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LEPROSY REVIEW

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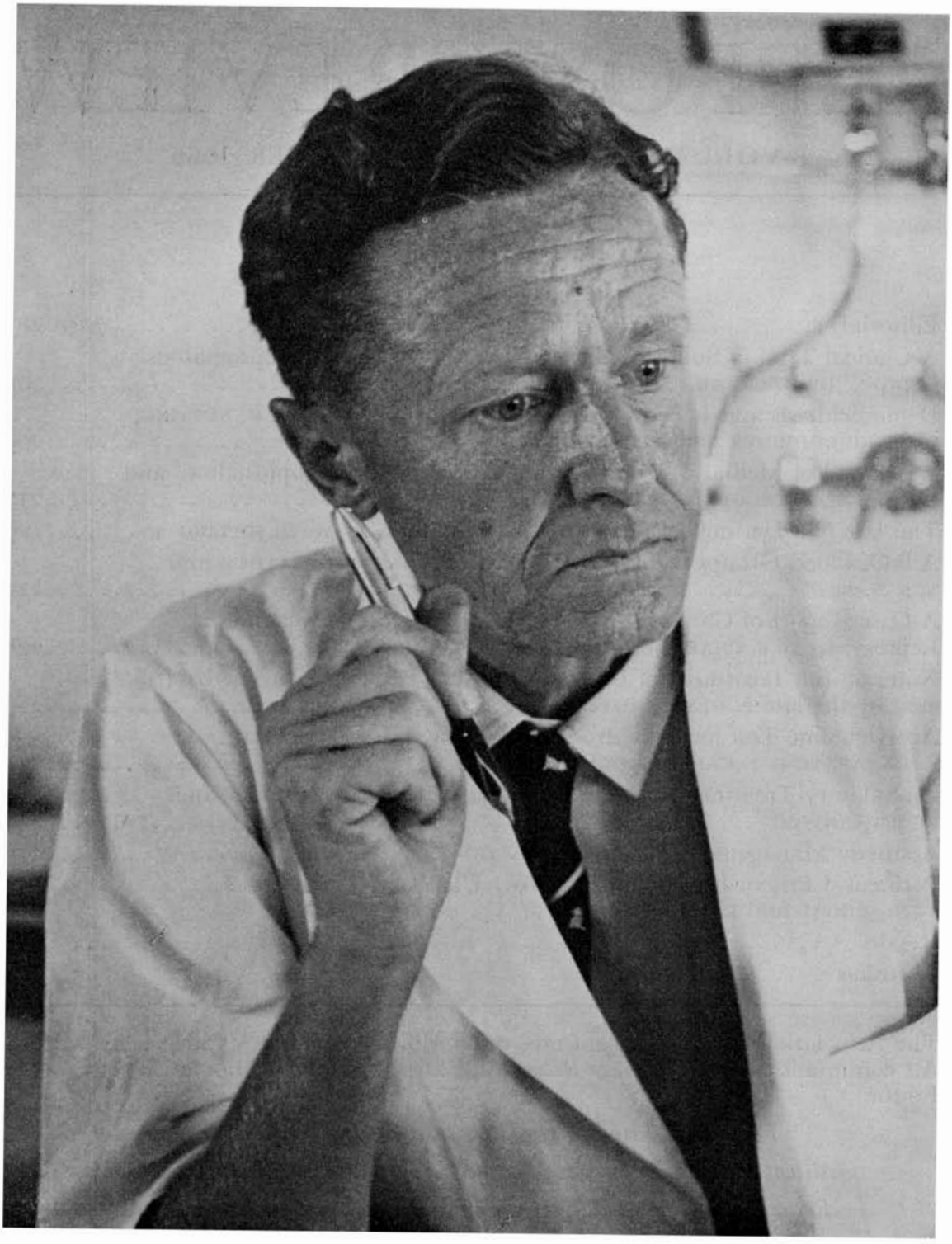

Dr P. Glyn Griffiths, M.C. Died 14 May, 1966

Editorial

1. OBITUARY—Dr P. Glyn Griffiths, M.C., B.SC., M.B., CH.B., M.R.C.P., F.R.F.P.S.G.

Dr Peter Glyn Griffiths, leprologist to the Republic of Zambia, died on 14 May 1966, aged 48. He was educated at William Hulmes' Grammar School and Victoria University, Manchester, where he graduated B.Sc. in 1938 and M.B., Ch.B. in 1941. He served in the R.A.M.C. with distinction and was awarded the M.C. during the Normandy campaign. After demobilisation he entered the Colonial Medical Service and served in Fiji where he became particularly interested in the problem of tuberculosis and leprosy. Fron 1952 to 1957 he was a consultant physician with the Malay Medical Service and from 1958 to 1960 administered a campaign against tuberculosis in Brunei. In 1961 he was a consultant chest physician in the National Health Service in Britain and in 1962 joined the Federal Ministry of Health as Leprologist for Northern Rhodesia continuing in this post under the Government of the Republic of Zambia until his death.

Mr James J. MacPherson, F.R.C.S., writes that he knew and respected Glyn Griffiths as a friend, colleague and outstanding physician for 13 years having first met him in the Malay Medical Service. By his enthusiasm and unflagging efforts he transformed Liteta Leprosarium, with the help of both Federal and Zambian Governments who were much impressed by his selfless work, from a settlement with minimal facilities to a modern leprosarium with over 700 patients whose cheerfulness is sufficient indication of his loving care for them. He was very insistent that his leprosy patients should never be referred to as 'lepers' as this term bore a stigma from Biblical times, again showing his compassionate feeling for his patients. He started a school, a scout troop, physiotherapy and other projects to improve treatment and amenities at Liteta and in these he was ably and enthusiastically helped by his wife. He was engaged in extensive drugs trials at the time of his death. He toured the country extensively and founded a leprosy register insisting on regular attendance at out-station clinics by all persons on the register. He also managed to maintain an extensive correspondence relating to leprosy. All this was achieved in the face of uncertain health and complete disregard for his own well-being. This greathearted physician was loved by both patients and staff and with truth it can be said that he sacrificed his own life for his patients and his profession.

He is survived by his wife, a son who recently graduated in medicine, and a daughter, and to all of them goes the sympathy of all who knew him.

Dr S. L. Gauntlett, Chikankata Hospital, Mazabuka, Zambia, writes: 'Glyn Griffiths' enthusiasm for and devotion to the cause of leprosy was infectious and our first meeting soon after his appointment as government leprologist in the then Northern Rhodesia made me at once a disciple and friend. I saw all too little of him during the ensuing years but my respect for him grew and even a brief visit was a stimulus to greater efforts and higher standards. When he first came to Africa he had extensive experience in leprosy and in general medicine and he had given up good prospects as a consultant in Britain to come to primitive and frustrating conditions when he established headquarters at Liteta. Liteta was intended to be the government's central leprosarium but accommodation for both staff and patients was poor – even primitive – with nowhere to examine patients properly and no runing water. From this he helped to build up a fine modern leprosarium which stands today as a model for other treatment centres. Glyn Griffiths was a perfectionist and made the greatest demands upon himself. He was a fighter in the cause of his main love and his long-fought battle against indifference and incompetence in some quarters, and staff and money shortages was aided by his fiery Welsh personality. These fighting qualities which, with his tenacity and drive, endeared him to me and many others in this and other countries also made enemies although I think most of these respected him. He was a good friend, sharing eagerly his successes and

hopes and also his defeats and frustrations, and ready to share in and understand yours. Glyn Griffiths hated insincerity and denounced what seemed to him to be the second rate, although this was not a destructive denunciation as he gave all the help and encouragement and challenge he could to treatment centres which he felt lagged behind the standard he accepted. He could be scathing in disagreement but he was eager and generous to a degree in his praise and he was ready to accept new ideas and give credit for them. His approach to his subject was not purely academic but he had a deep concern for the spiritual and moral as well as physical welfare of leprosy patients and this concern led him to fiercely oppose anything that conferred a stigma upon them. When I saw him recently after a gap of several months I was shocked at how ill he looked. It was obvious that he was driving himself well beyond his powers but all the pleading of friends and medical advisers to ease up were of no avail. To the end he was travelling widely along bad roads and under difficult conditions, working into the early hours of the morning in a vain effort to keep up with correspondence, and giving attention to his drug trials. He set us all a high standard in the meticulous care with which he conducted his investigations and the thoroughness of administration of the leprosy service, but all this proved more than one man could possibly do – even Glyn Griffiths. His sudden passing came as a great shock to his friends and colleagues but not as a surprise. He had "burnt out" and had left us with a great debt to pay and a challenge to carry on where he left off. Nevertheless in this country and in international leprosy investigation his place will be difficult to fill. To his wife who has shared so fully in his devotion to his work and who is still helping in leprosy organisation here in Zambia, we pay tribute and offer sincere sympathy, as well as to his two children.'

2. We draw attention to a very interesting and valuable report appearing in this issue of *Leprosy Review* (p. 255). This is the report by Dr S. G. Browne, O.B.E., on the Lepra Conference held at Farnham, Surrey, England, in May 1966. There is a great deal of detail about the progress of the project instituted in Malawi aimed at the control of leprosy. It is gratifying to us to note the considerable progress of this project from what seemed a 'pipe dream' in 1961 when, as Medical Secretary of Lepra, we mooted the project. It was due to the enthusiasm and support of the Medical Committee of Lepra that the idea was taken up and thoroughly discussed at a series of medical committees, and guidance given in various practical problems. We remember discussing the possibility of the project in January 1962 with Dr Ernest Muir, C.M.G., C.I.E., F.R.C.S., who at that time was Chairman of the Medical Committee and Medical Adviser to Lepra, and we recall the meeting of the Medical Committee at which the project was eagerly discussed. We emphasize that a debt of gratitude is owed to the Medical Committee for their wisdom and guidance on the Malawi Project and their various meetings under the chairmanship of Dr R. J. W. Rees, M.R.C.S., F.R.C.P., F.C.PATH., who succeeded Dr Muir in the position in 1962.

3. Dr Ernest Muir who was born in Banffshire, Scotland, in 1880, has recently retired as Honorary Medical Adviser to Lepra. He has had a long and wonderful career and is loved and revered over the whole world wherever leprosy is actively under attack. He has given us a summary of his career starting with his work as a medical missionary of the United Free Church of Scotland in Kalna, Bengal, where he treated many leprosy patients; then to the Calcutta School of Tropical Medicine to start work on leprosy when the School first opened in 1920, and eventually to become an examiner in Tropical Medicine and act as Professor of Tropical Medicine for two years. On retirement he became first 'Secretary' and later 'Medical Secretary' of the British Leprosy Relief Association. He is one of the founder members of the International Leprosy Association, was for many years its Secretary-Treasurer and is now its Honorary Vice President. He has travelled the whole world acting as adviser in leprosy to many governments and institutions and even after retirement has returned to the field several times to help out in staffing difficulties. We remember in particular travelling to India in the same ship as Dr Muir in 1928 and his eloquent insistence that in our forthcoming career in India we should take an interest in leprosy. It happened that the very first hospital of which we had charge had an accessory leprosarium of 300 patients and it was possible to

hearken to Dr Muir in practical issues from the start. Furthermore it was very useful to have his encouragement at the next stage when we ventured into active leprosy survey work in the Solomon Islands in 1937, and later when we went to Africa as leprologist to the East Africa High Commission.

We wish Dr Muir every health and happiness for the time of his retirement.

4. The STAR was 25 years old in September 1966. For this happy occasion we wish to send our hearty congratulations to Stanley Stein and his staff and best wishes for the future. The STAR began as a small mimeograph sheet with a circulation of a few hundred and today is a printed publication of 25,000 going to about 70 countries. It has always been a stout supporter of the interests of the patient.

5. The attention of subscribers to *Leprosy Review* is drawn to the Renewal of Subscription form which is enclosed in this issue. In order that our records should be accurate all subscribers are asked to complete Section A, Nos. 1 *or* 2 *or* 3, whichever is applicable. All subscribers must complete Section B of the form showing the exact name and address to which the journal is to be sent. This is to avoid delay and the many reports of lost journals which we receive. Comments would be welcomed about the condition of the journal and its container on arrival at destination.

Lep. Rev. (1966) **37,** 4, 205/208

A Clinical Trial of Sulforthomidine* ('Fanasil' Roche) in Lepromatous Leprosy

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Sulforthomidine ('Fanasil' Roche) is 4-sulphanilamido-5,6-dimethoxypyrimidine, a long-acting sulphonamide which has low toxicity and good antibacterial efficacy. As the half-life of this drug exceeds 100 hours in the majority of humans it need only be given once a week. The concentration of sulforthomidine in the skin is comparatively high (about 1/3 of the plasma concentration) and the drug has proved useful in a number of bacterial skin infections including leprosy. Sulforthomidine, supplied by Roche Products Limited in the form of 500 mg. 'Fanasil' tablets, was subjected to a clinical trial in human leprosy.

Selection of Patients

Thirty-two patients suffering from lepromatous leprosy and lepromin-negative were selected of whom two absconded during the trial period, both in the control group. All patients had received dapsone for a short period (2 to 12 weeks) prior to the clinical trial and all patients resumed dapsone at the end of the six month trial period. Of the 30 patients who completed the trial 16 received sulforthomidine 1 g. once a week and 14 received dapsone 0·3 g. twice a week, serving as a control. Ideally patients submitted to trial should not have had previous treatment (Jopling, 1965) but a large number of new untreated cases can seldom be collected at one leprosarium and the selection of cases already treated for a short time with dapsone permits interesting comparisons.

Methods of Assessment

Biopsies were taken and smears were made from both ear lobes and from the sites of the biopsies. Local anaesthesia was used to permit adequate incision and scraping of the dermis which can be difficult in nervous patients. The Bacterial Index (1—6 plus) was assessed by the method of Ridley (1958) and the Biopsy Index and Granularity Index established, also by the methods of Ridley (1964), both at the beginning and at the end of the six month trial period. Patients were observed twice a week throughout the trial and special attention was given to the incidence of erythema nodosum leprosum (ENL) and of side effects of the drugs. The progress of the sulforthomidine and dapsone groups is set out in the following tables.

Results

TABLE 1

Bacterial Index, assessed 1 to 6 plus
(Ridley, 1958)

	Before Trial	*After Trial*	*Improvement*
Sulforthomidine Group, 16 patients	4·7	4·1	13%
Dapsone Group 14 patients	4·3	3·9	9%

TABLE 2

Percentage of Dermis occupied by Granuloma

	Before Trial	*After Trial*	*Improvement*
Sulforthomidine Group, 16 patients	22·7%	11·0%	51%
Dapsone Group 14 patients	24·0%	10·5%	56%

*The B.P. Commission approved name is sulphormethoxine.

TABLE 3

Biopsy Index

Product of Bacterial Index x Percentage of Dermis occupied by Granuloma (Ridley, 1964)

	Before Trial	*After Trial*	*Improvement*
Sulforthomidine Group, 16 patients	1·07	0·45	58%
Dapsone Group 14 patients	1·03	0·41	60%

TABLE 4

Granularity Index

The Percentage of Bacilli Exhibiting Irregular Staining Granularity (Ridley, 1964)

	Before Trial	*After Trial*	*Improvement*
Sulforthomidine Group, 16 patients	85%	98%	15%
Dapsone Group 14 patients	84%	95%	13%

It will be noted from the above Tables 1 to 4 that there is no significant difference in the rate of bacteriological improvement in the two groups.

Side Effects

As already stated all patients received dapsone for a short time prior to the trial. This permitted the incidence of side effects attributable to dapsone to be assessed in all patients.

During the six month trial period the incidence of side effects to sulforthomidine and to dapsone respectively was noted, and the results are recorded in Tables 5 and 6 below. It will be seen that during the first month of dapsone therapy about 75% of the patients experienced side effects attributable to the drug. In the control group, after persevering with dapsone, the incidence gradually fell to about 25% over the six month period. In the trial group, however, when the regime was changed to sulforthomidine, the side effects ceased with relative abruptness (i.e. within one week) and only one patient out of 16 admitted to any side effects at all. This patient had suffered from neuritis while receiving dapsone prior to instituting sulforthomidine and it was not certain that the 'burning' sensation which he experienced could be attributed to sulforthomidine. In this trial, therefore, sulforthomidine proved singularly free from side effects.

The difference between the control group and the sulforthomidine group was more striking than Table 7 indicates. The ENL in the sulforthomidine group was mild. In the dapsone group not only were 8 patients (57%) affected, but 4 of these were severe and 2 were grave patients. One of the latter exhibited Lucio-like sloughing of the lesions. In this small series, therefore, sulforthomidine showed no tendency to exacerbate ENL. This was also the experience of Wilkinson and Barclay (1964) who treated 33 lepromatous patients with sulforthomidine for periods varying from six months to three years. They comment that this drug appeared less prone to give rise to leprotic reactions than other anti-leprosy drugs and could even be administered during reactional phases.

Other Complications

Four patients had mild neuritis while on dapsone therapy prior to the trial but none suffered from active neuritis during the trial and no comparison can be made. Two patients (female) were found to be suffering from endemic colloid goitre. In view of the tendency of sulphonamides to interfere with thyroxine synthesis these patients were watched carefully. No aggravation of the goitre occurred. Another 2 female patients in the sulforthomidine group were pregnant. Their pregnancies and deliveries were uneventful, and there was no exacerbation during the subsequent six months of lactation.

As sulforthomidine has been shown to be a potent schizonticide in falciparum malaria (Laing, 1965) and dapsone also has antimalarial properties (Archibald and Ross, 1960) it was considered of interest to examine blood films for malaria parasites. Thick and thin films were taken from all patients in the first and in the sixth month of the trial. Scanty ring forms resembling Plasmodium falciparum (three parasites per 100 thick film fields) were found in one patient only in the first month while receiving sulforthomidine. No parasites were found in any other patient whether on dapsone or sulforthomidine.

TABLE 5

Incidence of Side Effects

	Prior to Trial	*During Trial*	*Reduction in incidence of side effects*
Trial Group	11 patients	1 patient	
	(69%)	(6%)	90%
16 patients			
	Dapsone 0·3 g. twice a week	Sulforthomidine 1 g. once a week	
Control Group	11 patients	4 patients	
	(78%)	(28%)	64%
14 patients			
	Dapsone 0·3 g. twice a week	Dapsone 0·3 g. twice a week	

TABLE 6

Type of Side Effect and Number of Patients Complaining of Each Side Effect

	Before Trial		*During Trial*	
	Control Group on Dapsone	Trial Group on Dapsone	Control Group on Dapsone	Trial Group on Sulforthomidine
Headache	5	8		0
Deep Aches	4	6	1	0
Formication	4	4	2	0
Itching	1	1	1	0
Lassitude	0	0	0	0
Abdominal Colic	0	1	0	0
Epistaxis	0	0	1	0
Dizziness	3	2	0	0
Burning	1	0	0	1
Dermatitis	0	1 (due dapsone)	0	0
Total number of complaints	18	23	6	1
Reduction in Incidence of Side Effects			66%	95%

TABLE 7

Incidence of Erythema Nodosum Leprosum (ENL)

	Before Trial (all patients on dapsone)	*During Trial* (6 months)	*After Trial* (all patients on dapsone)
Trial Group 16 patients	2 patients (12%)	2 patients (on sulforthomidine) (12%)	2 patients (12%)
Control Group	3 patients (21%)	8 patients (on dapsone) (57%)	6 patients (43%)

Clincial Progress

The apparent improvement was greatest in the sulforthomidine group but in the absence of a double blind technique the assessment may be suspect. Improvement occurred in all patients, both subjectively felt and objectively seen, and was assessed as 'good' or 'very good' (Table 8).

TABLE 8

Clinical Improvement

The Number of Patients whose Improvement was Assessed as 'Very Good'

	Patient's Assessment (subjective)	*Clinician's Assessment* (objective)
Sulforthomidine Group, 16 patients	10 patients (62%)	14 patients (88%)
Dapsone Group 14 patients	7 patients (50%)	7 patients (50%)

The clinical improvement in the dapsone group was obscured by a greater tendency to ENL reactions and assessment was often difficult especially when focal exacerbations of ENL co-existed with appreciable general subsidence of leprous infiltration. All that can be said is that the clinical progress with sulforthomidine is as good as that achieved with dapsone.

