Difficulties arose with the patients also. The withdrawal of credit facilities at the colony's shop caused a strike of the labour force. A limited experiment of issuing rations in lieu of daily wages was tried, but was found to be more expensive and to require extra supervision.

Early in 1959, BELRA suggested subsidising the colony to the extent of £500 per annum for a period of five years, to assist in getting the Leprosarium 'on its feet' and in further expansion of the work. The Board did not feel able to commit the Leprosarium to increasing recurrent expenditure until the present position could be consolidated. However, three months later, £1,000 as an outright grant and the first instalment of £500 for capital expenditure, was received from BELRA.

Before any further expenditure was incurred, a complete survey of the buildings was made and a formidable list of repairs and replacements was presented. The cost of these could not be met, even with the grants, and, after a full account of the position had been compiled, a Committee of Enquiry was set up by the Director of the Government Medical Service. This Committee found that the Leprosarium could remain solvent but with no margin for maintenance of buildings, that the financial future based on expected farm profits would be extremely precarious and that the Leprosarium was not carrying out the function for which it was designed. The Committee expressed the opinion that the total abandonment of leprosy work at Mkunya would be undesirable and suggested that some form of outpatient centre, with or without a resident BELRA worker, should be maintained.

Mkunya Leprosarium Doomed

The 1959 cashew crop exceeded expectations and produced the highest income yet achieved. But before the Committee's report had been received by the Board, the elements took a hand in shaping the future of the Leprosarium. On 10th December, 1959, the Makonde Plateau was subjected to a severe tropical depression, with winds of hurricane force, followed by prolonged heavy rain. The Leprosarium lay in the area most severely affected and suffered considerable damage as a result. Few, if any, of the buildings escaped and a considerable number of the cashew trees were uprooted. No habitable accommodation remained for the patients, and there was no alternative but to discharge them to their homes. Some of the cashew trees recovered, however, and harvesting continued into January, 1960.

The recommendations of the Committee of Enquiry were followed in general by the Board. The assets of the Leprosarium were placed for disposal, and after the cost of the replacement of the BELRA worker's worn-out vehicle had been met, the proceeds were divided among the agencies who had met the capital cost, in proportion to their contributions. The work of the Mkunya Board was to continue in the supervision of outpatient treatment facilities, and was to be modified and widened to include facilities provided by the local authorities of other districts willing to come into the scheme.

Discussion

Ten years have passed since the recommendations on which the Mkunya Leprosy Control Scheme was founded were made. At the time of its inception, the placing of the control of a public health service of this nature in the hands of African local authorities, and relying on their financial support and encouragement, had not been tested. The experiment can be judged to have been successful.

The indigenous population were aware of the unfortunate effects of the disease in an area of such high incidence, its low fatality rate and the considerable disabilities from which its victims suffered. Yet sufferers from leprosy were accepted as part of the community; they lived with their families in the village homes and offered themselves for any treatment which would bring them relief. Their chosen representatives and administrative leaders were generous in providing public funds for treatment schemes. £14,000 was contributed by three local authorities to the Mkunya funds over a period of seven years, in addition to grants to the Missions and provision for treatment in their own local dispensaries.

The conception of being segregated in a colony was foreign to their nature. It involved separation from their families and from their own land for a period of at least three years, and the treatment provided could, in most cases, be obtained at the nearest dispensary.

Great persuasion was required before patients would be admitted, and absconding from the colony was not infrequent.

Those admitted were expected to work to be able to live. Such patients as actually wished to be admitted—the 'burnt-out' cases with gross deformity—were turned away because the facilities provided for patients requiring chemo-therapy only; no surgery or physiotherapy was possible at Mkunya. Yet the colony's accommodation was kept full up to the last few months, when admission was restricted for financial reasons.

The settlement was planned before the therapeutic effects of the sulphone drugs had been fully evaluated and their bearing on the policy of segregation fully realised. In the original planning of the scheme, Ross Innes states (personal communication) that the prime reason for his advising the establishment of the colony was not as a centre of segregation, but to raise the standard of the local anti-leprosy work by the creation of a laboratory, the training of African workers, facilities for research and for the medical treatment of reactions. For this purpose, the colony would have to be expanded to accommodate 1,000 patients with a medical officer, two nursing sisters, a lay supervisor and a laboratory technician heading the resident staff. The estate was developed and planted to provide work for this number of patients, and could not be run economically with the number eventually available, many of whom were disabled by the disease. It could not have become self-supporting under such conditions.

It must also be admitted that both the financial and general administration was placed in the hands of those untrained for it, or engaged in too many other duties to be able to deal with it efficiently. Until 1958 there was not even an African clerk on the Leprosarium staff to assist the Manager, who was also expected to be farmer, mechanic and clerk of works.

The Medical Department of Central Government provided the specific drugs used in the treatment of leprosy free of charge to all institutions providing a treatment service, and for the last two years of the scheme, the author, as the Government District Medical Officer, acted as Visiting Medical Officer to the colony, and assumed a general supervisory capacity over the outpatient treatment centres administered by two of the three local authorities contributing to the scheme. The day-to-day supervision of these centres was carried out by the two BELRA workers.

There was active and friendly liaison between the various agencies administering the leprosy treatment service, but, except for the control on expenditure of drugs supplied through Government channels, no overall co-ordination of the service. This was one of the functions that it had been intended the Board of Visitors should assume.

In the pilot stage, which the Leprosarium had reached by the time it ceased to function, no facilities for the confirmation of the diagnosis of the disease type, or for the evaluation of progress in the treatment of patients by laboratory techniques were available, with the exception of simple microscopy from skin smears and the estimation of the haemoglobin levels. The necessity for treatment, and the period of treatment required, was judged almost entirely on clinical grounds.

Further, little or no provision was made for the treatment of the neural forms of the disease, nor for the prevention or correction of the disabilities resulting therefrom. Yet it was these manifestations of the disease which most affected the working capacity and mental outlook of the patients who suffered from them. Such facilities as were available at general hospitals near the Leprosarium were limited by lack of isolation accommodation, and of trained staff, particularly those conversant with physiotherapeutic techniques.

Except for the encouragement of sufferers from the disease in seeking treatment at the centres, little or no education of the patients, or of the general public,was attempted. The African staff at work in these centres had received no training in the educational aspect of their duties, and there was no centre available where such training could be given by example.

General Considerations

In the present situation, when drugs are available which will control, if not cure, the majority of the infectious cases of leprosy, is the expense involved in the provision of centres for the segregation of infectious cases from the rural areas of under-developed territories justifiable? Ross Innes is of the opinion that the idea of segregation of all patients in institutions must be given up, firstly because it is too expensive and secondly, because it is of doubtful value; but a focus of hospitalization, special care, research and training is needed in strategic areas. W.H.O. (1958) states: "Leprosy patients no longer tend to avoid treatment because of its possible association with segregation. They now come forward spontaneously". Although the drugs can produce an acute leprotic neuritis, which is destructive if not treated, mass treatment is feasible, especially when bi-monthly intramuscular injections of D.D.S. suspension in chaulmoogric media are used.

On the other hand, Cochrane (1959) gives a warning "that it is a dangerous form of wishful thinking to consider that the control of leprosy can be achieved by pressing for more and more treatment centres without adequate regard for other preventative measures". He points out that statistics have shown that only in certain areas in the world has there been a general decline in the incidence of leprosy, while in other areas there has been an apparent increase,

despite intensive treatment campaigns. Because of the failure, to date, to isolate and culture the infective organism, the study of the epidemiology of the disease has been severely limited, and such studies as have been made have shown considerable variations throughout the world. From studies in the United States, Badger (1959) concludes that leprosy is as contagious or more contagious than is poliomyelitis. Like the latter disease, however, few of the persons infected present with clinical evidence of the disease. The period of incubation has yet to be accurately determined. It is apparent that leprosy is transmitted by direct contact, and, contrary to previous belief, this contact does not have to be unduly repetitive nor over a long period. The contact has to be with an infective case, and as pathological investigations have become more accurate and discriminatory, it has been shown that more cases are infective and remain infective over longer periods than was previously thought.

If, then, segregation is to be an essential part of the leprosy control programme, to what extent can adequate provision be made commensurate with reasonable cost? Cochrane stresses that adequate control measures must be related to the general public health service, as has been done in the case of the prevention of tuberculosis, syphilis, sleeping sickness and malaria. The sympathy of the whole medical profession must be enlisted and the services of para-medical personnel utilised. Specialists will be needed to advise the public health service, but should not form a special cadre of officers, except where there is a need for a limited number of special clinics and hospitals. The fundamental principle, he states, is accepted by all, that leprosy control and treatment is an inescapable responsibility of the national government.

Ekambaram and Sharma (1958) describe a small centre in South India and compare the methods used there with those in Nigeria Ceylon, Siam and Malaya. They came to the conclusion that the problem could only be solved if tackled together with the treatment and control of other diseases, and not as a isolated entity. Segregation is practical only insofar as it is possible in the patient's own home; both the treatment teams and the public health staff educate the public on the nature of leprosy and its prevention, laying special emphasis on the protection of the children.

Mallac (1960) gives a two-year assessment of a control scheme in the Gambia, based on village treatment clinics. The need for a focal leprosarium is stressed where the sequelae of the neural type of the disease can be treated, as well as all the reactive cases. No segregation methods are attempted.

Kinnear Brown (1952, 1956, 1957, 1960) describes the evolution of leprosy control in Uganda. The need for adequate local survey is stressed, and the evolution of special treatment villages is des-

cribed. These provide a measure for segregation in combination with treatment of the infective patient. Again the necessity for a leprosarium for the treatment of the disability of the individual patient is stressed. He is the unit who unconsciously controls the destiny of the control campaign, and his confidence must be gained. The centre also provides the focus for the training of the therapist, both in the social background of the patient, as well as in the treatment of his disease.

Wheate (1957, 1960) describes a small control scheme centred on a leprosarium in the Southern Highlands of Tanganyika, where the associated outpatient treatment centres were administered by the African local authority, under the supervision of the medical officer of the leprosarium.

