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CONTENTS

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EDITORIAL

I. Genetics and the Epidemiology of Leprosy

We are grateful to Dr. S. G. Spickett of Cambridge for raising this important question by his paper on the subject which appears in this issue of *Leprosy Review* (pp. 76–93). The study begins with a review of the variation in the incidence of leprosy in different populations. Dr. Spickett finds that the variation of populations in their susceptibility to leprosy is in part due to genetic differences, i.e. differences in gene frequency and manifestation. From his study of familial leprosy he suggests that the evidence is in favour of susceptibility to the invasion of the leprosy bacillus being controlled by a single irregularly dominant gene. There was one instance where this gene had a penetrance of 83.3%.

The influence of genetic systems on the epidemiology of leprosy is of considerable interest. We are glad that Dr. Spickett will continue his studies and also appeals for collaboration in the furtherance of such studies.

II. Leprosy Work in Ethiopia, Uganda, Northern Rhodesia and Tanganyika

Dr. N. D. Fraser, Medical Secretary of the Mission to Lepers, made a tour of these countries in May and June, 1961, and has kindly given us an informative report on his findings which we publish in this issue (pp. 141–153). In connection with Ethiopia we also publish a report by Dr. K. F. Schaller, Chief of Leprosy Control in Ethiopia, on the proceedings of the Second National Leprosy Conference held in Addis Ababa November–December, 1961. Both these reports are of great interest and we thank the respective authors.

III. Latex Compound for the Karigiri Boot

In connection with the treatment of plantar ulcers (W. F. Ross in *Leprosy Review*, Jan. 1962) we draw attention to a letter to the Editor from R. R. Stapleton, M.Sc. (in this issue p. 154) of Dunlop Chemicals Products Division. Practical details are given which will be of value to workers on the field.

IV. Footwear in Leprosy

This subject is also dealt with by Mr. D. Ward, M.C.S.P. of Karigiri in his paper in this issue (pp. 94–105). It is encouraging to find nowadays so much interest and study given to the orthopaedics and physiotherapy, prevention, and rehabilitation of deformities and ulcers of the feet in leprosy.

V. The Hyderabad Conference of January 1962

Dr. E. Muir attended this interesting and valuable leprosy conference in India and has kindly sent his report which appears in this issue (pp. 156–161).

VI. Classification of Leprosy for Research Purposes

Drs. D. S. Ridley and W. H. Jopling have been studying this subject and their stimulating paper appears in this issue (pp. 119–128). They attempt to define 5 group classifications of leprosy in which the groups represent 5 grades of resistance of the patient to infection. They suggest we can define this resistance on clinical and histological characters and by reference to the bacteriological response to treatment. Their basic idea seems eminently practical and it would be interesting to have their scheme worked out in full with all relevant details for each of the five groups. Also we have the useful paper by Dharmendra and S. N. Chatterjee (this issue, pp. 106–118) on the Indian view of maculo-anaesthetic leprosy and its relation to classification.

VII. Lepromin Reaction

Kooij and colleagues contribute an interesting paper (this issue, pp. 129–140) on the lepromin reaction evoked by normal liver preparations.

GENETICS AND THE EPIDEMIOLOGY OF LEPROSY

I. The Incidence of Leprosy

By S. G. SPICKETT*
Department of Genetics, University of Cambridge

Introduction

Ancient writings describe leprosy either as a highly infectious disease or as an hereditary disease. In more recent times the work of DANIELSSEN and BOECK (1848) gained widespread support for the view that leprosy was an hereditary condition. Hansen's discovery of *Mycobacterium leprae* as the causative organism of leprosy was considered to disprove Danielssen and Boeck's theories.

It is generally accepted that *Mycobacterium leprae* is the causative organism of leprosy, however some authorities have argued that the bacillus cannot produce the disease in all human beings. A variety of factors have been invoked to explain this supposed variation in susceptibility; these include diet, climate, the incidence of debilitating diseases, and factors variously described as innate, inborn, constitutional, familial and hereditary.

AYCOCK (1940; 1941; 1948) considered that there were genetic factors that determined susceptibility to leprosy. Other workers, notably ROTBERG (1937), STEINIGER (1941; 1950) and KINNEAR BROWN (1955; 1956; 1957; 1959), have held similar views to those of Aycock, nevertheless the theory of a dual etiology of leprosy depending upon the coincidence of effective contact from an open case with a genetically determined susceptible individual is not generally held.

It is the object of this paper to make a review of the literature relevant to the problems of genetic mechanisms in the incidence of leprosy, in the hope that this will stimulate workers in the field to provide the information needed if they are to be elucidated.

The distribution of leprosy

The frequency of leprosy is not uniform; variations in incidence are apparent between nations and races. However the distribution of leprosy is not random The social units between which variations in incidence of leprosy may be demonstrated are genetically rather than politically determined; tribes and races show more distinctive patterns of leprosy than do administrative territories. Such observations

*Medical Research Council Scholar.

on the distribution of leprosy suggest that some genetic factor or factors may be of importance in the epidemiology of leprosy.

The concept that the distribution and frequency of a parasitic relationship depends upon the interaction of genetically determined characteristics is not new. It has been shown to hold for several infectious diseases including tuberculosis in man. It is probable that all parasitic associations are controlled in some measure by genetic variability in host and parasite, and it would be surprising if this were not so for the relationship between *M. leprae* and man.

It is difficult to make an accurate assessment of the number of persons suffering from leprosy in a given population, so that data from different populations derived by different methods and gathered by different people cannot be used to make valid comparisons. Some investigators have, however, collected data of different populations by similar methods. MUIR (1927) has given data of the frequency of leprosy in three castes of Hindus cohabiting in the provinces of Bihar and Orissa; Table 1. Each caste forms an inbreeding community, and it is clear that there are considerable differences in the frequency of leprosy between them. The standard of living is different in each group although climate is obviously the same for them all. It has been suggested that hygiene is a factor of great importance in the epidemiology of leprosy, but it is clear that it is not of predominant importance here since the Bowris, who suffer the highest leprosy rate, have a higher standard of living and of hygiene than the more aboriginal Sonthals, but lower standards than the Brahmins.

TABLE 1

Incidence of Leprosy in Different Castes Living in Bihar and Orissa

Caste	*Incidence*
Bowris	145/100,000
Brahmin	28/100,000
Sonthal	29/100,000

GEHR and MUNDAR (1954) have published data relating to the frequency of leprosy in the different components of a multiracial society in Surinam. It is evident from these data: Table 2; that there are significant differences in the incidence of the disease between the various races, since $\chi^2_{(6)} = 435.0169$ and $p \ll .001$.