Summary and Conclusions

Sixteen lepromatous leprosy patients were submitted to a six month clinical trial of sulforthomidine ('Fanasil' Roche), a long-acting sulphonamide administered orally in a dosage schedule of 1 g. once a week. A control group of 14 patients received dapsone 0·3 g. twice a week.

The clinical and bacteriological progress of the patients on sulforthomidine was as good as that achieved by dapsone. The incidence and severity of ENL reactions and the incidence of side effects attributable to the drug were much less in the sulforthomidine group than in the dapsone group. From this limited trial it appears that sulforthomidine is an effective anti-leprosy drug singularly free from side effects and reactions.

ACKNOWLEDGEMENTS

I wish to thank Roche Products Limited for supplies of 'Fanasil' and in particular Dr John Garrod of their Department of Clinical Research for providing information and for his constructive criticism. I am grateful also to Dr R. Park, Permanent Secretary, Ministry of Health, Malawi, for permission to publish this paper.

The B.P. Co m. approved name is sulphormethoxine Outside the United Kingdo drug is, however, known as sulforthomidine.

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Lep. Rev. (1966) **37,** 4, 209/216

Demodicidiasis and Leprosy

(Review and Proposal)

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Despite a wealth of speculation there is no proof that any arthropod serves as transmission agent for human leprosy (Dungal, 1961). As a suspect vector the acarine *Demodex folliculorum* is in some respects unique since it is (1) apparently ubiquitous with an incidence of 100 per cent (Fuss, 1933), (2) found in intimate association with *Mycobacterium leprae* in the skin complex (Borrel, 1908), and (3) probably passed from mother to young during the nursing process. Furthermore, Spickett (1961b) reported the presence of acid-fast bacteria in the gut of *D. folliculorum* and that the gut contents of the mite can be regurgitated. These observations point up the need for continuing re-evaluation and for further studies on the possible causal relationship between demodicidiasis and leprosy.

The present paper represents an attempt to examine all facets of our knowledge of the association of *D. folliculorum* and leprosy, to present information on the biology of other demodicids pertinent to an evaluation of this relationship, and to indicate a programme of study which could materially advance our understanding of the role, if any, of demodicidiasis in the initiation of leprosy.

Demodex folliculorum

Borrel (1908) was apparently the first to suggest an association between *D. folliculorum* and *M. leprae.* He found, in sections of skin from leprosy patients, that the bacteria were investing, i.e. closely surrounding, the mite (1909a). From this he speculated (1909b, p. 126) 'Le transport et l'inoculation dans le système pilaire peut certainement se faire au moment de la migration des parasites d'un nez lépreux à un nez sain.' He suggested (1909c) that *Demodex* as it fed on sebum could take up the bacillus and so transfer the organism to another host. His reports thus associated demodicid mites with sebaceous gland activity and leprosy transmission.

In some respects as pointed out by Spickett (1961b) the careful work of Gmeiner (1908) retarded investigation based upon the speculations of Borrel. He reported that in twelve different skin diseases demodicids were no more common than in normal skin. On this basis and from examination of skin sections which showed no inflammatory reaction associated with *D. folliculorum* he concluded that this demodicid was non-pathogenic (see Beerman and Stokes, 1934) and held no causal or cooperative position with respect to any disease. In a later paper (1909), however, Gmeiner discussed a consistent relationship in red mange of dogs wherein *D. canis* is associated with *Staphylococcus albus.* He stated that here the demodicids had prepared the way for the bacterial infection. He assumed that a like situation may well prevail in blepharitis associated with *D. folliculorum.* The analogy here with *M. leprae* is obvious and had this latter work been better known it undoubtedly would have served as a spur to leprosy-demodicid studies.

In 1910 LeFebvre, familiar with the work of Borrel, reported on studies of leprosy and *D. folliculorum.* He found a 25 per cent incidence of this mite in his examination of 100 patients with leprosy. He stated that this figure was nearly identical to that obtained from an examination of 'healthy' individuals. Although he found both the mite and *M. leprae* in the same hair follicle he could not find bacilli within the mites. He noted that demodicids are not found on the

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appendages of man, a predilection site for leprosy[sic], and also that in his studies no children were *Demodex* positive. His conclusion was that *D. folliculorum* was not a likely transfer agent of leprosy.

The work of Bertarelli and Paranhos (1910) was based also on the findings and speculations of Borrel. They examined 60 patients from the leprosarium at Guapira. According to their report only 15 of these [only 59 listed!] were positive for *D. folliculorum*. Furthermore, in their sample patients with abundant 'comedoni' (indicative of involvement and hyperactivity of the sebaceous glands) were rarely positive for *Demodex* (only 3 of the 59). They stated that many leprosy cases with advanced facial lesions had an abundance of the mite. This led them to the interesting idea that *Demodex* is a secondary invader of an area in which skin defences had been reduced by the leprosy bacillus. In a remark unfortunately not documented by data they noted that demodicids are scarce in negroes even though facial lesions of leprosy were present. Bertarelli and Paranhos concluded that their study gave no information in favour of the transmission of leprosy by *Demodex*.

Majocchi (1914) reported on some observations similar to those of Borrel. He suggested that the fusion of leprous nodules was responsible for placing the leprosy bacteria in contiguity with *D. folliculorum*. These last could then spread the disease either over the body of the infected host or to healthy individuals.

In two papers A. Serra (1912, 1921) reported the results of his examination of patients with leprosy for *D. folliculorum*. In brief his data show 32 of 80 positive for *D. folliculorum*. He found a higher incidence in 'tuberculoid' and 'mixed' (63+ per cent) when compared to 'anaesthetic' leprosy (36+ per cent). This mite abundance does, however, seem to correlate not so much with the kind of leprosy but rather with the presence or absence of comedones. His figures (1921) show that of 28 patients with abundant comedones 22 (or 78 per cent) were *Demodex* positive. Also in his study of 1921 he found 15 of 58 patients with *Demodex* and bacilli together in the examination samples. Serra smeared a mixture of *Demodex* and leprosy bacilli on a patient assessed negative for both but showing symptoms of 'anaesthetic' leprosy. Mites and bacilli were recovered in two months. He also experimented with applications of like material on dogs (no positive results) and inoculated a glucose preparation of the same material into the anterior chamber of the eye in rabbits (negative results). His attempts at demonstrating *Demodex* and bacilli in the hair follicle of man or bacilli in *Demodex* failed. Serra notes the difficulty of establishing *Demodex* as a vector if the bacilli are rarely found within the hair follicle or sebaceous gland. He also suggests that *Demodex* could produce an irritant which would induce mobile elements of the connective tissue to act as mediators between mite and bacilli.

In assessing the value of all of these survey accounts (Borrel through Serra) one should bear in mind that Gmeiner (1908) found normal people 97 per cent positive for *Demodex*. It is also true as noted by Serra (1921), and others since his report, that mites may readily be missed on one examination; subsequent study will often reveal their presence.

Since the work of Serra (1921), with the exception of Spickett (below), accounts of the *Demodex*-leprosy problem are either text-book allusions (e.g. Neveau-Lemaire, 193
papers commenting on the work of Borrel, Majocchi, or LeFebvre (e.g., Hirst, 1919; Dungal, 1961).

Included in his review of the possibility that *D. folliculorum* is a vector of leprosy bacilli Spickett (1961b) reported the following information:

1. *D. folliculorum* will ingest minute bits of plastic and resin.
2. These ingested particles are regurgitated by the mite.
3. Acid-fast bacteria are occasionally (in two ovigerous females) found in the gut of *D. folliculorum*.
4. *D. folliculorum* does penetrate the sebaceous gland to the dermis.

He also suggested that *D. folliculorum* might transport bacteria between hair follicles. This, however, is open to question since Spickett's assumption is based on very circumstantial evidence (Spickett, 1961a) that ovigerous females must have recently entered a hair follicle. This is certainly not assured as is indicated by such studies as Nicholas (1943) who

found large numbers of *D. folliculorum* in hypertrophied sebaceous glands and from studies of other demodicids as *D. caprae* where marked populations build up in one locale. There is certainly the added possibility that the bacteria within the mites as reported by Spickett were obtained from within the same hair follicle.

Spickett's (1961a) account of the biology of *D. folliculorum* which might be useful to studies of the *Demodex*-leprosy relationship does not take into account many interesting observations in older publications. Fuss (1933) in a very careful study of 104 individuals in age groups from children to 70 years found 100 per cent infestation with *D. folliculorum*. This mite has been found in man from all major areas of the world and in Caucasoid, Negroid and Mongoloid races (see LeFebvre, 1910; Yokayama, 1941; G. Serra, 1942). *Demodex* would, therefore, seem to qualify under Spickett's criteria that a transfer agent be ubiquitous, and be found in areas endemic for leprosy.

Hirst, in 1919, provided excellent figures to show that the mouth parts of *D. folliculorum* are stylet-like chelicerae admirably suited to cell penetration. He also noted the absence of an anus and the sac-like nature of the digestive tract. These two features plus the obvious undercutting and destruction of cells by this and other species led Nutting and Rauch (1963) to contend that all demodicids are primarily cell feeders. The implication or statement that *D. folliculorum* feeds only on sebum (Gmeiner, 1908; Spickett, 1961a – although revised 1961b) would appear unfounded. Several accounts are in existence of the occurrence of *D. folliculorum* in loci other than sebaceous glands (see Nutting, 1965). It has been noted (Nutting, 1964) that because of its low nitrogen content sebum is an unlikely product to sustain mite development.

It should be further borne in mind that the details of the life cycle of *D. folliculorum* (Spickett, 1961a) are based on short-term *in vitro* studies (6+ days on sebum) coupled with limited and circumstantial *in vivo* evidence. We need confirmation of the suggested mechanism and stage of transference (direct contact during the nymphal stage?), span of the life cycle ($14\frac{1}{2}$ days?), and movement between hair follicles (adults or nymphal stage?) as postulated by Spickett. As yet no complete study of the anatomy of any demodicid has been published although certain systems and a review account of our current position in this regard may be found in Nutting, 1950 and Nutting, 1964.

To date no attempt has been made to examine critically the physiology of any demodicid. Spickett (1961a) using *D. folliculorum* maintained on sebum or lanolin reported negative phototaxy for all stages, positive stereotaxy for larvae, protonymphs, and females with shifting stereotaxy for deutonymphs and males, no reaction in any stage to gravity, and that larvae feed continuously, males rarely and deutonymphs not at all. Although no survival studies for this species have been attempted Daniel *et al.* (1959) did find one mite viable in dry cerumen after four months.

Until we have more secure observational or experimental information on the biology of *D. folliculorum* we are in a weak position to assess the *Demodex*-leprosy problem.

Demodicids would seem to have access to *M. leprae* in the lumina of the hair follicles or sebaceous canals or even from within the cells of the pilo-sebaceous complex. They would, furthermore, appear capable of opening the pilo-sebaceous apparatus both by enlargement of the canals (distension and undercutting) and by actual penetration of the cells. Bacteria could be held in the sac-like gut and upon regurgitation or on death of the mite be liberated to the host tissue. In this last circumstance the problem of elimination from the exoskeleton is discussed below. Unlike many arthropods, demodicid salivary glands are solid (holocrine) cell masses (Nutting, unpublished) so that here only the hollow salivary duct could house bacteria unless these are able to survive intracellularly in the mite tissues.

Entry of *M. leprae* bacilli to the host cells from *D. folliculorum* could conceivably come about not only through regurgitation but also through phagocytosis of the infected mites by mesodermal giant cells (see Nutting and Beerman, 1965). Khanolkar (1959) has noted that *M. leprae* multiplies within phagocytic monocytes in silent cases of leprosy. These last are noteworthy for the fact that giant cells are also present both free in the dermis and associated with the nerves (Lever, 1961). Giant cells were found

in man by Bergstad (1925) in a tumour infested with *Demodex*. Similar cells have been reported in cattle (Nemeseri and Szeky, 1961) and dogs (French, 1964) as phagocytic for demodicids. In sections of skin infested with *D. bovis* which were recently examined in the laboratory of the senior author it appears that the chitinous exoskeleton is rapidly degraded even before degeneration of the internal cells of the mite. Definite lacunae are found in the exoskeletal wall sufficient in size to permit passage of bacteria to the cytoplasm of the giant cell. It would seem logical to presume that one should search here for a likely mechanism of bacterial inoculation. Infected mites could be the source for seeding giant cells with bacteria which could then multiply and spread from the giant cells to the surrounding tissue.

Fuss (1935) has discussed and depicted the marked polymorphism present in *D. follicularorum*. Specimens obtained by one of the authors of the present report (Pfaltzgraff) in North-east Nigeria are in several respects different from her account. The specimens from Nigeria are very similar to a human demodicid photographed but not discussed in taxonomic terms by Daniel *et al.* (1959). A recent paper (Akbulatova, 1964) states that two distinct subspecies of *Demodex* (*D. f. longus* and *D. f. brevis*) do occur in man.

With few exceptions due to the limitations of the host organism the studies on *D. follicularorum* are restricted to superficial examinations or study of biopsy material. Incidence surveys of cadavers (Gmeiner, 1908) have been few and have been carried out on carcasses available rather than on selected specimens with heavy demodicid infestations.

Demodex spp.

Since all 38 species and subspecies (Nutting, 1964) of the genus *Demodex* are remarkably alike in structure (see Hirst, 1919) and niche requirements (Nutting, 1965), it would seem profitable to examine facets of their biology which may be useful in studies of the *Demodex*-leprosy association.

Of all demodicids, *D. canis*, of *Canis familiaris* is the most thoroughly known. It is also of more direct interest to our problem in that it shares a relationship with a bacterium. Although normally an inhabitant of the hair follicle it has been reported free in the dermis (Krulikovskii, 1878), in the lymph nodes (Canepa and da Grana, 1941) and in most other viscera (Koutz, 1957; French, 1964). Canepa and daGrana found all stages of the mite life cycle in the lymph nodes which may indicate mite reproduction in this location. French stated that he could find no evidence of bacterial infection in the invaded lymph nodes. This is, however, not usually the case in the above mentioned dermal invasions which are associated with *Staphylococcus albus*. Apparently for this relationship no attempt has been made to locate bacteria within the mites. Bacteria and debris do adhere externally to *D. canis* as they move *in vitro* (Nutting, unpublished).

Several papers on *D. canis* purport to have discovered the mechanism of mite transference (Enigk, 1949; French *et al.*, 1964; Sako, 1965). This is reputedly not by an *in utero* route (see Unsworth, 1946) but rather by direct contact between bitch and pup during nursing. As suggested elsewhere (Nutting, 1965) the observational and experimental measures used by these investigators are not sufficiently critical to settle this issue.

Demodex caprae of *Capra hircus* have been found in papular lesions which may be either infected with or free of bacteria. Nutting (1950) reported that the contents, mites in all stages and an ether soluble product, of unruptured papules were commonly sterile. A suspect relationship in the goat between demodicids and lymphadenitis due to *Staphylococcus* spp. has been noted (Nutting, unpublished). Durant (1944, and personal communication) does not believe that a vector relationship is present in this association. The nodular lesions due to *D. bovis* in *Bos taurus* are said to be bacteria free (Nemeseri and Szeky, 1961) but as in French's account for *D. canis* no procedure for ascertaining this is given. Open nodular lesions are, however, often markedly suppurating in bovine demodectic mange. Lesions due to *D. caprae* represent the only assured source of large numbers of bacteria-free mites useful for vector studies.

Other than the dog, most laboratory animals so far examined in our University of Massachusetts laboratory (rabbit, guinea pig, rat, mouse, cat), have been either negative for demodicids or harboured very small mite

populations. The Golden Hamster, *Mesocricetus auratus*, is an exception to this. In these a remarkable host-sex difference in parasite load is apparent with low populations in females and high populations in males (Nutting and Rauch, 1963). In the latter populations are occasionally so high that one or more mites may be found in nearly every hair follicle! Mites have not been found in internal tissues including the uterus or in foetuses (Nutting, 1965). They have been recovered from the muzzle of suckling young at five days postpartum from mothers isolated in screened and sterilized cages (Nutting, 1950). The transference mechanism here seems to be by way of direct contact which in our studies proved 100 per cent effective. Both species of *Demodex* in the hamster have been shown to be low grade pathogens which harvest cells of the epidermis (*D. criceti*) or of the follicular epithelium (*D. aurati*) (Nutting, 1961). As noted elsewhere (Nutting, 1964) the hamster is an ideal laboratory animal for work on demodicidiasis, and may under improved experimental conditions prove to be a choice subject for *Demodex*-leprosy studies.

As far as we can discover no attempt has been made to see whether populations of *D. folliculorum* fluctuate with time of year. Such changes have been reported for *D. equi* (Bennison, 1943) and *D. bovis* (Poliakov, 1958). In these papers no experimental evidence is available to indicate the mechanism of population fluctuation. So far we have not been able to find any seasonal differences in *D. aurati* of the Golden Hamster under controlled laboratory conditions.

It should be mentioned here that other associations between demodicids and disease organisms have been suggested (Table I). We have yet to obtain any proof of a causal or cooperative connection between the mites and any disease entity. The work of Magnusson (1929) would seem to rule out a transfer role for *D. bovis* in hoof and mouth disease of cattle. As a working hypothesis demodicids should be held suspect as cooperative agents for any disease organism of the skin.

Facets of Investigation

From considerations of our knowledge of the biology of demodicid mites and the information on the association of *D. folliculorum* and leprosy certain fertile facets for investigation become apparent.

In laboratories associated with leprosaria it would be relatively easy to determine:

1. The incidence of *D. folliculorum* in leprosy patients *versus* 'controls' with attention to race, sex, drug regimen, age of the host and time of year.
2. Distribution of *D. folliculorum* in body areas and with respect to lesions of leprosy.
3. Whether or not *M. leprae* is found in the gut of *D. folliculorum* and confirmation of Spickett's observation on mite regurgitation.
4. If *D. folliculorum* commonly invades the dermis with especial attention to infections or degenerative changes in the skin.
5. Whether or not *D. folliculorum* is found in internal organs in man.

Other problems such as (1) if offspring delivered by Caesarean section with no history of nursing, which may negate Demodex transfer, develop

TABLE I

Suspect cooperative relationships, with some degree of circumstantial evidence, between demodicids and disease organisms.*

Disease	*Demodicid*	*Authority*	*Date*
Acne	*D. folliculorum*	Simon	1842
Pustulous mange	*D. canis*	Nunn	1878
Blepharitis	*D. folliculorum*	Stcherbatchoff	1903
Cancer	*D. folliculorum*	Borrel	1909d
Red mange	*D. canis*	Gmeiner	1909
Hoof and mouth	*D. bovis*	Magnusson	1929
Lymphadenitis (?)	*D. caprae*	Aynaud	1931
Nodulous mange	*D. bovis*	Momberg-Jorgensen	1943

*demodicids have been found in most skin diseases (see Gmeiner, 1908).

leprosy, and (2) if siblings from parents arthropod-free (i.e. other than *Demodex*) develop leprosy, could be resolved in long term studies.

Techniques for incidence studies of *Demodex* are simple and quickly performed. Mites are most readily recovered by examination of expressed sebaceous material from the facial naso-labial area. Lawrence (1916) recommends expression with a small silver spoon. One could also use a comedo expressor although this is relatively tedious. Expressed material may be examined under the microscope (mites are under 0·5 mm.) in the living condition by simply adding a drop of mineral oil. Permanent mounts can be made with Hoyer's solution (may be purchased from Wards Natural Science Establishment, Inc., Rochester, New York).

Biopsy or necropsy material should be fixed in 4 per cent formaldehyde. Sections, 10 microns thick, should be cut from paraffin blocks and stained with hematoxylin and eosin (HE). By noting their morphological and tinctorial characteristics it also is possible now to examine for presumably viable *M. leprae* on, in, or around demodicids *in situ* (Rees and Valentine, 1962). A further refinement could be made using carefully washed and crushed demodicids injected into the foot pads of mice (Shepard, 1960).