Conclusions

Health and education services consume a considerable proportion of the national expenditure of emerging states, such as Tanganyika, but the proportion of the allocations on health services which can be devoted to the control of a disease such as leprosy is very limited, when there are many other urgent requirements to receive priority. Nevertheless, it is felt that too little attention has been directed towards this disease in the past. Two main reasons are suggested. Firstly, the low mortality rate, and the failure to recognise the disablement caused by the neural form of the disease, have placed it low in the priorities of international health control programmes. States which rely on the advice and assistance of the World Health Organisation and its special agencies have felt, therefore, that they would elicit little sympathy in embarking on comprehensive control measures.

Secondly, the study of this disease is attractive to few of the medical profession, and its advocates are also few. There are eminent authorities throughout the world, but, on average, such control measures as are undertaken by the undeveloped countries are placed in the hands of enthusiasts with little training in the specialty, and who have to reach proficiency by their own experience. Much could be gained by the scientific study of the disease in a co-ordinated and intensive manner at centres where officers assuming charge of control schemes could be trained in the scientific disciplines of diagnosis, including pathological aids, and in the statistical assessment of the disease incidence and the effect of control measures on such incidence.

Local surveys are of the utmost importance before any expenditure is incurred; the absence of the most elementary vital statistics in undeveloped areas makes this a slow and laborious process. Yet the planning of local control measures must be based on accurate incidence trends, so that the resulting treatment schemes

are not overloaded, and hampered by financial and staffing shortages. The conduct of such surveys, and the general overall supervision of the control measures instituted, should remain the responsibility of the national health service, and would require the allocation of a special cadre of medical officer and ancillary staff in the first instance. In areas of low incidence and where the proportion of infective cases to the total leprosy patients is low, the resultant control scheme could well be integrated with the general public health and therapeutic services, with overall control by a specialised officer. The district general hospitals would then provide inpatient accommodation for the treatment of the simpler complications and sequelae of the disease, together with limited isolation facilities for the infectious cases.

In areas of high incidence—and the area in which the Mkunya scheme has been operating would be classified as such—the necessity for a special residential treatment centre is still apparent, despite the advances made by the advent of the sulphone compounds. Not only would such a centre provide for the segregation of the infectious cases, but it would also be the focus for the prophylaxis and treatment of the disabilities resulting from the disease. In addition, it would serve as a training centre for the staff engaged in the treatment, in the social welfare and in the health education of the patients, as well as the education of the general public. A centre of this nature should also be the responsibility of the national government. Patients should be accommodated and treated free of charge, and be given a small reward for the product of their work in the rehabilitation side of the treatment. Attached to such a centre, there should be a training centre, where disabled patients could be taught new skills, so that when they are discharged to their homes, they could become active members of the community and no longer a burden on their relatives nor the object of public philanthropy. The residential centre would need to be equipped with facilities and staff for the operative surgery of the nerve and bone lesions, for remedial physiotherapy and for the special pathological techniques involved in the diagnosis and the assessment of progress—these last including facilities for histo-pathology.

In both low and high incidence areas, the treatment of the non-infective patient without potential or actual disability should be the responsibility of the local authorities; such village treatment centres would be supervised by the staff of the residential centres or local general hospital, and be manned by personnel trained in the detection of the various clinical types of the disease and the prophylaxis of the early disability or potential disability. In low incidence areas, the village centre could well be accommodated in the general dispensary, but where a large number of patients was anticipated, special buildings within the enclave of the general health

centre would be required and the specially trained staff employed full-time.

Public health staff should receive a limited training in the epidemiology of the disease, so that instruction in its prevention could be given individually and to village groups in the course of their routine work. In areas of high incidence, special public health staff would need to be trained and allocated specifically to leprosy control duties, engaged in case detection, including the follow-up of contacts and in specific health education programmes.

It is obvious from the above, that the areas covered by such control measures would be limited by their cost. With technical and financial assistance available from the international agencies, these would not of necessity be limited in size. When requests for assistance are made, the greatest stress should be placed on the need for trained staff, especially in the para-medical field. Although leprologists and surgeons acquainted with the neural and orthopaedic complications of the disease are sadly lacking, the need for the physiotherapist, the laboratory technician, the occupational therapist and the trained social worker is even more urgent. Not only the patient of today, but the local staff to be trained by them for the continuation of the scheme tomorrow, require their help. It is in this field that such organisations as BELRA could concentrate their energies.

And what of the voluntary agencies, such as the Missions, who have done so much in the treatment of the leprous patient in the past? The problem is a national one; the disciplines, of its control become more complex and beyond the resources of the majority of such agencies. Their help is urgently needed, but should be directed under a national policy and under closer national supervision and co-ordination. The patient, if he is to be attracted to receive the full benefit of the scheme, should be offered not only the drugs, but all the other known beneficial methods of treatment, and these should be standardised and be adaptable as research and experience provide further benefits. In the final event it is the patient who will determine the success or failure of any public health control scheme.

"No organisation controled by the State can do more than exert a favourable influence upon a subject so personal and so intimate as the health of the individual. The main influence will continue to be exerted by the individual himself through the habits and customs of his daily life, affected as they are by his intelligence, education and environment. The State has, however, its important part to play. It can provide a favourable environment both in the home and in the factory; it is able, within limits dictated by economic and political circumstances, to influence for the better the standard of living of the worker; and it is within its competence to secure for

him in old age or sickness the means whereby he can continue to live a satisfactory life.

"It is necessary to emphasise the fact that these desirable provisions which influence so much the health of the worker, can only be made by a highly-organised State which has at its command very great resources, and which possesses competent central and local government machinery adapted for this purpose". Fraser (1950).

Summary

The story of the five years' experience of a pilot leprosy control scheme in Southern Tanganyika has been described. The scheme was an experiment in that the administrative control and the financial backing was placed in the hands of a Board of Visitors representing three African local authorities, with the assistance of the British Leprosy Relief Association and two Missionary organisations. The supervision of the medical service of the national government was kept to a minimum. The original function of the scheme was not realised.

An assessment of the success or failure of the scheme is made. Reports of some recent limited leprosy control schemes throughout the world, but especially in the African continent, are reviewed and the basic principles of control measures in an emerging undeveloped State with limited financial resources, suggested.

I wish to thank the Board of Visitors to Mkunya Leprosarium, who gave me access to the records of the institution since its inception, to the Medical Secretary of BELRA for his advice and encouragement, and to the Director of Medical Services, Tanganyika, for permission to publish this paper.

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FOUR SURVEYS OF LEPROSY IN THE LANGO DISTRICT OF UGANDA

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Introduction

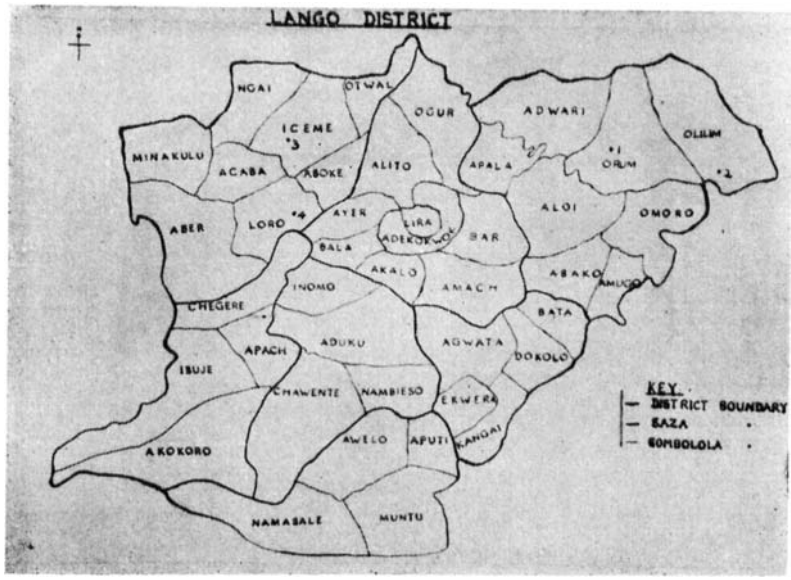
Four leprosy surveys were carried out in the Lango District of Uganda in 1960. At that time the author was a worker of the British Leprosy Relief Association assigned to assist in carrying out the policy of the Ministry of Health in the Northern Province of Uganda. The Lango District lies between 1° 45′ and 2° 40′ N. and 32° 15′ and 33° 30′ E. The average altitude of the survey areas is 3,500 ft. (1,076 m.) above sea level. The area is 4,464 sq. miles (about 12,080 km.^{2}, plus 595 sq. miles (about 563 km.^{2}) of open water and swamp. The population at the 1959 census was 354,311, with a density of 79 persons per sq. mile (about 30 per 1 km.^{2}).

Method of Survey

The survey team consisted of the District Medical Officer, Dr. S. M. McKenzie, and Medical Officers Dr. P. N. Williams (for Surveys 1 and 2) and Dr. C. J. Lewthwaite (for Surveys 3 and 4), and 2 Health Inspectors, E.A. (Mr. D. Omole for Surveys 1 and 2, and Mr. L. Ochero for Surveys 3 and 4); and Mr. Ellis.

In order to obtain information on population distribution, the team carried out a domestic census before the sample areas were selected, by permission of the Hon. the District Commissioner. The social structure of the Lango people lends itself to an intimate study of this nature. The Lango District is divided into 7 counties, varying in population from 94,780 to 24,197. There are sub-counties which vary in population from 3,916 to 15,740. Sub-counties are further divided into parishes, which vary in population from 539 to 2,714. All chiefs are salaried, but the leadership contains also the unsalaried work leaders or *adwong-wan-tics*. The male members of the community choose these adwong-wan-tics, who are in charge of 17 to 273 people, and their number in a parish will vary with population density. These leaders have or gain an intimate knowledge of the people, and are invaluable in a domestic census, and their work in a census is regarded as reliable. Their figures agreed to within 3.4% with the results of the main census carried out shortly afterwards. The team selected the four survey areas at parish level, taking into account the question of the greatest number of people who could be handled in 6 hours by the survey team at the actual survey, and the necessity of confining the investigation to the northern part of the district.

The next step was to compile a nominal roll of family groups in each area, and for this purpose the two health inspectors toured the



areas in company with the adwong-wan-tics. The nominal roll, once formed, was then checked against tax registers. These preliminary measures excited the curiosity of the people, and this was satisfied, and expected benefits pointed out, at a one-day course at District Headquarters, where chiefs were instructed also on the mechanics of the survey and in a social atmosphere enjoyed rehearsing their parts. The success of this preliminary explanation was shown later by an attendance of the people at the survey of 95.5%. The method of survey was similar to that of J. A. KINNEAR BROWN, specialist leprologist in Uganda, and described by him in the *East African Medical Journal*, 1956, **33**, 7.