Similarly, analysis of data from HUMPHREY (1952); Table 3; gives a significant difference between the frequency of leprosy in Australian Aborigines and persons of mixed European and Aborigi-

nal parentage: $\chi^2_{(1)} = 7.91659$, $p < .01 > .001$. WAYSON (1934) has given comparable data of the frequency of leprosy amongst different races from Hawaii: Table 4. It is notable that the incidence in part Hawaiians is approximately midway between that in Hawaiians and that in other races.

TABLE 2

Incidence of Leprosy in Different Races from Surinam

Race	*Population*	*Number with Leprosy*
Creole	89,280	874
Hindu	72,960	254
Indonesian	41,280	135
Bushman	23,040	16
American Indian	3,840	4
Chinese	3,120	6*
European	3,120	4
Others	3,360	0
TOTAL	240,000	1293

TABLE 3

Incidence of Leprosy in Australian Aborigines and in those of Mixed Aborigine European Parentage

Race	*No. Examined*	*No. with Leprosy*
Aborigine	4181	264
Aborigine × European	800	30

TABLE 4

Incidence of Leprosy of Different Races in Hawaii

Race	*Incidence*
Hawaiian	0.850/1,000
Part Hawaiian	0.480/1,000
Japanese	0.019/1,000
Chinese	0.030/1,000

The frequency and distribution of leprosy in North America have been the subjects of reviews by HOPKINS AND DENNY (1929); DENNEY (1933); HOPKINS (1938); MCCOY (1938); AYCOCK AND MCKINLEY (1938); AYCOCK (1940, 1941) and AYCOCK AND HAWKINS (1941), so that the facts need not be detailed here. Aycock has shown that the main concentrations of leprosy in the United States attributable to the immigrant population occur in different parts of the country from the main endemic foci. He has also shown that in those states with the highest incidence of leprosy there are distinct foci in which racial restriction is marked and between which there is no epidemiological relationship.

The leprosy rate may become very high in small inbreeding communities. This is exemplified by the experience of a colony of Bavarians established in Colonia Tovar, Venezuela, over a hundred years ago. 113 of the 1,126 members of this colony had leprosy when examined by CONVIT, GONZALES AND RASSI (1952). This rate of leprosy is far higher than that in the surrounding indigenous population.

Demonstrable differences between the incidence of leprosy in the different groups of a multiracial society have been shown in very many studies. Even in populations which are relatively homogenous racially there is evidence of some degree of limitation to certain breeding groups; See KINNEAR BROWN (1952). COCHRANE (1959a). However, although differences in the frequency of leprosy are found between populations, this does not necessarily mean that these differences are genetically determined.

BADGER (1959) has shown that one of the principle factors controlling the incidence of leprosy is the chance of contact with an open case; he has argued further that this is the predominating factor in the epidemiology of the disease. Also he has shown that the chance of contact with an open case is not dependent upon the frequency of such cases alone but that it depends very largely upon the behaviour and social structure of the community. Evidence has been put forward that strongly suggests that the actual mechanism of transmission of the bacilli from an infected individual to an uninfected individual may involve skin parasites; SPICKETT (1961); and that the relationships of these parasites with both host and bacillus must add further epidemiological complications which may vary between populations. The point at issue is that different populations may vary in a number of characteristics controlling the probability that any individual will come into effective contact with an open case, and therefore that variations in incidence of leprosy between populations may be unconnected with biological susceptibility to *M. leprae.* It would seem very probable that these factors do explain at least in part racial variations in incidence of the disease. BADGER has argued that the differences in incidence between the various races in Hawaii

and in Louisiana are functions of the probability of contact with an open case. If the argument that the predominant reason for differences in racial incidence is the frequency of open cases holds, it would be expected that an immigrant population from a country where leprosy was not endemic would have a lower rate than the native population of the country to which they move if leprosy is endemic in that country. The data of ROTBERG AND BECHELLI (1956) are not in accord with this expectation. In a population of 6,557,423 Brazilians there was a leprosy rate of 0.204/1,000 whereas in an immigrant European population of 815,108 (the majority of whom originated from Italy in which country there was very little if any endemic leprosy) the leprosy rate was 0.303/1,000. This is the reverse of what would be expected if chance of contact with an open case was the controlling factor. BECHELLI and ROTBERG have also made a study of the incidence amongst the contacts of patients in a leprosarium, their data are given in Table 5. The incidence amongst Brazilians of foreign extraction is significantly higher than that amongst native Brazilians ($\chi^2_{(1)} = 12.7303$, p. $< .001$). It is clear that the variation in the incidence of leprosy between populations cannot be explained on the basis of variations in the probability of coming into contact with an open case alone. It must, therefore, be concluded that there is a variation in the frequency and/or degree of susceptibility between populations.

TABLE 5

Incidence of Leprosy amongst Native Brazilians and Brazilians of Foreign Extraction

	Native Brazilians	*Brazilians of foreign extraction*	*Total*
Affected	7,614	4,873	12,487
Unaffected	5,815	3,232	9,047
TOTAL	13,429	8,105	21,534

Although it may be conceded that populations vary in their pattern of susceptibility to leprosy, this does not necessarily mean that these variations are genetically determined; unless "genetic determination" is taken in the broadest sense, including the influence of genetic mechanisms on choice of diet and the like. Several of the environmental factors that have been thought to exert an influence on the incidence of leprosy have already been mentioned. It has been demonstrated that climate is not of itself a factor of overriding

importance nor is hygiene or standard of living, nor is it possible to draw any correlation between diet and the incidence of leprosy. No environmental factor can of itself be shown to be of predominant importance in influencing susceptibility to leprosy, nor can any combination of them be shown to be of great effect in this respect. It is possible that different environmental factors have a different intensity of effect in different populations; however this implies genetic differences between populations relating to susceptibility although their influence may be remote. It may be considered that there must be some factor other than the environment influencing the susceptibility of the body to parasitism by *M. leprae*, and that this factor must be genetic.

Even though it may be concluded that there are genetic effects upon susceptibility to leprosy, there is no indication in the evidence presented so far as to what the nature of the relevant genetic system may be. These effects could be manifestations of known genes; as for example those controlling blood groups; or they could be manifestations of genes hitherto unknown. Furthermore it is not possible, at this stage, to make any hypothesis as to whether the genetic control of susceptibility to leprosy is mediated through one or many genes.

