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LEPROSY REVIEW

VOLUME XXXVI NO. 3 JULY 1965

Contents

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Editorial

1 PRICE INCREASE OF LEPROSY REVIEW

The first warning of prospective price increase was given in Vol. 36, No. 2, April 1965.

With much regret it has been found necessary to double the subscription to *Leprosy Review*. This has been due to investigation of the rising costs of printing and it is intended that, in order to cover the cost of production, the price for a single copy of the Journal will be sh10/– whereas hitherto only sh5/– per copy has been charged. It is hoped that all subscribers will give us their support and pay the new annual subscription which will be raised to **£2 per annum from 1st January, 1966.**

2 ANTIBIOTICS IN THERAPY OF LEPROSY

In the past antibiotics have not achieved a dominant position in the therapy of leprosy largely because of toxicity and cost. In this issue we publish a paper by D. V. A. Opromolla, Lauro de Souza Lima and G. Caprara, on an antibiotic which has been used in leprosy therapy with some success, page 123.

3 Two interesting subjects are dealt with by Dr S. G. Browne on pages 119 and 133 viz. 'A positive Kveim reaction in a case of leprosy' and 'Leprosy in Eastern Nigeria – reflections on cases diagnosed at Uzuakoli 1959–64'.

4 The importance of surgery in modern leprosy is maintained by Dr W. M. Lennox, page 109, 'Plastic Surgery of the Anaesthetic Foot of Leprosy'.

5 Dr A. R. Davison's article on 'Six Years Follow-up of Diphenylthiourea Treatment', page 145, takes up a subject on which he wrote before his retirement, and we believe that Dr Schulz is also working on a similar subject.

6 The important subject of Chemoprophylaxis is clearly raised in the paper 'Chemoprophylaxis with DDS, mainly in Children: A short trial' by Dr R. A. Brèchet out of his experiences.

7 News from Africa of great importance is that Dr. S. G. Browne, who has been Director of the Research Unit, Uzuakoli, for the past six years, has resigned on being invited to succeed Dr. Cochrane as Director of the Leprosy Study Centre in London. He will be leaving Uzuakoli in September of this year.

This Centre is noted for its good study facilities and its valuable investigations into various aspects of leprosy, especially problems of treatment. Its work is of the highest value in the control of leprosy in Africa and throughout the world.

As a matter of great urgency, anyone who feels capable of tackling such an important job as Director of the Uzuakoli Leprosy Research Unit, which has an adjacent leprosarium, should communicate either with us, or with Dr. S. G. Browne direct at the Leprosy Research Unit, Uzuakoli, Eastern Nigeria, and to Dr. S. O. Egwuatu, Chief Medical Officer, Ministry of Health, Enugu, Eastern Nigeria.

It is necessary that the person appointed should possess a higher qualification and should have had a wide experience in leprosy, including if possible familiarity with investigative procedures as applied to leprosy.

Lep. Rev. (1965), **36**, 3, 105/108

Five Years Experience in Upper South Vietnam with Dialide, and Comparison with DDSO

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4, 4′-Diethoxythiocarbanilide (Dialide), a tuberculostatic agent discovered by R. L. Mayer, was introduced in Vietnam for the chemotherapy of leprosy in 1953 – the first thiourea to be used anywhere for this purpose – and rapidly proved successful in all forms of the disease, either alone, or in combination with drugs belonging to other families ([1], [2], [3]). The rationale for proposing this compound for clinical trials was based on (a) the high tuberculostatic activity of many thiocarbanilides (or NN′-diarylthioureas), including this very one ([4], [5]), coupled with some growth-inhibiting effects towards certain pathogenic fungi (an association of properties that is thought to be significant for the selection of potential antileprosy drugs ([6]); (b) the compound's exceedingly low toxicity, both acute and chronic (its LD^{50} *per os*, determined in rats, is well over 5 g./kg.); (c) the very low cost of its preparation, a particularly attractive feature for its use in under-developed countries; (d) and last but not least, its lack of tendency to induce or maintain reactional states in the patients. Since these initial observations, other thiocarbanilides have been introduced in leprosy therapy with considerable success, notably Ciba-1906 (a compound with an amine function) by Davey ([7]) and others, and Isoxyl (a higher homologue of Dialide) by our group ([8]) and by Griffiths ([9]). Dialide itself has been successfully used in Japan ([10]); in the Soviet Union it has been advocated as a subsidiary chemotherapeutic agent for tuberculosis, and reports have appeared in the recent Russian literature on its good effects in all forms of leprosy ([11]).

During the past 12 years, Dialide has been one of the major drugs used throughout South Vietnam for both hospitalised and ambulatory patients, and the experience thus acquired in a very great number of cases, some following a regular pattern of treatment, others undergoing therapy erratically (as is so often observed in this part of the world), allows some conclusions as to the influence of the drug, and perhaps to its mode of action.

In view of certain favourable local conditions (existence of close-knit communities and of a dedicated medical and paramedical staff) the upper regions of South Vietnam have provided the most reliable ground for such an evaluation. This report will therefore deal mainly with the results obtained in that area, above all in the province of Thua Thien. This coastal province, of which Hué is the capital, lies some 80 km. south of the 17th parallel (the demarcation line between North and South Vietnam), and has a population of some 400,000. As the incidence of leprosy estimated for the lowlands‡ is 3·5 per thousand, this would give an approximate figure of 1,400 patients for that province. During the five-year period of our campaign, we registered 700 patients. It is worth mention that the execution of our project was fraught with difficulties, due to the conditions of war prevailing.

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†Former Dean of the Faculty of Medicine and Director of the Central Hospital, Hué.

‡South Vietnam is divided into lowlands, inhabited by people of Vietnamese stock, and highlands, where the main population is made up of tribes of different ethnic origin; the incidence of leprosy among the latter is considerably higher (estimated at at least 7 per cent). Another difference is the frequency of the lepromatous form in the lowlands, in contrast with the predominance of the tuberculostatic form in the highlands (12).

Organisation of Campaign

The Leprosy Wing of the Central Hospital of Hué contained 65 beds and an out-patient department. Those of our patients who were in reactional states, the severe lepromatous cases, and some patients with extensive and painful perforating plantar ulcers, were hospitalised; the rest attended as out-patients. Laboratory tests included monthly nasal smears and skin biopsies; once smears and biopsies had remained negative for three consecutive months, the hospitalised patients able to walk were discharged and became out-patients. Among the nursing staff were four former patients whose 'negativation' dated from at least four years and who had undergone training both in the ward, and as outside visitors, where, in the outlying villages, they identified the sick and were, by their personal example, the most apt for encouraging the newly-detected cases to join in the chemotherapy project.

Protocol of Chemotherapy

Dialide, prepared in almost quantitative yield by the reaction of carbon disulphide on phenetidine (an inexpensive chemical intermediate widely used in the pharmaceutical and dyestuff industries) and recrystallised from ethanol, is a white crystalline powder melting at *circa* 176 °C, odourless, and with a bitter taste; it is insoluble in water and barely soluble in vegetable oils, and the most suitable galenic form is therefore tablets. The tablets, each containing 250 mg., were made at the pharmaceutical section of the Ministry of Health in Saigon, and put at our disposal. During the entire 5-year period, the patients received from 500 mg. to 750 mg. per day, without interruption whatsoever.

In order to assess the possible beneficial influence of a combination of drugs, a certain number of patients were given, along with the Dialide, 50 mg. of DDSO (4, 4′-diaminodiphenylsulphoxide) daily, six days per week (the earlier-advocated dose of 100 mg. [13]) was reduced by half when several separate chemotherapeutic trials with DDSO alone had demonstrated the adequacy of the lower dosage and the lesser occurrence of side-effects [14], except when a reaction episode set in, whereupon the patient was put back on Dialide alone. For a study of comparative long-term efficacies of Dialide and DDSO, a third, small group of patients was treated with DDSO alone; here again, administration of the drug was interrupted during reactional periods.

Adjuvant therapy in all cases comprised vitamins of the B complex.

Tolerance of Drugs

Daily administration of Dialide, even prolonged over five years as in the conditions of our trial, led to no side-effects nor signs of intolerance, and it was possible to administer it throughout reactional onsets without any exacerbation of the course of the reaction; in no case was there evidence that administration of Dialide had directly induced *erythema nodosum leprosum*. DDSO, in the lower dosage of 300 mg. per week, and given to patients on an adequate liquid intake, did not produce the transient renal lesions reported by Browne *et al.* [15] and which we ourselves observed in some cases receiving the higher 600 mg./week dosage. On the other hand, reactional episodes induced by administration of DDSO (alone or in combination) were frequent.

Results

Out of the 700 patients registered, we retained only 519, the remaining 181 having been found to take their drug irregularly, or having been lost from sight. The breakdown of these 519 is as follows:

	DRUG		
Form	*Dialide*	*Dialide + DDSO*	*DDSO alone*
L	248	70	24
T	68	71	38
TOTAL	316	141	62

Patients classified for practical purposes as 'apparently cured' were those whose routine laboratory tests showed persistent bacterial negativization of nasal smears and constant bacteriological improvement in serial skin-biopsies, together with disappearance of the evolutive skin lesions and of the tenderness and swelling of the nerves; these patients were then returned to normal life, whilst being maintained on therapy. In the light of these norms, results were as follows:

Form	Dialide		Dialide + DDSO		DDSO alone	
	Number of patients	*Apparently cured*	*Number of patients*	*Apparently cured*	*Number of patients*	*Apparently cured*
L	248	106 (42·7%)	70	29 (41·4%)	24	12 (50%)
T	68	26 (38·2%)	71	39 (54·9%)	38	17 (44·7%)
TOTAL	316	132 (41·8%)	141	68 (48·2%)	62	29 (46·7%)

From the above figures, it appears at first glance that Dialide is only slightly less effective than either the combination Dialide + DDSO, or DDSO alone (which latter is at least as active as diaminodiphenylsulphone ([16])). If this were indeed the case, then Dialide would hold a distinct lead over DDSO and the sulphones, being, unlike them, free from side-effects. Unfortunately, however, several of the patients on Dialide who had been 'negativized' and who were then switched to DDSO, developed reactional bouts, with bacteriological and clinical reactivation of the disease, and had to be put back on Dialide alone. This phenomenon was so regular an occurrence that patients kept on Dialide refused to be switched to another drug 'for fear of a relapse'. It is therefore probable that Dialide acts, in leprosy, less as a bactericidal than as a bacteriostatic agent, leaving in the body of the apparently cured patient, foci of residual infection which, under the effect of a reaction-inducing drug, can temporarily flare up. But so long as patients are kept free from such a 'therapeutic' triggering off, and are not attended by any breakdown in health, Dialide, in adequate dose levels, is able to maintain them in a state of 'apparent cure', seemingly for an indefinite period.

A Limited Trial in the Highlands

Since it is known that response to therapy tends to vary with the genetic stock of individuals, it was deemed of interest to investigate the effects of Dialide in leprosy among people of the highland tribes. A limited study, started in 1956, was carried out in the Leprosy Settlement of Ea-Ana, near the town of Ban-Me-Thuot, some 400 km. north of Saigon. Thirty-four patients in this area were treated with Dialide, in a lower dosage of 100 mg. per day, six days per week. Because of the conditions of war, records were obtainable for only 21 among them. Out of these 21, 12 were lepromatous cases, six tuberculoid, two dimorphous, and one indeterminate; eight patients were known to be reaction-prone.

Nine patients showed, after three years' Dialide therapy, the same type of improvement as those in the lowlands. In two tuberculoid patients previously treated during four years with sulphone with little effect, regression of the macules and anaesthesia was spectacular; in two other patients (one dimorphous, one lepromatous, and both reaction-prone), bacteriological negativation was achieved in under two years, with recession of the skin lesions and anaesthesia.

For comparison, a group of eight patients was placed on DDSO, in a dose of first 50 mg., then 100 mg. per day, six days per week. The following Table shows the results:

Form	*Previous Therapy*	*Reactional Episodes*	*Bacterial Index and Comments*
L	New patient	1	Bacterial index from ++ to + after 39 months; 1 psychotic episode.
L	Dialide	10 in 3 years	Negativized after 4 years; anaesthesia mildly improved.
L	New patient	1	Negativized after 41 months; anaesthesia almost completely disappeared.
L	New patient	nil	Negativized after 3 years.
L	New patient	3 moderately severe	Negativized after 21 months.
Dimorph.	DDS (anaemia)	nil	Haemoglobin level improved; negativized after 10 months; anaesthesia decreasing.
T	DDS	nil	Resolution of skin lesions; anaesthesia and bacilli persisting after 2 years.
T	DDS	nil	Skin lesions and anaesthesia improved after 16 months; bacteria still present.

CONCLUSIONS

Insofar as five years' experience in Upper South Vietnam allows conclusions to be drawn, it can be said that Dialide, in adequate dosage, is a highly active therapeutic agent in both lepromatous and tuberculoid leprosy, free from side-effects, and can be used throughout reactional episodes; the 'apparent cures' achieved are however less stable than those effected with the considerably more toxic DDSO, or with the combination Dialide + DDSO.

ACKNOWLEDGEMENT

We thank the Minister of Health at the time, the Medical Staff of the American Leprosy Missions in Ea-Ana, and Dr Ton-That-Niem (Ban-Me-Thuot), for help in this study.

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Plastic Surgery of the Anaesthetic Foot of Leprosy

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Department of Orthopaedics, C.M.C. Hospital, Vellore).

Some of the orthopaedic principles governing the correction of leprosy foot deformity have been discussed. Even when the orthopaedic condition of the foot is satisfactory, ulcers may occur when the quality of tissue between the bone and ground (or shoe) is poor. The normal sole contains a highly specialised superficial fascia which is a fibrous microcellular structure filled with fat (Maisels). A sheet of this tissue extends from the pulps of the toes anteriorly to the lower third of the back of the calcaneum behind, and laterally for about $\frac{2}{3}$ of an inch (2 cm.) round the lateral and medial borders of the foot. The layer is thickened under the metatarsal heads and under the heel. The fascia occurs in sufficient thickness in non-weight-bearing areas to form a useful reserve of tissue for transfer to strategic sites when trophic ulcers destroy or distort the shock absorbing mechanism.

Every ulcer leaves a scar and every scar increases the susceptibility of the foot to further ulcers. In certain cases a scarred foot fails to obtain sufficient protection from its shoe, and scars break down in spite of the best efforts of the shoemaker. A scar which breaks down when the patient walks is known as an 'unstable' scar, and this event is an indication for plastic surgery. It is the purpose of this paper to describe the principles which we follow in the management of these cases. Our object is to render unstable scars safe for walking with the protection of a microcellular rubber shoe.

Our experience has led us to recognise certain sites and types of scars which are particularly liable to cause trouble, even in the relatively normal foot. In the deformed foot a scar on a weight bearing area is almost certain to ulcerate. The first line of treatment is correction of the deformity. Thereafter attention is directed to

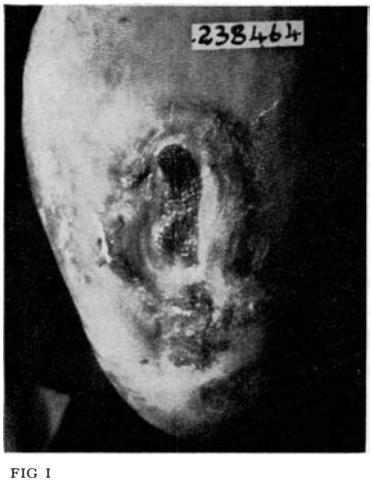
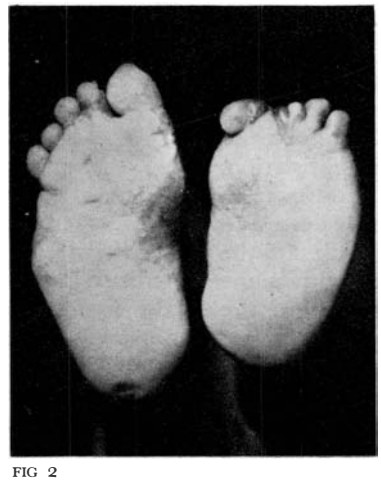


FIG 1



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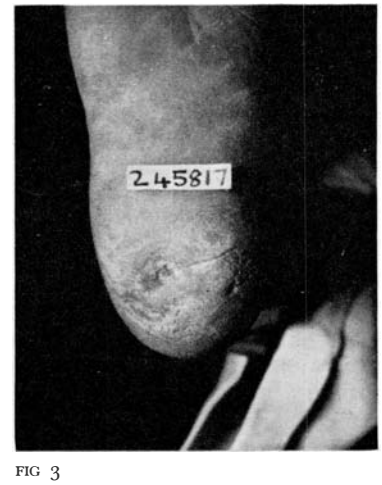


FIG 3

FIG 1 This heel was extensively ulcerated. The ulcer is healing but the scar is thin and closely adherent to bone. This heel requires trimming of the calcaneum and a direct flap.
FIG 2 The scar on the heel of the right foot has an adherent depressed centre, but mobile resilient margins, and is stable. The antero-medial corner of the left foot contains a plastic sponge implant (See text).
FIG 3 This narrow scar has poor resistence to shear: Plastic surgery indicated.

the plastic aspects of the case.

The following types of scar are notoriously unstable:

(1) Scars over the normal pressure points of the foot, i.e., heel, heads of the first and fifth metatarsals.

(2) Scars over abnormal pressure points – usually in the badly distorted foot.

(3) Scars which are adherent to bone.

In the heel, we recognise three types of scars:

(a) Extensive scars closely applied to the underlying bone without interposition of plantar fascia. (Fig. 1).

(b) Depressed scars in which the base is closely adherent to the bone but with resilient thick margins. (Fig. 2).

(c) Localised or linear scars deeply adherent to bone and extending in depth through a heel fascia of normal thickness. (Fig. 3).

Type (a) allows crushing and necrosis of cells on weight bearing, and therefore breaks down as soon as the patients walks. Type (b) usually possesses sufficient resilience of the margins to allow walking in a microcellular rubber shoe with a closely fitting heel counter. Type (c) withstands weight bearing satisfactorily, especially if a heel-counter is fitted to the shoe, but has poor resistence to shear. Types (a) and (c) generally require plastic surgery.