The Survey Areas were as follows:

(1) *Survey* 1 in Moroto County, with a population of 73,495; in the sub-county of Orum, with 8,407 people; in the Parish of Ating, with 1,153 people. The population density was 45 per square mile (about 19 per sq. km.).

(2) *Survey* 2 in Moroto County, in Olilim sub-county with a population of 9,260; in Ogwete Parish with 1,545 people. The population density was 50 per sq. mile (about 19 per sq. km.).

(3) *Survey* 3 in Oyam County, with a population of 67,194; in Iceme sub-county with a population of 8,398; in Omolo Parish, with 949 people. The population density was 53 per sq. mile (about 20 per sq. km.).

(4) *Survey* 4 in Oyam County, in Loro sub-county with a population of 5,815, in Agulutude Parish with 1,257 people. The population density was 63 per sq. mile (about 26 per sq. km.).

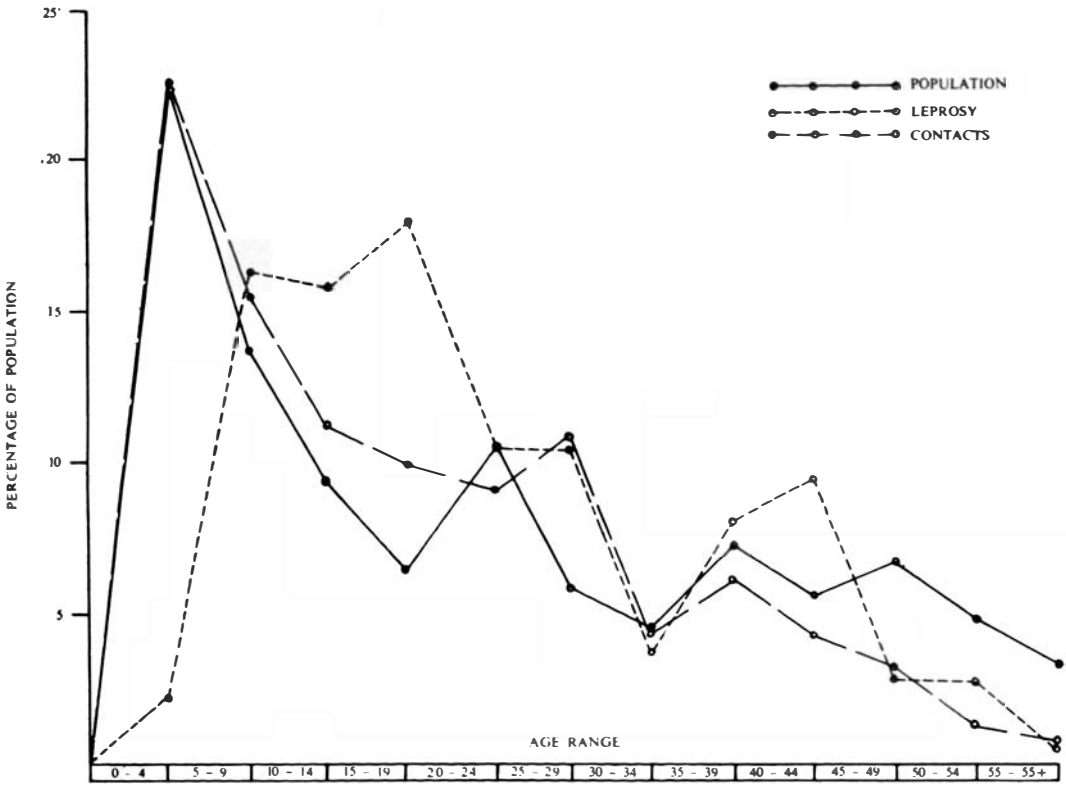


FIG. 1. GRAPH SHOWING AGE DISTRIBUTION OF THE SURVEY POPULATION, CASES AND THEIR CONTACTS.

Survey Results

Follow-up examinations were carried out during the month after the main surveys.

TABLE I

The Number of Persons Examined

Age Range	*Survey 1 Ating*		*Survey 2 Ogwete*		*Survey 3 Omolo*		*Survey 4 Agulurude*		*Total*
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	
0 — 4	116	131	161	173	95	91	134	148	1049
5 — 9	90	71	108	86	58	47	97	78	635
10 — 14	57	43	75	75	49	38	58	44	439
15 — 19	32	39	57	37	28	23	37	45	298
20 — 24	46	75	73	77	39	46	50	81	487
25 — 29	32	37	37	44	26	26	33	38	273
30 — 34	17	21	28	58	14	32	18	23	211
35 — 39	34	43	81	36	44	21	47	38	344
40 — 44	29	34	32	49	18	25	34	37	258
45 — 49	47	39	49	35	27	22	52	44	315
50 — 54	26	31	30	32	18	19	28	36	220
55 — 55+	30	13	36	4	20	3	36	15	157
Total	1133		1473		829		1251		4686
Percentage Attendance	98.2		95.5		87.6		99.7		95.5

TABLE II

Age, Sex and Type Distribution of Leprosy Cases

The Surveys are grouped together.

Age Range	*Male*		*Female*		*Total*
	L	*T*	*L*	*T*	
0 — 4	—	2	—	1	3
5 — 9	—	12	—	10	22
10 — 14	—	11	2	8	21
15 — 19	2	11	—	10	23
20 — 24	—	3	—	11	14
25 — 29	1	1	2	10	14
30 — 34	—	4	—	1	5
35 — 39	3	2	3	3	11
40 — 44	3	4	1	5	13
45 — 49	—	2	1	1	4
50 — 54	—	2	—	2	4
55 — 55+	—	1	—	—	1
Total	9	55	9	62	135

TABLE III

Number of Persons in Close Contact with Cases

Age Range	*Survey 1 Ating*		*Survey 2 Ogwete*		*Survey 3 Omolo*		*Survey 4 Agulurude*		*Total*
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	
0 — 4	12	9	30	43	10	9	13	20	146
5 — 9	10	7	22	27	6	5	17	6	100
10 — 14	12	4	17	10	4	8	11	7	73
15 — 19	3	3	22	16	7	2	4	8	65
20 — 24	4	17	7	11	5	4	4	6	58
25 — 29	7	15	13	24	4	2	1	5	71
30 — 34	6	1	10	5	3	2	1	1	29
35 — 39	7	1	10	8	4	5	2	4	41
40 — 44	2	1	6	1	—	4	5	7	26
45 — 49	—	2	2	2	5	3	5	4	23
50 — 54	1	—	1	1	1	1	2	2	9
55 — 55+	—	—	—	—	2	—	1	4	7
Total	64	60	140	148	51	45	66	74	648
Percentage of Sample	11.24		20.23		11.94		11.45		13.61

TABLE IV

The Family Group and Leprosy

Number	of	families	of	26	in	number	1	had	1	case	of	leprosy.
,,	,,	,,	,,	25	,,	,,	1	,,	3	,,	,,	,,
,,	,,	,,	,,	16	,,	,,	1	,,	1	,,	,,	,,
,,	,,	,,	,,	15	,,	,,	3	,,	3	,,	,,	,,
,,	,,	,,	,,	12	,,	,,	2	,,	2	,,	,,	,,
,,	,,	,,	,,	11	,,	,,	2	,,	2	,,	,,	,,
,,	,,	,,	,,	10	,,	,,	5	,,	6	,,	,,	,,
,,	,,	,,	,,	9	,,	,,	9	,,	11	,,	,,	,,
,,	,,	,,	,,	8	,,	,,	15	,,	15	,,	,,	,,
,,	,,	,,	,,	7	,,	,,	10	,,	10	,,	,,	,,
,,	,,	,,	,,	6	,,	,,	14	,,	15	,,	,,	,,
,,	,,	,,	,,	5	,,	,,	20	,,	20	,,	,,	,,
,,	,,	,,	,,	4	,,	,,	11	,,	11	,,	,,	,,
,,	,,	,,	,,	3	,,	,,	11	,,	12	,,	,,	,,
,,	,,	,,	,,	2	,,	,,	20	,,	20	,,	,,	,,
,,	,,	,,	,,	1	,,	,,	3	,,	3	,,	,,	,,

Thus 783 people in 128 families produced 135 cases of leprosy.

TABLE V

Summary of the Four Surveys

Area	*Number Examined*	*Number of Cases*	*Number of Cases*		*Incidence per thou.*	*Leproma Rate*	*Child Rate*
			Adult	*Children*			
Survey 1	1133	30	22	8	26.4	16.6%	26.6%
Survey 2	1473	51	29	22	34.6	19.6%	43.1%
Survey 3	829	25	18	7	30.1	4. %	28. %
Survey 4	1251	29	20	9	23.1	10.3%	31.3%
Total	4686	135	89	46	28.8	13.3%	34.1%

Discussion

It will be noted that 217 persons (4.5%) failed to attend the surveys. The cause of this were death in 8, permanent change of address from the area 106, and unexplained absence in 103.

Of the leprosy cases diagnosed in the survey, only 17 out of the 135 were undergoing treatment.

Analysis of the age groups of the subjects of the surveys reveals that 2123 persons (46.5%) are children of 14 years of age and under, and this group contains 1049 (49.4%) of 4 years of age and under. This distribution resembles the average pattern of the district. Fig. 1 is a graph of the relationship between the age distributions of the survey group and the whole population.

Summary

In 4 surveys a total of 4686 people were examined for leprosy in the Lango District of Uganda, and 135 cases of leprosy were found. The lepromatous rate reached 19% in one of the surveys, and in another the child rate reached 34%. The incidence per thousand of leprosy lay between 23 and 34.