It is apparent from the evidence that has gone before that racial differences in susceptibility are not of the kind that can be used to distinguish virtually all the members of one race or population from virtually all the members of another race or population. This implies that differences between populations with respect to the relevant genetic system, are differences either in gene frequencies or in the manifestations of the gene or genes. The causes of variation in manifestation of gene activity may be manifold and complex. A gene may have no manifestation with regard to a particular character in some individuals whereas it has in others. Such a gene is referred to as being non-penetrant in those individuals, the percentage of individuals carrying the gene who show manifestations of its activity with regard to that character is equal to the penetrance of the gene in that respect. There may be many reasons for lack of penetrance of the gene. It may be due to the presence of other genes modifying its activity or it may be due to environmental variation. Clearly genes controlling susceptibility to *M. leprae* will be non-penetrant if the individual carrying them does not come into contact with the bacilli.

The manifestation of a gene may also vary with respect to the degree to which the character is expressed. For example; in a family reported by LUCAS (1881), some members of whom carried the dominant gene for polydactyly, one person had a normal number of fingers but an extra toe on each foot, whereas another had an extra finger on each hand as well as an extra toe on each foot. This varia-

tion is said to be in the expressivity of the gene, and it may be due to environmental and/or genetic factors. It is obvious that populations may vary in gene penetrance and in expressivity though the latter need not be considered here.

It is possible to summarise the hypothesis as follows; the susceptibility of man to leprosy is influenced by some genetic factor, and human populations vary in the frequency of this factor and in its manifestations, so that its behaviour and significance may vary between populations.

The distribution of leprosy within affected populations is not random, there being a tendency, first noted by DANIELSSEN AND BOECK (1848): see Table 8; for the disease to be limited to certain family lines. This limitation is, as might be expected, more obvious in those populations where leprosy is infrequent than in those where it is common, and has been reported by AYCOCK (1940) from New Brunswick; BRACKEN (1900) from Minnesota; MELSOM (1953) from Norway; BJARNHEDINSSON (1909) from Iceland, MARIANI (1931) from Italy, MUIR (1940, 1943) from Cyprus and Barbados and by STEINIGER (1950) from the Eastern Baltic States. There are many reports from countries with a high rate of endemic leprosy confirming the tendency for limitation to certain families. DENNEY (1917) has shown, with data from the Phillipines, that 33% of children not separated from parents with leprosy showed signs of the disease, and LAMPE has given data from the East Indies that show a frequency of 26% in the children of parents with leprosy. AYCOCK (1941) has quoted details of a study by SAND AND LIE of 2,010 children of 587 couples one or both of whom had leprosy. They found that when the mother alone had leprosy 14% of the children contracted the disease, whereas only 7% did when the father alone was infected, however when both father and mother were infected 26% of the children acquired the disease. The incidence when both parents have the disease is more than the sum of the incidence when the mother alone has the disease and when the father alone has the disease, it is however nearly equal to twice the incidence when the mother alone has leprosy. From this it might be suggested that contact with the father alone is insufficient to give full expression of all the susceptible children, whereas with the mother it is, therefore when both parents have leprosy full expression is gained from contact with the mother, and there is twice the chance of having genes for susceptibility when both parents have such genes as when only one parent does.

Estimates of familial leprosy are usually too low, as has been pointed out by AYCOCK (1941). This is because the index cases do not always have full knowledge of the frequency of the disease in their own families, and moreover, they are often reluctant to admit that a disease regarded as shameful has occurred in their families before. Also studies of the incidence in children involve an under-

TABLE 6

Family relationships between patients with leprosy in St. George's Hospital, Bergen

Total number of cases of leprosy	*In the line of direct descent*						
	Number of cases in the paternal family	*Number of cases in the maternal family*	*Number of cases in both families*	*Series of generations in the lines of both families*			
				1st Generation	*2nd Generation*	*3rd Generation*	*4th Generation*
213	29	40	69	20	40	1	8
	In the collateral line						
	Number of cases in the paternal family	*Number of cases in the maternal family*	*Number of cases in both families*	*Series of generations in the lines of both families*			
				1st Generation	*2nd Generation*	*3rd Generation*	*4th Generation*
	52	64	116	38	58	7	13

estimate since the probability of uninfected children contracting the disease may still be high.

The data show that the tendency for concentration of leprosy in family lines is found in all types of community which have leprosy. However the demonstration of limitation of leprosy to certain family lines while consistent with an hypothesis of genetically controlled susceptibility does not prove it since it is also consistent with a purely contagion theory of the epidemiology of leprosy, and a decision in favour of one theory over the other cannot be made, on this evidence, until much more is known of the epidemiology of leprosy.

DUARTE AND LIMA (1936) examined 9,239 contacts of persons with leprosy and found that 456 of them had leprosy, the relationships of the infected contacts with the index cases are given in Table 7. Unfortunately no data is given of the proportion of each type of contact infected, however the limitation to the family is quite clear. It can be argued that this familial limitation is a function of the greater probability of contact within the family than between unrelated persons rather than a function of heredity. It was found that of the 456 infected contacts 189 did not live in the same house as the index case, this suggests that intimacy of association is not the only factor operable in the limitation of leprosy to certain families.

FERNANDEZ (1948) compared the incidence of leprosy amongst the children of leprosy patients with that in conjugal adults, his data are quoted in Table 8.

These results show that children usually acquire the infection from within the household in which they live, since when susceptible children live in a household with a relatively non-contagious case (tuberculoid) they rarely contract the disease. However the incidence in conjugal adults is not significantly higher in the households in which there are relatively contagious (lepromatous) cases than in those households in which there is a non-contagious case. It is, therefore, clear that child incidence may frequently be underestimated since distinction is not usually made between tuberculoid and lepromatous index cases. Also it is clear that adults leading an active life are as likely to acquire the disease from contacts outside their home as within it. It is, therefore, difficult to explain the limitation of the disease to certain families if it is as freely contagious as these data indicate.

It is rare for an entire family to be affected by leprosy. Several pedigrees have been established in illustration of the very high frequency of leprosy that may be found in certain families. The proportion of wholly affected sibships in all the available published pedigrees is shown in Table 9. These data are derived from: FERNANDEZ (1948), STEINIGER (1942), THIN (1892), GUINTO, RODRI-

TABLE 7

Relationships of Affected Contacts with the Index Case

Relationship of the index case to the affected	*No. affected*	*% of total affected attributable to each relationship*
Father	112	24.6
Brother	83	18.2
Mother	76	15.7
Sister	70	15.4
Husband	30	6.6
Wife	24	5.4
Daughter	16	3.6
Son	10	2.2
Uncle	7	1.6
Grandfather	6	1.3
Sister-in-law	3	0.6
♀ Cousin	3	0.6
Grandmother	2	0.4
Father-in-law	2	0.4
Aunt	2	0.4
Friend	2	0.4

Mother-in-law; Nephew; Niece; Brother-in-law; Employer; Acquaintance; ♂ Cousin and Daughter-in-law; all have 1 affected; that is 0.2% of the total.