PLASTIC MANAGEMENT OF OPEN ULCERATION

Open ulcers are of two types; those which heal satisfactorily with conservative treatment, and those which require skin grafting to accelerate healing and reduce scar formation. It is possible to excise clean ulcers and to treat the defect by one of the measures to be described but in general it is preferable to wait for the ulcer to heal spontaneously. This reduces the risk of sepsis and scar contraction reduces the amount of tissue excised subsequently. Plantar ulcers, once clean, can be split skin grafted as a primary measure, but in small ulcers this is unnecessary and in the larger ulcers it may result in an unstable scar. One experience has been that the principles governing plastic surgery in the non-anaesthetic foot are equally applicable to the anaesthetic foot providing that the 'rules of delay' are respected and that flap ratios do not exceed 1 : 1½ or 2.

SPLIT SKIN GRAFTING IN THE ANAESTHETIC FOOT

This is useful as a first-aid treatment for clean granulating ulcers. Most writers (Blair *et al.*, Brown & Cannon, Ghormley, Lewis), agree that these grafts are successful as a definitive treatment if a pad of normal plantar fascia exists between the graft and the bone. The fascia allows the graft to slide over the bone in response to shear stresses, without rupture of cells. This condition is not met where the graft is placed on a base of granulation tissue. Subsequent contraction produces an adherent scar lacking the elastic quality of the plantar tissues. Bearing in mind the above conditions we have found split grafts to be successful in the leprosy foot under the following circumstances:

(1) In defects due to loss of skin only, e.g., burns (Fig. 4).

(2) Defects over non-weight-bearing areas (Fig. 5).

(3) As a surface covering after flaps of plantar fascia have been swung in to form a resilient bed.

Srinivasan and Mukherjee report the use of local fascial flaps for the prevention of recurrent ulceration of the heel.

Sites which are particularly suitable for split skin grafting are therefore the instep, lateral border of the sole, undersurface of the heel when the pulp is intact (Fig. 6), and the back of the heel. At first we took skin from the thigh, but we now use the instep of either the same or contralateral foot.

SCARS OVER WEIGHT BEARING AREAS

These require excision down to bone, which must then be covered with pulp and skin. Experience with leprosy feet confirms the point stressed by Maisels (1961) that trimming of the underlying bone enhances the chances of successful weight bearing afterwards, and makes it easier to suture without tension. This is an important part of the repair of pressure sores over the ischial tuberosities and greater tuberosities in paraplegics (Yeoman & Hardy, 1954), and conditions in the anaesthetic feet are not dissimilar. Bony prominences commonly associated with overlying scars in the leprosy foot are:

(1) Spurs on the undersurface of the calcaneus.

(2) Prominence under the head of the first

FIG 4 A large anterior skin defect: Suitable for a split skin graft.

FIG 5 Suitable for split skin grafting.

FIG 6 Superficial heel defects treated by split skin grafting. Pre and post operative condition. Heel now stable in microcellular shoes.

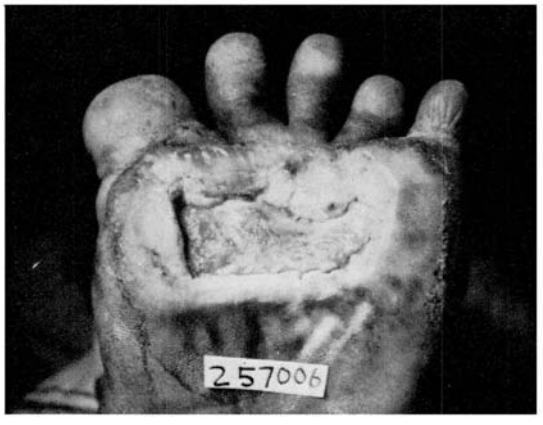
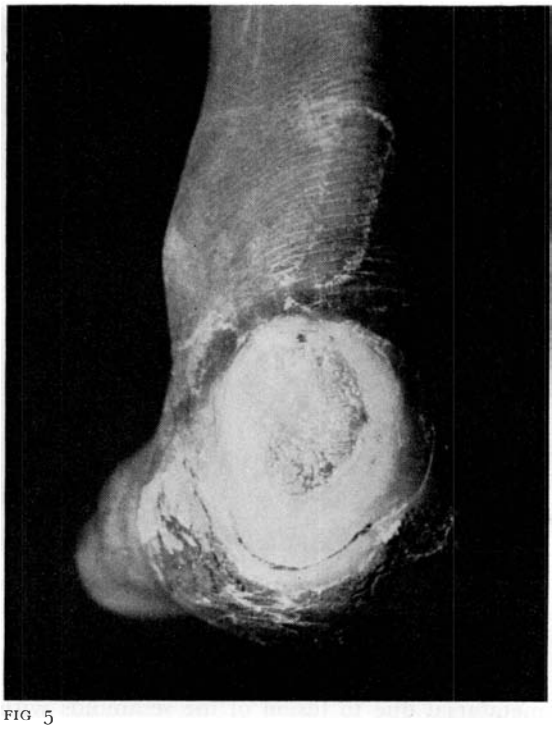


FIG 4



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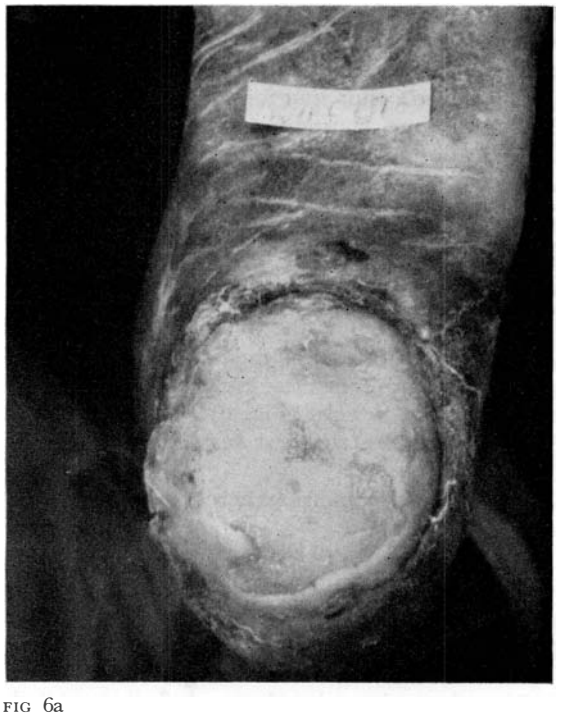

FIG 6a

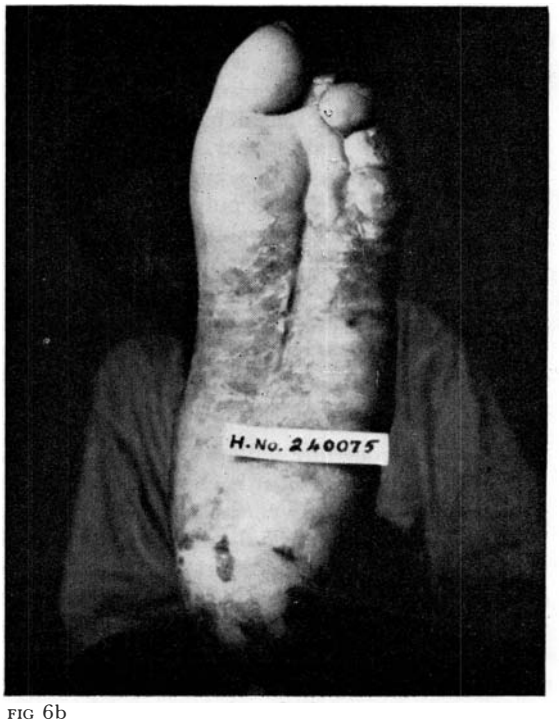

FIG 6b

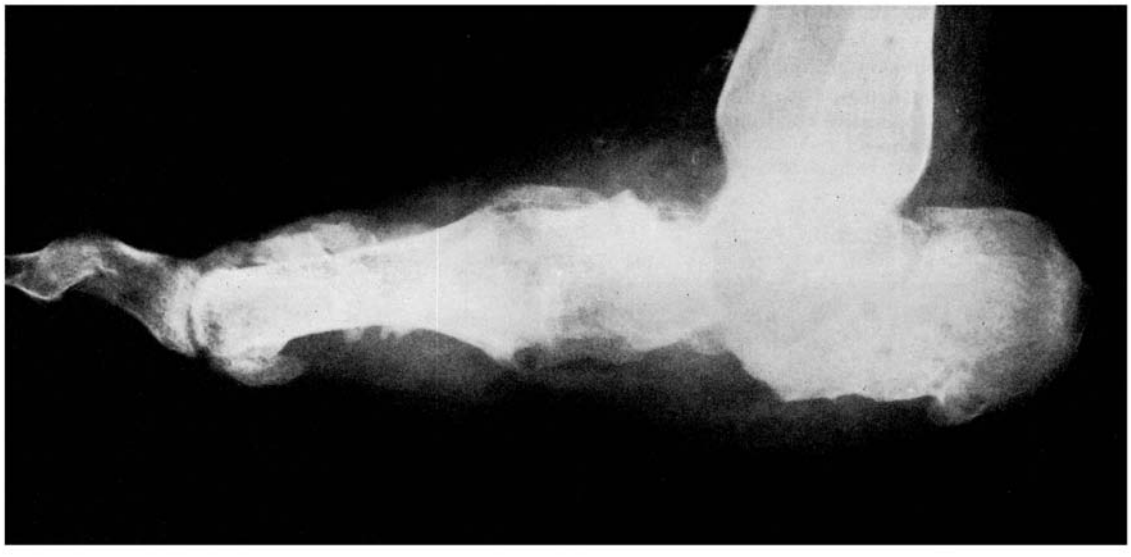

FIG 7 Triple Arthrodesis: Ankylosis of sesamoids to head of first metatarsal creates a localised high pressure point aggravated by ulcer scarring.

metatarsal due to fusion of the sesamoids with the head (old septic arthritis), (Fig. 7).
(3) The base of the fifth metatarsal.

After excision of a scar in depth, a defect remains which requires a flap composed of skin and subcutaneous pulp. Occasionally it is possible to close the defect by primary suture, giving a linear stable scar. This is usually possible in children, and sometimes in adults. It is important to close the pulp layer separately in order to insulate the skin from the bone. Catgut is used for the deep sutures in order to minimise fibrosis. If there is the slightest doubt about tension on the suture line, a flap should be employed. A linear scar well insulated from deep structures by a subcutaneous cushion is stable even on weight bearing areas.

After any procedure which leaves a scar on a weight bearing surface, it is essential to obtain mobility of the skin over the underlying bone. We now carry out gentle digital massage on all fresh scars (employing a circular motion) in order to stretch deep adhesions before they mature. The object is to obtain several millimetres of horizontal skin motion in all directions. During this phase of management the patient is allowed partial weight bearing on crutches.

THE USE OF FLAPS IN THE ANAESTHETIC FOOT

When combined with bone trimming, the use of flaps in the leprosy foot is usually safe and effective. Distant flaps do not have the specialised architecture for absorbing impact and shear, and are thus inferior to local foot tissue. They are time consuming and not devoid of complications. We therefore employ local flaps whenever possible. The rules governing local flaps in the leprosy foot are:
(1) Always shift non-weight-bearing skin to the defect.
(2) All flaps should be larger than would be used in the non-anaesthetic foot.
(3) Use large lateral or medial calcaneal flaps whenever possible, as these are based on anatomically constant vessels. (Fig. 9).
(4) Delay on the slightest suspicion of arterial insufficiency.
(5) Avoid making incisions across weight bearing areas.

We have found the following local flaps to be useful in the leprosy foot:
1. *For the forefoot:*
(a) Filleted toe flaps (Sangman & Guidin, Giannini). The scar is excised, and the defect fashioned to triangular shape. A flap is rotated

back into the defect. The skin of the filleted toe is turned back to cover the defect left by the flap. If the defect is not large, a partial proximal phalengectomy allows toe skin to slide proximally to cover the defect. The toe is temporarily immobilised with a Kirschner wire.

Feet are not uncommonly encountered in which one or more toes are functionless appendages carrying their own special risk of ulceration from pressure against a shoe. Such digits are ideal sources of pulp and skin.

(b) For scars just proximal to the big toe, the above method is useful, or a medial plantar transposition flap may be tried. Always excise underlying bone, and delay if necessary (Anderson). (Fig. 10).

(c) In more extensive scarring of the forefoot, with prominent metatarsal heads, make a transverse incision just anterior to the metatarsal heads, off the weight bearing area. Remove or trim the underlying metatarsal heads. Partial toe filleting will give closure without tension when particularly bad scars a re-excised at the same time.

(d) In some cases, excision of all the metatarsal heads may be required, so that the operation becomes in effect a conservative transmetatarsal amputation.

REPAIRS OF THE HEEL

Large heel defects are frequently associated with chronic osteomyelitis of the calcaneum, with sinuses opening on to the sides of the heel. A careful examination is therefore important in every case of heel ulcer, for to graft in the presence of bone sepsis is to invite disaster. In our experience, subacute osteomyelitis of the calcaneum does not do well with conservative treatment, and cases with sinuses, need operative treatment. This consists of excising a generous slice of bone from the undersurface of the calcaneum, taking with it prominences and depressions, and opening up deep bone recesses to the curette. A marginal heel incision (fish mouth) may be used, but we prefer to omit the medial limb of the incision, thus preserving the blood supply from the medial calcaneal vessels. Side sinuses are curetted, and the flap is then sutured back with drainage.

Once infection is controlled, the problem of the unstable scar arises. For scars where the main cause of breakdown seems to be localised adhesion to the bone, trimming of the undersurface of the calcaneum (V.S.), followed by a course of digital massage, is sufficient to render them stable. (Fig. 11). Scars which remain unstable should then be treated by one of the methods now to be described.

(a) MEDIAL AND LATERAL CALCANEAL FLAPS: These have given good results (Fig. 9). But should be large, and delayed.

(b) BUCKET HANDLE FLAP

This is a bipedicle local flap which is swung forward from behind the heel. Maisels points out that the heel can be divided into 3 parts – (1) the sole part covered by thick skin overlying the plantar cushion, and normally bearing weight; (2) an area over the back of the calcaneum, structurally similar to the sole part, but not bearing weight; (3) the area overlying the tendo-Achilles, similar in texture to normal skin. This flap brings area (2) into contact with the ground, and the defect over the tendo-Achilles is split grafted. The ratio should not exceed 1 : 2. (Fig. 8).

(c) DIRECT FLAP

These are required when the defect is too large to be covered by a local flap. The main application is for large defects under the heel, but defects of the forefoot can also be treated in this way. These methods are time consuming, involve immobilisation of the patient in difficult positions, and the tissue which is brought in is inferior in quality to the fascia which it replaces. Unsightly scars are also created. However, such flaps give good service in cases where special attention is given to aftercare. Underlying bone should be trimmed. Donor sites include:

The upper $\frac{1}{3}$ of the apposite calf (Ghormley).

The inner side of the opposite thigh (Browne and Cannon).

The buttock.

The selection of donor site depends on:

(1) The availability of blood supply. At levels below the upper $\frac{1}{3}$ of the calf the arterial supply is risky:

(2) The presence of a superficial fascia sufficiently thick and fatty to withstand trauma in its new location.

In Indian patients, this may be a problem. Many who need this operation lack subcutaneous padding. This makes the selection of a donor site difficult. Hence the occasional recourse to a buttock flap. However, we have observed thin

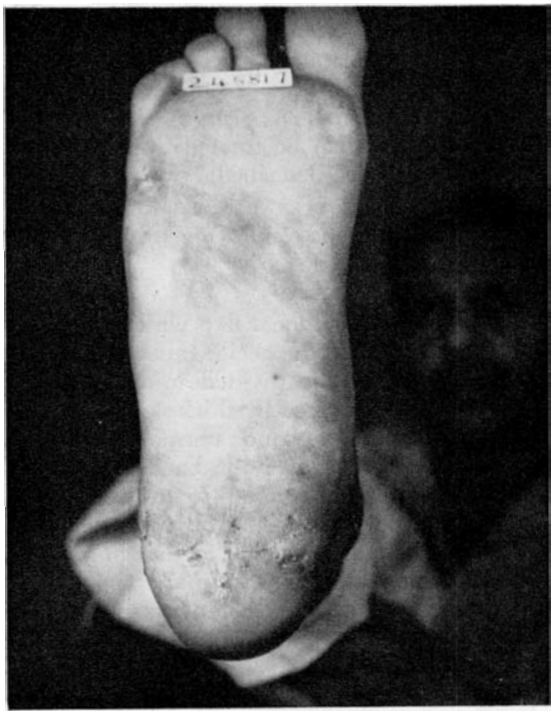

FIG 8 Bucket-handle flap.

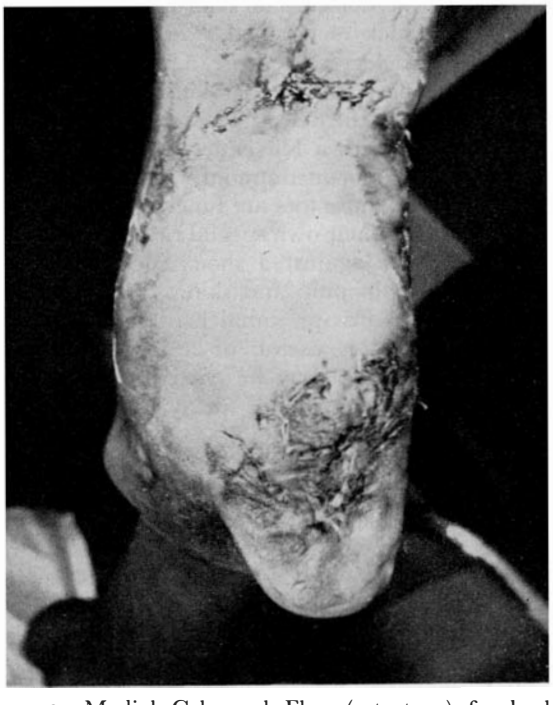

FIG 9 Medial Calcaneal Flap (1st stage) for heel scar. (Courtesy of Dr. A. J. Selvapandian).