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PLANTAR ULCER IN LEPROSY: A REVIEW OF THE LITERATURE, 1890-1960

E. W. PRICE, F.R.C.S.E.

Introduction

Recently there has been renewed general interest in plantar ulcers, and in their control as part of the process of rehabilitation of leprosy patients, and this paper will present a critical review of the literature to aid this work. We found *confused terminology* in the early papers on plantar ulcers. By some, any ulcer of the extremities in a subject of leprosy is called "leprotic". Others used the term "trophic" but included ulcers evidently hypostatic, and some even included the superficial ulceration of lepromatous lesions. Today the plantar perforating ulcer makes up most of the problem and it is found mainly in the tuberculoid and borderline kinds of leprosy. In our present review we have not included papers on the orthopaedic and plastic surgical procedures used in treatment of the complications of plantar ulcer. The modern literature on leprosy we found to begin with the recognised leprosy journals (Japanese journals should be included but were not available to us at the time of this study), namely *Leprosy in India* (1929), *Leprosy Review* (1930), *International Journal of Leprosy* (1933), *Revista Brasileira de Leprologia* (1934). Papers were few and scattered before 1930. The Tropical Diseases Bulletin, which began in 1912, gave a very useful service by its summaries. But as early as 1900 Lepra, of Biblioteca Internationalis, Leipzig, had also performed this function. In 1890 and 1891 appeared the Journal of the Leprosy Investigation Committee, which seems to be the earliest publication.

The Years 1890-1937. The Journal of the Leprosy Investigation Committee for 1890 has the earliest reference to specific treatment for plantar ulcer. It referred to the practice of stretching the enternal popliteal or great sciatic nerve. ARONGOM in 1905 stretched the posterior tibial nerve for the treatment of perforating ulcer. ROY (1934) was the first to recommend metatarsectomy, and GUIDA (1937) the first to report on therapy using a presumed vasodilator (acetyl choline). ARANGOM as above and SANDES (1913) described the "surgery of leprosy" but with little notice for plantar ulcers beyond the remark of SANDES that "nearly all lepers have ulcers".

The Years 1938-1960. Modern literature on plantar ulcers begins with a study by BECHELLI in 1938. There have been more than 90 papers since then, but many describe a few cases treated without controls and claiming good success. It is rare for the clinical condition and natural history of the lesion to be described. It is only in recent years that a serious attempt has been made to describe plantar ulcer.

Clinical Studies

In 1938 BECHELLI and colleagues described clearly from a study of 1600 cases in Brazil the development of the lesion. He noted that the distribution of plantar ulcers corresponded to "walking pressures" and concluded that the cause was "nervous", and secondarily mechanical stress. In the Compendio de Leprologia (1951) he repeated these conclusions. There seems little progress in the 20 years since this paper. COCHRANE (1947) gave a full account of the state of knowledge then, and clinically there was no further advance on BECHELLI. In recent years BRAND has referred to the subject, but there is no recent paper specifically studying the clinical picture until PRICE (1959) who gave an analysis of 2400 patients in Nigeria and developed the knowledge of the natural history of plantar ulcer, laying stress on the significance of the "necrosis blister". In 1960 LANGUILLON and colleagues followed by reporting on 3000 patients in Africa and attempting a full analysis of plantar ulcer. They pointed out that the sensory state of the foot is not always so anaesthetic as was thought.

Aetiological Studies

These did not begin until 1944, when SILVEIRA wrote as follows: "The pathogenicity is subordinated to a series of purely theoretical ideas invoked to explain it, namely mechanics, the influence of nervous and vascular lesions, the dyscrasias, and certain intoxications. These alone or together have been held responsible, but we must admit that basically it is difficult to say what exact part each factor plays in pathogenesis". This could almost have been written at the present day. SILVEIRA concludes that the major factor is mechanical, stresses the importance of rest, and notes that the uncomplicated ulcer will heal in a plaster cast without any other treatment; he also emphasizes frequent re-examination of the patient so as to avoid the recurrence of ulcer. KHAN (1939) made the important observation that plantar ulcers will heal with rest, including rest if the foot is encased in a plaster cast. This was not at once applied to aetiology, but MUIR in 1943 suggested that the provocative factor was the loss of the plantar cushion due to atrophy of the small muscles of the sole. COCHRANE (1947) stressed the relation of trauma to the aetiology. BRAND (1950) supported this, emphasizing sustained pressure and active injury. PRICE (1959) noted that the distribution of plantar ulcers was related more with walking than standing pressures. GUIDA made an early study (1937) on blood-supply but BARNETSON (1950) made the first detailed study, using oscillometry on neural cases. He showed that local blood vessels had not lost dilatability but vasomotor control was defective. He thought that the neurotrophic changes depended on more factors than vasomotor control damage. GOKHALE (1959) studied temperature changes in feet by

blocking the autonomic system and found that vasomotor control is defective in ulcerated feet of leprosy patients. LEITNER (1938) did arteriography and showed that there is an ample blood supply even in advanced cases, and BANG and colleagues (1938) found normal arteriograms in 26 of 34 ulcerated feet. LECHAT and colleagues (1959) repeated this and could establish no correlation with results of cutaneous thermometry and plethysmography. From all these studies there is no evidence that vascular inadequacy has any part to play in the aetiology of plantar ulcer. Workers in diabetes found the same thing (MARTIN, 1953, 1954).

Methods of Treatment

Some of the suggested therapies have been based on the foregoing theories of causation, but many have been empirical or aimed at suppression of local infection. A few have used local application of antileprosy drugs.

Local nonspecific therapy for which success is claimed includes the sulphonamides (A. ATUCHA, 1945; CHORINE, 1943); streptomycine (FITE et al., 1947); chloramphenicol (IYENGAR, 1959); tyrothricin (CABRERA et al., 1948; MOM et al., 1946); mercurochrome (OBERDORFER et al., 1939); iodoform (LANG, 1930); gentian violet (MUIR, 1941); trichloracetic acid (LAURET et al., 1956). Others were the local application of vitamin A (RYRIE, 1939), of madecassol (LANGUILLON, 1949), beef suet (MAYNARD, 1938), placental implants (FONTILLES, 1955; LUONG et al., 1958), and the infusion of barks of certain South American trees (FLORIANI, 1937), sodium dehydrocholate (HERMANS, 1957; LAVIRON, 1955; REZETTE, 1956), Dettol (RYRIE, 1938), Rivanol (DAS, 1940; MEHTA, 1938). The results recorded a monotonous success suggesting ulcers will heal easily.

Local antileprosy treatment. To use a local injection of an antileprosy drug suggests the suspicion that the ulcer is a specific lesion. Hydnocarpus preparations have been injected in and around the ulcers by LOWE et al., 1937; BOUSEFIELD, 1938; BOSE, 1938; COCHRANE, 1940; MUIR, 1943; BROWNE 1959. In the same way sulphone preparations have been used by DHARMENDRA et al, 1955 and FERREIRA, 1957. Leprolin was used by CALDEIRA in 1948. Results reported were uniformly good.

Treatment by Vasomotor Paralysis

Some workers tried to interrupt the tonic effect of the vasomotor control to try to improve the chronicity of the lesion on the supposition that this was due to inadequacy of blood supply. Thus lumbar sympathectomy was tried by GOHEEN in 1933 and GUADAGNINI in 1950, perifemoral sympathectomy by PY et al. in 1929, C. RUIZ et al. in 1931, BLACK, 1933, VIRNICCHIL in 1941, KIRKALDY-WILLIS in 1945. Epineurectomy or nerve blockage was tried by RANADE et al. in 1957 and VISHNEVSKY in 1938. Also, injection intra-

arterially of vasodilators was tried, ergot derivatives by GOKHALE in 1957, LAVIRON et al. in 1958, WATT-MANEY et al. in 1958 and FRITSCHII in 1959. Acetylcholine has been used for the same purpose by GUIDA in 1937, LANGUILLON in 1946, and A. CASTRO in 1940. All this had discordant results.

Treatment by Orthopaedic Methods

It was soon noted that simple protective footwear had no effect on either the healing or the recurrence of plantar ulcer; hence it seems that the cause could not be simple trauma. Attempts were next made to avoid the concentration of pressure on small areas by using moulded insoles so as to spread the weight. The plaster cast is the simplest method, and its value in healing an ulcer was confirmed by KHAN (1939), HAYTHORN THWAITE (1943), SILVEIRA (1944), FISHER (1955), NEWMAN et al. (1955), BOSE (1956), and LANGUILLON (1960). With a boot of Unna paste GENU et al. obtained similar good results. The plaster boot method for healing the ulcer is the simplest and best, and the patient can remain ambulant. Most cases heal in 4 to 6 weeks.

Treatment by Surgical Methods

Formerly most surgical methods were directed at the chronic bone infection. MILROY (1936) advised it, and others, and many have tried metatarsectomy. The general feeling is that the surgical mutilation does not solve the problem of healing or recurrence. SILVEIRA at the Havana Congress in 1948 protested that "amputation has become a frequent initial treatment of plantar ulcer" and recommended rest and plaster casts.

The Problem of Recurrence

The prevention of recurrence of plantar ulcer is the real acid test of any method or theory of treatment. So far no method of local therapy or surgical intervention successfully meets the difficulty. Why does the ulcer heal in a plaster cast even though the foot carries added weight? BRAND thought it was due to the spreading of the weight over a wide area of the sole by the moulding of the plaster, and he planned moulded insoles of plastic. ROBERTSON (1956) tried the same with moulded leather, also DREISBACH (1959) followed the same line. PRICE (1959) however suggested the interruption of the walking roll was the important factor, and that any type of rigid sole footwear, even wooden clogs, would be beneficial. Soft insoles can be used in addition to the rigid sole. Work is continuing on these lines.

Discussion

It will be seen that the plantar ulcer of leprosy poses three problems:

1. What is the neuropathic lesion responsible for the occurrence of ulceration?
2. Why does the ulcer occur in some neuropathic feet and not in others?
3. Why does the ulcer recur so readily after healing?

The *neuropathic lesion* underlying the lesion has not been the subject of any published study. Some workers are, however, investigating the matter. WEDDELL (WHO, 1960) reported on this and stated that as many as 25% of the sensory fibres to the skin may be destroyed before any sensory deficit can be detected clinically.

It has been generally believed (and stated) that a foot with an ulcer must be anesthetic to pain—and so exposed to unrecognised injury. Recent reports, notably by LAMBILLON (1960) have stressed that this is not in fact the case and that not more than half the cases clinically show this degree of anesthesia. It is also generally stated that there is no loss of deep sensation including joint sense. All these matters need further careful study, and are by no means clarified. It would be of considerable value to be able to recognise by some simple clinical test, which feet are likely to ulcerate and which not. A contribution to this is the recognition of the "pre-ulcerative state" by PRICE (1960).