GUEZ, DOULL AND DE GUINA (1954), MUKERJEE AND GHOSH (1958), DREISBACH (1954), MELSOM (1953), and NEFF AND SNODGRASS (1930). When it is considered that most of these sibships have been chosen as illustrations of high incidence the proportion of wholly affected sibships would appear to be very low, unless it is allowed that leprosy is very feebly contagious indeed. The data of Fernandez, which has already been quoted, suggests that leprosy is not as feebly contagious as the within family restriction implies. The literature abounds in reports of isolated cases of leprosy which cannot be traced to any known contact which implies that the contact must have been brief. Similarly KINNEAR BROWN (1956) has pointed out that in Uganda the disease must in many instances

TABLE 8

Incidence of leprosy in children and conjugal adults

Type of disease of index case	*Unaffected*		*Affected*		*Total*	
	Conjugals	*Children*	*Conjugals*	*Children*	*Conjugals*	*Children*
Lepromatous	91	184	24	90	115	274
Tuberculoid	59	122	16	4	75	126
Total	150	306	40	94	190	400

originate from a casual contact. Valuable information concerning the communicability of leprosy is available from the work of QUAGLIATO (1956) who followed up a large number of contacts over several years. The majority of cases that occurred in the contacts were detectable within six years of the first contact, this period includes the time between invasion of the new host by the bacilli and the appearance of the first clinical manifestations of the disease. Similar conclusions may be reached from consideration of the data of COCHRANE AND RAJAGOPALAN (1943) and of FERNANDEZ (1948) and of DUARTE AND LIMA (1936). Comparison can be made between the incidence of leprosy in the older and younger halves of affected sibships; such data are given in Table 10. There is no significant difference between them ($\chi^2_{(1)} = 0.470$, $p < .50 > .30$). On the basis of this evidence it seems unlikely that the limitation of the spread of leprosy within families is attributable to the feebly contagious nature of the disease. It must, therefore, be concluded that there is variation in susceptibility to leprosy within families, and, since the effect of environmental factors is minimised within families and no correlation is evident between the order of birth and the frequency of leprosy within sibships, it must be concluded that these intrafamilial variations are genetic and moreover that the evident segregation of the different genes within the family indicates that the appropriate genetic system may well be simple.

TABLE 9

Proportion of Sibships Wholly Affected by Leprosy

Size of sibship	*No. of sibships wholly affected*	*No. of sibships partly affected*	*Total No. of sibships*
2	3	12	15
3	3	9	12
4	—	10	10
5	1	8	9
6	—	4	4
7	—	3	3
8	—	2	2
9	—	2	2
10	—	3	3

There are several requirements that must be fulfilled in the taking of pedigree data for the estimation of genetic ratios, these requirements are discussed in the appendix. The majority of published pedigrees concerning leprosy are very far from satisfying these requirements and cannot, therefore, be used for the elucidation of the

genetic system controlling susceptibility to leprosy. The pedigree shown in Fig. 1 has been taken from STEINIGER (1942) and is from the Acadian French community in New Brunswick. It suggests that susceptibility to leprosy is controlled by a single irregularly dominant gene, that is a dominant gene that is not fully penetrant as a heterozygote. The sibship of 3 comprising III (1, 2, 3) has one parent with leprosy and one without, one of the sibs has leprosy. The sibship of 4 comprising IV (11, 12, 13) also has one parent with leprosy and one parent without and one sib with leprosy. These families suggest that there is a single dominant gene controlling susceptibility to the disease. However neither III 10 nor III 11, both of whom have leprosy, have an affected parent and this suggests that the gene is recessive. The entire pedigree, therefore, suggests that the gene is irregularly dominant and this is in accord with the appearance of other published pedigrees.

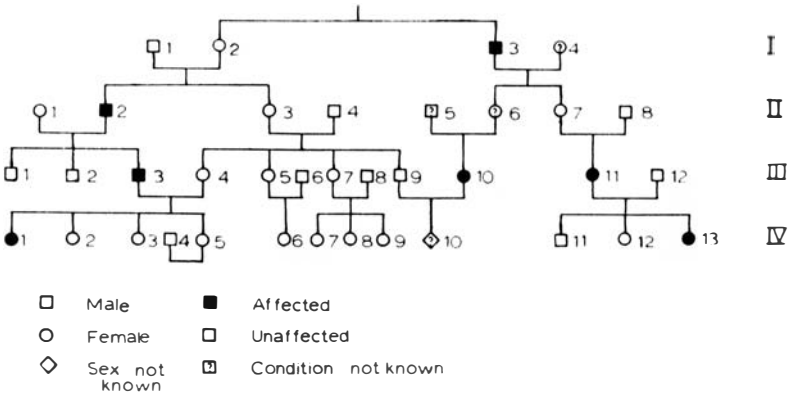

Fig. 1.

A very large pedigree also taken from the Acadian French community in New Brunswick has been given by AYCOCK AND MCKINLEY (1938). It is probable that all the geneological information that can be gained from this community has been published and that ascertainment is complete within these limits. It is, therefore, possible to calculate a value for the penetrance of the gene in this population. Since the frequency of leprosy and by implication the gene frequency, is high, and since the gene is not fully penetrant the most satisfactory value is that to be obtained from a consideration of sibships none of the parents of which had leprosy. It is assumed that where leprosy occurs in a sibship one of the parents must have carried the gene and that the mating is probably of the normal by heterozygote type. If matings of individuals with leprosy by normal individuals were taken there is a higher probability that the mating would be of the heterozygote by heterozygote type or of the homo-

zygote by heterozygote or normal. Data concerning sibships with one or more sibs having leprosy but with parents free from the disease have been abstracted from the pedigree and are given in Table 11.

TABLE 10

The Incidence of Leprosy in the Older and Younger Halves of Sibships*

Age	*Affected*	*Unaffected*	*Total*
Older half	58	59	117
Younger half	63	54	117
Total	121	113	234

* Where the size of a sibship was an odd number the middle sib was recorded as a half in both the older and younger groups.