Sako and Yamane (1962) found that internal structures, especially lymph nodes, which were adjacent to skin areas with the greatest parasite (*D. canis*) loads were most heavily infested. It would, therefore, appear most profitable to examine cervical or axillary lymph nodes in cadavers with high populations of *D. folliculorum*. Lymph nodes may either be digested in KOH (5 per cent), centrifuged and examined for mite exoskeletons or they may be sectioned (10 μ), stained (HE) and examined under the microscope.

Three ideal experimental animals are currently available for *Demodex* studies, the dog (*Canis familiaris*), Golden Hamster (*Mesocricetus auratus*) and the goat (*Capra hircus*), all of these with large populations of demodicids.

As noted above *D. canis* of the dog is easily obtained and should be re-investigated in order to resolve (1) the mechanism of mite transference, (2) the relationship of *D. Canis* to *S. albus*, and (3) the origin and function of giant cells. Such information could offer some valuable leads to studies of the leprosy problem.

The large populations of demodicids in the male Golden Hamster seem ideal for experimental purposes. Not only are two species present, *D. criceti* and *D. aurati*, but these inhabit distinct niches in the skin complex and are rather generally distributed over the body of the host. Furthermore, in *D. aurati* a differential position in the hair follicle is apparent for the stages of the mite life cycle. Since moderate infections of *M. leprae* have been obtained in the ear and testis of the hamster (Binford, 1959) it would seem feasible to concentrate on this animal in studies of *Demodex*-leprosy relationships.

Hamsters are the present host of choice in screening drugs for the control of *Demodex*. So far no absolutely dependable measure is available to extirpate demodicids (see Koutz, 1957; Nutting, 1964). Should such measures be devised massive prevention or treatment in endemic leprosy areas would answer our major question. Whether or not these mites transmit leprosy we still need an effective control procedure to prevent other demodectic diseases (see Nutting, 1965).

Only in the goat do we have massive populations of demodicids (*D. caprae*) and these free of bacteria. The mites are found in large (to 32 mm.) papules from which they are easily obtained by sterile puncture. The University of Massachusetts laboratory is currently attempting to find whether or not *D. caprae* will ingest bacteria and if these are transported or regurgitated. We are also concerned with the possible vector role of this species in lymphadenitis. Goat demodicids are also well suited for studies of the *in vitro* effects of chemicals which might be useful in control.

Giant cells are reputedly obtained from preparations of whole blood (Lewis, 1925). It would be instructive to examine with the Lewis technique the response of giant cells to demodicid mites, *M. leprae* and if possible the result of giant cell phagocytosis of *Demodex* which contain *M. leprae*. As has been shown for *Trichomonas vaginalis* (Honigberg, personal communication) in man, it seems plausible that *M. leprae* may subvert or destroy giant cells and thus be in a position to cause further damage to the host. It is certainly possible that destruction by phagocytosis of demodicids with an internal flora of bacteria would liberate these to the detriment

of the phagocytic cell and subsequently to surrounding cells.

We should not overlook the suggestion of Gmeiner (1909) that demodicids may pave the way for the establishment of bacterial infections. Their activity which enlarges the lumen of the hair follicle and their ability to penetrate cell membranes may well be necessary features in leprosy invasion. Such factors coupled with the apparent ubiquity and sure mechanism of mite transfer from mother to young could account for the long term close contact which may be necessary for leprosy transmission. It could also explain the baffling and spotty results of such studies as Worth's (1960) where various rearing procedures for children from mothers with leprosy gave conflicting results for incidence of the disease.

Undoubtedly most of the suggestions above will be studied and the questions resolved in the next few years. A large laboratory could conceivably undertake the entire programme but it is more likely that independent workers will attack one or more of the separate facets of the problem. In either case it would seem profitable to pool our thinking and our experimental programmes along these lines so that cooperative timing or the benefits of new perspective may reduce the period necessary to determine whether or not demodicids are in any way causally related to human leprosy.

Summary

1. The literature on *Demodex folliculorum* pertinent to the problem of the possible transmission of *Mycobacterium leprae* and the initiation of leprosy is reviewed.

2. Information on other demodicids (esp. *D. canis D. caprae* and *D. aurati*) is also presented with an eye to its use in resolving the suspect relationship of *D. folliculorum* and *M. leprae*.

3. A number of suggestions are made which would materially aid an attempt to settle the problem of whether or not there is any causal relationship between *D. folliculorum* and leprosy.

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IN MEMORIAM

Dr Edgar B. Johnwick, Medical Officer in Charge, Public Health Service Hospital, Carville, La. passed away on October 14, 1965. His pleasant, helpful and catalytic personality will be missed deeply by all of his friends and by his associates in problems of leprosy.

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A Method of Medial Tarsorraphy for Correction of Lagophthalmos and Ectropion

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In recent years the operation of 'Temporalis Musculo-fascial Sling' has become the operation of choice in many patients with lagophthalmos. The older operation of 'tarsorraphy' still has its place in the protection of the eye in older patients, and in patients where temporary protection is needed until recovery occurs or more extensive surgery can be done.

It has been stated that a closure of at least one third of the fissure is necessary for an effective result but this frequently results in an unsightly appearance and hence many patients refuse lateral tarsorraphy. Also ectropion of the lower lid may occur especially at the inner end causing watering. A combination of lateral and medial tarsorraphy is frequently more cosmetically and more functionally effective than a lateral tarsorraphy alone.

Various modifications of operations recommended for ectropion and lagophthalmos have been tried and found unsatisfactory. Basically I feel that this is because little attention has been paid to the basic anatomical defect. It will be noticed that when a normal eye is tightly closed the skin of the forehead and cheek is pulled inwards towards the medial angle of the eye. This is the normal function of the obicularis occuli muscle that is not functioning in lagophthalmos, and hence a sagging of the skin away from the medial angle of the eye results. In an attempt to correct this defect the following operation was devised and has been found effective over a period of four years.

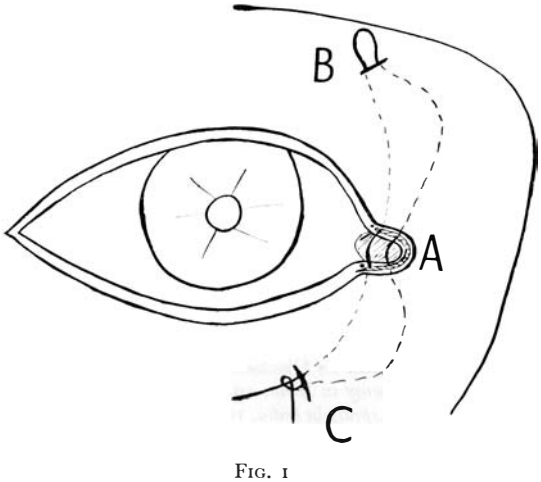

FIG. 1
Diagram of the Suture route.

Method

(*a*) The medial epicanthal skin is prepared as for a routine tarsorraphy. The incision extends along the grey line from the level of the upper punctum to the lateral side of the lower punctum. If the incision is kept to a depth of 1 mm. and on the outer edge of the lid there is little danger of damage to the lacrymal apparatus whose position can be checked by the passage of a probe. The incision is deepened by blunt dissection to make a raw surface about 2 mm. wide.

(*b*) An incision is made, about 2 mm. long, slightly lateral to the upper punctum and just below the orbital margin.

(*c*) An incision is made, 2 mm. long, about 1 cm. lateral to and 1·5 cm. below the lower punctum, and deepened slightly.

(*d*) A length of monofilament nylon (No 6x0) is passed from (C) to the lower half of (A) near the punctum. It passes across the caruncle and into the upper edge by the punctum and out at (B). Here the direction is reversed so that the needle enters at (B), biting deeply to catch the fascia around the orbit and to take a different path back to the upper border of (A), more medial than the point of entry, then across the caruncle and by a different route to (C).

(*e*) One or two small black cotton sutures are used to ensure eversion of the skin edges of A. (Remove in 3 days.)

(*f*) The nylon is then pulled sufficiently tight to slightly over-correct the defect. It will be noticed that the skin is pulled in towards the medial angle of the eye. It will also be realised that the lower lid can be shortened relatively to the upper lid by careful selection of the sites where the nylon passes across the caruncle. The nylon is knotted at least three times to prevent slipping and cut short. It is usually possible to bury the ends without suturing the incision C.

(*g*) The minimum of dry dressings may be applied but it is frequently not necessary.

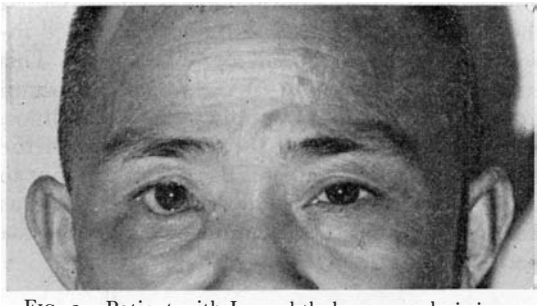

FIG. 2. Patient with Lagophthalmos on admission.

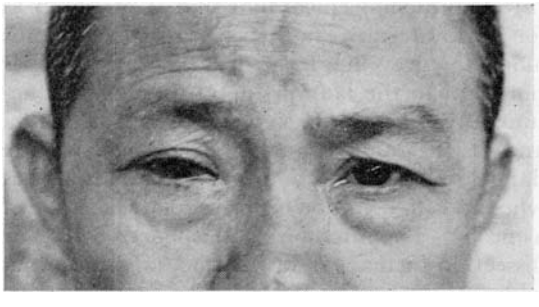

FIG. 3. Same patient after Medical Tarsorraphy with eyes open.

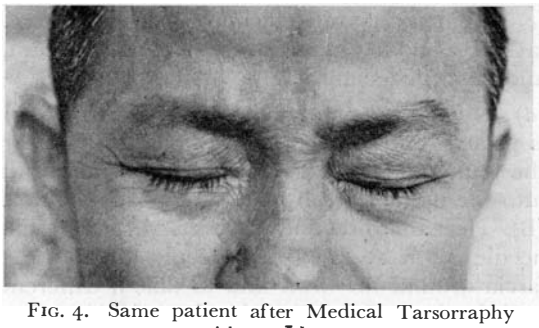

FIG. 4. Same patient after Medical Tarsorraphy with eyes shut.

This procedure has been used on over 25 patients; some previously failed by other methods. The first patient was in December 1960 and is still functional with the nylon *in situ*. It has caused no trouble though previously he had had several types of closure that had produced inadequate results.

This method generally gives better functional and cosmetic results than more conventional procedures. The patency of the lacrymal apparatus has been checked on a number of cases after surgery and found patent. Many patients claim marked relief from watering which is often the original complaint; this is easily explained as the lower punctum is brought into better apposition with the eyeball.

Failure has occurred but is is usually due to insufficient tension in tying the nylon.

Summary

A method of medial tarsorraphy using a buried nylon suture is described. The suture does not have to be removed and so provides a more permanent as well as a more cosmetically acceptable answer to the problem of lagophthalmos than many other methods.

ACKNOWLEDGEMENTS

I am very grateful to Dr Margaret Brand for her careful tuition in the care of the eyes of leprosy patients and for her encouragement and assistance in the production of this article.

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The Use of a Dermojet Injector for Skin Biopsies

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Since the report by Krantz (1960) on the successful use of a dermojet injector for local anaesthesia, this instrument has been found to have a wide range of usefulness: in dental surgery (Stephens & Kramer, 1964); in dermatology (Juel-Jensen & MacCallum, 1965; Moynahan & Bowyer, 1965); in large-scale programmes of B.C.G. vaccination (Griffiths *et al.*, 1965) and of measles vaccination (Cooper *et al.*, 1966). The object of this paper is to show that it can also be of value in carrying out skin biopsies.

The dermojet injector ('jet-gun') is a compact apparatus 16 cm. long, and when held at right angles to the skin, with the nozzle 0·5 cm. away, painlessly delivers 0·1 ml. of fluid into the dermis when the trigger is pressed by the thumb – fig. 1. The problem was to find the best way of delivering the local anaesthetic into the skin using the minimum number of applications, and it was soon found that the actual region of skin injected was of no value to the histologist because of tissue disruption. By a process of trial and error a successful method evolved, and consisted of cleaning the skin with ether, drawing a circle 1 cm. in diameter around the biopsy site with a skin-marking pencil, and then administering a jet of local anaesthetic at eight points around, yet close to the circle – fig. 2. It is simple enough to space the eight insertions of local anaesthetic outside the circle as a wheal appears immediately at each site, and after waiting a minute or two the region within the circle is ready for biopsy. Slight discomfort may be experienced when the deepest part of the tissue is removed but is no worse than with standard methods of anaesthesia. As the chamber within the dermojet holds 4·0 ml. of fluid, five biopsies can be carried out before refilling, so there can be a considerable saving of time if a large number of biopsies are required as, for example, under field conditions; also expense is curtailed as the only syringe required is the one with which to fill the chamber.

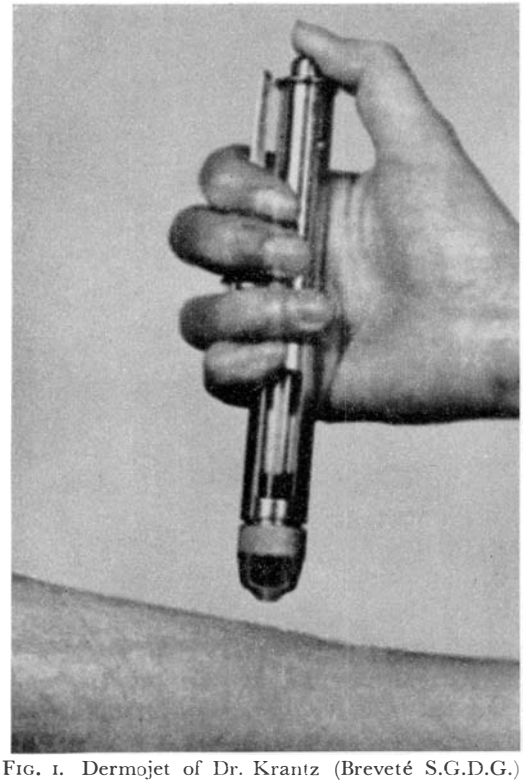

FIG. 1. Dermojet of Dr. Krantz (Breveté S.G.D.G.) as used in this trial.

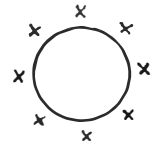

FIG. 2

ACKNOWLEDGEMENTS

I would like to thank Dr R. J. W. Rees of the National Institute for Medical Research for suggesting that this trial should be carried out; Dr P. W. Muggleton of Glaxo Group Ltd. for supplying a dermojet on loan; and Dr D. S. Ridley of the Hospital for Tropical Diseases for the histological examinations.

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A.B.O. Blood Groups in Leprosy

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The exact mode of transmission of leprosy is still controversial, despite numerous epidemiolocal studies in leprosy. It has been shown beyond doubt that exposure to the infection is not the sole factor in the spread of the disease since a number of individuals exposed to an open patient do not develop the disease.

A few factors other than mere contact with *Mycobacterium leprae* have recently been emphasized. Genetic factors have been considered significant in this direction (Ali and Ramanujam, 1964, and Ali, 1965) and were recently discussed in an international conference at Washington (Blumburg, 1965, and Lechat, 1965). Hsuen *et al:* (1963) from South India reported an association between the incidence of leprosy and A.B.O. blood groups. They have shown that its incidence is nearly twice in O group as compared to the B group. Beiguelman (1964), however, pointed out that a significant excess of A frequency was found in the lepromatous as compared to the tuberculoid samples. With respect to O frequency, a similar, but slight excess of this group was found among tuberculoid patients as compared to lepromatous patients. On the other hand Sato (1949), Yankah (1965) and Verma and Dongre (1965), recorded no specific relationship between leprosy and A.B.O. blood groups.

The present study was undertaken in Varanasi district in Uttar Pradesh, India, to further evaluate the observations made by aforesaid workers.

Material and Methods

623 patients of leprosy were drawn from the outpatients of Sir Sundar Lal Hospital and leprosaria in Varanasi. The patients were diagnosed clinically by salient diagnostic criteria (Dharmendra, 1960) and classified into lepromatous and non-lepromatous types, whereas in doubtful patients histological studies were undertaken to confirm the clinical impressions.

In the control series 615 first time blood donors at Sir Sundar Lal Hospital were taken for the blood group frequency examination. Only those persons who belonged to Varanasi district were included. Leprosy in all these cases was excluded by thorough clinical examination.

Blood for blood grouping was taken by finger prick method, but where this was not possible, it was obtained from the cubital vein. The blood grouping was done immediately by the slide method.

RESULTS AND DISCUSSION

The frequency distribution of lepromatous and non-lepromatous patients is shown in Table 1.

The distribution of blood groups in control and leprosy patients is given in Table 2.

The statistical analysis of the data reveals that the blood group incidence in control series and leprosy series is significantly different ($X^2 = 41 \cdot 125$ df $= 3$ $p < 0 \cdot 001$) while no significant difference is observed between lepromatous and non-lepromatous leprosy groups in their blood group distribution ($X^2 = 3 \cdot 917$ df $= 3$, $p > 0 \cdot 20$). On further analysis of the data comparing the blood group distributions of control, lepromatous and non-lepromatous series separately it is found that the blood group distributions of the two types of leprosy are significantly different from the control series ($X^2 = 11 \cdot 510$ df $= 3$ $p < 0 \cdot 01$) and $X^2 = 41 \cdot 728$ df $= 3$ $p < 0 \cdot 001$ respectively).

The B group in control series is 39·7% while in Leprosy series is 25·4%. This differ-

TABLE I

Type	NUMBER OF PATIENTS	
	Number	*Percentage*
Lepromatous	169	27·13
Non-Lepromatous	454	72·87
Total:	623	100·00

TABLE 2

Distribution of Control and Leprosy Series According to their Blood Groups

Blood Group	*Control Series*		*Lepromatous Series*		*Non-Lepromatous Series*		*Combined*	
	No.	%	No.	%	No.	%	No.	%
A	119	19·3	49	29·0	155	34·2	204	32·7
B	244	39·7	49	29·0	109	24·0	158	25·4
O	191	31·1	59	34·9	144	31·7	203	32·6
AB	61	9·9	12	7·1	46	10·1	58	9·3
Total:	615	100·0	169	100·0	454	100·0	623	100·0

ence is highly significant ($X^2 = 28·92$ df $=$ 1 $p < 0·001$).

While the A group is found in excess in the leprosy series (control 19·3% and leprosy 32·7%), this difference is also significant ($X^2 = 29·80$ df $= 1$ $p < 0·001$). It is evident from the data charted above that there is an association between leprosy and blood groups. Observations of the present series are thus in conformity with the results of those of Hsuen *et al.* (1963) and Beiguelman (1964) who have reported an association between leprosy and blood groups. However, these results do not support the observations of Yankah (1965) from Ghana and Verma and Dongre (1965) from Baroda.

SUMMARY

623 patients of leprosy and 615 normal controls have been studied in a section of the community in Varanasi district, UTTAR PRADESH, INDIA. The distribution of A.B.O. blood groups in relation to leprosy is analysed and it seems that there is an association between leprosy and A.B.O. blood groups.

ACKNOWLEDGEMENTS

We express our thanks to Dr K. N. Udupa, Principal, College of Medical Sciences, Banaras Hindu University, Varanasi, and the Civil Surgeon, Varanasi district, for their encouragement and help during this study. We are indebted to Dr R. S. Shukla, Blood Bank Officer, and his staff for their timely help.

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An Appendix to the Article

A.B.O. Blood Groups in Leprosy

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The distribution of individuals according to their blood groups varies from group to group. Especially in a country like India which has various tribes and groups of people, there are many blood group distributions. This difference is even more predominant from one part of India to the other.