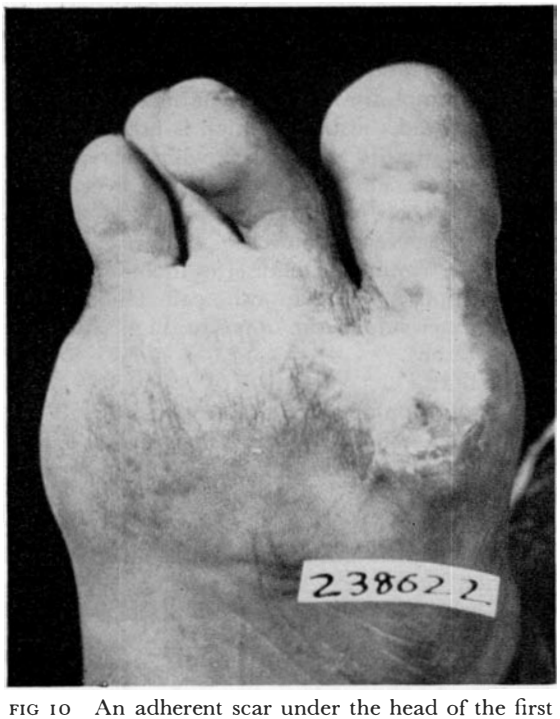

FIG 10 An adherent scar under the head of the first metatarsal. Suitable for filleted Hallux flap.

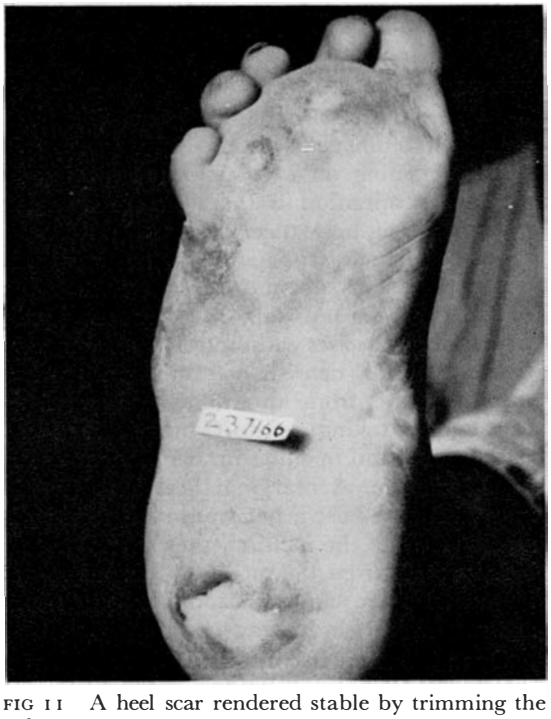

FIG 11 A heel scar rendered stable by trimming the calcaneum.

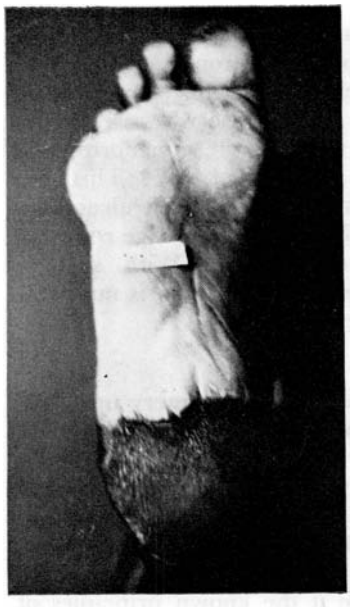

FIG 12

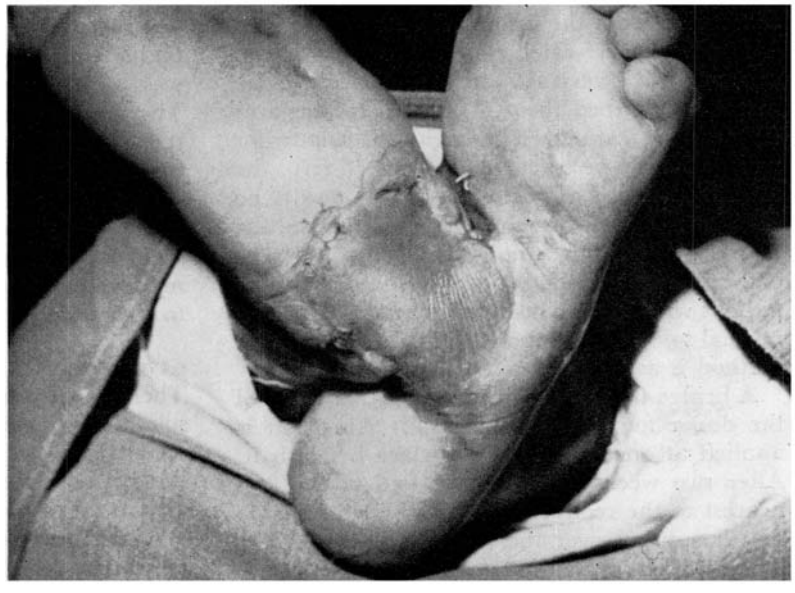

FIG 13

FIG 12 A cross leg (direct) flap 15 months after the operation.
FIG 13 A cross plantar flap (MIR-Y-MIR) immediately prior to division of the pedicle.

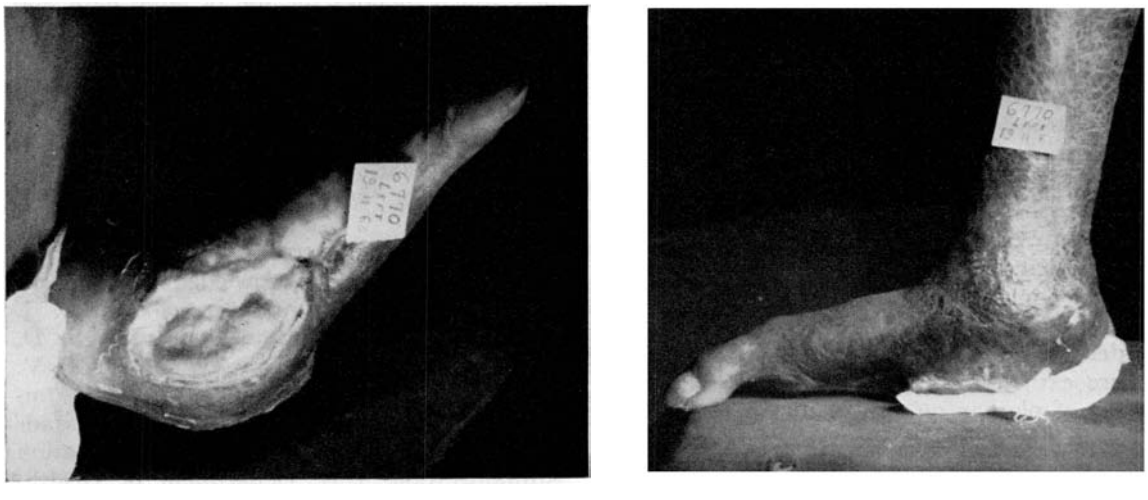

FIG 14 An uncommon reconstructive problem: See text.

flaps which initially adhered closely to bone to become supple and develop a functionally satisfactory subcutaneous layer after about six months from operation. This requires insight and co-operation from the patients, who must understand the need for restricted ambulation until the graft becomes mobile. (Fig. 12). On the other hand, a gratifyingly thick pad will ulcerate in the patient who takes no care. This prompts us to state a third selection criterion.

(3) The patient should be co-operative, and have insight into the problem and into what is being attempted for him.

In 1954, Mir-Y-Mir described the use of a

direct flap from the instep of the opposite sole. The advantages which this method appears to offer make it a very attractive alternative to the methods described above. These advantages are: (i) the tissue transferred has an ideal structure for withstanding pressure and shear; (ii) the technique is not difficult; (iii) there results no functional damage to the donor foot, since the flap is raised from a non-weight-bearing area of the sole. The method appears to be ideal for the patient with a large heel defect and a relatively normal sole on the opposite foot. In outline, the method is as follows.

A bridge flap is fashioned across the instep of the donor foot, and a thick split skin graft is applied at once to the raw surface beneath it. After two weeks ('delay'), the end of the flap nearest to the recipient heel is divided and the flap is sutured over the defect. (Fig. 13). The legs are immobilised in a comfortable position, using plenty of padding for anaesthetic areas. After three weeks the base of the flap is divided, and suture to the recipient heel is completed. Weight bearing may commence about four weeks later.

MISCELLANEOUS PLASTIC PROBLEMS

It is not uncommon to encounter cases in which standard procedures cannot be used. For these it is necessary to devise special procedures. Two examples will be mentioned.

Fig. 2 shows a shortened left foot which was badly scarred anteriorly, but with remnants of toes present. The pattern of absorption suggests neglected claw toes as the cause. In spite of microcellular footwear, ulcers regularly occurred under the anterior end of the first metatarsal, where existed the unfortunate combination of a loss of plantar pulp, and thin scarred skin. After monkey experiments, the underlying bone was trimmed sub periosteally, and a piece of 'silastic' sponge was inserted. The periosteum was united over the sponge with a catgut stitch, and the incision, forward of the scarred area, was closed. The patient has walked on this piece of sponge for 10 months without further ulcers.

This procedure is not recommended for routine use. Meticulous asepsis must be observed; an infection might well have left the foot much worse than before.

Figure 14 shows an inverted foot in which ulcers have destroyed the lateral ray. The foot was reduced to a single ray bearing a relatively undamaged big toe at the front. A large ulcer was present under the weight bearing area. The management in this case was resection of the foot skeleton through the cuneiform, and turning back of the filleted flap. This was sutured over the site of the excised ulcer scar. After primary healing a lateral wedge resection and fusion was carried out. With suitable microcellular footwear, this patient is now able to walk without ulcerating.

DISCUSSION

There is a tendency to avoid surgery upon the sole of the anaesthetic foot, and to rely mostly on footwear (after corrective surgery) to keep the patient free from ulcers. This is a sound attitude, but in certain instances shoes are not enough. It is then that a plastic procedure should be considered. Our experience indicates that much can be done if the known principles of this type of surgery are adhered to. Denervated tissues heal almost as rapidly as normal tissues providing a good blood supply exists: it is this fact which dictates the use of large flaps and broad pedicles.

SUMMARY

Plastic procedures which have been found to be useful in the management of the ulcer prone anaesthetic foot are reviewed. Some of the indications for these procedures are discussed.

ACKNOWLEDGEMENTS

It is a pleasure to acknowledge the constant encouragement and guidance of Dr. A. J. Selvapandian, and also to thank Mr. S. D. Sigamoney for the photography, and Mr. B. V. Venkatesan for his careful typing of the manuscript. This work was made possible by funds donated by the Vocational Rehabilitation Administration, U.S. Department of Health, Education and Welfare, Washington, and the British Leprosy Relief Association.

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A Positive Kveim Reaction in a Case of Leprosy

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The intriguing question of the relation subsisting between sarcoidosis and leprosy, raised long ago by Rabello (1936) and Reenstierna (1937), has been revived recently both by researches into sarcoidosis (Scadding, 1960; D'Arcy Hart *et al.*, 1964; and many others) and by the symposium-by-correspondence on sarcoidosis and leprosy reported in the International Journal of Leprosy (1962).

The Kveim reaction is now generally held to be specific and positive in the great majority of histologically proved subjects of sarcoidosis. It was at one time suspected that false positives did not occur (Brit. med. J., 1960), but they have been reported in granulomatous disease of known causation (Daniel and Schneider, 1962), and also in leprosy (Kooij, 1958; Dugois *et al.*, 1960) and referred to by other workers (James and Jopling, 1961; Brit. med. J., 1964). Kooij (1964) suggests that leprosy may be misdiagnosed clinically as sarcoidosis by clinicians insufficiently acquainted with the varied cutaneous manifestations of leprosy. The converse also is possible, and leprologists may be missing cases of sarcoidosis because of their preoccupation with their specialty.

All the patients receiving treatment at Uzuakoli Leprosy Settlement have been periodically reviewed with this possibility in mind. Eleven patients have been intensively studied because their cutaneous leprosy lesions bore some resemblance to the various lesions of sarcoidosis associated with the names of Besnier, Boeck, Schaumann, Darier, Roussy and others, and hence might be diagnosed as sarcoidosis if encountered in Caucasians living in countries where leprosy is not endemic.

All the 11 patients were deeply pigmented Nigerians, healthy apart from leprosy. Nine were males, and two females; four were children, and seven adults.

Bacterioscopic findings

In seven patients, no *Myco. leprae* could be found on prolonged searching of material obtained by the slit-smear method from the lesion itself or from the ear-lobes and nasal mucosa. In three patients with clinically similar but multiple lesions, *Myco. leprae* were found at all these sites, and one patient had a high Bacterial Index, with globi at all sites.

The lesions

The commonest lesion was a slightly raised plaque involving the nose and perhaps extending to adjacent areas of the face – the cheeks, upper lip, and centre of the forehead. The limits might be well-defined or might merge imperceptibly into the surrounding normal skin. In colour, the lesion was reddish or violaceous, or slate-grey. The surface was generally smooth and shiny, but not of the greasy appearance associated with diffuse infiltrative lepromatous leprosy. Sensory loss was minimal. Such lesions were also found on the forearms, deltoid region, scapular region, etc.

Mantoux reaction

The Mantoux reaction (1/1000 PPD) was negative in four patients, slightly positive in four and moderately positive in three.

Lepromin reaction

The early (Fernández) and late (Mitsuda) reactions were comparable in each case. They were completely negative in three cases classified as lepromatous or borderline, moderately positive in two classified as borderline on the tuberculoid side, and highly positive in the remaining six.

Kveim reaction

0.15 ml. of Kveim antigen (kindly supplied by the Standards Laboratory of the Medical Research Council, London) was injected intracutaneously into the extensor surface of the arm just above the elbow. The site of injection was examined daily for the first three days, and then at weekly intervals.

Slight infiltration and local tenderness developed at the site during the first few days in eight patients, but disappeared more or less rapidly. In two patients, a papule developed which disappeared by the seventh day in the first case, but which persisted till the seventh week in the other. One patient, a boy of 12 years, who had slight transient tenderness of the site of inoculation, developed a palpable nodule during the sixth week which subsequently increased in size.

Under local anaesthesia, an elliptical portion of skin and subcutaneous tissue (including the site injected) was removed from each patient during the seventh week, and dispatched in formal saline solution for histological examination.

Dr A. H. T. Robb-Smith, of the Radcliffe Infirmiry, Oxford, kindly processed and examined the specimens of tissue. He reported that all were negative except that from the boy referred to above, which showed a 'typical positive reaction'. In three others, there was a very slight cellular reaction.

DISCUSSION

The patient whose Kveim test was positive had been under treatment with dapsone for 18 months. A few weeks before he was admitted to the Settlement, many small, slightly raised, violaceous lesions had made their appearance on the face, trunk and limbs: some were plaque like or dome-shaped, and scaly. Other lesions appeared, which were hypopigmented and contained a ring of papules within a flat hypopigmented advancing halo. This case bears some clinical resemblance to that reported by Flock and Mailloux (1958), in which similar lesions occurred after BCG inoculation.

All the main peripheral nerve trunks were slightly enlarged and slightly harder than normal. A blister had recently appeared on the left great toe, giving place to an indolent ulcer.

All bacteriological examinations (of lesions, ear-lobes, and nasal mucosa) were negative. The Mantoux test was negative. The Fernández and Mitsuda reactions were strongly positive, the site ulcerating. The lepromin test had been performed but once before: it has been suggested that repeated microvaccinations with mycobacterial antigen might provoke a positive, lepromin – and possibly a positive Kveim reaction. The patient had not received BCG vaccination, which also might induce a positive Kveim reaction (Ellman and Andrews, 1959; Hoffbrand, 1963).

The serum proteins were found to be 9.5 g. per 100ml.: albumin 4.8 g., and globulin 4.7 g.

The patient continued to improve under standard treatment with dapsone, and was eventually discharged symptom-free. At no time did he develop any abnormalities in the eyes, glands, or chest. No suggestion of erythema nodosum appeared: one patient in four with sarcoidosis is likely to have erythema nodosum at some time (Greenberg *et al.*, 1964), but patients with abacillary borderline leprosy never experience erythema nodosum leprosum. No essential difference could be detected, clinically or pathologically, between this patient and the others in the group in whom the Kveim reaction was negative.

To those familiar with leprosy and its typical accompanying peripheral neuropathy, the diagnosis of this case is not in doubt. Local changes in the main peripheral nerve trunks of the limbs, principally at the well-known sites of predilection, are generally regarded as pathognomonic of leprosy, but attention should be drawn to the case of sarcoidosis reported by Garrod (1964) in which trigeminal neuralgia and transient peripheral neuritis were observed.

Histological examination of skin lesions discloses round-celled infiltration around and within the terminal nerve fibrils in the dermis – a picture not observed in sarcoidosis – and focalization around the skin adnexa superficially, with a more diffuse granulomatous infiltrate situated in the deeper layers.

The pathological interest of the positive Kveim reaction in a single case in the series lies in the 'specific' alteration of tissue reactivity associated in some way with a hyperergic response to a paucibacillary leprosy infection. This response was shown clinically by the sudden

appearance of multiple skin lesions of characteristic aspect. The significance of the positive Kveim reaction must remain a matter for conjecture.

The hope is expressed that the reporting of this isolated case may stimulate further research into the relation between leprosy and sarcoidosis.

SUMMARY

A patient with leprosy is reported in which the Kveim reaction was 'typically positive'. In ten other patients whose leprosy lesions also bore some resemblance to cutaneous lesions of sarcoidosis, the Kveim reaction was negative.

ACKNOWLEDGEMENTS

My thanks are due to Dr Patricia Bradstreet for supplying the Kveim antigen used; to Dr A. H. T. Robb-Smith for his help in reporting on the histology of the specimens sent to him; and to Dr S. O. Egwuatu, Chief Medical Officer, Ministry of Health, Eastern Nigeria, for permission to publish this article.