The *reason for ulceration* in a foot already neuropathic is the second problem. The various theories have been examined in the preceding review:

(i) "Ulcer is due to unrecognised external trauma".
This theory fails because protection of the foot by footwear does not, in fact, prevent ulceration.

(ii) "Ulcer is due to prolonged standing".
This suggestion is untenable because ulcers will heal with the addition to the leg of the weight of a plaster cast, and the added immobility it entails.

(iii) "Ulcer is a specific leprosy lesion".
This view is untenable because of the occurrence of the lesion in diabetes, tabes etc. Nevertheless, as recently as 1959, a paper has appeared describing the use of locally injected anti-leprosy drugs.

(iv) "Ulcer is due to loss of the plantar pad of intrinsic muscles through atrophy".
This suggestion is abandoned because treatment of the foot by using a padded sole had no effect.

(v) "Ulcer is due to prominence of a bony projection in the sole".
This led to metatarsectomy, which is still widely practised. It is significant that no paper has been published stating the value and results of this, but most of those who use the method admit that the ulcer may not heal, may heal and then recur, or may heal and another occur elsewhere on the sole.

(vi) "Ulcer is an expression of local nutritional defect".
This is the reason for the numerous attempts to increase local blood-supply, using chemical or surgical interventions. The results have been reviewed and are not consistently favourable.

(vii) "Ulcer is an expression of deep plantar damage caused by walking".
This recent hypothesis is based on the observations of the effects of walking plaster casts. It should be confirmed by other workers, and may suggest a means of avoiding and treating ulceration.

The *problem of recurrence* has defeated all efforts at solution until recently. All methods of foot-protection, of local therapy, and of locally increased blood-supply have failed to affect the tendency of ulcers to recur.

The recent observations of the effect of plaster casts does, however, suggest an effective method of preventing recurrence of ulceration. It is based on the deduction that as the ulcer has healed while the cast was in position, it would remain healed if the cast was left on the limb indefinitely. As this is not practical, efforts are being made to define the factor that was responsible for initial healing and would, therefore, in all probability, maintain healing. Several workers are following up this suggestion, which appears likely to bring fruitful results.

Conclusion

The recent Conference at Vellore (WHO, 1960) accepted the statement that: "If the present state of knowledge is properly applied, plantar ulceration need not occur in leprosy".

THE LITERATURE ON PLANTAR ULCERS IN LEPROSY 1890–1960

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ABSTRACTS

Preliminary Report on DPT (Ciba–1906) in the Treatment of Leprosy. (Name of Author not given.) The Med. J. of Malaya, **14,** 4: June, 1960, p. 249.

This brief report is of a trial of Ciba–1906 in 12 leprosy cases at 1 g. to 2 g. per day orally, with control cases given DDS by injection. The results were very good in borderline cases and considerable in lepromatous. The drug seemed non-toxic and is considered worth expanded trials. The higher cost, and the inconvenience of daily administration, are not thought to be of importance.

Leprosy in Papua and New Guinea. D. A. RUSSELL, Papua & New Guinea Med. J., **4,** 2; July, 1960, pp. 49–56.

Dr. Russell, who is specialist m.o. (leprology) has given this interesting study of the problem in those countries. He recognises leprosy as endemic in most parts, and quotes various preliminary survey figures which gave leprosy incidences from 36 to 39 per thousand, with lepromatous rate low, and tuberculoid rate high. The policy of control is on the "*open-up*" modern lines, based at present on oral DDS and Avlosulphon therapy, and other drugs will be tried. There is enlightened recognition of the need to introduce physiotherapy and reconstructive surgery to assist in rehabilitation of those with deformities and stigmata. Dr. Russell also is keen on *training* in leprosy work for nurses and medical auxiliaries, education and propaganda, extension of rural aid and care, and on continued practical research. His refreshing article should be studied in detail by all workers.

The Application of Quantitative Electronmicroscopy to the Study of M. lepraemurium *and* M. leprae. R. J. W. REES and R. C. VALENTINE and P. C. WONG, Journal Gen. Microbiol, **22**, 2; April, 1960, pp. 443–457.

The authors refer to previous reports by HANKS, 1955, and MCFADZEAN and VALENTINE, 1960, who showed that *M. lepraemurium*, when kept in a phosphate buffer loses its viability and shows morphological changes under the electron microscope. The uniform density of the bacilli is lost and the picture changes to an empty cell wall, except for some disorganised material. The present authors confirm the morphological changes and further show that the proportion of degenerated bacilli is inversely proportional to the infectivity of the suspension. The change was also noted in bacilli in tissue cultures in which the tissue cells had degenerated, but not in healthy cultures. The authors also found a third distinct morphological change in which the bacillus divided into many bodies clearly outlined and often dense. This change took place in a medium con-

taining a high percentage of citrate—viability tests showed that such bacilli were dead.

The beading seen in human leprosy bacilli under Z.N. stain seems equivalent to the degenerative change seen under electron microscopy. Death of the bacilli in the host and during storage can thus be detected under the electron microscope. Death in the host but not during storage can be detected by a study of the bacilli under the light microscope after Z.N. staining.

Serological Findings in Leprosy. H. G. S. RUGE, G. FROMM, F. FUHNER and R. S. GUINTO, Bull. World Health Organization, **23,** 1960, pp. 793–802.

The authors seem unaware that The V International Leprosy Congress of Havana in 1948 recommended the abandonment of the word "leper" for a patient of leprosy, and it creates a painful impression in their paper to read phrases like "sera from lepers" instead of "sera from leprosy patients". They have studied the serological finding in leprosy. Leprosy sera often give biologically false positive reactions in serological tests for syphilis, which may be due to the presence of lipid antibodies in the sera, or of errors in technique or unfavourable working conditions in the laboratory. The authors investigated several hundred sera from leprosy subjects by means of 4 of the standard serological tests for syphilis with cardiolipin or crude lipid antigens. They used also the PR test with Reiter treponemes, and the Trep. pallidum immobilization test. It was found that the number of biologically false positives was not so high as expected, and that the lipid antigens were those mainly responsible for the non-specific reactions. They think the PR test will give sufficiently accurate results in the serodiagnosis of treponematoses, but it is not able to differentiate between syphilis and yaws infections.

Leprosy and Coccidiomycosis. J. GONZALEZ, Dermatologia, Rev. Mexicana **4,** 2; June, 1960, pp. 113–119.

The author describes the clinical history and successful treatment by Amphotericin B. of a case of borderline leprosy who also had coccidiomycosis of the neck. The case was seen in Monterrey, Mexico, and is the first case of the diseases combined. The treatment of the leprosy at the same time was carried on with Avlosulphone with success.

Biochemical Aspects of the Chemotherapy of Leprosy. G. A. ELLARD, East African Med. J., **37,** 12; Dec., 1960, pp. 765–775.

The author has been working for 2 years at the East African Leprosy Research Centre at Alupe, Kenya.

He opens his paper by stating that quicker acting drugs are urgently needed for the treatment of leprosy, and sets out to study the biochemical aspects involved in the choice of potential new

drugs. He points out that because of the similarity of the causal agents of tuberculosis and leprosy, almost all the promising antitubercular drugs have been tried in leprosy. This has had partial success, for the best antitubercular drugs are of little value in the treatment of leprosy, while the best antileprosy drugs are not now used in tuberculosis (with a possible exception in the case of Etisul). No drug has yet been found effective in leprosy which is entirely without activity in tuberculosis. Testing of antileprosy drugs in rat leprosy has been done by some, with good but by no means sure correlation with human leprosy. Others think that antileprosy drugs should have metal-chelating properties, lipid solubility, and antifungal activity. The general approach of using antitubercular drugs did result in the discovery of a curative drug, DDS. With the sulphones, leprosy became curable, though slowly, but *if sulphones alone are used* the author thinks that *the eradication of the disease in this generation will be impossible. New drugs are urgently needed, which will cure the disease in a year or less.*

The requirements of a good drug for the treatment of leprosy are very exacting. It should be well absorbed but slowly excreted, so that blood levels do not diminish rapidly. As most leprosy cases are treated on an outpatient basis, drugs active by administration only once or twice a week are desirable. As most leprosy occurs in the poorer countries of the world, a good drug should be cheap to produce (though cheapness in a drug is a factor secondary to effectiveness: it will be more economical to use a very effective drug which is dearer, as it will be needed for a shorter time—Editor). An anti-leprosy drug should be non-toxic in therapeutic doses, because of the paucity of skilled staff. Biochemical approaches include:
(1) *The designing of antimetabolites is proving a very profitable approach in the search for new chemotherapeutic compounds.* Antimetabolites are compounds which inhibit the pathogen by interfering with some vital enzymic process in which the antimetabolite is bound on to an enzyme in place of the metabolite it mimics. Consequently only small molecular changes are needed to turn a metabolite into an antimetabolite. Examples are sulphonamides derived from PAB, and PAS from benzoic and salicylic acids. Sometimes combining two antimetabolites in one compound gives a potent new one, e.g. INH from the active chemical groupings of INH and thiosemicarbazones. The difficulties in the way of the cultivation and transmission of *M. leprae*, perhaps from the lack of some vital growth factor, reduce the chances of its synthezising an antimetabolite, but mycobacteria possess permeases and also have adaptive enzymes so there are yet possibilities. By synthezising antimetabolites, new classes of antimycobacterial compounds may be discovered, which must then be tailored into a suitable form for absorption by the bacillus.
(2) *For effective in vivo activity* a drug must be well abso bed, and

the absorption processes are highly specific. At present, many compounds have to be made and the best absorbed found by experiment. Absorption in man is often very different from in the animal, and after absorption there are differences in metabolism which will cause variation in therapeutic action. To obtain *in vivo* action, a drug must reach the infective agent. In both tuberculosis and leprosy this is particularly difficult because the bacilli are intracellular and maybe walled in by fibrous tissue or lipid.

(3) *The evasion of drug resistance* in leprosy at present depends on the hope that such strains will be few and slow to appear; so it is with the slower sulphones in therapy. For quicker drugs, the appearance of drug-resistant strains may often be prevented by the concurrent use of two or more drugs, with the extra benefit of synergic action to be expected.