Various studies have been done on the comparison of blood group distribution of normal persons with leprosy patients (Tables 1 and 2). Amongst them Hsuen *et al.* (1963) from South India have shown that the blood group distributions of normal and leprosy patients are significantly different. Verma *et al.* (1965) from

TABLE 1

Showing the Blood Group Distribution of Normal Persons and Leprosy Patients by Various Workers in India

Blood Group	*South India* HSUEN *et al.* (1963)				*Baroda District* Verma *et al.* (1965)				*Varanasi District* *Sehgal *et al.* (1966)			
	Control Series		*Leprosy Series*		*Control Series*		*Leprosy Series*		*Control Series*		*Leprosy Series*	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	214	21·4	130	24·7	242	24·2	156	26·3	119	19·3	204	32·7
B	331	33·1	123	23·4	347	34·7	231	38·9	244	39·7	158	25·4
O	397	39·7	257	48·9	335	33·5	177	29·8	191	31·1	203	32·6
AB	58	5·8	16	3·0	76	7·6	30	5·0	61	9·9	58	9·3
Total	1000	100	526	100	1000	100	594	100	615	100	623	100

*Present Series

TABLE 2

Showing the Blood Group Distribution of Lepromatous and Non-Lepromatous Types of Leprosy by Various Workers in India

Blood Group	*South India* HSUEN *et al.* (1963)				*Baroda District* Verma *et al.* (1965)				*Varanasi District* *Sehgal *et al.* (1966)			
	Lepromatous		Non-Lepromatous		Lepromatous		Non-Lepromatous		Lepromatous		Non-Lepromatous	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A	62	24·0	68	25·4	74	25·7	82	26·8	49	29·0	155	34·2
B	68	26·4	55	20·5	111	38·5	120	39·2	49	29·0	109	24·0
O	121	46·9	136	50·8	92	31·9	85	27·8	59	34·9	144	31·7
AB	7	2·7	9	3·4	11	3·8	19	6·2	12	7·1	46	10·1
Total:	258	100	268	100	288	100	306	100	169	100	454	100

*Present Series

Baroda have stated that there is no significant difference between the two groups in their blood group distributions. Further in the series reported in this article from Varanasi an association is found between leprosy and blood group distribution.

On a comparison of the blood group distribution of the normals as well as the leprosy patients, separately, in these three series it is observed that the distributions are significantly different ($X^2 = 27{\cdot}63$ $P < 0{\cdot}001$ for normals and $X^2 = 87{\cdot}73$ $P < 0{\cdot}001$ for leprosy patients).

If a consolidated study of all these 3 groups is to be made it is not advisable to conjoin the observations of control and leprosy patients of all the 3 series into their respective blood groups. Hence a suitable method used by Doll & Hill (1956) and referred to by Radhakrishna (1965) to conjoin the data from different contingency tables is utilised.

By this method we calculate X^2 from the formula $X^2 = \Sigma \frac{(O-E)^2}{E}$ where O and E are the cumulative observed and expected values in each of the cells calculated on the basis the respective individual distributions.

Analysing the data utilising the above method the following results are observed:

1. The blood group distributions of control and leprosy series are significantly different ($X^2 = 32{\cdot}93$ $P < 0{\cdot}001$).
2. No significant difference is observed between Lepromatous and Non-Lepromatous types of leprosy in their blood group distributions ($X^2 = 4{\cdot}995$ $P > 0{\cdot}10$).
3. An excess of A group is observed in the leprosy series compared with the control series ($X^2 = 18{\cdot}98$ $P < 0{\cdot}001$).
4. An excess of B group is found in the control series compared with the leprosy series ($X^2 = 16{\cdot}75$ $P < 0{\cdot}001$).

All these results are in conformity with the observations of Hsuen *et al.* and the author's present series of Varanasi data.

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A Case Report of Gangrenous Balanitis in Progressive Reaction in Leprosy

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INTRODUCTION

Erythema nodosum leprosum is the most common reactional manifestation of lepromatous leprosy. It occurs as crops of discrete nodules, more rarely as raised patches varying in size from a few mm. to a few cm. in diameter. The nodules are usually found on the face and extremities and less often on the trunk. They are painful and tender. The individual nodules last from 3 to 4 days to a week or longer. In the subacute or chronic form, the condition continues unabated and constitutes a serious reactional condition which Cochrane (1964) describes as 'Progressive Reaction'. The subcutaneous nodules in this type of reaction have a tendency to break down and ulcerate resulting in great distress to the patient. A description of a case of such progressive lepra reaction in a young African where ulcerative breakdown resulted in gangrenous balanitis is given in this paper.

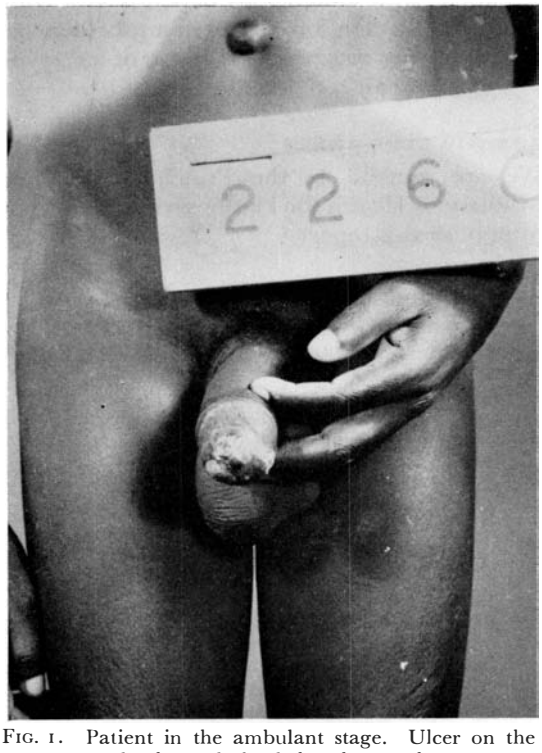

FIG. 1. Patient in the ambulant stage. Ulcer on the glands partly healed and scarred.

History

A lepromatous Ghanaian boy of 15 years, admitted to Ankaful Leprosarium, developed progressive lepra reaction. On admission the patient was graded as infiltrative lepromatous leprosy. His general health was poor and he had oedema in both feet. Prior to his admission to Ankaful Leprosarium, he had treatment for one year at Ho near the Eastern Border of Ghana. Later he was admitted to Ho leprosarium for treatment of frequent subacute reactions. He was referred to Ankaful from Ho. On admission to Ankaful, the following laboratory findings were obtained:

Skin smear — B.I. = 2+(Ridley)
— 50% Fragmented
50% Granular
Haemoglobin 68% — 9·9 g.% (Eel)
Sickling — Negative.
Blood film for malaria and filaria — Negative.
Blood Group — A
Skin snip for Onchocerca Volvulus — Negative.
Examination of urine for *Schistosoma haematobium* — Negative.
Urine examination for Albumen and Sugar — Negative.
Examination of stool for hookworm and roundworm — Negative.

Histopathological Report

'Epidermis shows flattening of rete pegs. Subepidermal zone partly invaded with lymphocytes. Infiltration mostly perivascular and around skin structures. No follicle formation noticed and few macrophages seen. Nerves invaded but mostly perineuritis. Picture suggests lepromatous leprosy with borderline features'.

Case History

The patient admitted for treatment in November 1963 has had very frequent erythema nodosum leprosum. He was put on parenteral DDS. 125 mgm. weekly and thiosemicarbazone 75 mgm. daily. In periodic reviews it was observed that B.I. remained fairly constant. He developed severe ENL in September 1964 and after 3 days, there was increase in the nodules with breakdown of a nodule on the glans penis forming a big ulcer. The edges of the ulcer were elevated and indurated. The ulcer covered nearly half the entire glans and extended mostly on the dorsal surface. The granulating base was covered with a thick purulent exudate and dirty necrotic detritus.

There was oedema in the rest of the glans. The patient was acutely ill and also developed several superficial ulcers on the soles of feet. There was no ulceration on the skin of the penis or scrotum.

Treatment

The management of the patient was by giving intramuscular injections of ACTH, and Fantorin (trivalent antimony), intravenous Terramycin in Dextravan drips, iron and multivitamin by mouth, liver extract and Largactil (chloropromazine) parenterally. The ulcer was dressed with nonad tulle. The recovery was complete although slow.

The ulcerated part of the glans healed with a scar. There was no difficulty in micturition. His general health improved and reactions settled down.

DISCUSSION

Gangrenous balanitis as a complication of progressive lepra reaction is not reported in the literature so far. Cochrane mentions orchitis, lymphadenitis, iritis, progressive cachexia and rarely amyloidosis as accompaniments or terminal complications in progressive lepra reaction. Molesworth (1965) confirms occurrences of similar ulcerative breakdowns and sloughing of indurated areas as frequent in Malayan patients. Andrews (1954) states that gangrenous balanitis is encountered mostly in young Africans suggesting a racial proclivity. He adds that the condition is extremely painful and sometimes fatal. The common conditions, he mentions, as causing this, are syphilis, chancroid and granuloma inguinale which were excluded in this case.

SUMMARY

A patient with gangrenous balanitis as a complication of ulceration arising in a subcutaneous nodule during progressive reaction of leprosy in a young African is reported.

ACKNOWLEDGMENTS

We are grateful to the Principal Secretary, Ministry of Health for kindly giving permission to publish this report.

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Notes on the Treatment of Ulcers in Leprosy Patients with Polybactrin

by the late Dr. P. GLYN GRIFFITHS, M.C., M.B., CH.B., M.R.C.P.,
Liteta Leprosarium, Zambia.

History of 2 patients with large ulcers successfully treated with Polybactrin spray, Cicatrin powder and Cicatrin cream at Liteta Leprosarium, Zambia.

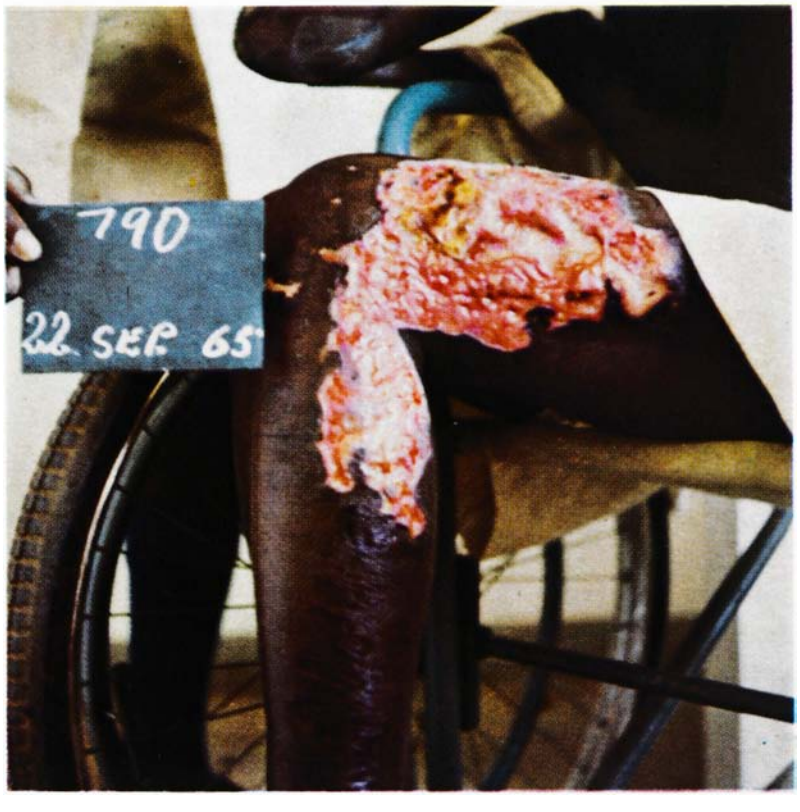
The following 2 patients with large ulcers were successfully treated with Polybactrin spray, Cicatrin powder and Cicatrin cream by Dr. P. G. Griffiths who intended to publish the results of these cases but wanted to treat a few more patients before publishing the results. The author died on 14th May and it has been possible to publish these notes posthumously by the help of Dr. F. Imkamp, Medical Officer in Charge, Liteta Leprosarium.

Polybactrin, manufactured in England by Calmic Ltd., Crewe, is an antibiotic powder spray containing bacitracin, neomycin and polymyxin.

Cicatrin is an amino acid antibiotic powder containing per g.:

neomycin sulphate	3.3 mg. base
zinc bacitracin	250 units
l-Cysteine	2 mg.
dl-Threonine	1 mg.
Glycine	10 mg.

NOTES OF PATIENT NO. 1 (*Liteta Patient No* 790)
Was admitted to Liteta on 29.9.56 with lepro-

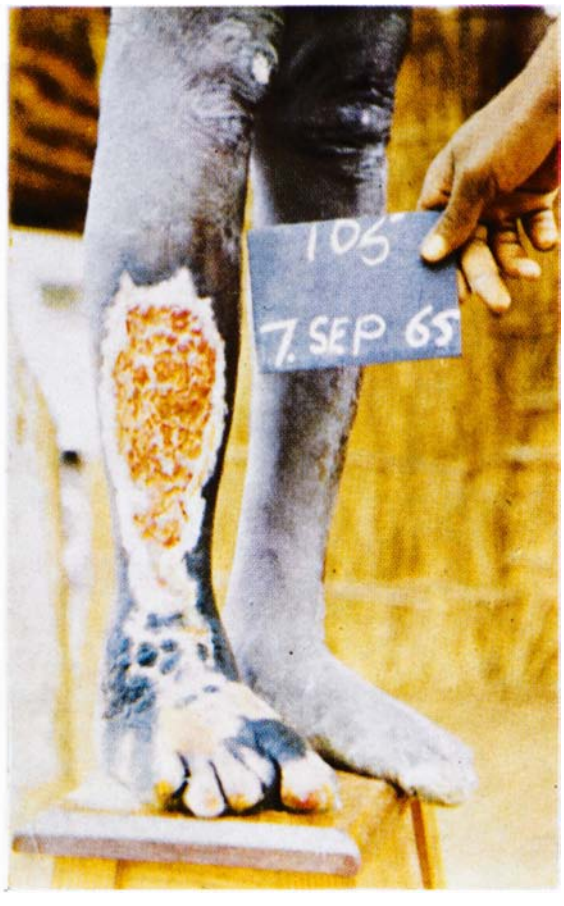


matous leprosy and discharged to outpatient treatment. He was re-admitted to Liteta on 18.9.65 with a huge, deep sloughing ulcer on his left thigh due to burning. (Photo: 22.9.65.) The ulcer was treated with Polybactrin spray first, followed by vaseline gauze and bandage, but as from 15.10.65 only Polybactrin spray was applied daily covering the entire ulcer and no dressings applied. Photo: 23.12.65 shows the end result and Griffiths' note, "completely healed." The patient was discharged on 12.1.66 and advised to return at once if the ulcer should break down. The patient was seen by Griffiths at Kampumba Clinic on 13.4.66 and Griffiths reported—"ulcer healed".

NOTES OF PATIENT NO 2 (*Liteta Patient No.* 105) Was admitted to Liteta on 20.10.60 with lepromatous leprosy and discharged on 18.5.65 to outpatient treatment. He was re-admitted to Liteta on 15.7.65 with an enormous ulcer of his right lower leg and right foot. Griffiths' remarks on 7.9.65: "patient still has a huge ulcer of right lower leg". (Photo: 7.9.65) Treatment was then started with Polybactrin spray followed by Cicatrin cream and bandage applied. 11.9.65 Patient much improved. "There is now a ½in. x 1 in. diameter healing area all round the ulcer". (Griffiths). 15.10.65 "Ulcer much smaller. Half the original size". (Griffiths)

From now on the ulcer was treated with Polybactrin spray only, bi-weekly and later daily, and no dressings applied. The ulcer was closed at the end of April and the last picture was taken on 9.5.66 by Griffiths when visiting Liteta. Unfortunately his camera was stolen. To complete the case history another photo was taken on 10.6.66. The ulcer is completely healed and the patient is doing full duties as a cleaner at Liteta Leprosarium.

It is not suggested that this method of treatment be used in the proximity of joints where scar contracture would produce disability.



SUMMARY

Under Dr. Glyn Griffiths 2 patients suffering from lepromatous leprosy complicated by ulcers of the thigh and leg were treated with Polybactrin spray, Cicatrin powder and Cicatrin cream (Calmic Ltd., Crewe, England) with very satisfactory healing of the ulcers.

ACKNOWLEDGMENTS

Thanks are due to Mrs. I. M. Griffiths for permission to publish this report, to Dr. M M. Nalumango, Permanent Secretary of Health, for permitting publication, and to Messrs. Calmic Ltd., Crewe, England, for their generous supply of Polybactrin spray, Cicatrin powder and Cicatrid cream.

Lep. Rev. (1966) **37**, 4, 231/237

Acetylcholine Test for Anhydrosis in Leprosy

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KAPADIA, B. I.,‡ and NAIK, S. S.‡

Since Father Joseph Damien de Veuster's observation in 1889 that on the early macules of leprosy which appeared on his own skin perspiration did not appear, many authors were inspired to investigate this localized anhydrosis in early patches of leprosy and also utilize this phenomenon for early diagnosis of the disease especially where the examination for the cardinal signs of leprosy gave doubtful results.

Physiology of sweat secretion

The physiology of sweat secretion is a complex matter. The sweat gland structures are supplied by the non-medullated sympathetic fibres, which form a close plexus on the outer surface and give off fibrils to the glandular and muscular cells. Unlike other sympathetic innervated structures they are not 'adrenergic' but are 'cholinergic'.

Anhydrosis, partial or absolute, may be due to deficiency, destruction or absence of the secretory apparatus.

It may result from congenital ectodermal defects and may be associated with other physical characteristics showing:

1. symmetric volar keratosis with follicular keratosis of the body.
2. keratosis of hands, feet and body with leukoplakia of mouth or
3. these changes combined with corneal alternation or cataract.

Localized anhydrosis may occur due to a variety of causes leading from disorders of the nervous system to the skin lesions. The anhydrosis is symptomatic in ichthyosis, ectodermal defects, extensive psoriasis, scleroderma, morphea, other cicatricial lesions including roentgen dermatitis, avitaminosis A, neuritis and leprosy.

Intradermal Tests

Anhydrosis resulting from the early denervation of sweat glands supplied by the cholinergic postganglionic sympathetic fibres, due to neuritis of leprosy has led many authors to devise intradermal sweat tests (sudomotor tests) for the early diagnosis of leprosy.

As pilomotor and vasomotor responses also seem to be affected in this way, a series of intradermal tests are available as diagnostic aids.

The following are the more important of these:

Sudomotor Tests:

(a) Pilocarpine nitrate, (Dubois & Degotte, 1938).
(b) Metacholine, (Arnold, 1948).
(c) Adrenaline, (Wada, 1950).

Pilomotor Test: Nicotine Picrate (Arnold, 1953); (Rothman, 1953).

Vasomotor Test: Histamine (Rodriguez and Plantilla, 1933).

It is not proposed to go into the relative merits of these various tests, as the majority of these are not being used widely either because they cannot be interpreted satisfactorily or these tests are positive in other dermatological conditions such as achromia parasitica, mycotic infection, scleroderma, morphea etc. It is also debatable whether the affection of sympathetic fibres occurs before the other fibres subserving heat, touch and pain sensations are affected by *M. leprae*. According to Arnold (1948) impairment of the sweat function precedes the development of demonstrable anaesthesia.

Aim of the Study

The increasing need for early diagnosis of leprosy among hypopigmented lesions due to various causes prompted us to study whether any simple and better intradermal test will be of

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help as a diagnostic aid, as a considerable number of such cases have to be kept under observation without arriving at a diagnosis for want of unequivocal demonstration of the cardinal signs of leprosy.

Material

The study was made in 159 patients who attended the clinic of the Acworth Leprosy Hospital, Bombay, with hypopigmented lesions. Of these, 87 patients had well developed characteristic lesions of leprosy where the cardinal signs could be easily elicited and hence a diagnosis of leprosy could be made. Out of these 87 patients, 9 had multiple lesions some of which had no anaesthesia. In all, the lesions studied number 96 in 87 patients. These act as a control for the study of the test. The remaining 72 patients had hypopigmented lesions of doubtful origin which simulated early leprosy as well as other skin diseases or conditions.