TABLE 11

Analysis of Pedigree Data

Size of sibships	*No. of sibships*	*Total No. of individuals*	*No. of affected individual*
s	n_s	t_s	T_s
1	14	14	14
2	7	14	13
3	2	6	5
4	2	8	5
5	0	0	0
6	1	6	3
7	1	7	2
8	2	16	5
9	1	9	6
10	0	0	0
11	1	11	3
	n_s	$t_s = T$	$T_s = R$

Since inclusion of a sibship in the data depends upon the presence of an affected propositus within it, the number of affected individuals within each sibship must be reduced by one to give an unbiased proportion of affected individuals.

The penetrance value can be calculated as follows:

Let s = size of sibship.
n_s = number of sibships of a particular size s.
r_s = number of individuals with leprosy within sibships of size s.
T = total number of individuals.
R = number of individuals with leprosy.

Then: $T = sn_s$

and $R = r_s$

The proportion, P, of individuals with leprosy is therefore:

$$P = \frac{R}{T}$$

Making allowance for the bias attributable to the propositi:

$$P = \frac{R - ns}{T - ns}$$

If it is assumed that the matings are all heterozygote × normal then the expected proportion is equal to $\frac{1}{2}$.

$$\text{Penetrance} = \frac{\text{Observed proportion}}{\text{Expected proportion}} \times 100$$

$$\text{Therefore: Penetrance for heterozygotes} = \frac{P}{\frac{1}{2}} .100\%$$

Substituting in values from Table 11.

$$\text{Penetrance} = 2\left(\frac{56-31}{91-31}\right) 100\%$$

$$= 83.333\%$$

The penetrance value for heterozygotes where neither parent has leprosy is therefore 83.3%. This is a maximum estimate since there is a possibility that some matings may not be of the heterozygote by normal type and the two parents may carry more than one susceptibility gene, in which event more affected progeny would be expected so that the calculated penetrance value would be too high.

It must be emphasised that the penetrance value for homozygotes may be different and also that the value might be higher where one or both parents have the disease. Also it must be emphasised that the penetrance value may well vary in different populations.

Discussion

The evidence strongly suggests that there is a human genetic factor involved in the epidemiology of leprosy. This controls whether or not the bacilli can become established in the human body and would appear to involve a single irregularly dominant gene, which may have a penetrance as high as 80%. There is evidence of a second gene complex that exerts an influence upon the course of the disease, and this will be discussed in a future paper.

It is probable that these genetic systems vary between different populations both in the frequency of the relevant genes and in the extent of their manifestations. It is, therefore, necessary that data should be studied from a wide range of communities. The implication of these genetic systems on the epidemiology of leprosy may vary widely between different populations and attempts to extrapolate from the knowledge of one community to another may be both misleading and dangerous.

The probability of genetic variation in the infecting organism must also be considered, there is some slight evidence that this might be of importance and *a priori* it would be improbable that it is not. It is perhaps appropriate here to draw attention to the risk that strains of bacilli resistant to modern drugs are being selected by the widespread use of these drugs and there is indeed some evidence that this is happening. This possibility might be thought to give an added urgency to the study of genetic variation in human populations with regard to leprosy.

If the problems of genetics as they affect leprosy are to be studied they must, for the reasons that have gone before, be studied on a world-wide scale. Obviously it is of some importance that the considerable effort that will be necessary for such a survey should not be misdirected due to ignorance of the particular requirements that must be fulfilled in the collection of data for purposes of genetical analysis. These problems will be discussed in a future paper.

The main object of this series of papers is to review the evidence that genetic mechanisms may be of importance in the epidemiology of leprosy, and so to stimulate workers in leprosy endemic areas to collaborate in a large scale survey. It is appreciated that many leprosy workers are extremely hard pressed for time and assistance, and it is, therefore, with some hesitation that this appeal is made. Any collaboration will be most welcome and every effort will be made to lighten the task of workers in the field.

Acknowledgements

I wish to thank both Professor J. M. Thoday of the Department of Genetics, University of Cambridge, and Dr. R. G. Cochrane for the advice and encouragement they have given me throughout this work.

Summary

1. A review has been made of variation in the incidence of leprosy in different populations.

2. The evidence suggests that populations vary in their susceptibility to the disease and that this variation is in part due to genetic differences, expressed as differences in gene frequency and manifestation.

3. The evidence concerning familial leprosy has been analysed and a large pedigree has been examined.

4. The evidence suggests that susceptibility of the body to invasion by *M. leprae* is controlled by a single irregularly dominant gene, and in one population this gene has a penetrance of 83.3%.

5. An appeal is made for collaboration in the furtherance of studies on the influence of genetic systems on the epidemiology of leprosy.

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FOOTWEAR IN LEPROSY

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Papers by PRICE in 1960, ANDERSON 1961, ROSS 1961, outlined the pathogenesis, natural history and treatment of plantar ulcers. The importance of mechanical factors in provoking plantar ulcers is stressed and PRICE describes a shoe to overcome certain of them. This paper offers an outline of the mechanical forces thought to be involved, a review of certain efforts to forestall them; a description of footwear now prescribed at the Schieffelin Leprosy Research Sanatorium, and Christian Medical College Hospital, Vellore, with some cautions to be observed and some suggestions for further developemnts.

Mechanical Factors in Plantar Ulceration

Plantar ulceration occurs on walking anaesthetic feet. Enforced rest, either in bed or a plaster cast produces healing in the very great majority of cases. Since the anaesthesia is permanent certain factors involved in the walking process would appear to be the provoking cause, because their removal or diminution permits healing. KELLY in 1958, when discussing the neurotrophic ulcers of diabetes mellitus states, "The distribution of ulcers indicates a mechanical factor". The work of PRICE in Nigeria supports this. It is difficult to differentiate between these factors at the various stages of the walking cycle, but provided it is borne in mind that they interplay with each other, the following stresses can be discerned.

Weight

The area of plantar skin in contact with the ground during walking is shown by a wet footprint. NAPIER (1957) points out that prints differ between walking and standing. We are concerned with the walking print, where the area beneath the metatarso-phalangeal joint of the big toe comes in contact with the ground (Diag. 1). It is seen that the inner longitudinal arch bears no weight, the heel, outer border, metatarsal heads and toe pulps successively transmitting the strain. Examination of the weight bearing foot through a sheet of plate glass reveals that the area of the foot transmitting weight is flattened and blanched. For the moment, the skin is ischaemic. This might be of significance if the foot was static for a long period but this is very seldom the case.