(4) *Personal variations:* every human being is now thought to have a virtually unique biochemical constitution; biochemistry applied to chemotherapy must take account of this. Individual human variations in drug response must never be forgotten, e.g. there are rapid, medium, and slow inactivators of INH, and the inactivator-type is genetically controlled.

Present Antileprosy Drugs were then discussed by the author, viz. chaulmoogra oil, the sulphones, DDSO, TB_1, DPT and Etisul. As regards DPT and Etisul he drew attention to the finding that a decline in the proportion of normal staining bacilli precedes the decline in numbers of bacilli. Both these drugs seem to act by rendering the bacilli susceptible to phagocytic destruction. He states that Etisul causes a rapid diminution of the numbers of normal staining bacilli and the bacterial index.

Angiography in Non-lepromatous Leprosy. S. P. BASU, S. K. GHOSH, N. MUKERJEE, and K. P. ROY, Bulletin of the Calcutta Sch. of Trop. Med., **8,** 4: Oct., 1960, pp. 166–167.

From investigations by angiography and other means findings led the authors to believe that vascular stasis and consequent failure to dissipate heat are noticeable in the human body parts in non-lepromatous leprosy. The experiments of CHATTERJEE on blister formation led to a similar conclusion. The authors now report angiographic results in the hands of 20 non-lepromatous cases. All the cases had slight or moderate polyneuritic changes in the upper limb. They injected 10 ml. of 30% Dionine into the brachial artery above the bend of the elbow and X-rays were taken. There was violent spasm of the arteries in almost all the cases, probably due to the dionine. The dye was seen well distributed in the arteries, with good visualization in most cases. Some cases showed *stasis* of the dye, engorgement of parts of the vessels, thinning of the digital vessels and delayed emptying.

REPORTS

Colonial Medical Research Committee: 15th Annual Report, 1959–1960.

In 57 pages this report deals with a wide range of research activities, including helminthiasis, malaria, virus diseases, tuberculosis, leprosy (pp. 116–129), Sickle-Cell Anaemia, etc. In Northern Nigeria, Dr. D. G. JAMISON made interesting histological investigations in formalin-fixed skin biopsies from 5 normal subjects in daily contact with untreated lepromatous cases. Even after examining 2,230 serial sections he could not detect the presence of acidfast bacilli in the skin. He also examined biopsies taken from enlarged nerves of patients with various kinds of leprosy, choosing in each case the dorsal cutaneous branch of the radial nerve. He used silver staining techniques. He also studied the Schwann cells in enlarged peripheral nerves after Indian Ink injections and injections of dead acidfast bacilli. Changes in skin and nerve structure were also studied in 15 leprosy patients under "Etisul" inunction therapy, and animal experiments of parallel nature are being carried on. It was found that in all the lepromatous cases that *with daily inunction of Etisul there was a very marked reduction of the number of bacilli in the dermis* following 3 weeks of treatment, though acidfast bacilli could still be found in peripheral nerves in the same biopsy. Lepromin and Tuberculin skin testing was carried out in 79 selected children in Katsina (the lepromin was made in Oxford by Dr. R. L. Vollum from material sent from Katsina). For the tuberculin test the Heath multipuncture method and PPD were used. It is hoped to extend the experiment to at least 1000 children. During each visit overseas lepromatous material was collected for making lepromin at Oxford and for culture studies. Dr. J. M. GARROD, of the *East African Leprosy Research Centre at Alupe, Kenya* has reported on therapy by DPT (Ciba–1906). Those who have completed 3 years of treatment showed some signs of drug resistance, first shown by apparent lack of further progress, then by the appearance of new lesions and an increase of bacilli in lepromatous cases. When transferred to DDS treatment, normal progress is resumed. *Etisul* was tried in combination with DDS or DPT, or TB_1 in 17 lepromatous, 5 borderline, and 1 tuberculoid cases. The tuberculoid did not respond much more quickly than usual, and of the others those on TB_1 did rather better than with the other accompanying drugs. *Etisul has a direct and speedy effect on the bacilli, causing granulation and beading, loss of acidfastness, and disintegration of globi. The bacillary index drops by a fourth in* 4 *months, and nearly half in* 8 *months. Clinical progress in speeded three-fold.* Progress then slows remarkably, even when the Etisul is continued and signs of resistance develop. It seems that all the benefit of Etisul is obtained in the first few months of its use.

This benefit is permanent and is maintained if DDS is the accompanying and following drug. There have been *no toxic effects with Etisul*. There is little objection to the smell.

Biochemical studies have been carried out by Mr. G. A. Ellard, M.Sc. on the estimation of DPT by a ferric chloride quantitative method and it has been possible to suggest *the optimum dosage of DPT* as 1.5 g. daily or preferably in 3 divided doses daily. The metabolites of DPT have also been studied, with hopeful results.

Dr. R. F. NAYLOR of the Dept. of Chemistry of Makerere College has continued studies on the measurement of dehydrogenase activity in saphrophytic mycobacteria by tetrazolium salts, and latterly *by radioactive tracers*. He is using C–14 to detect protein synthesis in *M.phlei*, and the actual uptake of DDS, DPT, and Etisul when labelled with S–35 (this in collaboration with Mr. Ellard).

From the National Institute of Medical Research, London, Dr. R. J. W. REES reports on his laboratory studies *on the morphology of leprosy bacilli* (with Dr. R. C. VALENTINE) *on the multiplication of* M. lepraemurium *in cell cultures* (with Miss Y. M. BARR and Miss E. W. GARBUTT); on *attempts to transmit* M. leprae *to experimental animals*. This last work is based on a colony of the strain of hybrid black mice in which K. R. CHATTERJEE of Calcutta claimed to have transmitted human leprosy. It is interesting that this hybrid strain of mice has proved to be much more resistant to tuberculosis yet more susceptible to rat leprosy than an albino strain of mice. These transmission studies are being closely integrated with those of Dr. M. F. R. WATERS at Sungei Buloh, Malaya, who also supplies much of the fresh leprosy tissue.

Dr. E. M. BRIEGER and Miss J. M. ALLEN of the Strangeways Laboratory, Cambridge visited several leprosaria in Uganda and Belgium Congo, Dec. 1958 to May 1959, for observations on behaviour of leprosy bacilli in tissues; electronmicroscopic studies were made of thin sections through lepromata (by treating osmum-fixed tissues with uranyl acetate one could avoid much of the distortion seen in previous studies). Many bacilli showed a defined general structure with definite close-fitting cell walls and a well-delimited cytoplasmic cortex, and the cytoplasm was interpenetrated by membranous sheets in a well-nigh parallel arrangement. Inclusions made up of a granular uniform material were found at one or both ends of the bacilli. These inclusions were bounded by a membrane and in texture were different from the cytoplasm itself. They are not likely to be spores but more probably are inclusions of metabolic material. A *nuclear structure* has not so far been identified in the bacillus. The correlation between structural anomalies in the bacteria and *viability* has not yet become possible. The potassium tellurite work in conjunction with Dr. NAYLOR at Makerere has not shown respiratory activity in *M.leprae*, indicating an absence of dehydro-

genase activity. Dr. NAYLOR also had a pilot experiment on the uptake of labelled amino-acids in bacilli recovered from explants after various lengths of time in culture. There was a meagre uptake in *M.leprae* compared to *M.phlei*.

East African Leprosy Research Centre (John Lowe Memorial): Annual Report, July 1959—June 1960.

Some patients still remained in the clinical trial of DPT (Ciba–1906). In 12 out of 18 remaining patients, signs of *drug* resistance in the shape of clinical regression, after an average of 35 months' treatment. The treatment had been DPT by mouth in a single undivided dose, and the giving of divided doses might well have prevented any clinical regression. Nevertheless, DPT might better be reserved for the first year only of treatment.

Etisul (diethyl dithiol*iso*phthalate) has been given trial at the Research Centre, combined with DDS or DPT, or Thiacetazone, and the results are favourable. In the first 4 months it has a marked antimycobacterial effect, first shown by a disintegration of the bacilli and globi, and loss of acidfastness. *Bacterial and histological effects and clinical progress in the first year are similar to that of* 2 *or* 3 *years of standard treatment*. It seems that most of the benefit from Etisul takes place in the first 3 months, and little is to be expected from continuance. When standard treatment follows, quick progress continues for some time, slowing gradually until at 18 months the rate of progress resembles that of standard treatment alone. In cases with few bacilli the effect is not marked. No toxic effects from Etisul have been noted up to a dose of 10 g. daily. The average dose is 5 g. by inunction as a cream into the skin twice a week, or 1.5 g. daily is effective.

In the Centre a guinea pig colony has been established. The Centre also has made lepromin. In biochemistry further study has been made of the ferric chloride method of estimating DPT, and studies of the amounts of metabolites excreted. Above 1.5 g. further increases in oral dosage cause no further increase in the amount absorbed. To clear 1.5 g. takes about 4 to 5 hours. *A dose of* 1.5 *g. DPT thrice daily is recommended for the best results*. Radio-isotope work on DPT has been done in conjunction with Dr. R. F. NAYLOR of Makerere. Extraction of urinary metabolites of continued and samples have been sent to U.K. The extracted metabolite seems to be even less soluble than the parent substance.

The Director of the Research Centre now acts as medical officer of the leprosarium.

First Course of Instruction in Dermatology—Leprosy for Doctors and Nurses, in Mexico. Dr. A. SAÚL reports on this course, in Dermatologia, Revista Mexicana **4**, 2: June, 1960, pp. 131–138.

The Director of the Course is Prof. F. LATAPÍ. Dr. AMADO SAÚL was the professor of the Course, which was held 15 Mar. to 31 July,

1960, in the Dermatological Centre PASCUA in Mexico City and in the Dermatological Institute of Guadalajara, Mexico. There were 12 weeks of theoretical and practical study, and 4 weeks of practical exercises in the field.