Method

After routine clinical and bacteriological examinations for the cardinal signs of leprosy, sweat test with intradermal acetylcholine was performed in all the cases.

Sweat Function Test:

Materials used: (1) Acetylcholine (0·1% aqueous solution).

(2) Bromophenol blue paper.

Bromophenol blue paper is made as follows: 100 mgm. of bromophenol blue powder is dissolved in 10 cc. of absolute alcohol to make a 1% solution. The solution is poured on a Whatman filter paper no. 4 with the help of a pipette. The paper is allowed to dry and cut into square pieces of 1″ x 1″.

Method:

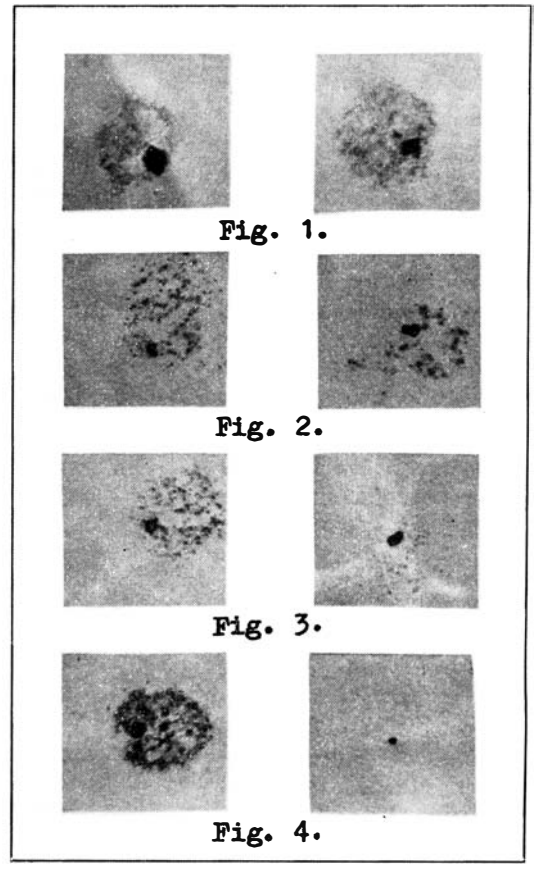
The lesion and a corresponding area of the skin on the other side which is normal are cleaned with spirit.

Acetylcholine (0·1% aqueous solution) is injected intradermaly in both the areas with a tuberculin syringe. 0·05 ml. is injected in each area. The droplets of solution that leak out from the injected sites are gently blotted off.

After 2 minutes 2 square pieces of bromophenol blue paper (which are actually yellow in colour) are pressed lightly on the sites of injection for 15 seconds and removed.

The sweat drops appear on the paper as blue dots. Interpretation of the test:

1. Normal: Number of blue spots close to each other with no appreciable difference as compared to the normal or control area. (Fig. 1).
2. Slightly diminished: Number of spots more than half but yet less than in the normal or control area. (Fig. 2).
3. Markedly diminished: Number of blue spots less than half the number found in the normal or control area. (Fig. 3).
4. Absence of sweating: No blue spots on the paper. (Fig. 4).



Bromphenol blue papers showing spots of sweat. The papers on the left represent the normal (Control) and those on the left the lesions.

TABLE I

Sensory changes	*Total*	RESULTS OF SWEAT TEST			
		Normal	*Slightly Diminished*	*Markedly Diminished*	*Absent*
Anaesthesia	41	1	—	14	26
Hypoesthesia	46	2	7	21	16
No anaesthesia	9	3	1	4	1
Total:	96	6	8	39	43

RESULTS

I. Lesions due to Leprosy (Control group).

Table 1 shows the results of sweat test in 96 anaesthetic as well as non-anaesthetic hypopigmented lesions of 87 leprosy patients of tuberculoid and maculo-anaesthetic type.

It will be seen from the table that out of 87 lesions which showed definite sensory impairment, diminution or absence of sweating could be demonstrated in 84 (96·6%) and only 3 lesions showed normal sweating. Out of 9 non-anaesthetic lesions, 6 (66·6%) had diminished sweating, while 3 showed normal sweat response.

Lesions of 'Indeterminate' leprosy (of the intermediate group) and lepromatous macules were not included in the present study as these lesions are bacteriologically positive for large numbers of bacilli and hence are easily diagnosed. (However, it may be stated that in two cases of leprosy of the 'Indeterminate' type in which the sweat test was done the lesions showed appreciable diminution of sweating.)

II. Lesions simulating early leprosy

Seventy-two patients had hypopigmented lesions resembling leprosy in which a diagnosis could not be arrived at after routine standard methods of examination. Histopathological examination was done in all these cases.

Out of these 72, 28 patients showed early infiltrative changes of a nonspecific nature suggestive of leprosy, as described by Khanolkar (1964), Dharmendra (1960), Ridley and Wise (1963) and Hasselmann (1963). The following criteria were considered for labelling biopsy slides as those showing nonspecific changes:

(i) Epidermis showing atrophy and narrowing of stratum malpighii or prickle cell layer with varying degrees of flattening of the rete-pegs.

(ii) Dermis showing infiltrative exudates predominently composed of lymphocytes, histiocytes and fibroblasts concentrated more around the pilosebaceous apparatus, sweat glands and neurovascular channels, with or without evidence of histiocytic granuloma in the formative stages.

Thirty-five patients showed more specific histological features of leprosy described by Khanolkar (1964) and Lever (1961). The following features were taken into consideration to grade cases into those showing 'specific' histology of leprosy:

(i) Chronic tuberculoid granuloma in the dermis with epithelioid cells and giant cells.

(ii) Evidence of infiltrated or destroyed nerves.

Nine patients showed features suggestive of diseases other than leprosy, namely allergic dermatitis (5 cases), secondary syphilis (2 patients), lupus erythematosus and scleroderma (one each).

The results of sweat tests performed on these 72 patches are as follows:

TABLE 2

Result of sweat Test	*No. of patients*	*Percentage*
Normal	17	23·6
Slightly diminished	12	16·7
Markedly diminished	32	44·4
Absent	11	15·3
Total:	72	100·0

It will be seen that 59·7% of the patients had either marked impairment or complete absence. 16·7% showed slight impairment and sweating was normal in 23·6%.

DISCUSSION

It may be concluded from the above results that in the lesions of the tuberculoid and maculo-anaesthetic type of leprosy showing definite sensory changes, anhydrosis can be demonstrated by the intradermal sweat test to the extent of 96·6%.

The majority of lesions which clinically simulate early leprosy but which have to be kept under observation for want of unequivocal demonstration of cardinal signs, have shown not only impairment of sweat function in varying degrees but also very early histological changes suggestive of leprosy.

TABLE 3

Histopathological Changes	*Total*	RESULTS OF SWEAT TEST			
		Normal	*Slightly Diminished*	*Markedly Diminished*	*Absent*
Non-Specific for leprosy	28	7	5	12	4
Specific for leprosy	35	6	6	16	7
Allergic Dermatitis	5	2	1	2	—
Secondary syphilis	2	1	—	1	—
Lupus Erythematosus	1	1	—	—	—
Scleroderma	1	1	—	—	—

Table 3 shows the correlation between histological findings and sweat tests in 72 patients where the cardinal signs of leprosy could not be elicited.

It will be seen that out of the 63 patients who were histologically suggestive of leprosy, 50 (79·4%) showed definite diminution of sweat function and 13 patients (20·6%) had normal sweating.

In three patients of allergic dermatitis, and in one patient with secondary syphilitic lesions also, normal sweating could not be detected with acetylcholine test.

Arnold (1948) has also found confusing results (diminished or absent sweating) in 4 or 5 conditions for which leprosy is apt to be mistaken. The sweat response is liable to be absent in the oval, hypopigmented, facial macules of so

called 'achromia parasitica'. He also states that histologically such patients show nothing to suggest leprosy and the great majority of such patches disappear after external application of either ammoniated mercury ointment or White's crude coal tar paste.

Our experience of sweat tests in similar patches has been the same; but when such patients were asked to apply antifungal ointment containing coal tar or hydroxy-quinoline derivative, the majority of these patches disappeared within about three weeks and sweat function returned to normal.

However, there are some drawbacks of sweat tests in general, as one has to make physiological allowance for varying amounts of sweating in different sites of the body owing to an unequal distribution of eccrine sweat glands. The function of the glands also diminishes with old age. However, these difficulties are obviated to some extent by choosing a control site in the opposite half of the body and by increasing the quantity of acetylcholine injected, (if necessary a maximum 0·1 ml. can be used in sites where sweat response is expected to be less).

In this study acetylcholine was used intradermally to induce sweating and bromophenol blue paper for the demonstration of sweat, whereas Arnold has recommended the use of mecholyl, a beta-methyl derivative of acetycholine to stimulate the sweat glands and Minor's Iodine solution with starch for the detection of sweat. Mecholyl was not available for this study and acetylcholine solution was found quite stable and adequate for the purpose. In this study bromophenol blue paper method was found much superior for the demonstration of sweat, as the blue spots can be observed, on a yellow background with photographic clarity.

The intradermal test, by virtue of the fact that it is extremely simple to perform and easy to read (in its present modified form) has been found very useful to detect anhydrosis in lesions suggestive of leprosy.

Considering the limitations of the sweat test, one has to take into consideration the histopathological evidences of early leprosy in the diagnosis of hypopigmented lesions. In view of the consistent anhydrosis and characteristic histological features suggestive of early leprosy observed in the hypopigmented lesions studied in this investigation, it was thought necessary to see if any correlation existed between the anhydrosis as detected by this test and the histological appearance of sweat glands.

The following table shows the correlation between these two features in the 72 doubtful patients:

It will be seen from the table below that out of 56 patients having diminished sweat response 48 (85·7%) showed either chronic inflammatory cells in relation to sweat glands, or infiltrative destruction and atrophy of glands. Out of 16 patients in whom sweating was normal, 9 (56·3%) showed infiltration around the glands.

Sato (1938) has described both atrophy of glands (in simple macules and in skin which is merely anaesthetic) and infiltrative destruction of them (in elevated tuberculoid lesions). These observations could not be confirmed by later workers. According to Arnold (1948), visible damage to the glands could only occasionally be seen in tuberculoid lesions and rarely in simple macules.

It is not possible from our figures to conclude that impaired sweat function is invariably accompanied by histological changes of the sweat glands, though in the majority of the patients showing infiltrative or destructive

TABLE 4

Sweat Test	*Total*	HISTOLOGICAL APPEARANCE OF SWEAT GLANDS			
		Normal	*Infiltration around glands*	*Atrophy or Destruction of glands*	*No gland seen in biopsy*
Normal	16	6	9	—	1
Diminished	56	6	42	6	2
Total	72	12	51	6	3

changes of sweat glands, the secretory function of the glands seems to be affected.

Our findings, namely that 96·6% of lesions caused by leprosy and 79·4% of those clinically and histopathologically suggestive of leprosy but without definite sensory impairment show diminished sweat response to intradermal acetylcholine may be considered as substantiating Arnold's suggestion that abnormal sweat response probably precedes the onset of demonstrable sensory changes. According to Figueredo and Martins (1959) the earliest visible sign of leprosy (primary lesion) is a hypopigmented or erythematous macule without sensory changes. In a comprehensive study which included a five year follow-up of 500 contacts of leprosy patients these authors observed development of lesions (without sensory impairment) in 73 contacts which remained static for variable periods of time, some of them finally vanishing. In 10 patients diagnosis could be confirmed histologically. It is obvious that one is likely to miss early diagnosis of leprosy if a thorough investigation is not done.

Where there is no anaesthesia, no single test by itself can be considered diagnostic of leprosy unless the lesion is positive for acid fast bacilli. Hence it is suggested that in all cases where clinical and bacteriological examinations have given inconclusive results, intradermal sweat test should be performed. Positive findings are of great significance when correlated with even non-specific histological features suggestive of early leprosy.

SUMMARY

A simple method to detect anhydrosis using 0·1% acetylcholine and bromophenol blue paper has been described.

In a study of 159 patients, anhydrosis has been demonstrated using this test in 96·6% of lesions caused by leprosy diagnosed by routine standard methods and 79·4% of those clinically and histopathologically suggestive of leprosy, but without definite sensory impairment.

As histological changes in relation to the sweat glands have been observed in the majority of hypopigmented lesions suggestive of leprosy in which anhydrosis could be demonstrated, it may be concluded that abnormal sweat response resulting from denervation of sweat glands due to neuritis due to leprosy probably precedes the development of demonstrable sensory changes.

CONCLUSIONS

1. An intradermal acetylcholine test to detect anhydrosis is extremely simple to perform and easy to read in the modified form as described.
2. It is recommended as a useful auxiliary diagnostic aid in leprosy where a diagnosis cannot be arrived at by clinical and bacteriological examinations only.
3. Using this test and histopathological examinations, it is possible to conclude that abnormal sweat response resulting from denervation of sweat glands due to neuritis due to leprosy probably precedes the onset of demonstrable sensory changes.

ACKNOWLEDGEMENT

We are grateful to Dr N. Figueredo, Special Officer, Acworth Leprosy Hospital, Wadala, Bombay 31, India, of international repute for his invaluable guidance in the conduct of this investigation and the preparation of this paper.

We are also thankful to Dr N. D. Katdare, Superintendent, Acworth Leprosy Hospital, Wadala, Bombay 31, India, for allowing us to present this paper and for his guidance.

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Ambulatory Treatment of Plantar Leprosy Ulcers

TIO (TIONG HOO),* HAN (SIK HIAN)† and KUTUT SANTOSO.†

A chronic feature of invalidism in trophic disturbance in leprosy is the plantar ulcer(s). W.H.O. reports[1,2] disapprove any walking without special protection and stress that it is *wrong*[1] to ask a patient to come to a clinic for dressing. They advocate complete rest of the foot for about a month otherwise use plaster casts. Absolute bedrest, as the W.H.O. reports correctly state, is very difficult in rural areas and plaster casts are preferable because these still allow limited walking.

Obviously complete rest is not very practical because most leprosy patients belong to the poor class and cannot afford to rest for a month. Plaster casts are not only inconvenient for the patient but a burden to medical personnel as well. And in rural areas it might even be impossible because they easily get wet or break during work in the field.

The authors, therefore, tried to find another simple method for treating these ulcers which will cause not too much inconvenience to the patients, are easy to apply in rural areas and require little effort from medical personnel.

Since it is known that walking causes ulcers or prevents their healing we have focused our attention on the way of walking and localisation of the ulcer(s). Natural walking is done by passing the legs (and ankles) closely to each other with the feet in parallel position. If this is done the foot unwinds on the ground as shown in figure 1, with push-off mostly at A-B.

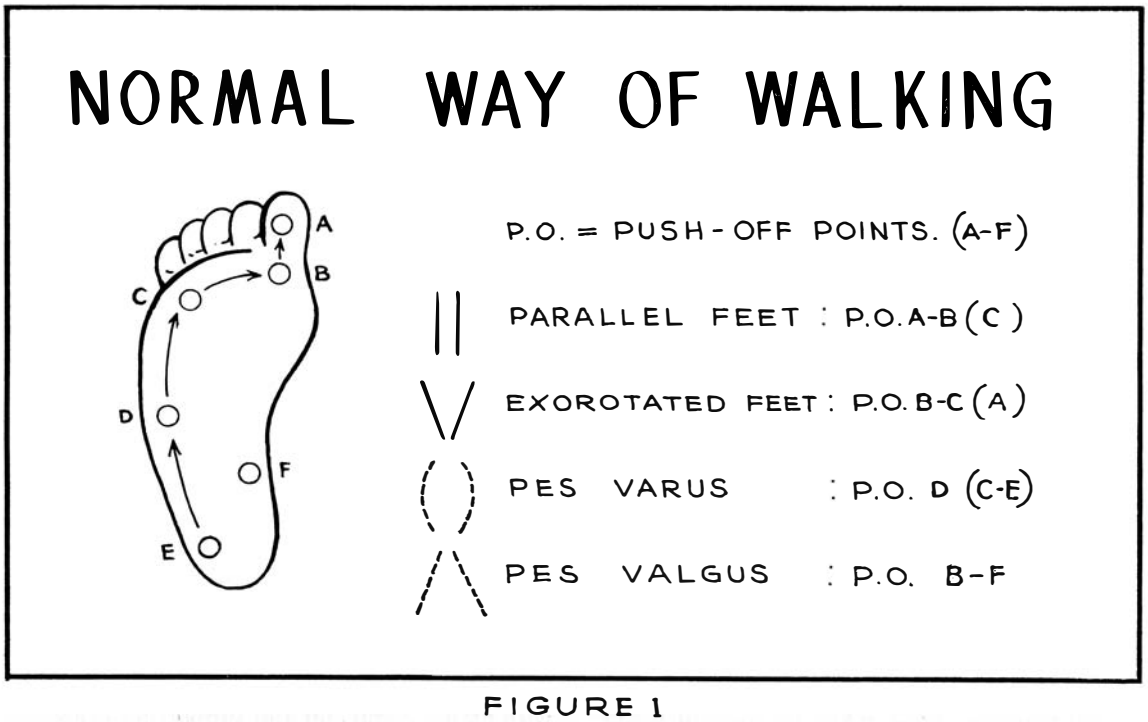

FIGURE 1

*National Institute of Health, Surabaya. †Provincial Directorate of Health, East-Java.

During push-off two important factors are obvious:

1. The whole body weight is concentrated on an area of less than one square inch.

2. Rubbing takes place at the push-off point. The provocative action of factor 1 is clear. Fig. 2 shows that rubbing (of the sandal belt) may cause ulcer(s).

The authors concluded therefore that *pressurized rubbing* is the causative external factor and consequently studied the push-off site and the localisation of the ulcer(s).

It was found that all ulcers occur on the push-off point(s). Except in cases of pes valgus, all push-offs take place along the line A–D. When the feet are held parallel the push-off points usually are in A or B, but in few cases the push-offs may be more lateral (B–C) in one or both leg(s). push-offs need not necessarily be found on similar sites on both *plantae* especially when one foot is held straight (parallel) and the other in a more exorotated position. Walking in exorotation moves the push-off laterally (B–C), or even to D in extreme exorotation and in *pes varus*. This will explain the finding of Srinivasan's[3] series where most of the ulcers were found in A and B and on the line B–C in front of the metatarsal heads, under the proximal phalanges. Ross[4] also found that these ulcers were actually lying in front of the metatarsal heads and not directly under them. These are obviously the push-off points.

More lateral push-offs, especially in flat feet, may not be restricted to one point and can cover several points.

It is furthermore not surprising that multiple ulcers and hyperkeratosis preceding or resulting from ulcers, can be found on the unwinding edge E–A along which the whole body weight moves with some rubbing (Fig. 3).

Initial trials for treatment of plantar ulcers were carried out at the National Institute of Health; 3% H_2O_2 was used for cleaning crypts in the ulcer followed by plugging with zincoil (75% zinc oxide + 25% cod liver oil) for drying weeping ulcers. The zincoil plug forces the patient to walk with the foot in a different position resulting in a different push-off point and as such relieving the ulcer from previous pressurized rubbing. Thus, while the patient walks about freely, the ulcer also gets appropriate rest. That the push-off points are moved to a different site, is clearly demonstrated by cases S 693/63 (National Institute of Health) see pictures 4–7.

From the above it was concluded that the guiding principles for simple treatment could be: '*give the ulcer(s) rest while allowing the patient to walk freely but in a different (therapeutic) way*'. This could cause another ulcer for which another solution, could be found (see discussion).

In trials in the National Institute of Health with outpatients, ulcers which were of years duration were healed in several weeks only, but correct evaluation of the therapy was rendered difficult by irregularity in the attendance of the patients.