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Rifamycin SV in the Treatment of Lepromatous Leprosy

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Rifamycin SV belongs to a family of antibiotics, the rifamycins, isolated in 1958 by Sensi *et al.* and produced by *Streptomyces mediterranei*, *nova species* [23-25]. Their chemical structure is entirely different from that of any other known antibiotic [18].

The pharmacological characteristics of Rifamycin SV, as demonstrated in animals and humans, are described in details in numerous papers (e.g. [1, 2, 4, 8, 9, 10, 30]).

This antibiotic shows, *in vitro*, a marked antimicrobial activity against gram-positive microorganisms at 0.002-0.05 mcg/ml concentrations, while against gram-negative microorganisms much higher concentrations are required. Against human and bovine varieties of *Mycobacterium tuberculosis*, Rifamycin SV is active at concentrations around 0.05 mcg/ml, determining arrest of the bacterial multiplication, rapidly followed by marked bacteriocidal effects. Its *in vitro* activity against tubercle bacilli is higher than that of Streptomycin and PAS and comparable only to that of INH [7, 14, 22, 31, 32].

In human tuberculosis, very satisfactory results have been obtained by topical application [5, 12, 13, 15, 20, 26, 32]; by intramuscular administration limited results have been obtained [5, 12, 13], while treatment with intravenous infusions seems to be promising [5, 6, 29].

The possible usefulness of Rifamycin SV in the treatment of leprosy has been suggested by the similarities believed to exist between the causative agent of this disease and that of tuberculosis, by the high *in vitro* activity of the antibiotic against the latter and by its clinical effectiveness in certain tuberculous conditions.

A relatively high dosage was used in our trial because of the lack of experimental data on the basis of which any reasonable assumption as to the clinically effective dosage could be made, and also because the distribution studies carried out in animals have shown that the concentrations obtainable in the skin after systemic administration are somewhat low in comparison with those obtainable in other tissues [9, 10]. In this connection, however, it should be noted that appreciable and long-lasting levels of antibiotic have been experimentally demonstrated in superficial inflammatory foci such as the 'granuloma pouch' exudate [9]; a significance of this fact with reference to the distribution of Rifamycin SV in skin lepromatous lesions in man is possible, although clearly hypothetical on the basis of the available evidence.

The intramuscular route of administration was chosen, as it is known that when the antibiotic is administered orally, therapeutically active concentrations can be obtained in the biliary tract, but usually not in the systemic circulation, while after intramuscular administration they reach a peak after 1-2 hours and last for many hours, depending on the administered dose. A sodium salt aqueous solution was used throughout, containing polyvinylpyrrolidone for better local tolerance.

Some preliminary results obtained in our clinical trial have been previously reported [16, 17, 27]: an assessment of the results of this clinical trial after a longer period of treatment is the subject of the present paper.

In the meanwhile, the therapeutic interest of Rifamycin SV in the treatment of leprosy has also been confirmed by the observation of other clinical investigators [3, 11, 21].

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MATERIAL AND METHODS

Eleven leprosy patients in advanced stage were submitted to the trial. Eight of them presented small or medium-size disseminated or isolated tubercles; in the other three there was a moderate, diffused infiltration.

One patient (No. 7) showed lesions which could be clinically classified in the 'borderline' group. We realize that objection could be raised as to the inclusion in a therapeutic trial of patients suffering from borderline leprosy, as these subjects usually react very rapidly and satisfactorily to any specific treatment. However, the bacterial and biopsy findings demonstrated that this case had to be eventually classified as belonging to the lepromatous type, and thus its inclusion in the caselist appears entirely justified.

Nine of these patients had not received any previous anti-leprosy treatment; two had discontinued a previous treatment, and presented a relapse.

Ages ranged from 18 to 54 years; three patients were females. The evolution of the cases was checked by clinico-dermatological examinations carried out at least once a month; photographs of the patients were taken on these occasions.

Each month a bacterial index was determined on the mucus and on the skin lesions. From a quantitative standpoint, the amounts of alchohol-acid-fast bacilli (AAFB) found in the smears were evaluated with a score (number of pluses), varying from 0 to 4; 0 indicates no bacilli, (+) rare bacilli, and (++), (+++), and (++++) from moderate to very high amounts of bacilli.

The mucus index expresses the average of the scores attributed to the material collected from each nostril.

The skin lesion index was calculated as the average of the scores attributed to the material obtained from the most active skin lesions.

From a qualitative standpoint, the alcohol-acid-fast bacilli (AAFB) encountered were classified as follows: (T) = typical bacilli; (G) = granular bacilli.

The abbreviation (R), which accompanies sometimes this classification, indicates that the form in question was represented only by rare bacilli.

The cases were classified as improved when the bacterial index became less or the bacillary regression was predominant; as deteriorated when the bacterial index was, even slightly, higher.

Biopsies were taken at the beginning of treatment and at different time intervals. The slides were prepared with haematoxylin-eosin and with the Ziehl-Neelsen method.

The evaluation was based on the following criteria: modifications of the lepromatous infiltration, quantitative and qualitative bacterial variations.

The infiltration was considered improved in the presence of the regressive lepromatous structures described by Rath de Souza and Alayon ([19]) and characterized by Virchow's cells and increase of intracellular fat.

Concerning the quantitative bacteriology of the infiltrates, it was impossible to work out reliable bacterial indices; only a rough comparison of the quantities of bacilli found in the examined lesions, expressed as scores (number of pluses), was carried out.

Concerning the qualitative bacilloscopy, the incidence of bacillary degeneration was evaluated.

Haemoglobin determinations, blood counts and urinalyses were also carried out at various intervals.

The general treatment schedule was 1 daily Rifamycin SV dose of 1 g., divided into two 500 mg i.m. injections, 1 every 12 hours; in 2 cases a 0.5 g. daily dose was also tried during part of the treatment period. The duration of treatment was 5 months in 2 cases, 10 in 1, 11 in 1 case, and 12 in 7 cases.

For evaluating the results, a blind-examination was utilized, with the co-operation of leprosy specialists from the State Leprosy Department of São Paulo. Two evaluations were generally carried out: one after 6 months and one at the end of treatment.

RESULTS

Case records are of course available of the 11 leprosy patients but because the full details would absorb considerable space we here include 3 tables of results.

DISCUSSION

Clinically, all the cases could be considered as improved (Table 1). This improvement consisted in diminution of the diffused infiltration; disappearance of the diffused erythema, of the

TABLE I

Clinical results of treatment with Rifamycin SV in 11 cases of leprosy

Case No.	*Name*	*Duration of treatment (days)*	*Dose (g)*		*Clinical result*
			daily	*total* °	
1	L.C.	372	1	371	improved, with erythema nodosum
2	A.C.	370	1	368	improved, with erythema nodosum
3	J.B.	360	1	355	improved, with erythema nodosum
4	G.A.	147	0.5–1	89	improved
5	O.O.	154	0.5–1	103	improved
6	J.F.M.	335	1	335	improved
7	M.A.P.	342	1	340	improved
8	M.J.M.O.	357	1	350	improved
9	B.G.	352	1	352	improved
10	E.L.S.	377	1	371	improved
11	P.S.	284	1	279	improved

°In most cases, the total dose is slightly lower than the value which can be calculated from the duration of treatment and the daily dose owing to temporary discontinuance of treatment (cases No. 3 and 5) or to occasional omission of some injections.

papules and maculo-papules; flattening of the tubercles and nodules, in many instances with disappearance of the latter. The intensity and rapidity of the regressive phenomena, which were generally evident already in the first 15 days and reached a peak within the first three months of treatment, were particularly impressive. The improvements which occurred after this period were, in our opinion, not quite as rapid, due partly to the progressively reduced number of clinically active lesions and partly to the tendency of the lepromas to fibrosis, manifested in some patients.

Another interesting aspect is that of the reactive phenomena, of the erythema nodosum type, observed during the treatment.

Cases Nos. 1, 2, 3 and 10 presented erythema nodosum outbreaks of low intensity, which varied from one single nodule in one case to a limited number of cutaneous elements with regional adenopathy, fever and moderate deterioration of the general condition. None of these patients had to interrupt the treatment, except for case No. 3, in whom Rifamycin SV was temporarily discontinued (five days) because the patient presented reactive nodules on the injection site.

Case No. 7 showed a recurrent but transient exacerbation of the specific cutaneous lesions during treatment.

On the other hand, case No. 4 showed early in the first weeks of treatment an acute episode of erythrodermia and oedema of hands and feet ('pseudo-exacerbation'); following this episode and possibly owing to the antibiotic effect, his immuno-clinical condition changed radically, with a remarkable improvement of the prognosis. Unfortunately the treatment could not

TABLE 2

Results of bacilloscopic examination of mucus and skin lesions before and after treatment with Rifamycin SV in 11 cases of leprosy

	Mucus			*Lesion*		
Case No.	*Initial index*	*Final index*	*Conclusion*	*Initial index*	*Final index*	*Conclusion*
1	0	0	unchanged	2.6/RT,G	3.6/RT,G	deteriorated
2	3/T	0	improved	3/T,G	2/G	improved
3	0	0	unchanged	3.6/T,G	3.6/T,G	unchanged
4	1.5 T	0	improved	3/T,RG	1.6/RT,G	improved
5	3/T	0	improved	1.3/T,RG	2.3/T,G	deteriorated
6	1/G	0	improved	4/T,G	3/RT,G	improved
7	0	0	unchanged	3.3/RT,G	3/RT,G	unchanged
8	0	0	unchanged	3.1/RT,G	2.5/RT,G	improved
9	1.5/T,RG	0	improved	4/T,G	1.3/RT,G	improved
10	0	0	unchanged	2.5/T,G	2.3/RT,G	improved
11	2/T,RG	0	improved	2.1/T,G	1.5/RT,G	improved

R = Rare bacilli, T = Typical bacilli, G = Granular bacilli

be continued in this patient because he was emaciated and suffering from mega-oesophagus and refused to go on with the intramuscular injections.

With reference to *bacilloscopy*, an evaluation may be made on the results of the examination both of the nasal mucus and of the cutaneous lesions.

The mucus became bacterioscopically negative in six cases (Table 2); the remaining five cases, which were already negative before treatment, persisted unaltered.

The disappearance of the bacilli from the mucus was observed within 2 months in one case (No. 11), 4 months in three cases (No. 4, 5, 9), 9 months in one case (No. 5) and 11 months also in one case (No. 2).

Examination of the cutaneous lesions revealed that the bacilloscopic picture after treatment was improved in seven cases, unchanged in two, deteriorated in two, in comparison with the picture observed before treatment.

In this connection it should be noted that in both the cases classified as deteriorated the increase of the bacterial index was moderate; furthermore, in one of them (No. 1) a persistence and in the other (No. 5) a relative increase of the granular forms were observed.

The bacilloscopic changes did not always proceed in a parallel way with the remarkable clinical results obtained. One of the reasons for this fact could reside in the defective evaluation criteria, since the bacterial index does not allow a satisfactory estimate of the actual numbers of infecting bacilli.

On the other hand, keeping in mind the enormous quantity of bacilli per mm^3 of infected skin it seems clear that, even if the microorganisms were no longer viable after the antibiotic treatment, a long period of time would be necessary for completing the elimination of this bacterial material.

As far as the *histopathological examinations* are concerned (Table 3), all the 10 cases who were evaluated at the beginning of treatment and after different time intervals were improved according to the previously mentioned criteria.

With reference to the bacilloscopic evaluation

TABLE 3

Results of histopathological examination of skin lesions before and during treatment with Rifamycin SV in 10 cases of leprosy.*

Case No.	*Histopathological results*							*Conclusions*
	1st Biopsy	*2nd Biopsy*	*Months of treatment between the 2 Biopsies*	*Quantitative bacilloscopy*		*Qualitative bacilloscopy*		
				1st	*2nd*	*1st*	*2nd*	
1	Intense lepromatous infiltration	Leproma in regression	5	++++	+++	T/RG	RT/G	improved
2	Leproma	Intense lepromatous infiltration in regression	4	++++	++	T/RG	RT/G	improved
3	Intense lepromatous infiltration	Leproma in regression	4	++++	+++	T/RG	RT/G	improved
5	Intense lepromatous infiltration in regression	Moderate lepromatous infiltration in regression	5	++	+	T/RG	RT/G	improved
6	Moderate lepromatous infiltration in regression	Moderate lepromatous infiltration in regression	5	+++	++	G	G	improved
7	Moderate lepromatous infiltration	Moderate lepromatous infiltration in regression	12	++++	++	T/RG	RT/G	improved
8	Intense lepromatous infiltration	Moderate lepromatous infiltration in regression	12	+++	+	T/RG	RT/G	improved
9	Leproma	Leproma in regression	$4\frac{1}{2}$	++++	++++	T/RG	RT/G	improved
10	Intense lepromatous infiltration	Intense lepromatous infiltration in regression	11	++++	+++	T/RG	RT/G	improved
11	Intense lepromatous infiltration	Moderate lepromatous infiltration in regression	8	+++	+	T/RG	RT/G	improved

*Carried out by Dr. P. H. de Mello, Head of the Pathology Division, Department of Leprosy Prophylaxis, São Paulo.

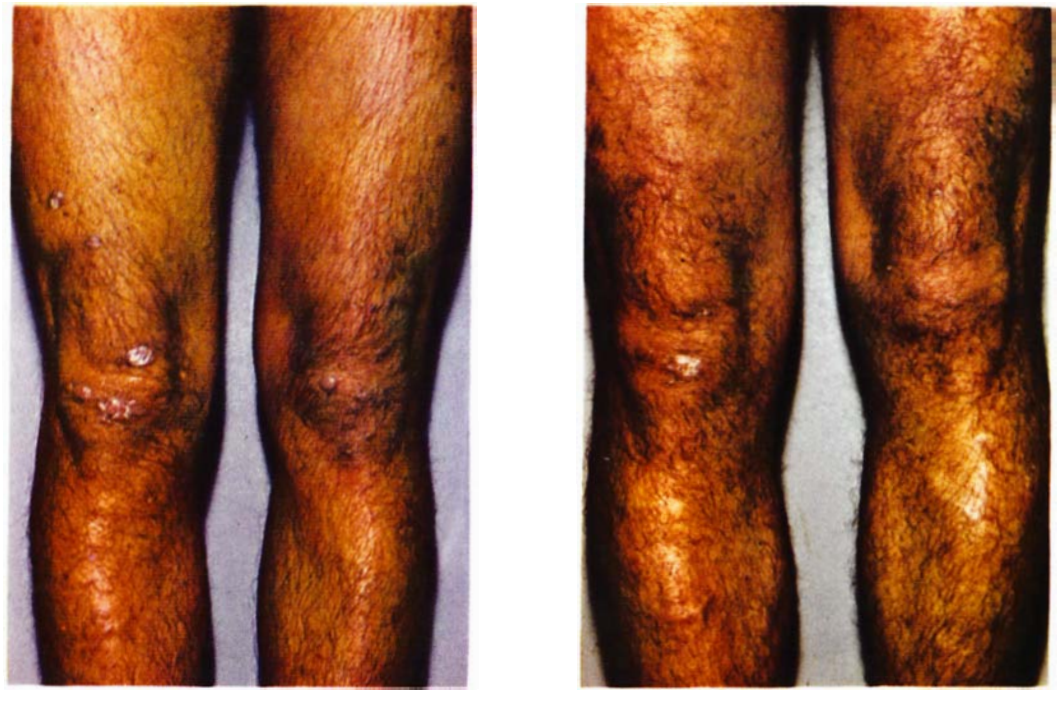

FIG 1 Case No. 1 at the beginning of treatment (a) and after 372 days of treatment (b).

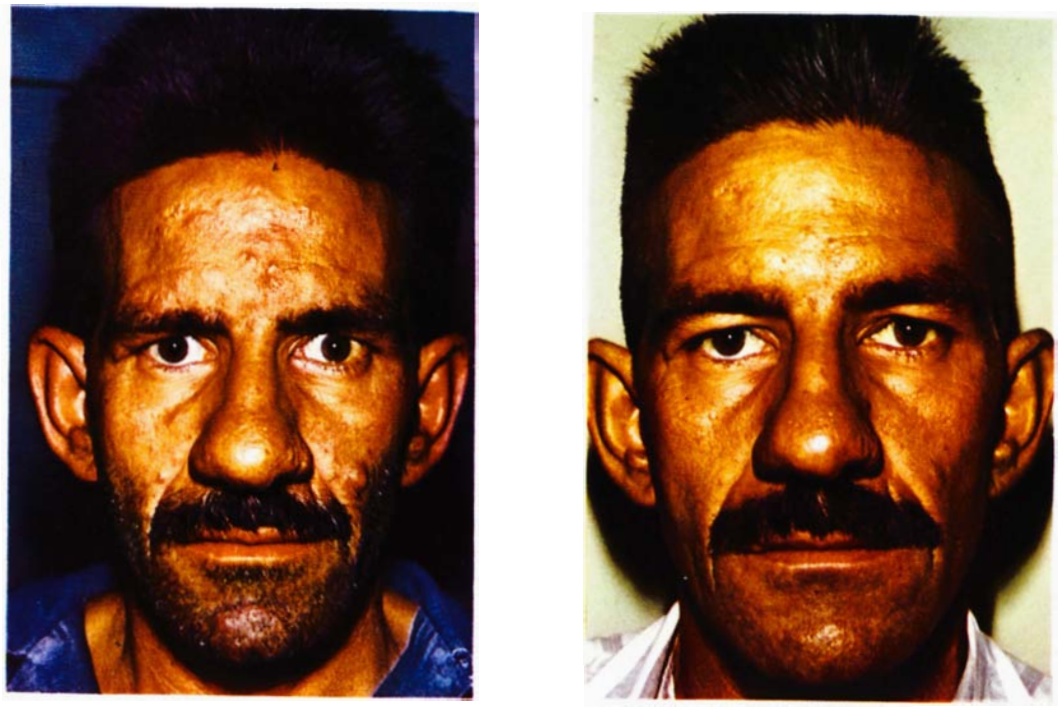

FIG 2 Case No. 2, at the beginning of treatment (a) and after 370 days of treatment (b).