In the walking foot, momentary ischaemia of the plantar skin

alternates with blood flow. For this reason necrosis of the skin is probably of little significance as a cause of ulceration. As scar tissue is formed in the plantar tissues however, as a result of ulceration, the viability of the remaining healthy tissues is endangered. Not only has the amount of the blood in the tissues been reduced but hard scar tissue concentrates pressure on adjacent structures. A result of this is that even the normal amount of weight applied to the foot during walking or standing, now becomes a dangerous factor in causing re-ulceration.

To meet this contingency it has seemed logical to utilise the skin of the inner arch as a weight bearing surface and so to reduce the proportion born elsewhere.

Impact

In the normal foot, during walking, the heel hits the ground first. This is sometimes referred to as "Heel strike". In the undamaged foot a soft resilient fibro-fatty pad is interposed between the calcaneum and the skin. The shock of heel strike is absorbed by compression and spreading of the pad. This is also easily seen by observation through plate glass. The metatarsal heads and the skin beneath them are protected from each other in a similar way. Impact stress in the forefoot occurs mainly during running and jumping, dancing, and in ascending and descending steps and slopes. In instances of muscle imbalance this pattern of impact being applied primarily to areas designed to meet it is disarranged. When the peroneal muscles are paralysed the unopposed pull of any remaining invertors causes the lateral border of the foot to strike the ground. The ulcer that develops beneath the base of the fifth metatarsal is the result, since there is no provision for absorbing impact in that area.

Ulceration of the plantar tissues, whether deep and unseen or more superficial and perceptible, results in the formation of scar tissue. Each such injury leaves less resilient tissue to counter even normal impact stresses. Therefore, in shoes designed to prevent re-ulceration a substitute pad must be provided to compensate for the loss of normal tissue. Preliminary experimental evidence indicates that peak walking pressures can be very markedly reduced by a soft insole in a leather shoe.

Shear and Thrust

When weight is transmitted through the metatarsal heads during the "take off" phase of walking, the tissues beneath are subjected to complex forces. As the heel rises, the metatarso-phalangeal joints are extended exposing the metatarsal heads which roll upon the tissues beneath. Apart from pressure there will be shear stresses as body weight and muscular effort force the metatarsal bones backwards

on the plantar tissue which are held in firm contact with the ground. The range of movement of the metatarsal heads in relation to the ground is often 40 degrees, while the plantar tissues permit $\frac{1}{2}$–$\frac{3}{4}$ cm. to and from movement of the foot skeleton without slipping. Many feet also exhibit a medial shift of the heel as it rises. This causes a twist between tissues and skeleton at the forefoot. These are normal phenomena.

The development of scar tissue within the $\frac{1}{4}$ in. thickness of the fibro-fatty pad is calamitous since it must materially reduce the gliding properties of the tissue. The metatarsal heads now roll over the tissue which has lost its resistance to shear strains and which is therefore stretched and irritated at every step.

Pressure and shear strains in the immediate region of the metatarsal heads increase in severity as the metatarso-phalangeal joints extend. By keeping these joints in a neutral position at all stages of walking the stresses can be markedly reduced.

Trauma

A variety of forces are grouped under this heading. The work of PRICE in Nigeria demonstrated that the great majority of ulcers start from within the foot. Those caused by direct damage to the skin form only a small minority. Certain causes will be familiar to all who examine large numbers of anaesthetic feet. Thorns or nails may pierce the skin. Burns may result from touching hot coals or walking long distances on scorching tarmac or concrete roads, while poorly fitting and badly designed shoes may cause shoe bites and abrasions. Pain is the greatest boon in preventing damage and its loss can only be overcome by constant and careful watchfulness.

The significance of each of these factors has been demonstrated by often removing only three and seeing the fourth cause re-ulceration. There is a further factor that is only imperfectly understood. What is the initial cause of the first ulcer? Granting the anaesthesia, it has yet to be demonstrated what initiates the development of the first scar tissue. It may be a sudden overstrain—an accenuation of one of the forces mentioned. It may be that there is faulty innervation of the plantar blood vessels which renders the foot susceptible to very minor stresses. Possibly the anaesthetic foot strikes the ground with greater than average force to compensate for a loss of proprioceptive reflexes, but this has yet to be convincingly demonstrated. Be that as it may, elimination or diminution of the mechanical factors outlined has been of great value in preventing re-ulceration in a large number of cases. In this connection it is exceedingly difficult to bring forward figures to prove the effectiveness of this or that kind of shoe in this country. For it is not customary to wear shoes within the house and it has been clearly shown to members of these units that *even ten minutes' walking without protective footwear is sufficient to cause*

re-ulceration in a healed but severely damaged foot. Experiments are now in progress however, which will show the comparative effectiveness of one kind of shoe versus another in reducing peak walking pressures on plantar tissues. This is being done with the help of pressure-sensitive discs. It is quite another thing however to ensure that the most effective shoes are worn constantly by those who need them. This will only be achieved as propaganda, education and practical proof combine their forces.

It is now postulated that the following points must be borne in mind when designing the ideal shoe for anaesthetic feet.

1. The fullest possible distribution of weight over the plantar surface of the foot.

2. The provision of a soft resilient insole or walking surface.

3. A rigid sole and rocker mechanism which renders movement at the metatarso-phalangeal joints unnecessary.

4. A soft, well-fitted upper.

Review of recent experimental shoe designs

In 1956 ROBERTSON described a method of moulding leather to the soles of individual feet in an attempt to distribute weight widely. The value of this when very carefully done was soon established. It was slow and time-consuming however and a very slight over-accentuation of the inner arch could result in a new pressure ulcer. Between 1958 and 1960 some 150 pairs of shoes were made at Schieffelin Leprosy Research Sanatorium using a modification of the technique of ROBERTSON.

Parallel with this work similar shoes with the addition of sponge rubber insoles or inserts were made. The concept of compensating for lost soft tissues was obvious to us but the results were not always very satisfactory. It became clear that this was in part due to the sponge rubber that we were using which was never designed for the heavy pressure and abrasive wear that was placed upon it. Even the firmest grade was easily compressed fully by the weight of the average man. A full insole lasted for only about three months and the cost of the rubber and the leather covering to protect it was a major item in the total cost of the shoe. With the introduction of microcellular rubber the situation changed remarkably. The Bata Shoe Co. made several grades of this rubber for our experiments and working down through higher numbers and harder grades of rubbers we decided that the resilience offered by the grade of "15 degrees Shore" best met out needs. The anti-abrasive qualities of this rubber when well made are excellent. It is easy to cut and work, can be sewn and stuck, buffed on a machine and very few insoles have had to be renewed in the past 18 months. With the help of the Madnas Rubber Factory a small unit to manufacture this special grade has been set up

in the Schieffelin Leprosy Research Sanatorium. Before microcellular rubber became available experiments were also conducted using rubber latex. BRAND had employed this as an outer covering incorporating a plastic insole on a visit to Kano, Nigeria in 1956, and in Vellore had also made moulded insoles with latex and cork dust. In 1959 he described a boot made with latex and rubber dust. This gave a very soft walking surface but experiments were stopped because of the technical difficulty of retaining the rigid member within the latex covering. Our interest in latex has been renewed recently as a means of making water-proof walking casts.