Controlled trials in a closed leprosy community were desirable for which a leprosy colony, Sumber Glagah, was selected. For convenience's sake the authors devised the symbols as shown in figure 8, for use on the patient's cards. Normal (causative) way of walking was studied and a different (therapeutic) way taught. If ulcers occured at A–B, mostly because of walking with parallel feet the patients were instructed to walk with exorotated feet, which as initial trials suggested, would be sufficient in most cases. The opposite treatment for lateral ulcers is obvious. If A–B–C ulcers could not be healed quickly enough, then walking in the knees by lifting the thighs was taught which moves the push-off closer to the heel. In this connection it is noteworthy that the traditional tight sarong of Indonesian women makes this way of moving about difficult. For medial ulcers a way of walking without *pes varus* manner via knees and ankles was also devised. Consequently for lateral ulcers walking with X-knees/ankles was taught.

From a theoretical point of view the following complicating factors were anticipated:

Drop foot

In such cases the logical site for ulcers is the distal side of the foot. Exo- or endorotation of the foot are impossible. The only way of changing the push-offs is lifting the thigh preferably supported by a walking stick. A low-heeled clog with higher distal end and supporting bridge in the rear could be helpful.

FIG, 2

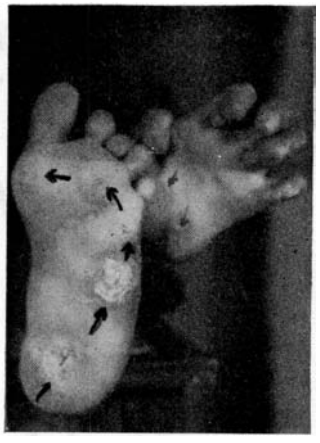

FIG. 3

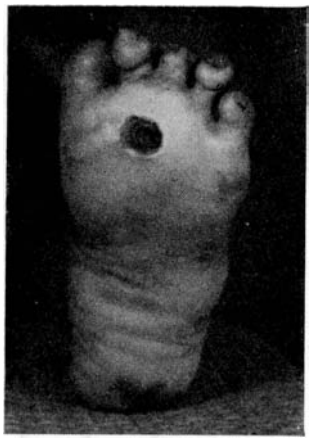

FIG. 4

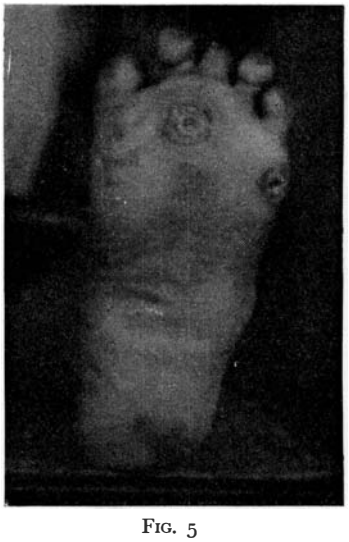

FIG. 5

FIG. 6

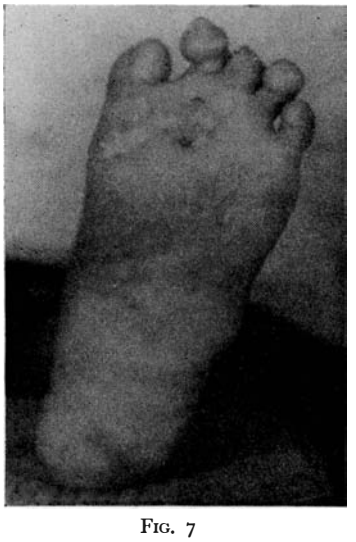

FIG. 7

Rigid foot and stiff ankle

This of course would impair free movement of the feet. A walking stick would seem to be of some help.

Flat foot and elephantiasis

Flat feet predispose to elephantiasis and can lead to multiple ulcers because the push-off point is widened to cover a large area. Manoeuvring of the foot is restricted and finding new push-off points difficult. A walking stick might relieve the pressure. Lifting the thigh is indicated in distal ulcers.

Intelligence

Low I.Q. might interfere in teaching new ways of walking.

In Sumber Glagah, 44 patients with plantar ulcers were submitted to the above mentioned treatment. After cleaning with peroxide, three different ointments, viz.

—75% zinc oxide + 25% cod liver oil.
— *idem* + 2% chloromycetin
—ung. zinci morrhuatis B.C.P. 1934*.

were tried out on approximately equal numbers of patients.

* Weight Layman & Umney Ltd., Southwark, London, S.E.1. courtesy of U.N.I.C.E.F.

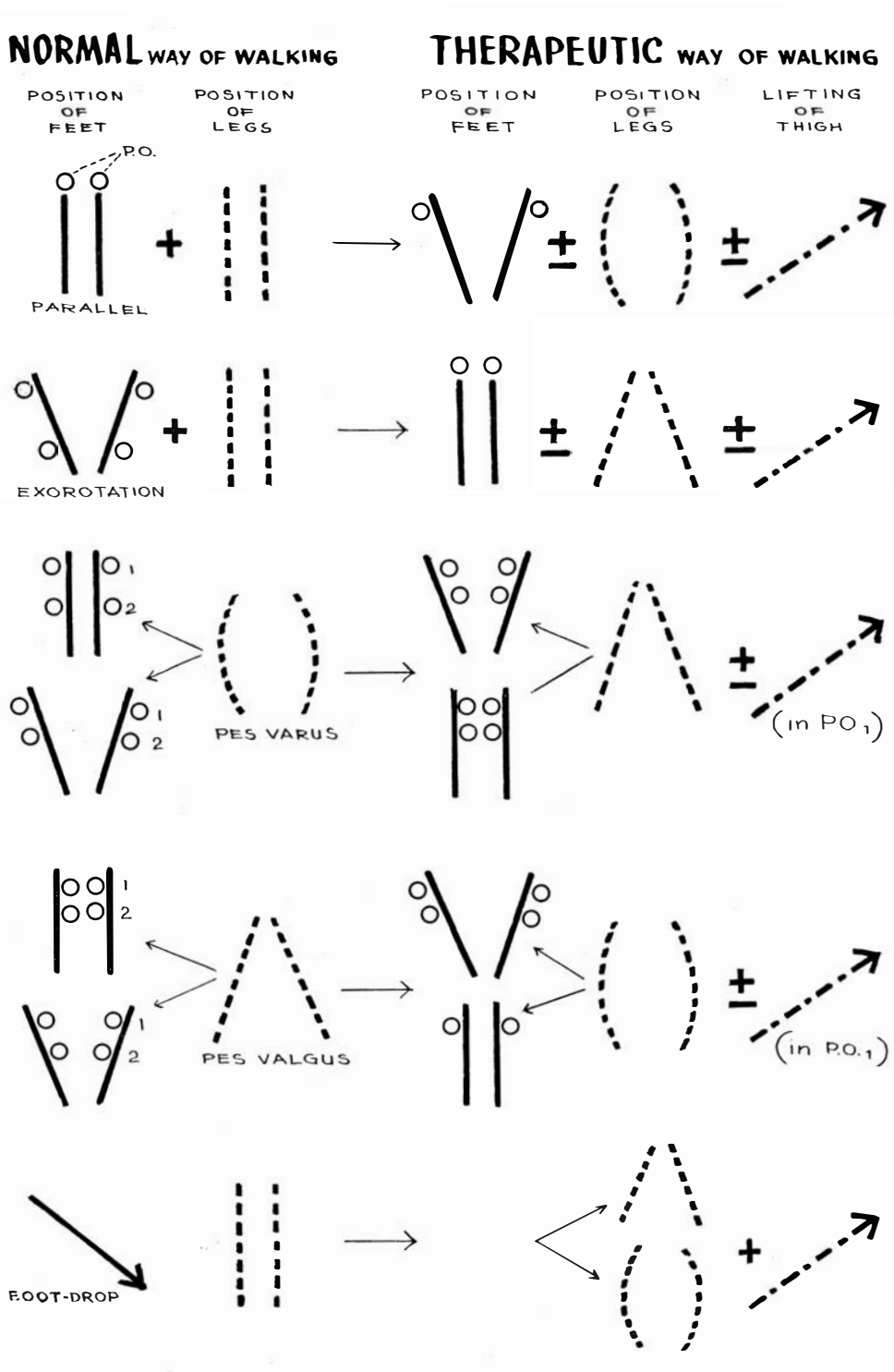
NORMAL WAY OF WALKING
THERAPEUTIC WAY OF WALKING
POSITION OF FEET
POSITION OF LEGS
POSITION OF FEET
POSITION OF LEGS
LIFTING OF THIGH
P.O.
PARALLEL
EXOROTATION
PES VARUS
(in PO1)
PES VALGUS
(in P.O.1)
FOOT-DROP

FIGURE 8

The results were as follows:
only 10 out of the 44 leprosy patients with plantar ulcers had none of the afore mentioned anatomical anomalies.

There were (mostly in combination):

10 drop-feet	: 4 bilateral
10 rigid feet	: 7 bilateral
21 flat feet	: bilateral, unequal
10 elephantiasis	: 8 bilateral, unequal
3 *pes varus*	: unilateral
3 *pes valgus*	: unilateral

This seems to indicate that, next to trophic disturbances, anatomical anomalies are another important intrinsic cause of plantar ulcers.

After 2 months (9 weeks) an evaluation was made of the results obtained:

— All ulcers showed clear and sometimes even dramatic improvement/healing

— Of 27 patients with ulcers on both *plantae:*
13 healed on both *plantae.*
11 healed on one foot; of the other 11 unhealed feet, 8 were on the right *planta* and 3 on the left.
in 3 patients ulcers on both *plantae* were not healed (yet).

— Ulcers on all 10 anatomical normal feet healed within 9 weeks.

— 71 ulcers (40 on the right, 31 on the left *planta*) of 1 month – 15 years duration were healed in those 9 weeks (as extremes: in 2 patients, 15 year old continuously existing multiple ulcers of various sizes and depths were healed in 1–4 weeks but in one patient ulcers of only 2 months duration required as much as 9 weeks).

— These 71 ulcers involved 6 drop feet, 18 rigid feet, 19 flat feet, 6 flat feet, 6 elephantiasis, 2 stiff ankles, 1 *pes varus* in various combinations. Three patients had a low I.Q.
Forty ulcers were on the right, 31 on the left *plantae.*

healed in	1*st*	week	: 5
,,	,, 2*nd*	,,	: 7
,,	,, 3*rd*	,,	: 17
,,	,, 4*th*	,,	: 17
,,	,, 5*th*	,,	: 10
,,	,, 6*th*	,,	: 6
,,	,, 7*th*	,,	: 1
,,	,, 8*th*	,,	: 3
,,	,, 9*th*	,,	: 5

— 22 ulcers, 9 on the left and 13 on the right *planta* were not healed after 9 weeks. All feet involved had anatomical deviations mostly in combination. There were 5 drop feet, 6 rigid feet, 14 flat feet, 7 elephantiasis, 6 stiff ankles, 2 *pedes vari* and 2 *pedes valgi.*

— Out of 4 patients with low I.Q. 3 recovered within 2 months; the only non-healed one suffered from a combination of rigid, flat feet and elephantiasis.

DISCUSSION

Although not all patients could be healed within 2 months this simple method can be regarded as satisfactory especially since all patients were allowed to walk as they pleased and 75% of the ulcers were healed and the rest showed clear improvement. In the not completely healed ulcers no X-ray pictures could be made for detecting *sequestra* and in one case even an amputation was originally thought necessary due to severe fixed *pes varus*. In other cases anatomical anomalies seemed to hamper the healing process.

This treatment can easily be applied in rural areas and no restrictions on walking need be imposed as long as the patients are willing and able to walk in the taught (therapeutic) way. When two out-patients did not turn up after running out of their supply of peroxide and zinc-oil, their improved ulcers (of 4 years and 5 months duration) were completely healed when they turned up again after several weeks, during which they claimed to have been walking in the taught way only without local treatment. This all the more stresses the therapeutic effect of this method.

For psychological reasons trials without ointment were not made in Sumber Glagah. No difference was found in the effect of the three ointments. The 75% zinc oxide +25% cod liver oil ointment, however, was preferred because it glued and stuck easier and better to the ulcer while *unguentum zinci* tended to fall out and needed supporting dressing. When for some days no zincoil was available ulcers started to 'weep' again.

Of the improved but not yet completely healed ulcers a greater number was found on the right *planta.* It seems possible that this is due

to the fact that most people are skilful and therefore have a more powerful kick-off on the right side.

In the duration of the ulcer neither its size nor depth need necessarily delay complete healing, although there was no doubt some correlation. The mysterious severity of the so-called 'trophic' disturbance seems to play an important role (see limits of healed ulcers).

Anatomical anomalies, although a hampering factor, need not necessarily prevent healing of the ulcer(s).

Low I.Q. would not appear to be an important factor because the sticky ointment seems to force the patient to walk with his/her foot in a different position.

When new ulcers on new P.O. points arose owing to the different way of walking, they can be treated by either changing the way of walking from day to day or, in case of distal ulcers, by walking in the knees by lifting the thighs. In more proximal ulcers walking on tip-toe might help or walking either in *pes varus* or *pes valgus* manner in the knees/ankles. All sorts of combinations can be taught to avoid a fixed push-off point.

COMMENTS

This treatment seems to be most practical especially in rural areas where zincoil can be handed to the patients wrapped in plastic. It would, however, appear that this method could be even more simplified for large rural areas if patients were only taught to walk differently (therapeutically) and to clean their ulcers with antiseptic decocts of local herbs. These trials will be carried out by one of us (H) in another leprosarium. Whether weeping of the ulcer is a disturbing factor for healing will then be estimated.

In *non-plantar* ulcers it was observed that pressurized rubbing existed from the inside viz. at malleoli, Achilles tendon or bone protuberances on a non-elastic thickened, hardened skin with no or little subcutaneous fat.

Here too a different way of walking relieves the pressurized rubbing i.e. for ulcers on the lateral malleolus and other parts of the foot, walking in *pes valgus* position in the ankle is a solution. For medial ulcers walking in *pes varus* style is advisable. For ulcers above the Achilles tendon walking on tip-toe assisted by a walking stick relieves the internal pressurized rubbing.

When sandals are used for feet with stiff, hardened skin, it would appear to be sensible to use foam rubber under the sandal-belts and ample talcum to minimize pressurized rubbing.

With regard to the primary cause c.q. the trophic disturbance it would appear that intra-neural injections of corticosteroids seem to be helpful as mentioned in an earlier paper[5]. Since then other similar encouraging results were obtained[6] and large scale trials in cases with various symptoms of trophic disturbances such as multiple ulcers, drop foot, elephantiasis, thickened toes, are now being carried out for further evaluation of this treatment. Unfortunately no intra-neural injectable sulphones are at our disposal which would be a real causal treatment for any trophic disturbances.

It is obvious that any treatment for trophic disturbances should start as early as possible to prevent formation of *sequestera* or other irreparable damage.

SUMMARY

A simple and cheap ambulatory treatment for leprosy ulcers, especially suitable for rural areas, is described and treatment of trophic disturbances is discussed.

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P.S. Owing to the departure of one of us (T) this investigation had to be restricted to two months only.

Lep. Rev. (1966) **37**, 4, 245/248

Aesthetic Management in Leprosy

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'Leprosy is dreaded most of all diseases not because it kills, but because it leaves alive'. (MUIR)

No truer words could have been written on leprosy than Muir's. It is well-known that leprosy patients suffer much more from mental depression rather than physical disabilities, and in his practice the writer has spent more time, especially during the initial consultation, comforting such patients rather than on drug and auxiliary treatment. The mental sufferings of leprosy patients can roughly be divided into two basic categories:

(a) knowledge of having a supposedly incurable disease which is thought to result in horrible disfiguration.

(b) constant fear that other people discover their disease and treat them as outcasts.

With regard to the former type of agony a clear explanation of the curability of the disease will boost the patients' morale. Although it is not easy to give it is far more difficult to soothe the patients' fear of becoming outcasts. It is the impression of the writer that this constant terror even overshadows the fear for the horrible somatic consequences. Visible symptoms of leprosy are dreaded, not so much for their unaesthetic appearance but rather because these symptoms will reveal the disease, so the writer feels that aesthetic management of leprosy is as important as the sulphone therapy, especially in the early stages of the disease, when the patient has to overcome his/her initial anxiety. This treatment seems to be appropriate for more well-to-do and intelligent people but the writer has experienced that the idea can also be applied to the poor. In a leprosarium, after undergoing two weeks of successful treatment for chronic plantar ulcers[2], the poor inmates generally wanted to know whether the writer could also restore lost eyebrows.

The visual symptoms on exposed areas, especially on the face, which may betray the patients are:

1. thickening of or noduli in the earlobes.
2. E.N.L., leproma and leprides.
3. erythematous maculae, sometimes swollen.
4. diffuse swelling of the face.
5. madarosis, mainly of the lateral part.
6. swollen digits.
7. dull, dry, scaling, hyperpigmented skin of extremities, especially of the legs.
8. elephantiasis.

All these symptoms are caused by infiltration, granulomata and/or widening of capillaries or as a result of trophic disturbance. They may occur as short attacks or persistently for long periods and can even become permanent. The writer has the impression that it is of paramount importance to treat these symptoms as early as possible not only for psychological reasons but also to curb further and possible irreparable damage. The earlier the therapy is started the quicker the results are obtained and the least psychic damage the disease can inflict. In coloured people every inflammation, especially if of long standing, may cause hyperpigmentation.[3]

Many of these symptoms can be improved with diathermic sparking[4] but similar results can be obtained by subcutaneous injections of preferable soluble corticosteroids. Local corticosteroid injections are very convenient and in many cases give much quicker and better aesthetic results than diathermic sparking but are far more expensive and therefore less suitable for mass campaigns. On the other hand diathermic sparking has, next to causing pain, the disadvantage that more time is required for the symptoms to disappear. Besides inflicting psychological harm the longer period before success is evident increases in coloured people the possibility of hyperpigmented sequels. Diathermic sparking itself may also give additional thermic stimulation to pigmentation. As such it is advisable to combine all diathermic sparking

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for aesthetic purposes with topical bleaching agents. While in fresh eruptions bleaching agents are generally not necessary, the need for them becomes all the more pressing in lesions of long duration. In sparsely disseminated lesions, especially on the face, local subcutaneous injections of corticosteroids are preferable to the much more easily administrable oral ones because of the latter's weakening effect on the general defence mechanism. Injections are also of great value when reaction-symptoms fail to respond to normal doses of oral corticosteroids (see case 17/64).

Although no wide experience has yet been gained, preliminary comparative results are herewith discussed with both methods in the aesthetic management of leprosy.

Thickening of or noduli in earlobes

Superiority of local corticosteroid injections over diathermic sparking was clear. Sometimes even one injection of 5 mg. prednisolone, especially in fresh cases, was sufficient to normalize the size of the thickened earlobe.

E.N.L., Leproma and Leprides

Although remote action of injected corticosteroids is known to exist (see under swelling of the face), it is, in the experience of the writer, by far the best method to inject all ENL lesions and lepromata separately with very small adequate quantities of corticosteroids. Complete flattening can be obtained very quickly leaving only hyperpigmented spots in more chronic cases. Recurrence of ENL may happen at short notice but in many cases this treatment gives long intermissions. Diathermic sparking reduces ENL at slower pace and with greater chances of hyperpigmentation.

In one L-type patient (17/64) with body weight of 33 kg. only, reaction symptoms flared up on 3 tablets of 5 mg. prednisolone per day. One series of injections of in all 25 mg. cortisone under the lesions at several places of the face cleared all symptoms within a week.

In one patient (G.S.T.) with persistent uniformly raised leprides on the face, however, repeated subcutaneous cortisone injections and oral prednisone could not reduce the plagues. Yet diathermic sparking had some softening and reducing effect.

Erythematous maculae

In coloured people, any chronic erythema if not treated may result in hyperpigmentation and bleaching agents are a necessity in the treatment of erythematous maculae of long duration. Subtcuaneous corticosteroids have a quick beneficial effect.

Early injections are desirable as demonstrated in one case of extensive erythema of one month on both cheeks for which the patient was expelled from her house. One series of subcutaneous injections of in all 25 mg. cortisone at several spots of the erythema almost cleared it in just 3 days. Chronic (swollen) erythema, in the experience of the writer, requires multiple injections (and bleaching agents).