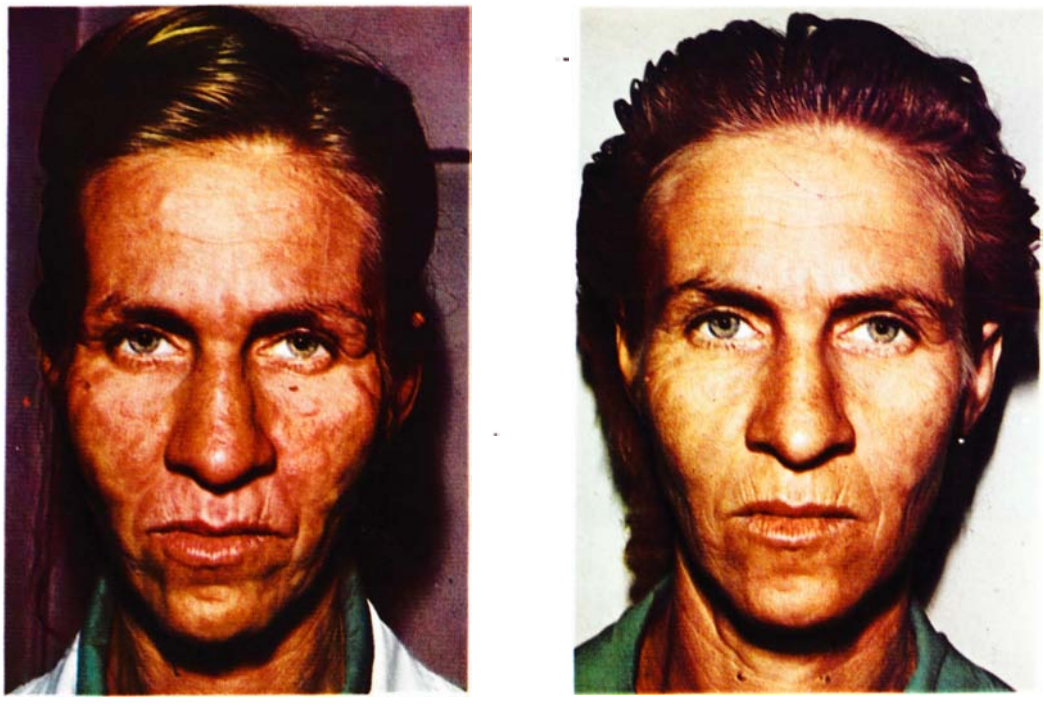

FIG 3 Case No. 7, at the beginning of treatment (a) and after 342 days of treatment (b).

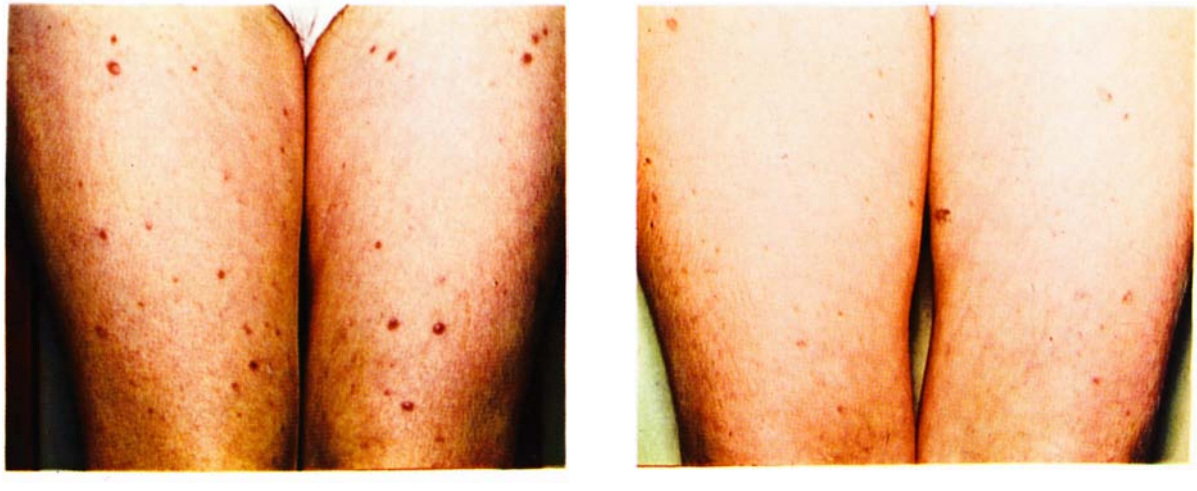

FIG 4 Case No. 10, at the beginning of treatment (a) and after 377 days of treatment (b).

of the biopsy specimens it should be noted, however, that its value appears to be clearly limited: in fact, the histopathological examinations were performed only at considerable intervals of time and thus could not give an exact estimation of the structural bacillary alterations due to the therapeutic influences. This seems to be especially true in consideration of the great number of lesions presented by each patient and of the possibility of a bacillary regression independent of any treatment.

It may therefore be stated that the available laboratory methods for evaluating the efficacy of an anti-leprosy treatment are still not very reliable. This is the reason why it seems preferable to rely more on the clinical results obtained and to attribute only a limited value to the bacilloscopic and histopathological data, even if they were favourable in the majority of the cases.

A further point which deserves a specific discussion *is tolerance*. The intramuscular administration of 500 mg. of Rifamycin SV every 12 hours was generally well tolerated: most patients received more than 350 g. of antibiotic.

One case (No. 8) presented itching, which started around the injection site and then extended to other areas. This symptom persisted for 2 months, was controlled by antihistaminics, and subsequently disappeared although the antibiotic treatment had not been interrupted.

Another case (No. 2) presented an urticarial rash with itching which subsided spontaneously after one month, without discontinuing the treatment. We have no reasons to believe that the symptoms presented by these two patients were due to the drug.

Two cases (No. 5 and 11) presented jaundice and gastric troubles with choluria and stained stools; neither fever, nor liver enlargement, nor erythema nodosum was noticed. The symptoms regressed within two weeks after discontinuance of the treatment and did not recur when the treatment was resumed.

In case (No. 5) the liver function tests (Lugol, Kunkel, thymol, Hanger and bilirubin serum levels) were positive. It is known that these tests can be positive in leprosy, even without jaundice; however, bilirubin serum levels (direct = 1.6; indirect = 2.4; total = 4 mg/ml) suggested the diagnosis of haemolytic jaundice.

On the other hand, similar symptoms have been observed with other anti-leprosy medications, such as sulphones, antibiotics or sulphonamides, regressing after discontinuance of the treatment and not recurring when the same treatment was resumed.

All cases, after 4 months of treatment, showed some hardening and slight pain at the injection site.

However, discontinuation of the treatment, was never required. No abscess occurred in any case.

An overall evaluation of the results obtained in the eleven patients reported here, who were all suffering from severe and long-lasting lepromatous leprosy, indicates that treatment with Rifamycin SV at the daily dose of 1 g. can be considered both effective and well tolerated. In this connection, it may be worthy of mention that other independent trials carried out by us on outpatients ([28]) and by other investigators who confirmed our results ([3, 21]) point to the possibility of adopting lower daily dosages, around 500 mg. daily. Furthermore, the usual promptness of the clinical improvement even in advanced cases suggests the possible interest of a short-term course of the antibiotic in the initial treatment of recent cases.

CONCLUSIONS

(*a*) Rifamycin SV shows a remarkable effectiveness in the treatment of leprosy. The very favourable clinical results obtained open interesting perspectives in this field.

(*b*) The histopathological and bacilloscopic results do not always proceed in a parallel way with the clinical evolution.

(*c*) The absence of toxic effects, and of any other side effects which could be definitely attributed to the drug, shows that Rifamycin SV is excellently tolerated, except for some local reaction at the injection site after the fourth month of treatment. The incidence of reactive phenomena of the erythema nodosum type is moderate.

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SUMMARY

Eleven cases of lepromatous leprosy, in advanced stages of the disease, were treated for periods up to one year with Rifamycin SV. All the cases were submitted to clinical, bacilloscopic and histopathological examinations.

Tolerance was excellent and the clinical results obtained, which were evident since the first weeks of treatment, were considered satisfactory.

Rifamycin SV has shown to possess a remarkable effectiveness in the treatment of leprosy.

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Leprosy in Eastern Nigeria - Reflections on Cases Diagnosed at Uzuakoli 1959-64

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The anti-leprosy campaign in Eastern Nigeria has been the subject of reports by Lowe and Smith (1949), Lowe (1952), Davey (1957) and others, and the results of investigations undertaken in this Unit in furtherance of the general objectives of the campaign have been published from time to time. The pattern of leprosy as a disease most difficult to eradicate from a tropical country is now emerging. Control measures and comprehensive treatment facilities together result at first in a dramatic fall in the total number of patients and a notable reduction in the number of new cases diagnosed annually. Thereafter, control seems to become rather less effective, new cases tending to counterbalance discharges, and eradication of the disease is seen to be protracted as a task and remote as a goal.

During the period August, 1959, to December, 1964, 1015 persons were diagnosed at Uzuakoli as having leprosy. This figure represents about half of those who presented themselves with signs they considered indicative of the disease, or nearly 30% of the total number of new patients with leprosy diagnosed during this period in the Uzuakoli leprosy control area (3477), the remainder having been seen at the district clinics. This paper will examine in detail only the 1015 patients diagnosed at Uzuakoli itself.

No trends are discernible in the total number of new patients diagnosed from year to year, or in the proportions of the different varieties of leprosy, as the table in next column indicates.

	Adults			*Children*			*Total*
	Lepro-matous	*Tuber-culoid*	*Uncharacteristic*	*Lepro-matous*	*Tuber-culoid*	*Uncharacteristic*	
1959	59	489	32	6	16	1	603
1960	61	414	53	12	51	12	603
1961	73	331	31	8	43	17	503
1962	59	435	17	11	40	25	587
1963	35	552	29	2	64	5	687
1964	63	350	28	8	41	4	494
	350	2571	190	47	255	64	3477
		3111			366		

Totals:
Lepromatous 397 patients, 11.4%
Tuberculoid 2826 ,, 81.3%
Uncharacteristic 254 ,, 7.3%

N.B. Annual returns (U.N.I.C.E.F.) are made according to the above categories.

Reasons given for coming to the Diagnostic Clinic

Although it may be difficult to discover the real reason, or combination of reasons, that brought the individual patient to the point of presenting himself at the Diagnostic Clinic, the following were given, in the approximate order of frequency: lesions that failed to disappear with time or to show improvement on the application of indigenous irritants or Western caustics; appearance of new lesions or extension of existing lesions; development of nodulation in unnoticed macular lepromatous disease; nerve pain; acute exacerbation; dermatitis from self-medication; ulceration of anaesthetic extremities; acute foot-drop, lagophthalmos, facial paralysis, or sudden paresis of the intrinsic muscles of the hand; epistaxis and nasal obstruction. Pressure to seek medical advice might be exerted on the patient by near relatives, neighbours or local government officials.

Delay in seeking treatment

In general, the more obvious and the more easily recognizable the lesion, the shorter the

delay in seeking help. Thus, frank tuberculoid lesions of the uncovered skin (especially the face and forearms) may bring the patient to the Diagnostic Clinic within a few months, whereas the generalized macular rash of lepromatous leprosy may remain unnoticed for several years. In fact, the commonest clinical finding in lepromatous leprosy nowadays in this district is a coalescent macular rash that leaves unaffected only small areas in the groins, the sacral region, the axillae and the scalp. In the ordinary contacts of everyday life in village and market-place, these patients pass for the lighter-hued, and it may be only the occurrence of nodulation or of neuropathic ulceration that brings the patient for diagnosis and treatment.

Of the 1015 patients in whom leprosy was diagnosed, 727 gave an indication of the time elapsing since they noticed some symptom or sign which they then or since attributed to leprosy: in 204 bacteriologically positive patients the average was 22 months, while in patients with tuberculoid or indeterminate lesions the average was 15 months. These figures are underestimates, certainly by several months and possibly by years. They have a bearing, however, on the age of onset of leprosy in Nigeria, and indicate that the infective contact or contacts must antedate the coming of the patient for diagnosis by the variably long latent period *plus* the (underestimated) average period of delay in seeking medical advice.

Epidemiological considerations

The epidemiological implications of these facts will not escape notice: not only do bacilliferous patients disseminate *Myco. leprae* for many months among their entourage, but the identification of the source case of many new infections may be quite impossible.

Another disquieting feature is that an educated generation is arising that fails to recognize the less obvious stigmata of leprosy. The wily old chiefs and headmen detected and correctly appraised an early macular rash as 'the mother of the bad leprosy', whereas their modern counterparts do not see, or do not see the significance of, the lesions that are barely visible or recognizable.

The urgent and practical question arises: is a method of case-finding adequate that depends ultimately and predominantly on non-medical suspicion? By this method and ancillary measures, the prevalence of the disease can be reduced – possibly below a hypothetical critical level – but present experiences in Eastern Nigeria do not foster any sanguine hopes of complete control and eventual eradication unless a more effective and practicable method of case-finding can be utilized in the field.

Bacterioscopic examination

All patients presenting themselves at the Diagnostic Clinic are subjected to examination of material by the slitsmear method obtained from six or eight sites, including the ear-lobes and nasal mucosa and the suspected lesion or lesions. In the majority of patients, the findings, whether positive or negative, served as confirmatory evidence of the clinical diagnosis.

In certain cases, however, the examination was of more positive value; e.g., in demonstrating the extent and intensity of the infection in lepromatous leprosy; in revealing bacilli in patients provisionally classified as having indeterminate leprosy, which was in reality macular lepromatous leprosy; in showing bacilli, sometimes numerous and sometimes in clumps, in cases of tuberculoid leprosy in exacerbation; in indicating the intensity of bacillary infection in certain cases of borderline leprosy.

The following table indicates the numbers and proportion of patients with bacilli at one or more sites, as revealed by microscopical examination of material obtained by the slit-smear standard technique.

	Total number	*No. with bacilli*	% *Bacteriologically positive*
Lepromatous	145	139	96
Borderline	153	100	65
Tuberculoid	673	12	2
Indeterminate	44	9	20
	1015	260	26

Of the 6 patients with bacteriologically negative lepromatous disease, 5 were in children (ages: 1, 10, 11, 11, 12) with multiple ill-defined macular lesions that in Africa may suddenly become highly positive.

Of the 139 patients with bacteriologically positive lepromatous leprosy, in no fewer than 122 all the 6 or 8 sites smeared were positive; in 3, only one site was positive (ear-lobes 2, nasal mucosa 1), and in the remaining 9, two sites were positive (skin 8, ear-lobes 6, nasal mucosa 4). In most patients, there was no significant difference at the several sites smeared either in the absolute height of the Bacterial Index or in the Morphological Index (the proportion of morphologically normal forms). Where there was a marked difference, the skin showed the highest Index in 20 patients, the nasal mucosa in 18, and the ear-lobes in 17.

With expert techniques, examination of material from the contralateral ear lobe or the contralateral septal mucosa does not add appreciably to the precision of diagnosis of the assessment of the Bacterial Index. If circumstances dictated the minimum number of such examinations, then a single examination should be made from material taken from the most active edge of a recent lesion; the second most valuable examination would be of material from an ear-lobe, and the third of material from the septal mucosa.

Based on Dharmendra's notation (maximum 4.0), the following table indicates the Bacterial Index in the patients with lepromatous or borderline disease:

Average Bacterial Index	*Lepromatous Leprosy*	*Borderline Leprosy*
0 – 0.9	27	74
1 – 1.9	29	20
2 – 2.9	40	6
3 – 4.0	49	0
	145	100
Average:	2.25	0.76

Of 666 sites smeared in 100 patients with borderline leprosy, 431 showed bacilli as follows: very scanty 33, scanty 127, 1 + 144, 2 + 89, 3 + 37 and 4 + 1.

The examination of the morphology of individual *Myco. leprae* in these initial routine smears was of interest. Sometimes the presence of a high proportion of grossly degenerate bacilli might indicate that treatment had been taken clandestinely, but the percentage of normal forms in the patient who had never had treatment might vary within wide limits, i.e. from 0 to 100%. There may be an ebb and flow in the susceptibility of *Myco. leprae* to inimical factors, or in the intensity of these factors, resulting in changes in the proportion of morphologically normal forms of *Myco. leprae* encountered in routine smears made in untreated patients.

Seasonal variation

Attendances at the Diagnostic Clinic month by month show no great differences likely to be dependent on season, the farming calendar, or on any other discoverable factor. Taking into account the variable delay in seeking treatment, there is no indication that the onset of leprosy or the occurrence of exacerbation is associated with changes in temperature or humidity, as has been suspected elsewhere.

Contacts

The time-honoured concept of 'close and intimate contact' long held to be necessary if leprosy is to be contracted, cannot be deduced or supported from a study of the series under review. In only 66 instances out of 1015 (6.5%) was any contact admitted or suspected. In a district that has been generously provided with treatment facilities for some years past, and in which the great majority of those suffering from active leprosy are probably under treatment, this low proportion admitting contact is probably accurate. The degree of contact varied from the intimate (mother-and-child) to the problematically remote and infrequent (neighbour in the same compound). The suspected or presumed index case was usually abacilliferous to standard methods of examination, and in most cases had probably been so always. The paucity of known patients arising in the families of highly positive patients, and the numbers of new patients in which no such sources are implicated, are alike remarkable. There may be an unsuspected source of infection, or an unrecognized bacilliferous case, or even possibly an extra-human '*réservoir de virus*'.

The epidemiological and practical importance of these considerations needs no emphasis. In particular, the regular examination of close contacts of a bacilliferous index patient may be economically sound, but it will not lead to the discovery of more than a small proportion of patients with leprosy in such a community and at such a stage in the history of the endemic.

The value of yaws survey and resurveys

It has been the practice to attach an auxiliary versed in leprosy, to itinerant yaws teams engaged in whole-population surveys and resurveys. The value of this procedure varies with the experience of the auxiliary and the thoroughness he displays in examination, and also with the state of the anti-leprosy campaign in the district concerned. Thus, in the neighbourhood of Uzuakoli, yaws teams directed to the Diagnostic Clinic only 16 patients suspected of having leprosy, and half of these proved to be either ex-patients whose lesions were residual or persons whose lesions had regressed spontaneously. In the remoter southern districts, however, where a greater number of patients with active leprosy remained undiagnosed and untreated, 70 patients needing treatment for leprosy were in one area directed to the district clinics.