Earlier attempts at obtaining rigidity employed a wooden sole similar to the Chinese clog and considerable work was done with Alkathene, an ICI thermoplastic, a polyethylene derivative. This necessitated the making of a plaster cast and a solid plaster or cement positive on which the hot alkathene sheet was moulded. A steel strip was riveted beneath to give added rigidity and a rocker added to facilitate walking. This shoe met the requirements of rigidity and a moulded weight bearing surface. It also had the advantage of providing lateral stability and support to the heel. But it was clumsy in appearance, heavy, and if the plastic came in contact with the skin abrasive sores were very likely to develop. Attempts were then made to render the ROBERTSON type shoe rigid. Some 60 pairs were made with a horse-shoe shaped piece of 8 SWG spring steel wire incorporated beneath the leather mould. The wire fitted into a second piece of soling leather so that it did not form a ridge in the mould. A car tyre undersole and a rubber or leather rocker was added. This proved fairly satisfactory for the first six months of wear but the steel gradually began to work loose within the sole with a resulting loss of rigidity. Very occasionally the steel snapped when used in an exceptionally long shoe. A wooden undersole was used thereafter and this proved more satisfactory and is the method still used.

Some shoes have been made using metatarsal bars. When these are properly applied they transpose the weight from the metatarsal heads to the region just behind. They do not prevent shear. Large numbers have been used at the Christian Medical College and the National Research Institute, Chingleput. CURRIER (1959) reports their use at Carville. That they have a value is not doubted but rigidity is much to be preferred from a medical standpoint.

Footwear now in use

Two main patterns of footwear are now used extensively among the out-patients of the Schieffelin Sanatorium. They are the microcellular chappal with car tyre under sole and rigid soled shoes. The rubber chappal, or sandal (Diag. 2), is prescribed for all patients who exhibit anaesthesia of the foot, who show superficial cracks at

the sides of the heels and for feet which have one very small mobile ulcer scar with no pain.

Ideally in the latter instance rigid soled shoes should be worn, but generally it seems wiser to provide a sandal that is socially more acceptable and is likely to be worn constantly rather than a rigid shoe which may, to the patient, appear unnecessarily cumbersome. The chappal consists of a ½ in. (1.27 cm.) layer of 15–20 degree microcellular rubber stitched to a car tyre undersole. One leather strap passes across the forefoot from first to fifth metatarsal head. A second lies just anterior to the ankle and a third, with a buckle on the lateral side passes around the back of the heel. The straps are inserted between the two soles and stitched. A stock of these sandals is kept and fitting and adjustments take only a few minutes. At present the cost of such a pair is about Rs. 5.00 (seven shillings and sixpence sterling, or rather more than 1 dollar, U.S.). The car tyre undersole is an essential part of the chappal which is not found on the commercial variety. It serves three functions. It stiffens the sole and to some small extent hinders metatarsophalangeal extension. It saves the microcellular sole from excessive wear from cuts and slashes on its underside. But most important it prevents thorns from piercing the soft rubber and entering the foot. This last is a very real danger under the conditions most of these sandals are worn.

The rigid soled shoe is recommended for all cases of healed plantar ulceration other than those suitable for a rubber chappal. These shoes should never be used as a means of achieving healing of ulceration for which the plaster cast is both designed and effective. Their purpose is to prevent recurrence. They are prepared while the plaster cast is being worn and are fitted as soon as the cast is removed before any walking is permitted after removal of the cast.

The shoes are made on wooden lasts. This is necessary in order to provide a covered heel, without which the effect of the rigid sole is largely lost, and which also prevents much lateral movement with a consequent increase in stability. We have used the ordinary commercial shoe lasts with certain adaptations rather than have special lasts made which discourage other institutions from taking up the work. The first adaptation is to cover the sides and top of the last with soling leather about ⅛ in. (0.32 cm.) thick. Thus the width of the last is increased in relation to its length (Diag. 3). This has been found necessary since most of the feet we cater for have been free of shoes during formative years and are therefore broader than the foot accustomed to shoes from an early age. The second alteration is to increase the depth of the last by ½ in. (1.27 cm.) by adding layers of leather to the undersurface on the heel, outer border and forefoot only. This is to allow the ½ in. (1.27 cm.) microcellular rubber insole to be inserted after removal of the last. Because the area of the inner longitudinal arch is packed to a lesser extent the inner arch of the

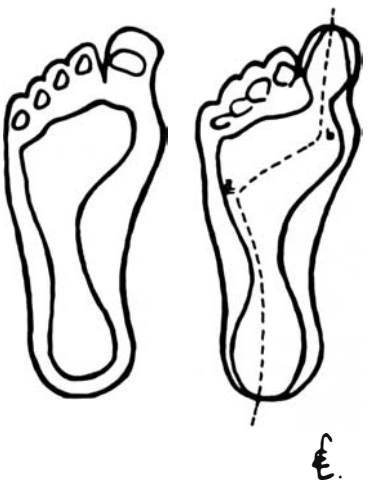


Diagram 1. The difference between a standing print (a) and a walking print (b). The dotted line shows the weight passing from heel to great toe.

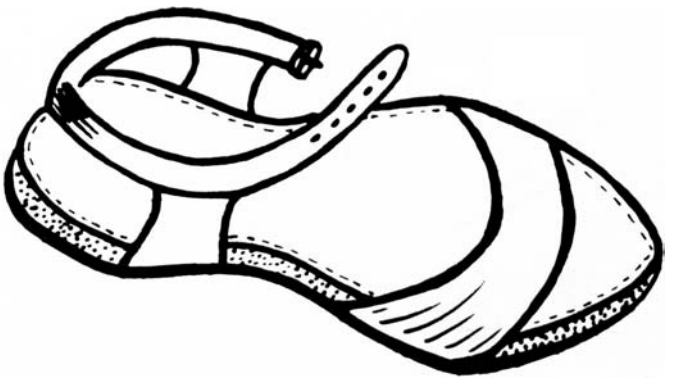


Diagram 2. The rubber sandal. A sole of car tyre is stitched to a ½ inch layer of 15-20 degree shore microcellular rubber.