Peroxide bleaching ointment in the above mentioned rather fresh patient, however, stimulated hyperemia and was therefore omitted. It seems possible that the use of bleaching agents should be restricted to chronic patients only but more experience must be gained for a final conclusion.

Swelling of the face

In a few patients quick flattening was obtained with both methods but injections of corticosteroid seemed to give quicker results. Although the two methods have remote actions (see under madarosis), when only one half was treated no effect was ever observed on the untreated half.

Special attention is drawn to red swelling of the nose which can be very unsightly, quickly draws concentrated attention and hence is of great psychological influence.

Local subcutaneous injections of corticosteroids make the swelling and redness quickly subside.

Diffuse swelling of the face does not necessarily require multiple injections on different spots. Remote action may render one injection of corticosteroid on each half of the face sufficient (see under madarosis case D103/65).

Swollen fingers

Although Hyfrecator sparking has beneficial slimming effect it takes several weeks or months to complete the treatment.

Quicker results were obtained with corticosteroids which can be injected locally as well as intra-neurally in the supplying nerve[2, 5].

Madarosis

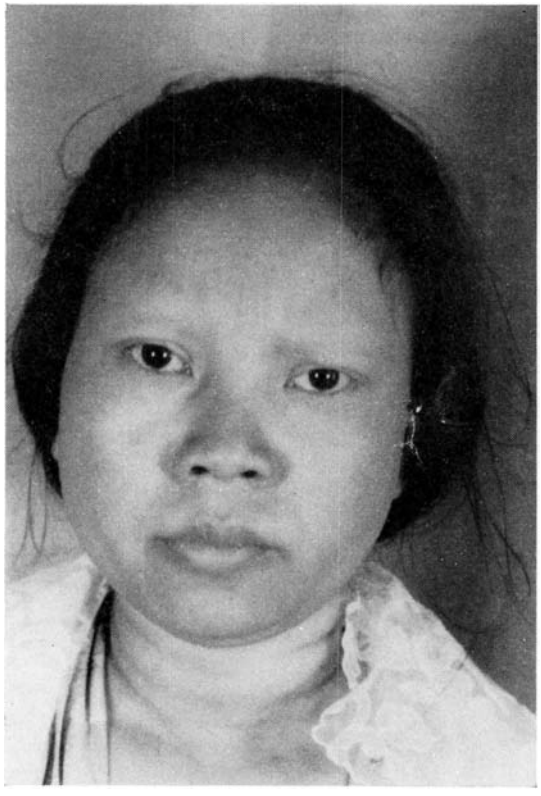
It is known that during swelling of the face, eyebrows may fall out and then grow again during remissions. It seems to be caused by pressure on the hair roots due to infiltration. In this chronic symptom both methods seem, in the limited experience of the writer, to be of equal value, likely because it takes the hair root a long time to restore its function. Furthermore diathermic sparking may also stimulate growth of hair via induced hyperaemia.

Remote action of corticosteroid was seen as flattening of the cheeks on the side of the injected eyebrow (see picture case D103/65).

Case D103/65 : female – 20 years.

– 3 years leprosy of L-type in reaction
– diffuse infiltration of face + ENL on body; madarosis.

After the first infiltration of 5 mg. prednisone subcutaneously under the L-madarosis flattening of the L-cheek was seen. Only after 4 months of regular weekly injections was sparse hair observed.



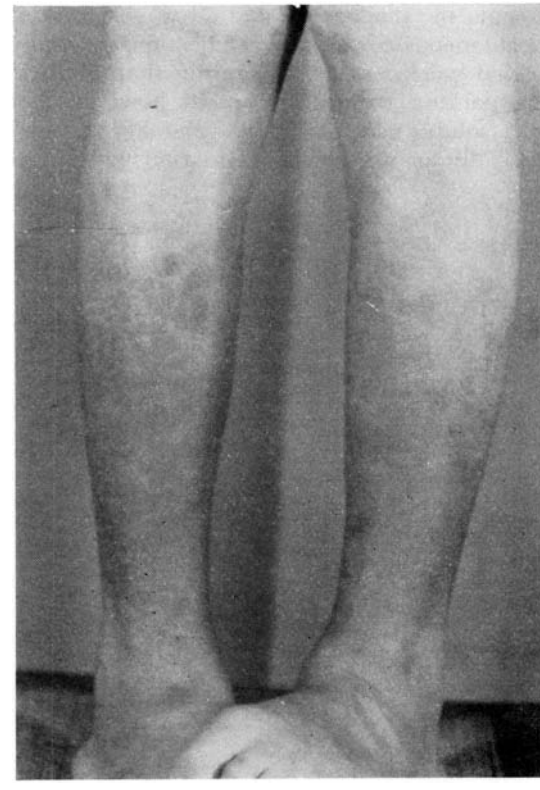
Case 103/65

Picture taken after 8 weekly injections. Left corner of mouth lifted due to flattening of left cheek.

In a leprosarium 35 male and female patients mainly of L-type were at their request[2] injected weekly with 5 mg. cortisone in one madarosis, the other serving as check. After 4 weeks new growth was clearly seen in 15 patients and questionable new eyebrow hair in 2 patients. After the 4*th* injection, however, further injecting became more difficult in many cases. Injections were abandoned because formation of granulomata due to partly insoluble cortisone was feared (see under discussion). Further evaluation of these preliminary trials can better be obtained with injections of soluble corticosteroids.

Dry scale hyperpigmented skins

In such cases intraneural prednisolone injections[5] resulted in visually similar sebaceous



Pat. L.K.S.

effects as from diathermic sparking.[4] Due to lack of technical facilities no quantitive measuring of the improvement of the function of the sebaceous glands could be carried out.

As in other cases of dry skin on the extremities equal parts of a lanoline, vaseline and water cream gave good greasing and moisterizing results[5] (see picture case L.K.S.) Addition of a bleaching agent such as ammoniated mercury is advised.

Elephantiasis

In one clinically observed patient beneficial effect was seen by intraneural injections in the sciatic nerve. Pain in the foot (? due to röntgenologically determined 'vanished bone'. caused by trophic disturbance) and volume of the elephantiasis decreased. Putting the leg in upward position expedited treatment.

Trials for further evaluation of this therapy will be carried out.[2]

DISCUSSION

Except in madarosis and dry scaly skin, subcutaneous corticosteroid injections generally yielded quicker and better results than diathermic sparking. It must be stressed, however, that only soluble corticosteroids should be used especially for madarosis. The writer was forced to utilize the less soluble cortisone-acetate and out of eight out-patients with madarosis, two male patients developed local swelling, in one patient even resulting in the total loss of previous remnants of the eyebrow.

In mass campaigns where the hyfrecator can be used[4] the author would endorse the use of this instrument for aesthetical purposes as well.

SUMMARY

Attention is drawn to aesthetic management in leprosy, and preliminary results with diathermic sparking and local subcutaneous injections with corticosteroid are compared.

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These trials had to be discontinued due to departure of the author. Partially soluble cortisone-acetate had to be used as the supply of soluble prednisolone ran out.

Lep. Rev. (1966) **37**, 4, 249/253

Perineural Priscol Injections in Leprosy Ulcers

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Leprosy patients with open wounds and ulcers are feared, despised and treated as outcasts. New drugs are being tried for the prevention and management of deformities so that these patients may become useful members of society.

Trophic ulcers are quite commonly met with in leprosy patients and are attributed to relative ischemia and loss of sensation triggered by trauma and sepsis. In the management of ulcers local dressings, plaster, physiotherapy and surgery have a limited role to play. In addition very few hospitals in India are undertaking plastic surgery.

Local use of some of the antileprosy drugs has shown some success. Injections of hydnocarpus oil at the base of the trophic ulcers give healing effects (Chatterjee, 1955); Saxena and Mathur (1963); Mathur and Saxena (1965) and Mathur (1965) have shown beneficial effects of Priscol in leprosy deformities and ulcers.

Material and methods

Twenty-five patients attending the research centre in the Department of Preventive and Social Medicine with ulcers in the hand and foot were selected for perineural Priscol injections. A clinical and laboratory diagnosis of leprosy was made in every case.

All the patients were treated under identical conditions. They pursued their routine work as before. They used ill-fitted shoes or walked barefoot because of poverty. In spite of repeated advice to avoid excessive strain the patients continued to perform the same physical actions. Most of them had to walk several miles to the Centre. No patient was given plaster casts. Surgical intervention in two patients before Priscol therapy did not improve the ulcers.

Priscol 1 ml. (25 mgm.) was injected twice a week by the technique of Saxena and Mathur (1963) near the ulnar nerve in the case of ulcers of the hand and round the lateral popliteal nerve in patients with ulcers of the foot. All the patients who were not already receiving antileprosy drugs were given 100 mgm. of sulphones for six days in the week. Twenty patients with trophic ulcers on hand and foot after cure are under observation for the last three to 12 months.

The ulcers were classified into two categories, small and big. Ulcers 12 mm. or more in length or breadth, or more than 4 mm. deep were classified as big ulcers and the rest of the ulcers were taken as small ulcers. Ulcers on the hand were generally small and were situated at interphalangeal joints or the terminal phalanx. Big ulcers were found in the region of the sole with profuse foul-smelling discharge. Patients were given acriflavin cotton and bandages to dress the ulcers. They were not given any antibiotics nor DDS. On the injection days the wounds of most of the patients were found undressed and covered with dust. Initial photographs of ulcers and final photographs after healing of ulcers were taken. A fortnightly record of progress of the ulcers was kept.

Observations

The details of ulcers are given in Table 1.

Number of ulcers treated and the results of treatment in each period are depicted in Table 2.

TABLE 1

Details of Ulcers, Size and Discharge, and Walking Habits

Location of Ulcer	*Size of ulcer*				*Discharge*		*Walking habit for foot ulcers*	
	< 12 mm in length or breadth and < 4 mm in depth	> 12 mm in length or breadth and < 4 mm in depth	any length or breadth and > 4 mm in depth	Total	Small	Profuse and foul smelling	Barefoot	Ill-fitted Shoes
Hand	10	2	2	14	13	1	—	—
Foot	—	—	11	11	—	11	5	6
Total	10	2	13	25	13	12	5	6

TABLE 2

Minor and Major Ulcers with Results of Treatment

Type of ulcer	*No. of ulcers*	*Duration of treatment in weeks*	*Number of ulcers treated in each period*	RESULT			
				Cured	*Reduced in size and discharge*	*Did not improve*	*Increased in size*
Minor	10 (hand)	1–2	10	2	8	—	—
		3–4	8	4	4	—	—
		5–6	4	3	1	—	—
		7–8	1	1	—	—	—
Major	15 (4 in hand and 11 in foot)	1–2	15	—	14	1	—
		3–4	15	2	12	1	—
		5–6	13	3	9	1	—
		7–8	10	4	5	—	1
		9–10	6	1	4	—	1
		> 10	5	—	4	—	1

TABLE 3

Shows Duration of Ulcer Cured or Improved and Period of Treatment

Period of treatment	DURATION OF ULCER				*Total*
	—15 days	*30 days*	*3 months*	*> 3 months*	
4 weeks	3	4	1	—	8
5-8 weeks	1	6	1	3++	11
>8 weeks	—	—	2	3+++	5
Total:	4	10	4	6	24

++ one each of 7 months, 10 months and 15 months duration.
+++ one of 9 months and two of one year duration.
Note: One ulcer of age above one year did not improve but increased in size.

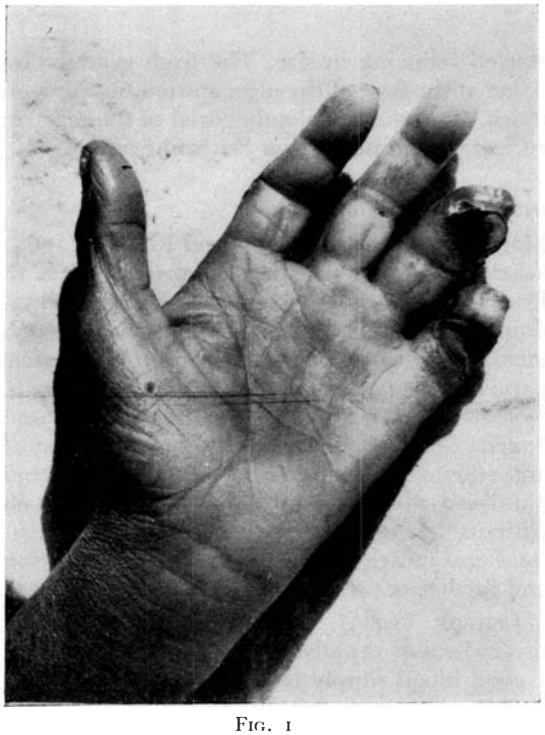

FIG. 1
Ulcers on small and ring fingers before Priscol therapy.

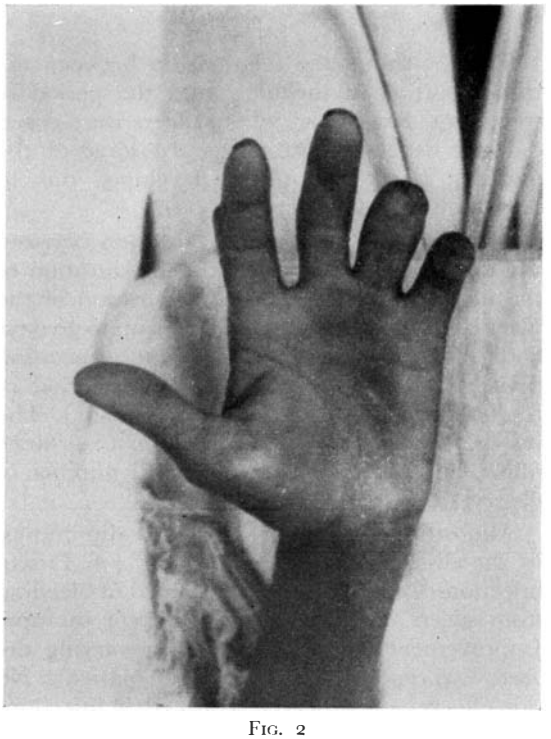

FIG. 2
Healed ulcers on small and ring fingers after Priscol therapy.

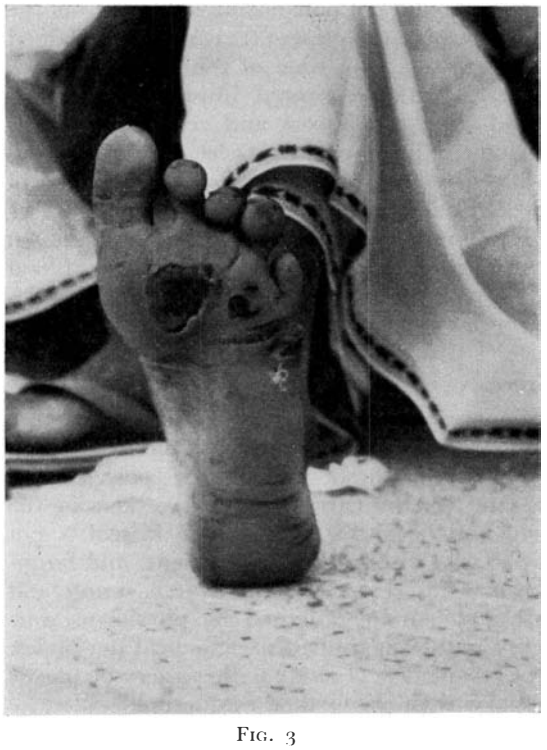

FIG. 3
Trophic ulcers in sole before Priscol therapy.

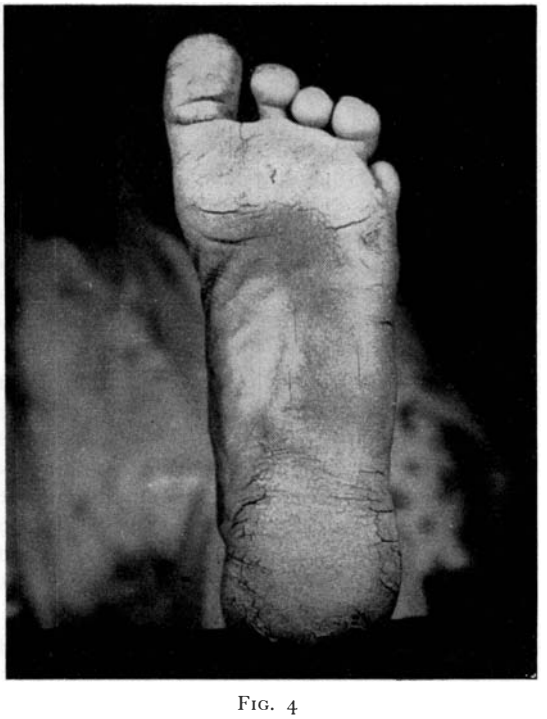

FIG. 4
Healed trophic ulcer in sole after Priscol therapy

Table 3 shows the relationship between the total duration of the ulcer and the period of treatment. Patients in whom ulcers were cured did not develop fresh ulcers. In some of the patients, burns and ulcers developed due to neglect, healed in shorter periods.

There was no significant association between the duration of treatment and the duration of the ulcer. However, when the duration of the ulcer is taken in two groups, that is up to 30 days and above 30 days, a significant association between the duration of ulcer and period of treatment is found ($x^2 = 6 \cdot 404$, P $0 \cdot 05$). The insignificance observed in the first instance might be entirely due to the small number of observations in each cell.

Almost all the patients reported diminution in the discharge from ulcers after 4–6 Priscol injections. Four patients complained of bleeding from ulcers on dressing after Priscol therapy. Improvement in the sensations in varying degrees was reported by most of the patients. No side effects were observed with Priscol injections in any of the cases.

Case 1. C. 35 year old male, complained of loss of sensation, deformities of fingers, wasting of muscles of the hand and blisters off and on for the last three years, and an ulcer in the small finger for the last 10–12 weeks. (Fig. 1). Perineural Priscol injections along the ulnar nerve were given. He was kept on 100 mgm. of sulphones. He was not given systemic antibiotics. Local dressings of acriflavin were applied. After 7 to 8 Priscol injections the ulcer completely healed (Fig. 2). The patient continued to get Priscol injections. Frequently occurring blisters and swellings of the fingers also subsided and sensations have improved in hand and forearm. He is under observation for the last three months.

Case 2. N.D., aged 45 years, female, complained of loss of sensation in the hand and deformities and ulcer in the sole for the last three months (Fig. 3). She used leather sandals and walked nearly three miles to reach the Centre. She was given perineural injections of Priscol along the lateral popliteal nerve at the neck of the fibula. She was advised to restrict her walking and was given only acriflavin dressings.

After four injections the foul smelling discharge decreased considerably and the ulcer started reducing in size. The fresh granulation tissue at the base of the ulcer started bleeding on touch. She was completely cured of the ulcer in 10 weeks with perineural Priscol injections.

DISCUSSION

Mathur and Saxena (1963) and Mathur (1965) have already shown the beneficial effects of Priscol in leprosy deformities and rehabilitation. Srinavasan (1964) had reported high incidence of trophic ulcers with intrinsic muscle paralysis in feet along with analgesis strain. Saxena and Mathur (1963) and Mathur and Saxena (1965) have shown the improvement of anaesthesia and muscle power in wasted and paralysed muscle of the hand. Priscol in such patients, by restoring to a variable extent sensations and muscle power, helps in the prevention and further occurrence of ulcers.

Lennox (1965) reported that denervated tissues heal as rapidly as normal tissue provided a good blood supply is maintained. Priscol is a vasodilating drug and dilates the blood vessels of nerves and parts supplied by them (Saxena and Mathur, 1963). It improves the vascular supply of the ulcerated region. Four of the patients who did not note oozing of blood from the wound before the present treatment complained of bleeding at the time of the dressing of the ulcers. Chatterjee (1955) improved the local blood supply of ulcers and recommended its periodical injection. Crutz *et al.* (1933) and Goheen (1933) were able to achieve healing of ulcers by improving vascularity by sympathectomy. Similarly Priscol injections can be given periodically to maintain the improved blood supply of the parts and prevent further occurence of ulcers.