Treatment recommended for the patients

The organisation of the anti-leprosy campaign provides for treatment as follows: as in-patients at Uzuakoli Settlement; at district leprosy clinics, the patient residing either in his own home or in a segregation village adjacent to the clinic; treatment prescribed from Uzuakoli, the patient coming for periodical clinical and bacteriological examination ('confidential treatment').

The choice of the appropriate course for the individual patient depends on medical and social factors, particularly the contagiousness of the patient and the home circumstances. A well-run Welfare Service, with indigenous auxiliaries attached to each group of district clinics, provides all relevant information concerning social factors.

Patients with the more contagious or potentially serious forms of leprosy (lepromatous or borderline) are advised to enter Uzuakoli Settlement; the same advice is given to those undergoing acute exacerbation of any form of leprosy, acute neuritis, any eye complication or paresis. Children are frequently admitted on social rather than on strictly medical grounds, so that they are spared the mental suffering of village ostracism and exclusion from school because of a leprosy infection, often relatively benign. Some patients are admitted because of neuropathic ulceration, or the need for surgical intervention, or the provision of footwear, after a sequestrectomy for example.

The accompanying table indicates the disposal of the 1015 patients, analysed according to the type of leprosy from which they were suffering.

	Lepromatous	*Borderline*	*Tuberculoid*	*Indeterminate*	*Total*
Uzuakoli Settlement	130	131	217	19	497
District Clinics	12	19	292	19	342
'Confidential' treatment	1	3	43	5	52
No treatment advised	2	—	121	1	124
	145	153	673	44	1015

'*No treatment advised*'

In no fewer than 124 patients in this series, no treatment was advised because their lesions were inactive. They had come because of pressure from relatives, neighbours or officials, or because of appearances they mistook for evidence of activity. More than half did not know how long they had had the quiescent leprosy lesions. Most of the 57 patients who had some idea of the duration of the leprosy lesions fall into two main categories: those with completely inactive residual lesions they knew to have been present for several years (24 patients), and those with early lesions regressing spontaneously (26 patients). The history and clinical indications were imprecise in the remaining seven patients. Knowledge of the natural history of the disease in West Africa and of the probable consequences of the decision not to treat is a *sine qua non* in dealing with these patients.

Neuropathic ulceration

Ulceration of the extremities, usually the lower, sometimes the upper, and sometimes both lower and upper, was present in 93 patients when they came to the Diagnostic Clinic. Some ulcers were obviously of long standing, whereas others were of recent appearance and had made the patient or his neighbours realize that something was amiss.

While secretion from ulcers rarely contains acidfast organisms, neuropathic ulceration

occurred in 34 patients whose skin smears were bacteriologically positive: 12 out of 14 patients with lepromatous leprosy, 19 out of 25 with borderline, and three out of 54 with tuberculoid.

SUMMARY

To judge from experience during the past five years at Uzuakoli, the anti-leprosy campaign in Eastern Nigeria has entered a difficult phase in which many sporadic cases of leprosy are still appearing. The reasons for this state of affairs and its epidemiological implications are considered.

Certain clinical and bacterioscopic aspects of the problem are recorded, and recommendations made regarding case-finding, slit-smear examination, etc.

ACKNOWLEDGEMENTS

I wish here to pay tribute to all those who have assisted in whatever capacity in the anti-leprosy campaign in Eastern Nigeria. My thanks are due to Dr S. O. Egwuatu, Chief Medical Officer, Ministry of Health, Eastern Nigeria, for permission to publish this article.

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Leprosy in Cuba

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(Original in Spanish, translated by Dr J. Ross Innes)

Cuba is a long narrow island which is situated in the sea of the Antilles between North and South America, at the entrance to the Gulf of Mexico, and sited in the torrid zone and between 19° 48′ and 23° 13′ of north latitude and 74° 08′ and 84° 57′ of longitude, west.

The lands nearest to Cuba are the United States of North America at 180 km., Mexico at 210 km., Haiti at 77 km., and Jamaica at 140 km. Cuba has a territorial extent of 114,524 square km. 1200 km., long and an average breadth of 100 km. The present population consists of 7,390,222 inhabitants.

The nation is formed of ethnic groups of white, black, mixed, and yellow races, chiefly.

Cuba has a hot tropical climate and according to Prof. S. Massip, 'The climate is determined by the neighbourhood of the mass of North America which restrains the effect of insularity. The temperatures and the winds are influenced by the high and low temperatures and the different pressures which appear in the continent. Normally without storms there is easy passage for the winds, and the great stabilizing influence of the sea attenuates the climatic variations.

The average annual temperature of Cuba is 25°C and the winter average is 21°C with a range of 10°C to 22°C. There are exceptionally low temperatures in some regions of the island when 0°C has been recorded. The summer average is 27°C, with fluctuations between 19°C and 36°C, and in a very rare case 36°C has been reported, as at Sagua de Tánamo in Oriente province in 1927.

We have only two seasons, the dry from December to April, and the wet from May to November.

The annual average precipitation is 1.40 m., 75% of it in the rainy season. The western region registers the most, and the south coast of Oriente province maintains the record for dryness.

The average relative humidity is 72%.

The average atmospheric pressure is 762 mm. The maximum is in January with 764 mm., and the minimum in October with 760 mm.

Cuba is an independent sovereign state. Its territorial divisions are 6 departments called provinces, each subdivided into municipalities and these again into wards.

There are 2 hospitals completely dedicated to the treatment of leprosy (1) Hospital of San Lázaro in Havana Province, with 300 beds; (2) the sanatorium of San Luis de Jagua in Oriente Province, with 400 beds.

Properly registered and supervised there exist in Cuba 4,020 patients suffering from leprosy.

With dispensary treatment there exist 3,470 patients, and there are 550 patients hospitalized.

There are 10 dermatological centres throughout the provinces. There is 1 at Pinar del Rio, 3 at Havana, 1 at Matanzas, 1 at Las Villas, 1 at Camagüey, and 3 in Oriente. The endemic leprosy is spread over the whole country.

Ages

Of the 4,020 patients there are 2.51% at age 0 to 14 years, and 97.49% at ages of 15 years and more. Most are met with at 20 years of age and more. There is an increase of incidence from 20 years until the third decade of life is reached, when the maximum incidence is found. The curve descends slowly at 32 years.

In studies carried out at the National Sanatorium of 'San Luis de Jagua' among 2,219 patients who had passed through it since its opening in 1944 we have been able to establish that more than 65% of the patients were included between age groups 20 and 35 years. The average age is 28.5.

Races

The white race was 56.68%, the black 15.45%, the mixed 27.33% and the yellow 0.54%. The racial percentages are approximately similar to those which exist in the healthy population.

Sex

Males were 59.24% and females 40.76%. These percentages are also approximately equal to those in the general population of the country, except for a slight preponderance of males in the general population.

Civil state

Unmarried were 39.48%, married were 52.89%, widow or widower 5.81%, divorced 1.82%. In this it will be noted that the percentage for unmarried is less than for the married. This throws into relief the opinion of some authors who think that in the affected population a greater number of unmarried exist. They attribute this to the terror which leprosy inspires, and above all the deformities caused sometimes by leprosy. This is the chief cause of their being rejected by the opposite sex. In our opinion it is not certain. The married predominate in official records of patients, and the unmarried predominate in records of the hospitalized. The reason is obvious. The married cannot abandon the hearth and leave the wife and children unprotected. They only come to hospital when there is no other remedy. The position of the unmarried is different. In most cases they do not have home obligations, and the hospital represents a welcome relief, as well as securing them health of body. It spiritually re-animates them, and frees them from a sea of misunderstandings among which they live.

Nationality

Cubans were 95.67% and foreigners 4.53%. We encountered leprosy among foreigners mostly among Spaniards, Chinese, Haitians, and Jamaicans, but these are the nucleus of those foreigners settled in Cuba.

Occupations

Farmers, wives and children	48.01%
Unemployed	8.35%
Housework	5.31%
Clerks	3.88%
Small traders	3.53%
Washerwomen	3.32%
Labourers	1.86%
Drivers, carters, and muleteers	1.54%

We wish to point out those occupations where the incidence is over 1%, also to explain those called 'small traders' are really ambulant vendors or bosses of humble establishments.

Clinical Forms

The lepromatous form occurred clinically in 44.43%, the tuberculoid in 24.01%, the indeterminate in 19.29%, the dimorphous in 0.32%, the unclassified in 12.04%. Patients under control were 87.30%, and uncontrolled 12.70%. At the present time we have under medical control 87.30% of all our patients. The terms 'under control' or 'controlled' mean that we were able to examine the patient and give him the treatment personally at least once every 60 days. When a patient comes to the dermatological clinic, after studying and examining the case he is given the medicaments which have to be used during 2 months, after previously completing all necessary laboratory examinations and tests. He is advised on the regularity to be followed and summoned to a return visit at the end of a given time. If he fails to do that, then he enters a group which we call 'tardy in treatment' and his file is delivered to responsible special auxiliaries, so that he may be visited in his domicile so as to find out the cause which has made him interrupt treatment, solve the difficulties behind the delay and bring him back to active and regular control.

When a patient has too much invalidism from disease or age and cannot attend the centre he is visited in his own home, and examined and treated, with his contacts. So we do with urban patients and contacts, and so maintain control.

Those who live in rural zones are visited by leprologists in their own homes. We have thus established a regular calendar of visits and we go regularly to the rural foci every 6 months. We carry out the rural work in conjunction with the doctors of the rural medical service, who in a total of 47 function in the whole national territory. Taking as base the hospital which is sited nearest the focus, the special auxiliaries in charge of the zone visit the focus, previously calling the patients, those living with them, and contacts together to the hospital on a chosen

date for examination by the leprologist and the general doctors resident in the hospital. Every patient is discussed with the general doctors. The necessary laboratory examinations and tests are carried out, the indicated drugs are given, and these patients continue directly under the control of the doctors of the rural hospital, to which the patient will return, to be visited by the leprologist at the end of 6 months, if not previously summoned. The patients who have not been able to attend the rural hospital are visited in their own homes, just as we do with the patients of urban zones. The mobile team which we have available for these tasks of each region consists of a jeep, a leprologist, and a special auxiliary.

SUMMARY

1. Leprosy is found uniformly spread through all the national territory in direct relation to the number of inhabitants in each province;

2. 3,470 patients receive outpatient treatment and 550 are hospitalized;

3. Minors of 14 years of age make up 3.51% of total number of patients;

4. Lepromatous rate of the Cuban leprosy patients is 44.43%;

5. We have under therapeutic control 87.30% of the total;

6. We can estimate approximately 6,000 leprosy patients existing in Cuba.

APPENDIX

Leprosy Patients in Cuba by Provinces

PROVINCE	*Area in Sq. Km.*	*Population*	*Density per Sq. Km.*	*Total of Patients*	*Prevalence per 1000 population*	*Patients per 100 Sq. Km.*	*Percentage of the total of patients*
Pinar del Rio	13,500	518,496	38.4	109	0.21	0.81	2.71
Habana	8,221	2,093,597	254.7	1,097	0.52	13.34	27.29
Matanzas	8,444	455,796	54.0	158	0.35	1.87	3.93
Las Villas	21,411	1,240,359	57.9	501	0.40	2.34	12.46
Camagüey	26,346	795,864	30.2	475	0.60	1.80	11.82
Oriente	36,602	2,286,116	62.4	1,680	0.74	4.59	41.79
CUBA	114,524	7,390,228	64.5	4,020	0.54	3.51	100.00

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Chemoprophylaxis with DDS, mainly in children: A short trial

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The Eighth International Congress of Leprology at Rio de Janeiro in 1963, stressed the importance of chemoprophylactic trials, and we report our experiences in an African 'milieu' facing the difficulties of effective protection of children from the infection.

We first tried chemoprophylaxis on a limited scale in two 'homes for healthy children of leprosy patients'. We do not report results in detail in this paper, but can say that the results were encouraging, except for one person.

In 1960 we began a larger scheme at our main leprosarium (Jamba). As no unfavourable results were noted, we progressively extended the scheme to 3 other institutions. So far the experiment covers only a few years and we hope to report fuller results after several more years.

In the present trial there were 97 adult leprosy patients who had 864 children as contacts: ('child' means 15 years of age or less). There was a loss of 161 children from the chemoprophylaxis trial, mainly because their parents left the institution. Only 9 children stayed in the institutions but they are not being given drug prophylaxis.

In spite of this, there are at present 703 children in our 4 leprosy institutions who are taking chemoprophylaxis, of whom 615 attend regularly and 88 irregularly. The total patient population of the institutions is about 1400.

The duration of the prophylaxis varies according to time of initiation of the drug prophylaxis. Thus in Jamba 363 persons have had $3\frac{1}{4}$ years of chemoprophylaxis, in Catala 141 have had 3 years, in Caluquembe 115 have had $2\frac{1}{4}$ years, and in Cavangu 245 children have had 2 years.

Age of onset of dosage has been 5 months to 12 months for infants, advantage being taken of the prophylactic effect of DDS in maternal milk and that giving of tablets to small children could be avoided. About 2 to 5 years 50 mgm. orally twice a week was given and from June 1964 reduced to once a week, the dosage being:

50 mgm. once a week for children up to 3 years of age.
100 mgm. ,, ,, ,, ,, the rest of the children.
200 mgm. ,, ,, ,, ,, adults.

Medical observations were simple and included recording of weight, haemoglobin level, and the lepromin reaction.

RESULTS

Not a single leprosy manifestation has appeared in the contacts up to end of November 1964. There was only one doubtful case who might already have been a leprosy infection but who disappeared from observation and later was reported to have died at home.

Toxic effects have been minimal.

BENEFICIAL EFFECTS

(1) incidence of other illnesses became less; (2) better general health; (3) lack of fear of leprosy and lack of psychological dread of separation from parents because the children could live a normal family life.

Attitude of Parents was good, with great satisfaction at this prophylaxis. They easily understood the principle of chemoprophylaxis. Co-operation has been very good.

DISCUSSION

We did not have a control group because of technical and psychological difficulties, and propose to use the experiences of former years as control. Thus in the years from 1947 to 1964

at least 360 children were treated for leprosy, and 178 (or 49.2%) had parents or relatives who suffered from leprosy. Of apparently healthy children there were in the past an appreciable proportion who developed leprosy later. This has ceased under the prophylactic regime.

SUMMARY

The dramatic disappearance of leprosy incidence in healthy children living in contact with leprosy patients, the absence of notable toxic effects, the additional benefits, together with the low price of DDS, makes chemoprophylaxis a simple and easy method of prevention of the more susceptible human group. The results encourages a wide use of this method.

ACKNOWLEDGEMENTS

Thanks to the 4 nurses directing the 4 institutions for their co-operation and help in preparation of much of the material of this report, namely Miss Alice Moreira, Miss Hanni Sigg, Miss Elsi Guildimann, and Miss Gandhi Marinova.

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Six Years Follow-up of Diphenylthiourea Treatment

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In 1957 lepromatous patients were selected for a trial of diphenylthiourea (DPT or Ciba 1906) and its effects were compared with the results obtained with diamino-diphenyl-sulphone (DDS). The results were analysed at the end of two years when the project was stopped and all cases were placed on DDS. The subsequent history of the cases were investigated after six years (i.e. in 1963). The results after two years and six years are here reported.

METHOD

We selected 30 lepromatous patients and formed 3 equal groups, taking into account (1) bacillary index, (2) degree of lepromatous involvement, (3) history of erythema nodosum leprosum (ENL), (4) sex, and (5) weight.
Patients in group A received DDS only.
Patients in group B received DPT only.
Patients in group C received both DDS and DPT.

Dosage

The dose of DDS was 200 mgm once daily for 6 days per week. (In 1959 the maximum dose of DDS was reduced to 100 mgm. daily).

The dose of DPT was 50 mgm per kilo of body weight given in one dose. The tablets contained 500 mgm so the dosage varied from 5 to 8 tablets daily.

The patient on combined treatment received full doses of each drug.

Examinations

(1) Clinical: every two months.
(2) Skin smears: every two months from 4 sites.
(3) Haemoglobin estimations: every two months.
(4) Reactions: daily observation when reactions occurred.

Dropped from Project

Group A One patient died.
Group B One patient died, one developed pulmonary tuberculosis and one absconded.
Group C One patient died, one transferred within the first two years and one died in the 4th year.

Results after second year

Patients are photographed at the beginning and end of each project and this is of help in assessing the changes in a patient. Patients are then assessed as e.g. improved, markedly improved, stationary or worse. In an attempt to make the changes statistically clearer we use what we call a 'Lesion Index'. In this the infiltrations, the maculae or plaques, and the nodules or papules are graded according to severity, from 0 to 3 in three sites, i.e. in the face, trunk and limbs. The maximum severity for one patient would then be 9.

The results after two years were:

TABLE

Lesion Indices after two years of treatment

Group	*Number of Cases Remaining in Project*	*Infiltration Index*		*Macules or Plaques Index*		*Nodule or Papule Index*		*Total Lesion Index*	
		Before	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*
A. DDS only	9	36	20	9	0	6	4	51	24
B. DPT only	7	30	14	9	1	0	0	39	15
C. DDS and DPT	8	31	23	8	5	3	2	42	30

From this it is obvious that DDS alone and also DPT alone have a definite effect on the clinical lesions. It also seems that combining DPT with DDS is not so good as either DDS or DPT alone.

Reactions

Reactions in the form of erythema nodosum leprosum, or neuritis or acute swelling of lesions occurred in all groups. However, they were much less in the group which received no DDS i.e. Group B.

Bacteriology

As there is a monthly fluctuation in the bacteriological index of all groups (and this applies to all our investigation projects) we took the bacterial smears for two months at the beginning and two months at the end of the second year. The results were:

Group A. (9 cases) Bacterial Index dropped from 17.2 to 10.
Group B. (7 cases) from 16.7 to 10.
Group C. (8 cases) from 16.6 to 9.7.

It may be inferred from this that DPT has the same suppressive effect on bacilli as DDS or the combined DDS and DPT.