Prof. SAÚL says that the modern Mexican approach to the control of leprosy began and developed gradually since 1937, and as in other countries, and changed the plan of internment of the patients in leprosaria with almost police persecution and devoted a more humane and wise attention to the patients in antileprosy dispensaries (which were afterwards called Dermatological Centres). These are now the basis of control and are sited in the areas of the country which have most endemic leprosy; on paper at least there are 24 of these centres now, but many of them are not fully completed and in full action. Because of the wide spread of the endemic zones of leprosy in Mexico, the poverty of the patients which hindered travel to the Centres, the poor performance of the Centres, and the imperfect treatment of the patients, the work of the Centres became changed to an intramural one with scanty rural effect. Little effort and interest and much "burocratismo" characterized the Antileprosy Campaign during recent years. The patient labour of Mexican leprologists, headed by Prof. LATAPÍ, the continuous and tenacious influence of the Mexican Association for Antileprosy Action, the recent international Leprology Congresses, and the visit to Mexico of distinguished leprologists of world-wide fame, awakened the interest of the national Health Authorities. By the express desire of the Secretary for Health and Social Assistance, Dr. J. A. AMEZQUITA, a different new plan was drawn up. This was called "Programme for the Control of Chronic Skin Diseases". It continues on all general and special lines as laid down often by Mexican leprologists. Its basic principle is to continue work in the rural zones where the patients actually live, by means of the creation of *mobile teams* made up by 1 doctor and 1 nurse, both properly trained in leprosy.

The Dermatological Centres continued their function of centralization of activities and dermatological consultations, of teaching of staff, and of study. Of the 24 Centres in the land, only 2 had any great development, namely the Pascua Centre in Mexico City and that in Guadalajara.

An important point in the new programme was to consider and repair the lack of doctors trained in leprology and dermatology. Mexico is one of the few countries which insist on the need of a basis of dermatological knowledge for the training of a good leprologist and the first Course of Instruction for doctors and nurses was planned with this in mind. The course contained 10 doctors and 10 nurses, as well as 3 health nurses. For the doctors the theoretic course covered theoretic and practical lectures, "round tables", and

time for the library. The lectures covered fundamental dermatology and leprology, epidemiology, statistics, health administration, hygiene, anthropology, and psychology. The subjects in dermatology occupied 33 hours and gave special attention to the diseases most common in Mexico, such as superficial and deep mycoses, microbial, parasitic, and virus dermatoses, reactional dermatoses, tumours, syphilis, Mal de Pinto and many others. The use of the laboratory in dermatology and ideas on treatment completed this part of the study.

The leprology classes occupied 73 hours and dealt with the following subjects: the importance of leprosy in Mexico, its distribution and causes and pathogenesis, transmission, immunity, clinical features, cutaneous, neurological, ophthalmological, and orthopaedic; the use of the laboratory in leprosy, modern therapy of leprosy, leprosy as a problem of the individual, the family, and the community; the management of the patient, the problem of leprosy reaction, prevention of leprosy and modern ideas on that. The classes in epidemiology dealt with the concepts of health and disease, transmissible diseases and epidemic diseases, and of course the epidemiology of leprosy. Anthropology and Psychology occupied 9 hours and dealt with important themes like the characteristics of urban and rural populations in Mexico; social, cultural, and psychological data of the chronic patient.

Complementary classes were given on health administration and hygiene, with emphasis on education of the patient and his family. Statistics classes occupied 8 hours. There were practical classes for most of the time. Books and periodicals were studied in the library. Professors and lectures at the course included F. LATAPÍ, C. ESTRADA, BEIRHNA, A. SAÚL, NOVALES, CASTILLO, and many others. For the nurses the theoretical and practical course lasted 1½ months and the course was on similar lines but simpler. *Field studies* were incumbent on all students. They brought the students into contact with people where they lived and were most valuable. They were divided into teams for this work. The whole course was highly successful.

Department of Health, Union of South Africa: Annual Report, 1958.

This Report was received by us in London Jan. 1960. It is mainly of statistical nature. Leprosy is mentioned on p. 2 where it is stated that Leprosy Boards meet at frequent intervals for the purpose of discharging patients. Discharges seem to be greater in number for it is stated that the institutions in Tanskei and Pondoland (Mjanyana and Mkambati, respectively) have less than half their accommodation taken up, and the vacant section has been converted for tuberculosis patients. This transfer of use for tuberculosis is also foreshadowed for Amatikulu in Zululand. On p. 27 there is a table of

incidence. There were 32 "white", 1418 "Bantu" and 56 "coloured" patients, and only 4 Asiatics, in leprosy institutions, *a total of* 1510 *leprosy patients*. Of these, Westfort, Pretoria had 327 new cases, 470 discharges and 25 relapsed cases. The other 3 institutions had 257, new cases, 494 discharges, and 49 relapsed cases.

Report of the Director of Health Services, Ceylon, 1959.

This Report, on pp. 209–212, deals with the Control of Leprosy. There was an "Antileprosy Drive" in 1959 which brought 339 new cases to light. The cases are simply and practically classified as lepromatous or non-lepromatous on a bacteriological basis. The total of known cases is 3547, and 881 are in institutions. The average lepromatous rate is something approaching 30%. Contacts are kept under observation by field officers, and attention is being given to rehabilitation of cured patients.

Report on the Health Conditions of the Maltese Islands for the Year 1958.

On p. 129 leprosy is reported under the heading St. Bartholomew Hospital. The number of patients remaining in hospital was 43 at the end of 1957. Two patients were admitted during 1958 and 2 discharged. The type of leprosy is mainly lepromatous. Compulsory segregation was abolished in 1953. Patients now come forward voluntarily. At the outpatient clinic attached to the hospital there were 652 attendances. Sulphone therapy remains the main therapy for all patients, but Ciba–1906 has been tried on a few patients.

REVIEWS

"*Leprosy, Its Challenge and Hope*", by R. G. COCHRANE, issued by the Mission to Lepers (i.e. To Leprosy Sufferers), 7 Bloomsbury Square, London, W.C.1.

This is a booklet of 35 pages and 12 illustrations, in which Dr. Cochrane sets out the challenge of the world leprosy problem as seen today, with perhaps 15 million leprosy sufferers existing in the world today, and the challenge to us of its curability, for not only are the standard drugs efficient but new drugs are becoming available. There is also the discovery of the prevention and cure of leprosy deformities by the use of physiotherapy and surgery. This pamphlet brings a message of hope to leprosy patients and a challenge to us to produce the personnel and the effort needed to eradicate leprosy in our time.

Sbornik Nauchnikh Rabot Po Leprologii i Dermatologii No. 13. (Collected Scientific Papers on Leprology and Dermatology No. 13); Rostov Experimental and Clinical Leprosarium of the Ministry of Health of the USSR, and the Chair of Skin and Venereal Diseases of the Rostov Government Medical Institute.

This symposium of papers is always of great interest. No. 13 contains 155 pages. Prof. N. A. TORSUEV on pp. 3–13 reviews *leprosy epidemiology*. He emphasizes the need of a comparative study of different endemic zones the regular use of the Mitsuda for contacts, the use of BCG vacination, and prophylactic sulphones. He thinks we need to find a perfect experimental model of human leprosy. G. TCHIRAKADZE, pp. 17–20 gives a paper on the *history of leprosy in Georgia* and deals of the documentary evidence of its existence there in the 11th and 12th centuries. R. A. TRAPEZONTSEVA and K. A. VESSELOVSKY, pp. 21–28 deal with *blood catalase in leprosy* and show that the level is reduced markedly, which is bound up with changes in the body in the processes of oxyreduction. R. A. TRAPEZONTSEVA and K. A. VESSELOVSKY also deal with the *metabolism of Bromine, Potassium, and Calcium in leprosy patients* (pp. 29–41). They carried out 1843 blood analyses and showed a reduced level of potassium and calcium in advanced lepromatous cases and at the same time a low Bromine level in any case of leprosy, of whatever type and stage. The alterations are probably connected with functional disorder of the nervous system. Prof. N. A. TORSUEV discusses on pp. 43–47 the use *of the preparation* RD *in leprosy treatment*. RD is the gamma fraction of oxydiphtherinic acid, and broadly speaking, is equivalent to use of salts of ethylesters of hydnocarpus oil. It is used in a watery solution of strength 0.25 to 0.5%, in a dose of 0.5 to 1.0 mg, given perineurally every second day to patients suffering from acute and subacute neuritis. It is said to cause a rapid disappearance of symptoms of pain. For intense pain he recom-

mends an endoneural injection. The use of a 1% solution is indicated by intramuscular injection in the case of neural disturbances, especially at the beginning. The injections are given every second day, up to a total of 20, at a dose of 0.2 mg. If the treatment is repeated, the injected dose increases each time by 0.2 mg. V. LOGUINOV and I. EFIMOV discuss the influence of the sulphones on the cardiovascular system of leprosy patients, pp. 48–51. They used electrocardiographic examination on 47 leprosy patients under sulphone therapy, and towards the end of treatment there were quite marked changes in 22. A. S. DICHKO, pp. 63–69 discusses *pruritis and changes in the peripheral nerve receptors in the skin in leprosy.* He used the dionine test to examine 29 leprosy patients. There does not appear to be much relation between pruritis and sensation to pain, temperature, and touch. In certain cases the application of dionine produced pruritis in a symmetrical zone on the other arm, which seems to indicate that pruritis is connected with cerebral cortical processes.

Vestnikh Dermatologii. Venerologii (*Journal of Dermatology and Venereology*), Nos. 11 and 12, Moscow 1960.

These two issues contain a total of 194 pages, and there are several paper on leprosy. In No. 11, pp. 3–6, N. V. NIKITINA, A. A. STUDNITSIN, and V. K. SHUBIN discuss "The Tasks of Leprosy Control in the U.S.S.R." In No. 12, pp. 3–6, Prof. N. A. TORSUEV has a paper on "Nerve Endings in the Human Skin", a subject of great importance in human leprosy.

Etude des Mutilations Lepreuses (*Study of Leprosy Deformities*), 1961. M. LECHAT.

This monograph contains 276 pages with an atlas of 85 X-rays and arteriograms. It is written mainly in French, but there are Summaries in English and Spanish. There are 221 References. The illustrations are of excellent quality, and well described. This valuable monograph should be in every library, personal or scientific and has appeared just as the right time in history when attention to leprosy deformities and honest attempts to prevent and relieve them have at last become a joyous part of the "Zeitgeist" of world leprosy.

Premier Colloque International Sur Les Mycobactéries (*First International Symposium on the Mycobacteria*), 4–6 Dec., 1959, Institut de Medicine Tropicale Prince Leopold, 155 Rue Nationale, Anvers. This booklet contains 198 pages, mainly in French, German, and English.