CONCLUSION

Priscol provides opportunity both for preventing and curing ulcers by improving the local blood supply, anaesthesia and muscle power. This method can be carried out by workers in the field and hospitals. The cost of Priscol is not prohibitive and most of the patients and hospitals can afford it. The technique is simple and safe and can be practised by physicians, surgeons and even trained paramedical personnel. The use of Priscol along with surgery or plastic surgery requires further evaluation.

SUMMARY

Twenty-five patients of small and big ulcers were treated with perineural Priscol injections. Smaller ulcers and ulcers of shorter duration healed early. Trophic ulcers in the sole healed with prolonged treatment. All the treated ulcers except one either healed or reduced in size. No fresh ulcers were reported in the regions after healing.

ACKNOWLEDGEMENTS

The present work could not have materialised without the constant encouragement from Dr K. N. Udupa, Principal, College of Medical Sciences; Dr S. M. Marwah, Professor and Head of the Department of Social and Preventive Medicine, College of Medical Sciences, Banaras Hindu University, Varanasi; and Dr K. N. Saxena, Professor of Dermatology, S.N. Medical College, Agra.

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Lep. Rev. (1966) **37**, 4, 255/257

Report of the Conference of Lepra Regional Organizing Secretaries

(held at Farnham, Surrey)

Kindly written by Dr S. G. BROWNE, O.B.E., M.D., F.R.C.S., D.T.M.
Medical Secretary, British Leprosy Relief Association, 8 Portman Street, London W.1., England

The British Leprosy Relief Association, now known as LEPRA (formerly BELRA), held a very successful residential conference for its Regional Organizing Secretaries at Farnham, Surrey, England, in May of this year (1966). Under the genial chairmanship of Sir George Seel, K.C.M.G., Chairman of Lepra, the participants not only considered questions of propaganda and organization and fund-raising, but also gave themselves as laymen to the study of leprosy as a major endemic disease in the countries of the Commonwealth.

Interesting factual reports of their recent visits to Africa were given by Mrs Peggy Morton, Regional Organizing Secretary for N.E. England, and by Mr Francis Harris, M.C., Deputy General Secretary of LEPRA.

Dr Gordon Currie, O.B.E., gave the conference up-to-date news concerning the Leprosy Control Project inaugurated recently by LEPRA in Malawi. In the chosen area of operations there are probably 10,000 people suffering from leprosy. Communications are quite good, and the people are courteous and friendly. The Project is assured of the personal interest and wholehearted co-operation of the President, Dr Hastings Banda. Dr Currie himself, who as Government Leprologist had an enormous fund of local knowledge and enjoyed the esteem of the people, directed the scheme in its initial stages. To the regret of all, circumstances have compelled Dr Currie to return to Britain. His place has been taken by Dr David Molesworth, formerly of Malaya and Ghana. He is assisted by two LEPRA field-workers, and will shortly be joined by an experienced nursing sister and a laboratory technologist.

Auxiliary staff are being trained on the spot in leprosy diagnosis and treatment, and rural surveys are under way. Already, many hundreds of leprosy patients have been brought under treatment.

It is hoped that expert surgical assistance will be available for the correction of deformities due to leprosy – all in keeping with the scope and objects of the Project, one of which is to demonstrate to countries with similar medical and financial problems a practical method of controlling and eventually of eradicating leprosy in a circumscribed area.

A small central hospital will be erected in the grounds of the Queen Elizabeth Hospital at Blantyre, where the laboratory, administrative headquarters, and rehabilitation unit will be installed.

Dr S. G. Browne, O.B.E., the new Medical Secretary of LEPRA, gave a stimulating address on 'Modern Leprosy Work'. He emphasized the need for hard work and adequate knowledge and perseverence in the struggle against leprosy. Gone were the days of easy optimism engendered by the advent of the sulphones, and by the popularization of orthopaedic surgery as applied to leprosy. Despite the numerous successes of the past decade, leprosy still constitutes a formidable medical, social and financial problem to those countries least able to afford or to face its ravages.

Leprosy work today entails bringing the known effective drugs to the people who need them, which in turn means discovering by surveys and examination of contacts all who are suffering from leprosy, and making available the standard drugs to them through static or mobile treatment centres. Dr Browne emphasized the importance of diagnosing leprosy early, diagnosing it correctly and placing patients under adequate treatment before irreversible nerve damage had occurred.

Secondly, leprosy work means training indigenous auxiliary workers in leprosy diagnosis and control, in surveys, in examinations of contacts, in simple microscopy and simple physiotherapy, in mass treatment. The role of these invaluable auxiliaries was to cure the individual suffering from leprosy, to prevent nerve and eye damage, to educate patients and their entourage, to supply simple footwear that will prevent neuropathic ulceration, and to ensure that patients under treatment or with arrested disease may retain or resume their place in the family and the community.

Thirdly, modern leprosy work includes the provision of a central hospital where patients with special needs may receive expert help. The over-emphasis on mass treatment in the immediate past must be counterbalanced by insisting on the need for a well-equipped and well-staffed centre where a variety of patients may be treated: those in acute exacerbation, or with incipient nerve or eye damage; those in drug reaction or needing stabilization of dosage; and those needing operation, physiotherapy, special footwear or prostheses.

Fourthly, leprosy work means education – education of leprosy workers themselves (doctors, nurses, physiotherapists, etc.), and of medical auxiliaries of all kinds. It means education of the patients, so that they may look after themselves and prevent the many avoidable disabilities. Thus it means educating the community by all means and at all levels, especially in the preventive aspects of leprosy.

Fifthly, leprosy work today necessarily includes research into leprosy. New approaches and new investigative techniques have recently become available. New drugs are urgently needed, to reduce the unconscionably long period now necessary for treatment, to facilitate the removal of effete mycobacteria, and to minimize the over-vigorous immunological response of the presence of mycobacterial antigen. The many and serious lacunae in our knowledge of *Myco. leprae* must be filled in as soon as may be.

Sixthly, modern leprosy work visualizes more than ever before the need for co-operation between all those engaged in the struggle. The Christian missions that have been in the forefront of the fight are now joined by non-confessional bodies, by Governments and by international agencies.

Lastly, it may be possible within the comparatively near future to make a definite pronouncement concerning the prophylactic value of B.C.G. inoculation in leprosy. If the present encouraging results are confirmed in the final reports from Uganda and elsewhere, there will be available a method for preventing the appearance of leprosy infection in three-quarters of the numbers of those exposed children who would otherwise contract it. If this happy result should prove to be true, then real and definite and lasting hope would arise in individuals and in countries where leprosy is still a scourge, an unresolved problem, and an economic incubus.

Mr W. Lennox, F.R.C.S., the orthopaedic surgeon who has been recently working in Vellore, South India, and at the Karigiri Leprosy Research Centre sponsored jointly by the Leprosy Mission and the American Leprosy Missions, Inc., gave an account, illustrated by coloured transparencies, of the complex activities of a Rehabilitation Unit.

He showed the various types of severe damage that may result from repeated neglected trauma sustained in the course of ordinary walking, walking over irregular ground, and working with the hands. When a specific action can be incriminated as causing damage to an anaesthetic part, appropriate steps to mitigate or avoid its effects could and should be taken.

The surgeon's task comprises not only the accurate and detailed assessment of the departure from the normal, but also an appreciation of the cause, and the determination of the part to be played by each member of the team concerned in the total rehabilitation of the patient. The actual operation was but an incident in this long process.

When deformity has been corrected by operation and physiotherapy, the task often remains of making the patient cosmetically acceptable to his community. Thus, where time and opportunity exist, plastic and reparative operations – while not strictly and surgically imperative – may make all the difference to a patient's life and welfare.

The skills of the shoe-maker and splint-maker are also enlisted so as to provide the patient with

shoes and splints to enable him to take his full place in the community. Tools and implements with specially made handles are often needed.

The psychological aspects of rehabilitation were also stressed, and the need to educate the patient to rethink his attitude to the disease and to any remaining disability he has. And then, prevention of recurrence is all-important, or the last state of the operated patient (who still has no tactile sensation in his extremities) may be worse than the first.

When asked what he considered the place of surgery in such a scheme as the Malawi Eradication Project, Mr Lennox admitted that early diagnosis of leprosy and adequate treatment would make virtually all reparative surgery unnecessary. If resources are limited, then money should be spent on bread, and not on the icing of a cake.

Lep. Rev. (1966) **37**, 4, 259/261

Abstracts

1. **Mycobacterium ulcerans** Infection. Clinical and Bacteriological Study of the First Cases recognized in South East Asia, by J. H. S. PETTIT, N. Y. MARCHETTE and R. J. W. REES, *Brit. J. Derm.*, **78** 4, Apr. 1966, p. 187–197.

This paper gives case reports and nine illustrations of four patients of skin ulceration with deeply undermined edges in Malaya. It is believed that these are the first patients with *Mycobacterium ulcerans* infection to be recognized in S. East Asia. It is gratifying to report that the authors have confirmed the finding of LUNN and REES that the administration of B 663 has been dramatically successful in all their patients. This riminophenazine derivative was originally developed by BARRY *et al.* (1957, 1958 and 1965) and has now been shown to have a therapeutic value for leprosy (BROWNE and HOGERZEIL, 1965, PETTIT and REES, 1966). At present the only available preparation is an 100 mgm. capsule and the authors have given 100 mgm. three times a day for six days a week.

It is suggested that the ulcers of *Myco. ulcerans* are probably not uncommon in humid tropical climates and a better knowledge of the disease and its bacteriology will enable more patients to be diagnosed and treated.

2. **A Prosthesis to restore Balance and Prevent Ulcers after partial Amputation of the Foot,** by W. A. WIGNEY, F.CH.A.V., S.R.CH., Senior Chiropodist to the Diabetic Clinic, Royal Melbourne Hospital, *Med. J. of Australia*, 1965, **1** : 852 (June 5).

The author describes a prosthesis made from inert silicone rubber for this purpose. This is of particular interest in surgery for leprosy. After conservative surgery of the foot it is impossible to avoid disturbing the natural balance and stability. If a metatarsal resection has been necessary or exposed bone has to be necessary, malfunction of the foot will result and inevitably some interference can be expected. Even the removal of the 5th toe can give the patient a sense of insecurity. Abnormal pressure areas are often produced which hasten the development of perforating ulcers or small areas of gangrene.

3. **Annual Report of the Ghana Leprosy Service, 1961–62,** by DR D. S. CHAUDHURY.

The report which has just been received indicates an increase in the number of patients treated showing that more have been brought under treatment at an early stage. The Laboratory trained six assistants in elementary routines for posting to different regions so that out-patient treatment is under laboratory control from the beginning. Co-operation and assistance have been received from UNICEF and Radda Barnen.

4. **New Orientation in the Control of Leprosy in Japan. Curability of the Disease,** by SHIGETAKA TAKASHIMA. *Internat. J. Leprosy*, 1965, **33**, 1, 1–17.

The author has reported on (1) arrested and discharged patients, (2) bacteriological, pathological, and immunological criteria of curability, (3) comparison with respect to antileprosy programmes of the present course in Japan and that of the World Health Organization, and (4) the trend of leprosy in Japan.

1. The curability of leprosy was found to be higher than expected, quite in contrast to socially prevalent opinions and also the general medical view.

2. The curability of leprosy has been acknowledged as proven from the bacteriological, pathological and immunological points of view.

3. In Japan, hereafter, leprosy control is to be directed to counter-measures among institutionalized patients, for antileprosy measures have been nearly completed for domiciliary patients in the communities.

4. Still further study is needed to bring about an increase in the resistance of a nation against leprosy and promote curability of leprosy.

5. **Chemotherapeutic Trials in Leprosy. 2. Comparative Trial of Dapsone plus Ditophal (Etisul) and Dapsone alone in the Treatment of Lepromatous Leprosy,** by M. F. R. WATERS and J. H. S. PETTIT. *Internat. J. Leprosy*, 1965, **33**, 3, 280–95.

A controlled clinical trial, using the 'double blind' technique, is reported of combined dapsone and ditophal therapy compared with dapsone and placebo in the treatment of pure lepromatous and near-lepromatous leprosy. Twenty-five untreated, matched pairs were admitted and the final analysis was made on 23 pairs and 47 patients studied for 1 year.

Dapsone and ditophal were commenced simultaneously, and over the treatment period 0–1½ months, a statistically significant (at the 1% level) greater decrease in the percentage of solid-staining bacilli occurred in the smears of pure lepromatous patients treated with ditophal and dapsone than occurred in the smears of patients treated with placebo and dapsone. Therefore, it is evident that combined therapy resulted in a faster rate of killing of leprosy bacilli than did dapsone alone. However, only one method of clinical assessment of the pure lepromatous pairs favoured combined therapy; the two other methods of clinical assessment used, and the bacterial index and biopsy index results, all failed to reveal any significant differences. between the two treatment groups. In addition, the incidence and severity of erythema nodosum leprosum did not differ in the two groups. Since the more rapid death of bacilli early in treatment had little effect on the rate of improvement of patients after 12 months, the widespread use of ditophal with dapsone does not appear to be justified Special circumstances are envisaged, however, in which ditophal would be a useful adjunct to treatment. The small number (11) of near-lepromatous patients studied showed a high incidence of lepra reactions, and four underwent histological change during their year in the trial. There was no evidence that the addition of ditophal to dapsone

treatment increased the rate of improvement, clinically, histologically or bacteriologically, in this type of leprosy which, because it is so unstable, appears unsuitable for formal clinical drug trials. Although the majority of the patients included were light-skinned Chinese no contact dermatitis nor other toxic effect of ditophal was observed.

6. **Experimental Infection of the Golden Hamster with** *Mycobacterium leprae*, by M. F. R. WATERS and JANET S. F. NIVEN. *Internat. J. Leprosy*, 1965, **33**, 3, 297–315.

Forty-eight golden hamsters, inoculated in the left ear and left testis with living suspensions of *M.leprae* and in the right ear and right testis with heat-killed suspensions, were maintained for 5–22 months. Sixteen of the 23 left ears examined histologically showed typical intracellular acid-fast micro-organisms in a variety of cell types. However, of 28 pairs of testes examined histologically, in only one left testis were intracellular mycobacteria found. Bacteriologically, acid-fast bacilli were recovered from suspensions prepared from nine left testes out of 19 pairs of testes examined, and these positive suspensions were used to attempt passage to 18 hamsters. After 18 months, 6 of 8 first passage ears examined histologically showed intracellular mycobacteria in sites similar to those found in the primary inoculation animals. Homogenates from nine other ears contained acid-fast bacilli, and counts on four confirmed a ten-fold increase, although the yield never exceeded 10^6 bacilli. It is concluded that a limited multiplication type of infection has been achieved in the hamster ear, but not in the testis, analogous to that described by Shepard in the mouse footpad.

7. *Mycobacterium leprae:* **Viability at 0°C, 31°C, and during Freezing,** by CHARLES C. SHEPARD and DOROTHY H. McRAE. *Internat. J. Leprosy*, 1965, **33**, 3, 316–23.

1. At 0°C (in crushed ice) suspensions of *M.leprae* in 0.1% bovine albumin balanced salt solution maintained their viability (as measured by their ability to multiply in mouse foot pads) with little change for about two weeks. There was a distinct loss in viability after three to four weeks.

2. At 31°C in bacteriological media containing about 1% bovine albumin and 0.2 M sucrose, *M.leprae* maintained viability with little change for two weeks.

3. Freezing and storage at —60°C caused serious losses in viability under most conditions. However, in the presence of 10% glycerol, losses of viability were sometimes only moderate (estimated as about five-fold).

Temperature Optimum of *Mycobacterium leprae* **in Mice,** by CHARLES C. SHEPARD. *J. of Bacteriology*, Nov., 1965, **90**, 5, 1271–5.

Mycobacterium leprae multiplied most rapidly in foot pads of mice kept at an air temperature of 20°C. At air temperatures of 15° and 25°C, bacillary multiplication was slightly slower; at 10° and 30°C, distinctly slower; and at 4° and 35°C, no bacillary multiplication was detected. The temperature of the foot pad tissues of mice kept at an air temperature of 20°C averaged 27° to 30°C and that of mice kept at 10° and 30°C averaged about 25° and 36°C, respectively. These measurements indicate that the optimal temperature for the growth of *M.leprae* in mice is in the range several degrees above and below 30°C. The comparative effect of different air temperatures on the growth of *M.leprae* in foot pads was very similar to that found earlier for *M.leprae* in this site, thus indicating that the potential growth of *M.leprae in vitro* might have a similar optimum of *M.marinum in vitro*, i.e., 25° to 35°C. The optimal temperature for the growth of *M.leprae* appears to be the same in mice as in humans. It is pointed out that the temperature optimum of *M.leprae* may be a reflection of the fact that most of the bacilli being excreted into the environment, where they may reach new hosts, have multiplied in the nasal mucosa, a cool tissue.

9. **Treatment of Acute Falciparum Malaria with Diphenylsulfone in North-East Tanzania,** by A. B. G. LAING. *J. Trop. Med. & Hyg.*, 1965, **68**, 10, 251–3.

Diphenylsulfone (DDS) was used in single doses of 200 mg. (and proportionately less for children under 12 years) to treat forty semi-immune African patients suffering from acute falciparum malaria in north-east Tanzania. There were five failures and, in addition, two recrudescences. The average duration of a sexual parasitaemia was 3.2 days and fever 2.4 days. Dissection of mosquitoes fed on one of the patients showed that the drug lacked sporontocidal properties against *P.falciparum*. It is considered that although diaphenysulfone is not a reliable drug for treating acute malaria, its antimalarial properties do merit a place in malaria chemo-therapy, particularly as a potentiator of other drugs such as pyrimethamine.

Influence of Repeated Lepromin Injections on the Mitsuda Skin Reaction, by B. BEIGUELMAN, R. QUAGLIATO and D. PIRES DE CAMARGO. *Internat. J. of Leprosy*, 1965, **33**, 4, 795–9.

A sample of 1,251 healthy leprosy contacts, not reacting macroscopically to lepromin, was injected a second time with lepromin. Of these, 834 were vaccinated orally with BCG after the first lepromin test. The remaining 417 were not vaccinated and were used as controls. No difference was found between the groups in the proportion of macroscopically positive late lepromin reactions revealed by the second test. The results suggest that lepromin has a sensitizing effect of short duration.

11. **Nature and Familial Character of the Lepromin Reactions,** by B. BEIGUELMAN and R. QUAGLIATO. *Internat. J. of Leprosy*, 1965, **33**, 4, 800–7.

The distribution of lepromin and Mantoux reactions was investigated in a randomized sample of 100 families living in a Brazilian rural area (Cosmopolis, State of São Paulo). A census was conducted in the studied area prior to the sampling order to include only white, complete, unrelated families of larger size.

Analysis of the data collected supports the following hypotheses:

1. The early lepromin reaction may be considered as an allergic response to leproproteins contained in lepromin.

2. The macroscopically positive late lepromin reaction reflects both the capacity of the subject's macrophages for

lysing leprosy bacilli, and the influence of sensitizing agents stimulating the lysogenic ability of the macrophages.

3. The lysogenic capacity of macrophages probably has a hereditary basis.

12. **The Genetics of Resistance to Leprosy,** by B. BEIGUELMAN. *Internat. J. of Leprosy*, 1965, **33,** 4, 808–11.

The late lepromin reaction was investigated among children of persons with polar, i.e., lepromatous and tuberculoid, types of leprosy. The data secured correspond with the view that the lysogenic capacity of macrophages for leprosy bacilli is a dominant trait, provided that allowance is made for a discrepancy found among children born to parents each of whom is lepromatous. The exception to the postulated inheritance may be ascribed to the influences caused by BCG vaccination, incomplete penetrance of the gene for leprosy resistance and illegitimacy among the offspring of leprosy patients.

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The letters after the entry have the following significance: Original Articles (O); Editorials (E); Letters to the Editor (L).

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