Results after six years

Patients who died, absconded, developed tuberculosis or were transferred were excluded from the final analysis. It was found that all remaining patients had become negative. One patient had died in the 4th year. The periods required to achieve negativity were:

Group A. (9 patients) averaged 5 years.
Group B. (7 patients) averaged 5 years, 2 months.
Group C. (7 patients) averaged 5 years.

The significance of this finding is that patients who were deprived of DDS for two years were not delayed in their healing.

CONCLUSIONS

DPT in its clinical effect and its effect on bacilli is as efficacious as DDS. However, it has to be given at the rate of 4 or more tablets per day as opposed to the one tablet of DDS. Also, tablet for tablet, it is 10 times the price of DDS, so the treatment costs at least 40 times as much.

We therefore do not consider it as a substitute for DDS and only give it under certain indications.

INDICATIONS

(1) DPT may be substituted for DDS where the patient has repeated reactions under DDS. We are not satisfied that this is of much avail.
(2) DPT may be substituted for DDS when the patient's response to DDS is slow. We have no figures to confirm that this is of use.
(3) DPT is definitely indicated when the patient shows any type of psychosis under DDS.

ACKNOWLEDGEMENTS

I am obliged to the Secretary for Health for authority to publish these notes.

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Abstracts

1 **Tuberculosis and Leprosy,** by ESMOND R. LONG, *Journal-Lancet*, Minneapolis, Nov. 1964, **84,** 11, 395-400.

Retrospective advances in the knowledge and control of tuberculosis and leprosy are described based on a symposium in 1937. Knowledge has since accumulated and includes that on a number of significant mycobacterial diseases, such as those due to *Mycobacterium kansasii*, *M. balnei*, *M. ulcerans*, and *M. fortuitum*, and the *Battey bacillus*. (Recently the powerful chemotherapeutic efficacy of 'B663', a new rimino-compound discovered by V. C. Barry, has been reported from Uganda as definitive against *M. ulcerans*. Strangely, B663 is concurrently being tried against leprosy, and there are previous reports of its action against *M. tuberculosis*. Editor). Dr. Long rightly looks to study of the other mycobacterial infections to provide leads for the difficult problem of isolation and cultivation of the infecting agent of leprosy, and of transmission of leprosy to experimental animals.

The diseases leprosy and tuberculosis are closely related in many ways, such as sharing of chemotherapeutic susceptibility and rather broad antigenic relationships in the components of the aetiological agents.

2 Mycobacterium leprae **in Mice: Minimal Infectious Dose, Relationship Between Staining Quality and Infectivity, and Effect of Cortisone,** by CHARLES C. SHEPARD and DOROTHY H. MCRAE. *J. of Bacteriol.* 1965, **89,** 2, 365-372, (14 refs).

The minimal infectious dose of *Mycobacterium leprae* in mouse foot pads was found to be of the order of 10 solidly staining bacilli. In a titration experiment, the actual number found was 3.4 to 34 solid bacilli, and the order of magnitude was confirmed by experience with inocula containing varying numbers of solidly staining leprosy bacilli from mouse passage and from clincial sources. The acid-fast staining quality of leprosy bacilli was related in a useful way to the subsequent rate at which bacillary growth appeared. When the proportion of solidly staining bacilli was high, the calculated generation time was shortest, and the lower the proportion, the longer the generation times. The results were in accord with the hypothesis that all viable bacilli are solid, and that when they die, most of them become non-solid. Varying proportions of the dead bacilli, perhaps up to 10%, remain solid, at least temporarily. The growth curve of *M. leprae* in mice was followed in several experiments with total counts of acid-fast bacteria and determination of the ratio of solid bacilli. What had been called a maximal stationary phase was seen to consist of sequential phases of conversion of solid to non-solid bacilli (death), reappearance of solid bacilli (growth), and conversion of solid to non-solid bacilli (death). When cortisone was administered, leprosy bacilli grew somewhat more slowly during the logarithmic phase, but attained a higher level, especially of solidly staining bacilli.

3 **Lepra Reactions and Basophil Granulation Test,** by DR. B. B. GOKHALE and DR. M. V. JOGLEKAR. *Indian Practitioner*, **7,** 4, April 1964.

The original basophil degranulation test described by Shelley *et al.* 1962, was used by the authors to study reactions caused by the sulphones and spontaneously. It was standardized by studying known cases of allergy to various drugs, e.g. sodium salt of penicillin-G, streptomycinsulphate, and others. Possibly the test will be applied to differentiate between lepra reactions and those precipitated by sulphones.

4 **Contamination of Healthy Mice with Murine Leprosy-like Acid Fast Bacillus,** S. NISHIMURA, Y. KAWAGUCHI, K. KOHSAKA, and T. MORI. *La Lepro*, **33,** 4, 1964, pp. 245-256.

This paper is in English and contains 4 tables and 8 figures in colour. The author found that caution must be exercised in murine experiments of inoculation with the leprosy bacillus because acid-fast bacilli present in natural circumstances must be noted as an infectious agent of natural murine leprosy. Mice were inoculated with organisms isolated from bacillus-positive animals. Leproma was produced and identification tests showed that many of the organisms had properties similar to the murine leprosy bacillus.

This murine leprosy-like acid-fast bacillus has several points of difference, such as the absence of active infection in the original animal, lack of leproma production, proliferation in the lungs in the next generation of mice, and the simple conglomeration of the organism rather than its presence in the cells.

A severe murine leprosy infection was reported in 1932 by Krakower and González in the brown wild house mouse (*Mus musculus*), but other reports are rare. The rarity of natural murine leprosy infection in the mouse compared to the rat may be due to lack of observation, or to an inability of the mouse to survive until the disease can fully develop.

The authors note that the murine leprosy bacillus proliferates only in certain cells of the rat or mouse and cannot grow in any artificial medium and is an obligate cellparasite and is not present widely in nature. Despite this, it is present in the lymph nodes and subcutaneous tissue of apparently healthy mice which have not contacted infected murine leprosy. It is probable that the source of infection is a micro-organism present in the earth. Acid-fast bacilli could enter the body of the rat through a defect in skin or hair follicle; some bacilli may have mutated already so as to grow *in vivo*, and ready to respond to transduction, lysogenic conversion, and other hereditary factors. Further investigations are needed.

When the acid-fast bacillus has succeeded in invading the animal and adapting itself, the question arises why a subcutaneous leproma is not produced. Nishimura found that in an experiment, 9 of the inoculated animals

developed leproma in the next generation in young animals mostly. The survival time of the experimental mouse is short while the generation time of the murine leprosy bacillus is long. This may play some part. Also it can be assumed in nature there is no invasion by a massive quantity of bacteria at one time, but a repeated invasion by small numbers of bacteria so that resistance is gradually built up by the host.

Pronounced pathological changes were found in the lungs in many cases rather than at the subcutaneous site of inoculation, and proliferation was greater. It was found that a leproma constantly was produced in the next generation of mice inoculated with material from the pulmonary lesion, but only a few animals inoculated with subcutaneous material developed leproma. The reason for this difference is not clear. Changes occur early and in a high percentage in the organs, especially the spleen.

The authors consider that the isolated organism is the murine leprosy bacillus, but use the term 'murine leprosy-like acid fast bacillus' in their title of the paper because of the several questions in the process of proliferation of the organism, such as the absence of leproma formation in the first generation of mice inoculated with the material from the original animal, the development of the leproma in the second generation of mice inoculated with material from the pulmonary lesion of the first generation, and finally the simple conglomeration rather than typical cellular proliferation. The authors surmise the presence of some factor by which the acid-fast organism is changed to the murine leprosy bacillus, and propose to call it 'leprosy-like acid-fast-bacillus', until the matter is clarified.

5 **The Need for Bringing Leprosy Research into Universities.** (Address given by DR R. G. COCHRANE, of 57a Wimpole Street, London, Acting President, International Leprosy Association, at a Conference of Research Workers at Washington held under the auspices of The Leonard Wood Memorial, 11 May 1965).

This was a very congenial subject for Dr Cochrane, as he had long emphasized the need for integrating leprosy into the total picture of leprosy research, and he welcomed the opportunity of introducing this subject.

The author does not claim to be a research worker, but insists that he is a clinician deeply interested in research and appreciative of the fact that significant progress in clinical medicine and therapy is absolutely dependent on the fundamental research worker, and has been successful in attracting many such to the problems of leprosy. He has found that scientific research with the rat leprosy bacillus is more readily accepted than with *Myco. leprae*, but the way to a more detailed study is now open since the great work of Shepard, Binford, and Rees. He suggests that there would be profit in extending the investigation of *Myco. leprae* to other animals. Those used so far have been the smaller animals with a life span of about 2 years. Small size of an animal hinders the harvesting of a reasonable number of acid-fast bacilli. Because *Myco. leprae* will grow in the foot pads of mice and hamsters, why should it not grow in the foot pads of larger animals, and animals with longer life span? There is a further potential problem. Growing *Myco. leprae* in a foreign environment may develop in it different characteristics which may be perpetuated. We cannot fail here to stress the importance of the genetic element in leprosy in the human tissue in which *Myco. leprae* grows, and also in the *Myco. leprae* itself. This is a completely new avenue of research. This is best done at University level and in co-operation with the Departments of Human Statistics and Bio-physics and with the assistance of clinicans well versed in leprosy and knowledge of its racial variations (It is well-known that leprosy in Caucasians and Mongoloids is very different clinically from that in Indians and Africans). Such a genetic research project should be long term, and adequately provided for financially. The addition of an epidemiologist would be of great value to the project. For the project, sporadic research would be relatively profitless Dr S. D. Spickett who initiated research on genetic lines said 'The most hopeful approach to leprosy would be the formation of large integrated research groups'.

At the present time university centres do not have a clear understanding of the importance of other scientific disciplines in leprosy. Relatively few persons have adequate training in scientific methods, and on the other hand research workers trained in scientific disciplines often become involved in peripheral matters because their lack of knowledge of leprosy precludes recognition of relevant points. S. D. Spickett also said leprosy research suffers on 2 counts, (1) those doing pure research in leprosy tend to have scanty clinical experience, and (2) those who have clinical experience are out of touch with potential research workers.

In any case the scientific worker has failed to produce regular growth of the micro-organism in *vitro*, so we still cannot study the life history, its metabolic requirements, its growth bye-products, and what is perhaps more important, the products of breakdown at bacillary death.

Over the past century numerous attemps have been made to culture *Myco. leprae*. None has been substantiated. Famous work is that of Doull, McKinley, Sister Marie Suzanne, and Sister Marie de la Trinité. The author thinks that the work of Khanolkar and Ranadive deserves more attention. Khanolkhar used the posterior root ganglia, and later found that the organism grew on a tuberculosis medium. Khanolkar's suggested 'first passage' through the small superficial nerve plexuses of the skin opens up interesting possibilities in the attempt to culture *Myco. leprae*. Dr Ranadive and her colleagues think that it is important to study the behaviour of this bacillus in the foot-pads of mice, and to study lepromin results from it against standard Mitsuda lepromin (histological picture should also be compared, as if the histology tallies there is additional circumstantial evidence that the bacillus is isolated; if they do not tally there is perhaps evidence of a close affinity and the degree of it). The author thinks that in study of *Myco. leprae* one must always remember that a change of environment may produce mutants of the organism.

Margaret Murray of New York University has made an important advance in sub-culturing Schwann cells, and her technique calls for mastery by other workers.

A very great significance attaches to the discovery of lysosomes by De Duve and Novikoff. The presence of these hydrolytic enzymes may explain why relatively so few persons develop leprosy even after most intimate and prolonged contact. There are various other matters that hint at the importance of lysosomes. They may explain,

for instance, why even in children who are constantly exposed to leprosy infection under greatly favourable conditions for the organism, as many as 70% escape infection. Schwann cells are rich in lysosomes. Could it be that natural immunity resides in the Schwann cells? Dr Cochrane suggests that most of the Schwann cells contain enough lysosomal activity to deal with any bacteria which may be introduced into their cytoplasm. Clinically he thinks of non-responding and reacting patients as those possessed of deficient or inhibited lysosomes.

Dr Brieger in his work with electron microscopy found lysosomes within the cells, and when Dr Cochrane heard from him that they had the property of destroying bacteria and bacillary debris, shortly afterward, in a patient with serious relapse Dr Cochrane found with Brieger's aid evidence of absence of lysosomes. This matter also bears on the action of corticosteroids (Dame Honor Fell commented that certain drugs in small doses activate lysosomes and in large doses inhibit lysosomes). Corticosteroids are very powerful in inhibiting lysosomes action. The matter bears on the dosage of sulphones. The author thinks we should reduce it considerably, such as to 10 mgm a week and not exceeding 30 mgm. This succeeds, and Dr S. G. Browne from Uzuakoli agrees. Lessening the dose improved the clinical condition in a recent one of the author's patients, and in a recent relapsed patient there was clear improvement. In a third patient in England, the patient, a chronic one, improved on 30 mgms. DDS a week. These 3 patients were long-standing but the improvement on moderate dosage of sulphones definite.

This opens up a wide field of investigation of lysosomes in Indian and African races. There may be more powerful lysosomal activity, with patients generally less prone to severe reactions and more easy to treat than in Caucasoid and Mongoloid races.

The author says that while *Myco. leprae* is the causative organism of the disease it appears to set up side reactions which make the bacterial invader merely an onlooker who is quite unable to intervene in the disturbances which have been set up. *Myco. leprae* merely serves to trigger a whole series of malignant processes. It is related to autoimmune processes, disorders of pigment etc.

The author comments that he has found in over 90% of patients that the first presenting sign or symptom was anaesthesia. In more and more patients it will be discovered retrospectively in the history. Diagnostic clinics are therefore very important in leprosy campaigns. If diagnosed, early leprosy becomes a controllable incident in life. In some patients in whom leprosy was diagnosed as early as the first presence of bacilli in nerves, it was noted that the disease treatment was highly successful. It would be helpful to find another name for leprosy. A name for the early lesions would be desirable. ('Mycobacterial neuropathic dermatosis' was suggested by J. Ross Innes but ignored largely by those who previously preferred the term Hansen's disease').

6 **Manifestaciones iniciales en la adolescencia y pubertad (Initial manifestations in adolescence and puberty),** DR FÉLIX CONTRERAS, *Revista de Leprología*, 1964, **6,** 2, page 105.

The initial manifestations of leprosy, though they pass unnoticed in most patients, have presented many years before. As long ago as 1797 Pfefferkorn said that leprosy commenced always by a sole and limited lesion in the skin. This same opinion was supported afterwards by Marcano and Wurtz, Leloir, Gougerot, Beurmann, Klingmüller and others.

Brocq in 1907 confirmed the existence of abortive forms which could even regress and not be reproduced, and at that time there was much disagreement between the infective and hereditary theories of the transmission of leprosy. Even it was held that infection could not take place in infancy and Goodhue published the history of some patients who illustrated this.

In fact initial lesions of leprosy were not known until a systematic study took place of the children of leprosy patients born in some leprosaria, especially in the Philippines leprosaria. The first to publish were Rodriguez, Manalang, Velasco and Chiyuto, who maintained that infection almost always took place in children by means of intimate and prolonged contact with the skin of the mother who was a patient. This skin to skin contact resulted in a hypopigmented macule in covered parts. These lesions were apt to coincide anatomically with the maternal bacilliferous lesions and those lesions which had been in intimate and prolonged contact.

Some years later Duarte do Pateo and Solano Lima, Souza Campos, Bechelli and Rotberg, Charria Tovar, Gonzaga, Souza Campos, Bungeler and Alayon, Fernández and other South Americans observed initial lesions, mostly always in children, which were afterwards confirmed by the medical officers of Fontilles. These were observed in patients of Fontilles who lived in some adjacent little towns. Shortly afterwards different doctors of the Spanish provinces began observing such patients, the endemic being more widespread than was thought.

The discovery of early lesions is extremely important, because it allows of easy and certain early treatment of leprosy without scars, and permits of social and public health welfare of patient and family, as well as early control of the infection. The value of early diagnosis is very great, even in less well civilized countries.

The difficulty of infection of adults is recognizable. Even in tuberculosis this is acknowledged, as by Lumiere, who pointed out that most tuberculosis patients were discovered as adults, and least in infancy and youth. The diagnosis must have been late. We should recognize that most of the patients of leprosy start their career in childhood. The greater susceptibility of children is aided by greater susceptibility to heredity (as studied by Aycock and Kinley, and by Fernández.

All leprologists agree in recognizing factors which favour infection and contribute to diminution of resistance to infection. Puberty stands out in these, preferably in women but also to some degree in men. However publications are few of initial lesions in adolescents and in puberty, which doubtless exist, because few are described on entry into military service. We are convinced that mostly these initial lesions pass unnoticed.

We have seen about 200 initial lesions in minors of 16 years, and between 11 and 17 years of age. They were adolescents who were children of leprosy patients, who live all their childhood in leprogenous environment. They showed some defectively pigmented area, and the rest of the skin marked with faint hypo chromia which never

reached the characteristic light macule. The sites were twice in the buttocks, thrice in the thigh muscles, twice on the shoulder, and twice in the forearms and once in the leg. In six patients the plaques coincided with an incomplete alopecia. In all there was sensory change. In six of these and in one other, there was anhydrosis in the hypopigmented lesions. The histamine reaction was incompletely positive. No lepromin reaction nor bacilli were encountered positively.

Recently we have seen the patient A.T.C. of 21 years, unmarried, living in Madrid. He has lived since his birth with his mother and a sister and both were lepromatous patients. He has had good health. Since childhood he thinks he has only had chicken pox. Three months before he attended at the consultation, he noted in the entire surface of the left thigh a small area near the knee that had lost hair and sensitivity, a macule of irregular oval form of 2 or 3 cm., less pigmented than the rest of the skin. There was also some loss of sweating and the histamine test was incomplete. We performed a biopsy which we sent to Félix Contreras Rubio who reported epidermis without histological changes. In the dermis, round some vessels and the nerve filaments there is an inflammatory infiltration consisting of undeveloped lympocitic cells. Bacilli were not encountered; the clinical suspicion of in-determinate leprosy is suggested. We had no doubt that this patient was indeterminate.