Prof. L. M. G. GUERDEN opens with *Introduction a L'Etude des Mycobactéries et des Mycobacterioses*, and states that mycobacteria are characterized by their acid-fastness which is conditioned by their waxy envelope. There are 3 groups, poikilotherms, homoiotherms,

and saphrophytes. They are identified by culture, animal inoculation, sensitivity to antibiotics, phage typing, histopathology, biochemical and antigenic structure, etc. They vary in pathogenicity and in stimulation of allergy and diagnostic procedures include bacterioscopy, culture, antigenic reactions, and serological tests. The present position includes the discovery of the "atypical" mycobacteria and of pathological conditions and epidemiological facts which do not conform to the classical picture. The author recommends research by different disciplines on a comparative plan. Dr. A. DEVOS discussed *Les Techniques D'Isolement des Mycobacteries* and surveyed the different media and current methods for isolation of mycobacteria. The choice of the medium and of the homogenisation technique should depend on the number of mycobacteria present in the pathological material and also on its degree of contamination by fungi and bacteria. It is necessary to use different media and different temperatures to allow the mycobacteria to obtain the most favourable conditions for growth. I. W. LESSLIE reported on *Purified Protein Derivatives from Mycobacteria.* He includes also PPD from *M. johnei.* The problem of non-specific reactions in animals free of tuberculosis has been solved in UK by the use of avian tuberculin, naturally taking into consideration the history of the herd and its environmental factors. The non-tuberculous mycobacteria are widely present in nature. Acid-resistant mycobacteria of rapid growth have been isolated in 2.5% of cases out of 5000 samples examined, all from a herd free of tuberculosis. From tuberculous mammitis of cows 3 different types have been isolated and from cattle a certain number of chromogenic strains of slow growth have been recovered. Three PPD preparations from saphrophytic mycobacteria (*M. smegmatis*, *M. fortuitum*, *M. phlei*) have been tested by intradermal injections in guinea pigs and with sensitized cattle. The specificity was shown to be useful and reliable for the rapid identification of saphrophytic mycobacteria. Cows and calves, experimentally infected with cultures of these 3 strains, developed an allergy uniquely corresponding to the respective PPD. The reactions obtained with *balnei* PPD increased in intensity thrice that to human PPD in animals sensitized previously with *M. balnei.* The specificity tests showed, that in guinea pigs sensitized by means of *M. johnei*, the reaction with *johnei* PPD was 2.9 times stronger than with avian PPD, and with those sensitized per *johnei* PPD and avian PPD, six times stronger with avian PPD than with *johnei* PPD. The differences between *johnei* PPD and avian PPD were not as marked in cattle as in the guinea pig. A fairly high proportion of animals clinically attacked gives a negative reaction. The author will continue his researches with PPD of new mycobacteria, and comparative studies with tuberculin PPD could contribute greatly to our knowledge of the allergic reactions, in animals as well as man.

Prof. P. HAUDUROY also discussed classification in his paper *Essai Sur la Classification des Mycobactéries.* He mentions some of the names, *Mycobacterium phlei*, *M. lacticola*, *Smegmatis friburgensis*, *M. smegmatis*, *M. butyricum*, *M. ranae*, *M. tuberculosis var. hominis*, *M. bovis*, *M. avium*, *M. leprae*, *M. ulcerans*, *M. balnei*, *M. kansasii*, *M. johnei*, *M. paratuberculosis*, *M. enteritidis chronicae pseudo-tuberculosis bovis*, *M. tuberculosis var BCG*. Mycobacteria as a whole possess group characteristics. Differences in the types (*hominis*, *bovis*, *avium* and *johnei* are shown by certain biological characters, such as possible pigmentation of cultures, tolerance to temperatures at different stages of growth and with different media, initial resistance to certain antibiotics, lack of pathogenicity to the guinea pig, etc. "Mixtures" with mycobacteria are a source of fatal errors. Strains that have been isolated should be lyophilized and preserved in a collection. The International Centre should preserve sample strains and be ready to supply them. In classification the only general agreement is on acidfastness. Classification needs much further study. The author proposes the formation of a study group for the mycobacteria.

Prof. G. PENSO gave a paper on *The Identification of the Mycobacteria in the light of their Antigenic Constitution.* His own research has been on the immuno-electrophoretic study of the pathogenic and saphrophytic mycobacteria. By electrophoresis the number of antigens was found to be constant for each species. There is a generic antigen in all the mycobacteria, and another specific one for the pathogenic strains. The bovine mycobacterium has the most complex antigenic structure. Each strain has a whole series of antigens specific for it. Phage-typing gives a very clear parallel result to electrophoresis. Strains sensitive to a phage have also a common antigen.

J. ASSELINEAU gave a paper on *Composition de la Partie Peripherique du Bacille Tuberculeux.* He studied the composition of the superficial lipids of *M. tuberculosis*, particularly the "cord factor", the cell wall, and Wax D extracted as per ANDERSON. He concludes that the D waxes are constituents of the cell wall. This explains the hydrophobic nature of *M. tuberculosis*, its acidfastness, the differences in the behaviour of the virulent and avirulent strains to neutral red, the parietal localization of the factor responsible for sensitivity to tuberculin. In spite of certain discordances one can say that *M. tuberculosis* has a cell wall rich in lipids, which at least in the virulent strains is itself covered by a lipidic film containing the "cord factor".

Prof. G. PALLASKE discussed the *Pathology of Mycobacterial Infections in Animals and Man.* He said that in man and animals a tuberculous infection causes inflammatory reactions which are proliferative, or exudative, or all stages between. In the horse the disease

is proliferative, as also the disease in the swine caused by the avian type. It 's the same but less so in carnivores, monkey, giraffe, mouse, rat, hedgehog, hamster, and guinea pig (sometimes). The exudative form is often typical in bovine and caprine tuberculosis but rarely in other animals. Johne's disease, or bovine hyperthrophic enteritis is striking because it is limited to the intestines and mesenteric glands. It is chronic and is invariably fatal. The cutaneous nodules of bovines have been studied in the U.S.A.: acidfast bacilli are always present and on culture they have never been found to be tubercle bacilli. These cutaneous nodules show a certain resemblance to those of leprosy.

Prof. Ch. GERNEZ-RIEUX gave a paper on *Le Sero-Diagnostic des Infections Provoquées par les Mycobactéries*. Either specific or non-specific biological reactions are caused by mycobacteria. The antigenic relationships between the various mycobacteria are one cause of the difficulty in identification of mycobacterial infections. The method of passive haemagglutination is the most sensitive, in which the red cells sensitized by an antigen or a haptene are specifically agglutinated by a serum containing the homologous antibodies. When alexin is present the agglutination is replaced by haemolysis. The antigens responsible are of 2 types, polysaccharides, and proteins. Group reactions are seen in man (tuberculosis–leprosy) and in animals (tuberculosis–hypertrophic enteritis). Though the phenomena are complex, the haemagglutination and the conditioned haemolytic reactions deserve to keep a high place in the serodiagnosis of mycobacterial infections. The precipitation reactions are useful for determining the atnigenic relationships between the various mycobacteria but so far it has not been possible to use them for clinical diagnosis. In serodiagnosis one must always be ready to take into account (1) cross reactions, (2) lack of antibodies due to changes in the general condition of the patient; (3) neutralization of antibody by excess antigen during long term infections.

Prof. J. MORTELMANS gave a paper on *Mycobacterial Infections in Animals in the Belgian Congo and Ruanda Urundi*. Human tuberculosis has been known a long time in these countries. The animal form is mostly sporadic, and Johne's disease still more sporadic. Skin lesions are sometimes caused by saphrophytic bacteria. The incidence of bovine tuberculosis is low, and indigenous cattle have only a very little. Avian tuberculosis is very rare. Bovine tuberculosis in Ruanda Urundi is widespread, as is human tuberculosis. In tuberculin testing, for European cattle in the country the position is much the same as in Europe, but there are many false reactions among the indigenous cattle, caused by the classical causes and also by mange, ringworm, demodecosis, skin microfilariasis, photosensitivity, eczema, ticks, skin trypanosomiasis, minute wounds caused by insects, actinobacillosis, etc. The influence of the tropical sun is a definite one.

Dr. H. HUITEMA discussed PPD *and Tuberculin Tests in Cattle.* He said that the only way to favour the eradication of tuberculosis in cattle was to suppress the animals reacting to tuberculin. To this end PPD tuberculin is a sufficiently trustworthy method: he gives his method of preparing and using it. He describes nonspecific reactions met with. He thinks it probable that the nonspecific allergy is caused by saphrophytic mycobacteria always present in the intestine.

Dr. M. J. QUERTINMONT gave a paper on *Les Plaies a Bacilles Acidoresistants* (*Ulcers due to Acidfast Bacilli*). He described a series of necrotic ulcers separating at the edges caused by unidentified acidfast mycobacteria in Maniema in the Belgian Congo. The disease is only mildly contagious and children are more liable to be affected. The lesions are destructive, accompanied by fever and intense osteoporosis and may result in functional deformities (in the disseminated as opposed to the localised form). By intradermal tests the condition seemed quite specific and not leprotic nor tuberculous. The pathology was of an acute infection of a predominately necrotic nature. Entracellular acidfast bacilli were found in the necrotic areas. These are *M. ulcerans* of a local form *M. kasongo* and the author thinks it is the only one to be disseminated by the blood stream and to cause bony or intra-articular lesions.

Drs. J. P. DELVILLE and S. R. PATTYN discussed the *Histology of Ulcers due to Acidfast Bacilli.* They studied 15 biopsies taken from ulcers. The bacteria may be found in the necrotic portions, which helps diagnosis from tuberculosis and leprosy. There is typically deep and extensive ulceration and chronic inflammatory lesions and massive necrosis of the subcutaneous fat.

Drs. F. SCATTOZZA and G. MONDINO described their attempt to grow tubercle bacillus on Hela cells. He studied the behaviour of certain strains of *M. tuberculosis* on Hela cells. Three strains were used and refreshed at regular intervals (8–12 hours) on a Dubos medium with tween-albumin. For inoculation, cultures at 5 to 8 days were used. The bacilli could be observed intracellularly. The Hela culture kept up well at least in the first stages of the infection. Results seemed to show the possibility of this method of culture, and behaviour of strains of mycobacteria can be differentiated by their behaviour on Hela cells.