We may comment that:

1. For a long time it was thought necessary to find *M. leprae* in our diagnosis of leprosy. I think that the presence of the leprosy bacillus should be guaranteed for a final diagnosis.
2. Yet in indeterminate leprosy it is exceptional to encounter the bacillus.
3. The histology in these cases is limited to a completely non-specific inflammatory reaction, especially round the vessels and the glands.
4. The most characteristic sign of indeterminate leprosy is given by the sensory changes. No other disease exists which produces maculae with anaesthesia.
5. Sometimes also there are changes in sweating and loss of hair. These changes are more evident in adults than in children.
6. In the two adolescents whom I saw, it is probable that the initial changes were analogous to those of childhood, which we know better. Frequently we come to recognise them retrospectively. In some patients useful indicators are disturbance of sweating and tendency of anhydrosis to be limited to a small macule. Pigmentary or sensory changes are useful. I remember one very interesting foreign patient who noted a hypochromic spot in the leg when she was on the beach, when some ants passed over the spot in which she noted a complete absence of sensation just outside the spot which was also lacking in hair.

The most marked symptom according to age consists in lack of pigment which is less marked in adults than in children, and on the other hand lack of sweating and loss of hair are more evident. The most characteristic sign is the anaesthesia which in our opinion is enough to attract the diagnosis, for we repeat that we have not known any other dermatosis with persistent and evident anaesthesia in the macules. There have been hundreds of children who have been saved from the disease by early diagnosis, though we know some of those diagnosed who have not persisted in the treatment and in whom the disease has progressed after some years. Therefore we believe that the discovery of initial lesions is the foundation of prevention in leprosy which should be studied in all contacts especially in children.

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Reports

Summarized Papers from the All Indian Leprosy Workers Conference, Madras, 29-31 January, 1965.

(After an inaugural address by Sir A. L. Mudaliar, Vice-Chancellor of the University of Madras and a presidential address by Dr. R. G. Cochrane).

(**1**) *Team Approach in the Rehabilitation of Leprosy Patients*, was a paper delivered by MR. H. D. PAVRI, which demonstrated that more practical results are achieved by a team approach. Such a team in the author's experience has been studying such varied projects as assessing the effects of social ostracism, moulded footwear in the welfare of the feet, heat resistant points in limb trauma, moulded tool handles to suit the needs of hands, evaluation of jobs and tools to prevent trauma, choice of a suitable job in which to be placed for the best progress of rehabilitation.

(**2**) *Occupational Therapy in Leprosy*, by PAUL REGIS. This paper is not concerned with specific treatment ideas but with leading the deformed patients to his highest capacity in living. Each patient is evaluated for his physical disability, functional status, and mental condition. The aim is to concentrate on occupational therapy goals of developing independent skills and pre-vocational therapy. Every effort should be made to improve the working capacity of the patient in his own profession, along with his handicap.

(**3**) *Effect of Leprosy on the Work Life of Patients* by MISS N. B. SHAH. The author analysed the out-patient register of the Acworth Home in Bombay, and of 2,507 patients recorded January to October 1960 noted that 14% were women doing household work, 12% were children below the age of 15 years, 5.5% were above the age of 55 years, 4% were mendicants, 8.9% were young adults with advanced deformity and 55.6% were young adults without deformity. Of the patients without occupation or without means of support, 90 persons were young adults with deformity and 199 persons young adults without deformity. The young adults are the special concern of rehabilitation and educational facilities should be provided for children with infectious leprosy.

(**4**) *The importance of Social Assistance and Rehabilitation in Leprosy Control.* DR. V. P. DAS emphasizes that patients hesitate to leave hospital for home and family not only because of the stigma of leprosy, but because of economic and personal reasons.

The patient is gradually displaced as an economic unit as physical weakness advances, and ostracism develops to him. In many cases the relatives have used the ostracism to alienate the property of the patient in one way or another. Such relatives are the core of resistance to the return of the patient. Strangely enough, ostracism is more predominent in the educated section of the community. This is becausa the social excommunication is aimed at the whole family. Explanation, and further education, can be assisted by the family doctor.

On the economic side there are several suggestions, (a) improving the general economic condition of the common man in India; (b) teaching the patient an extra trade while he is under treatment, perhaps a better trade; (c) allowances for graded assessed disability; (d) explaining the leprosy problem to those in charge of the department on which the patient works or has worked; even the idea of rehabilitation centres at district level may be inspired in them; (e) in hospitals occupational therapy can be linked with the organized programme of rehabilitation; (f) sheltered industries outside the leprosaria should be arranged for the disabled, and help a non-mendicant morale; (g) every child patient should be found a place in a leprosarium, where they can be taught trades.

With early detection, deformities need not occur. A panel of lawyers, giving honorary service in the way of advice to patients to save many being ill-treated by the public on account of the disease, will be very helpfu! in a community. Re-assuring the public should also be done by doctors and social workers, and a special effort is needed by doctors to convince educated people.

(**5**) *Vocational and Psychological Rehabilitation*, by SRI D. V. KULKARNI, deals with present efforts in India in rehabilitation and social adjustment. The basic concept is of total rehabilitation. This includes physical as well as psychical means. The author considers that institutions are not out-moded but should be given special tasks, such as a supportive psychotherapy as well as specialised vocational training, therapeutic occupations, reconstructive surgery, and suitable medical treatment. The author makes several suggestions; (a) total rehabilitation should be a wider aim beyond physical; (b) the regular framework of therapy should be streamlined; (c) examine how anti-mendicancy legislation could be used for social adjustments of mendicants who have leprosy; (d) some kind of social insurance should be interwoven; (e) such as some kind of grant-in-aid; the leprosy programme needs help; (f) training for workers should be extended; (g) top priority should be given to emotional rehabilitation in any leprosy programme; (h) treatment centres should have specific and purposeful objectives towards social adjustment, with help of a team of specialised personnel, and encouragement of the corporate sense of the patients by themselves having a corporate sense.

(**6**) *Attitudes of leprosy patients to Their Rehabilitation*, by MISS O. PEREIRA. This paper deals with the response and active participation of the patients. Complete faith in the therapy is essential for its effectiveness. Studies show that most patients have faith in a complete cure with good treatment. This faith is stronger in women than in men, and more in the literate than the illiterate.

Many of the patients go home for shorter or longer periods, and there is benefit in this. The strongest fears in the patient concern social status and this fear affects relatives. Reconstructive surgery, artificial aids and adaptive devices are hard to find for cured patients, and their future seems insecure. Whether a patient wants his old job or is willing to find a new job is important.

Recreation is important. It goes a long way in building up a positive attitude to rehabilitation.

(**7**) *Control of Leprosy Among Students*, by SRIMATHI INDUMATI S. RAU is a paper recording a study of progress of the patients in clinics at the Victoria Hospital, Bangalore. Most patients are under 30 years of age and a great number about 13 years of age. Out of 650 patients registered as out-patients in 15 months 25 were below 10 years, 112 were between 10 and 9 years, and 194 were between 20 and 28 years. The group of young people contained 81 who were students in the schools and colleges of Bangalore, but none was sent by schools medical officers, and their diagnosis seems to be by chance. Many teachers suffered from leprosy. Efficient periodical medical examination is essential, as well as general and special health education.

(**8**) *Social Obstacles in Combating Leprosy*, by DR. Y. K. SUBRAHMANYAM. The paper poses the problem of instilling in the mind of the patient the understanding of leprosy and courage to come forward for treatment. It might help if the leprosy worker approaches the leprosy patient as one suffering from mental anxiety as well as physical disease. In all cases special love and care are needed, and the worker himself should be fearless. The leprosy paramedical worker, on whom control depends so much today, should realise this.

(**9**) *Health Education in Leprosy in Urban Areas*, by SHRI M. S. MEHENDELE. The author indicates various groups in each community such as leading persons, doctors, government and municipal officials, heads of institutions and clubs. These should be indoctrinated and given a task to do, as well as the teacher, the patient and relatives, and the man in the street. Various methods are suitable for tackling each group. Certain suggestions are the individual approach, short term courses for doctors, approach through voluntary workers, group discussions and meetings, newspapers, radio, pamphlets, films with lectures, integration with general health work. The author also suggests revision of text-books.

(**10**) *Health Education in Leprosy*, by DR. RANJITH RAO. The author who is in Health Education in the Research plus Action projects in Poonamallee, Madras, relates his experience in 2 villages. In these the main difficulty was the reluctance to come early for treatment and to maintain regularity. A large amount of success followed the formation of village health committees among influential village leaders, and the practical help of the Research cum action Committee. Local health committees have been found active. Regular treatment of the patient over long periods is helped by these local health committees.

(**11**) *Leprosy Eradication in the Villages*, by DR. R. VEDABODAKAM. The author gave an account of health education of the villages adjoining St. Luke's Leprosarium in Tirunveli District in Madras State. When a village is selected the panchayat president is informed a week in advance. The party arrives at the village at 7 p.m. in a van fitted with loudspeakers and gramophone, and the van moves round the entire village and gathers crowds successfully. Slides are shown and speeches made.

(**12**) *Health Education About Leprosy*, by DR. V. EKAMBARAM. The author thinks that public meetings and wall posters are not enough, and that health education about leprosy should be integrated into general health education and planned for urban and rural populations. He suggests that all students of the higher secondary and college classes should be given a course of instruction about general hygiene and about communicable diseases, including leprosy. The subject should culminate in a general examination, and in this subject all students should be required to get a class mark. He suggests that all officials and municipal and government employees should pass a first aid and general public health examination before being appointed to services. Traders might well be expected to pass such a course. Rurally, village committees should participate, and the efficiency of a panchayat should be judged by their active knowledge of such a health programme. The press, radio, and journals could help in the spread of health education.

(**13**) *Integration of Leprosy with General Health Services*, by DR. N. JUNGALWALLA. The author points out that the national leprosy campaign has not achieved the status of a mass campaign, for in 1963 the total registered was 530,000, whereas treated reached 496,000. Of these there were 394 'S.E.T.' or official treatment centres which covered 50,000 patients and voluntary agencies 20,000 patients.

The organisation of leprosy control work through S.E.T. centres is already in process of integration with basic health services, based on the primary health centre. With hospitals only partial integration has been attained. The separate leprosy treatment institution seems to be the pattern. It is debatable whether it should be increasingly favoured. The teaching hospital still needs to develop community consciousness. It is found that some self-sufficient institutions can find and treat fairly large numbers of patients and treat them, e.g. Polambakkam covered 570,000 population and registered 23,500 patients in $3\frac{1}{2}$ years; the Danish Mission covered 680,000 population and registered 23,000 in 3 years against 87,500 registered in the whole state. In Uttar Pradesh 13,000 patients were registered in 1 Taluk in 3 years by a similar voluntary organisation.

The Wallajapet scheme has tried to use the staff on a vertical mass campaign basis and tries to forge a link between the medical institution and the groundwork of primary health centres.

Co-ordination will progress when funds are available to strengthen district and subdivisional hospitals and peripheral services. The control of leprosy may yet achieve a mass campaign as in malaria and tuberculosis. Considerable experience has been built up in other campaigns, and integration and consolidation of the leprosy campaign should be planned now, with a pilot phase as soon as possible.

(**14**) *Review of Leprosy Control Programme in India*, by DR. P. N. KOSHOO. The author recalls the recent estimate of 1,500,000 leprosy patients in India and that a quarter of these patients are of infectious type. The 8 states which have a big problem are Andhra, Madras, Bihar, Maharashtra, Mysore, Orissa, Uttar Pradesh, and West Bengal. Other states have a rather low prevalence. Of the 450 million population of India there are 300 million people living in zones of high and moderate endemicity.

The national leprosy control programme has been in existence since 1955. Up to the end of the second plan a population of over 14 million people was covered and 6.6 million persons physically examined and 180,000 patients registered. In the third plan the concept of the S.E.T. Centres introduced, established in less endemic areas, and form the first step towards the integration of leprosy work with general public health and medical institutions. Leprosy subsidiary centres were reformed into leprosy control units. During the period of the third plan so far a population of 24 million has been covered and out of 12.2 million persons examined 250,000 more patients have been registered.

There have been financial and administrative difficulties, but now there are 166 leprosy control units, 487 S.E.T. Centres, and 32 voluntary organisations.

Training programmes have gone on for medical and non-medical personnel, and a rehabilitation training programme has not been forgotten.

The draft fourth plan envisages the establishment of 110 more leprosy control units, and 4,490 S.E.T. Centres in rural and urban areas, and 11 more training centres: 21 additional voluntary organisations may receive grants-in-aid, and a handsome amount will be spent on health education, reconstructive surgery, and a training programme for rehabilitation.

(**15**) *Voluntary Institutions and Changing Pattern of Leprosy Control Work*, by DR. R. V. WARDEKAR. The main burden of leprosy work since Swaraj has shifted from voluntary institutions to Government. In the same period sulphone therapy has shifted the emphasis from in-patients to out-patients. Voluntary institutions need to re-orientate their policy so as to contribute to the national programme by sharing their knowledge, and make practical field investigation of special problems, and especially if their institutions have 4 wings such as hospital, vocational training, settlement, and infirmary. If they are interested in out-patient treatment centres, they can take up S.E.T. work, if necessary helped by Government grants. Voluntary organisations can take up health education in urban areas, or establish referral centres.

(**16**) *An Approach to Leprosy Control and the Achievements of the Pogiri Control Centre*, by DR. KEJA. The Danish Fund started a leprosy control project with the approval of the Government of India and the interest of WHO, the Gandhi Leprosy Memorial Foundation and the Hind Kusht Nivaran Sangh. Soon construction of a headquarters building is to begin at Pogiri near Rajam, Palakonda Taluk of the Srikakulam District, which is a hyperendemic area. The approach to the problem on the advice of WHO has been ambulatory treatment through static control units, with visiting supervisory staff. The plans for 1965 are to extend the project to 2 adjacent taluks, and later to begin a similar project in Orissa. The Palakonda taluk project covers an area of 1,500 square miles with a population of 798,391. The prevalence rate is 18 per thousand, child rate 24.5% and lepromatous rate of 21.5% and the total number of patients is 20,884.

(**17**) *A Review of Anti-Leprosy Campaign in Gaya*, by DR. R. S. SHARMA. This anti-leprosy work in Gaya developed under the auspices of the Gram Nirman Mandal, led by Shri Jaya Prakash Narayan. There are many out-patient clinics spread over the area. The author points out from his experience that sulphones are not the last word in therapy, for there are baffling relapses: nor distribution of tablets through paramedical workers is the last word. There is need for suitable doctors. All Government dispensaries and hospitals should take more interest in anti-leprosy work and should treat leprosy and make special arrangements for reconstructive surgery. There should be more co-ordination of funds and supervision of voluntary institutions, and the allotted funds should be available in time. All leprosy workers should be one in spirit and devoted to the common cause.

(**18**) *Integration of Leprosy Relief with General Medical Relief Measures*, by DR. V. EKAMBARAM. The author stresses the importance of integration and suggests how the difficulties can be overcome by sufficient coaching of undergraduates in leprosy, by training house-surgeons in leprosy for 15 days, by asking questions about leprosy in the M.B., B.S. exam, by training medical officers in service as well as general practitioners by the State Leprosy Officers, by making a record of good leprosy work as one of the qualifications for promotion of Medical Officers.

Book Reviews

Physiotherapy in Leprosy, by MERRILL MENDIS, M.C.S.P., with a foreword by PAUL W. BRAND, C.B.E., F.R.C.S., 83 pp. published by John Wright & Sons Ltd., Bristol, 1 plate, 17 figs. paper covers; price 15s. postage 7d.

The extremely beneficial revolution for the leprosy patient is here for the first time systematized and described by the author who has practised it, and the surgeon who initiated it writes a foreword. The book should be in the hands of every leprosy worker. The book deals with nerve involvement, ulnar, median, combined ulnar and median, radial, lateral popliteal, and posterior tibial. Post-operative pysiotherapeutic treatment of hands is next dealt with. Splinting of digits for correction contractures, and re-education following surgery, are next carefully explained. Other subjects are preoperative treatment after lateral popliteal nerve palsy, re-education following tibialis posterior transfer, plantar ulceration and its prevention, shoes in leprosy, prevention of secondary deformity and ulceration.

If anyone wants to take part in the modern treatment of patients, this manual of physiotherapy is very valuable.

An Inn Called Welcome by A. DONALD MILLER, 241 pp. price 4/6 limp, is the story of the Mission to Lepers, 7 Bloomsbury Square, London W.C.1.

Tells of 43 years of world-wide compassionate service to leprosy patients from 1874-1917, and is published during the 90th anniversary year. It is hoped later to continue the absorbing story from 1918. Mr Donald Miller's own service began in 1922 and since 1963 he has become a Vice-President of the Society.

This is a noble and refreshing book. The author traces the story, with many an intimate detail, of the foundation of the work of the Mission by Wellesley Bailey and the sisters Pim to the present wide establishment of 'Inns of Welcome' in all parts of the world for leprosy sufferers and growth to embrace and support all sorts of remedial measures for them from shoes to electron microscopes. Many have co-operated and do co-operate, and the clear, growth of help for so many patients is a work of Grace which is a fit subject for rejoicing. The original book is worthy of immediate purchase, and study in detail. It is hoped that in a future edition it will be possible to add many illustrations.

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S.7. A NEW ANTI-FUNGAL AND ANTIBACTERIAL AGENT

S.7. provides di- (2-hydroxy-5-chlorophenyl) sulphide, B.P. approved name 'Fenticlor', a powerful fungicidal and antibacterial agent which has been found extremely effective in the treatment of a wide range of mycotic infections of the skin and mucous membrane.

As a fungicidal agent S.7. shows marked inhibition of Monilia albicans, Aspergillis Niga and Trichophyton interdigitale and other pathogenic fungi commonly met in mycotic infections of the skin.

Formula

Each preparation contains:
1% di-(2-hydroxy-5-chlorophenyl) sulphide

Packs

Available as: Jelly, Cream, Powder and Pessaries.

Full Technical Data and Literature on any of the above preparations available on request from:

CALMIC LIMITED, CREWE, CHESHIRE Telephone CREWE 3251 (7 lines)

LONDON: 2 MANSFIELD STREET, W.1 Telephone LANGHAM 8038