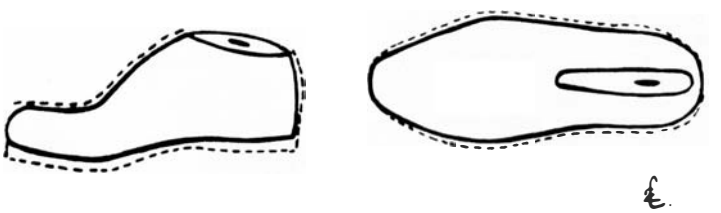


Diagram 3. To allow for an increase in width and depth of the finished shoe, the wooden lasts are packed with leather or cardboard. The instep is packed less than the heel and forefoot.

finished shoe is raised in relation to the rest of the sole (Diag. 4). This makes the longitudinal arch of the foot bear a proportion of the body weight. A complete set of lasts is treated in this way and thenceforth needs only small adjustments to compensate for such minor deformities as are met with, such as claw toes and enlarged joints. Gross deformities at once fall into a group needing the attention of a skilled surgical shoe maker.

The upper of the shoe is cut, lined and sewn to the welt of the last in the usual way. If this phrase is reminiscent of the directions in a cookery book it is because, as with cooking, this work is best done by someone with basic "know-how". A detailed dissertation on the elements of shoe making is not intended. The diagram illustrates the type of upper we employ. The reason for interwoven straps is that they permit the fit of the shoe to be easily checked and adjustments made on the spot. With the enclosed shoe the cobbler has to depend on the report of the wearer and when sensation is lost and shoes are in any case an unfamiliar item of attire such dependence is most

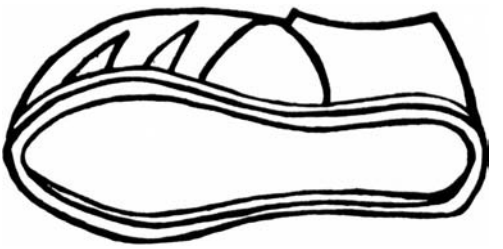


Diagram 4a. Shoe is on the last and the strip of leather has been stuck to the welt making a bed for 4b the 5-plywood insert marked with drill holes.

4c. The wooden rocker and heel 1¼ ins. high.

unwise. It does have the disadvantage that toes sometimes catch between the straps when putting the shoes on but this momentary annoyance is outweighed by the advantage of always being able to make a rapid check of correct fit. The straps are quite acceptable in this area of India.

When the upper has been sewn to the welt the accentuated arch of the insole is supported by several layers of leather stuck together. A second welt is then stuck to the first with paste or rubber solution. A strip of good soling leather ½ in. (1.27 cm.) wide and long enough to reach around the whole shoe is used (Diag. 4a). This extra strip must be the same thickness as the wooden stiffener for which we use 5-ply wood. In this way a bed is formed. The last is now removed from the shoe, and the stiffener placed in position. Screw holes are drilled from the inside of the shoe through the heel seat, the stiffener and into the wooden heel. Also through the area behind the metatarsal heads, the stiffener and into the rocker. The ends of the holes within the shoe are countersunk so that the heads of the screw lie flush with the leather insole. Three screws each for the heel and rocker usually suffice. The heel and rocker are now screwed in place. The forepart of the stiffener is then covered by sewing car tyre to the welt. The rocker and heel have car tyre tacked to them with ½ in. (1.27 cm.) nails. When the microcellular insole is slipped into the shoe it is ready to be fitted (Diag. 5).

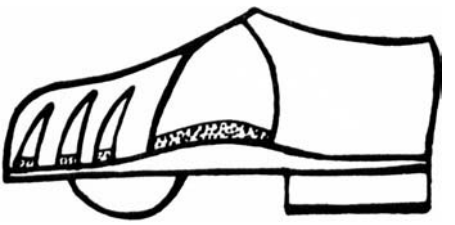
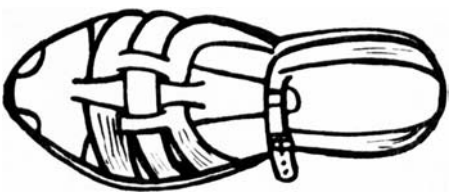


Diagram 5a. The rigid soled shoe complete with rubber insole and raised medial arch.

5b. Showing the interwoven straps of upper.



£.

The best position for the rocker has not yet been proven. We have tended to keep it as far back as possible without the empty shoe tilting forward. This is in order that the metatarsal heads should not be directly over the rocking line. But the further back the rocker is placed, the higher it must be to maintain the normal walking angle of 30–40 degrees (Diag. 6). If this is not maintained, the front of the shoe will tap the ground at each step. Another factor controlling the height of the rocker is the length of stride. A person who walks with a small step can manage with a much lower rocker than a person with a long stride. It must be remembered, too, that the metatarsal joints are the normal line at which to bend and the nearer the centre of the rocker is to these joints the more natural the gait and the less the strain placed on the heel buckle strap. The shape and dimensions of the rockers and heels that we use are shown in Diagram 4. These, with the stiffeners may be made in quantity.

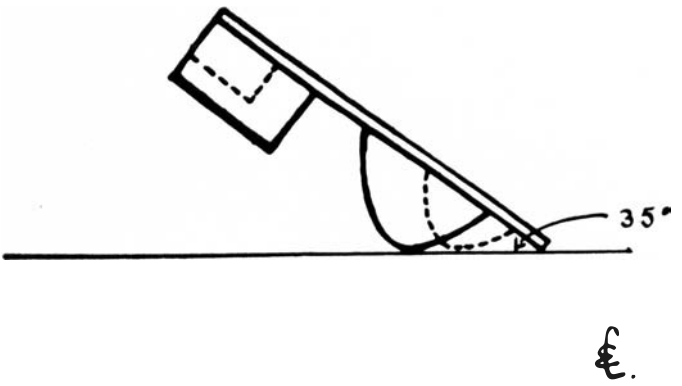


Diagram 6. The walking angle depends on the length of stride. Maintenance of the angle in a rigid sole shoe depends on the height and position of the rocker.

The finished shoe is shown in Diagram 5. If wedges are required for mild and mobile foot imbalance they may be added without difficulty. The shoes are effective in preventing re-ulceration when properly made and used, are durable, but not, it must be admitted, very elegant. This was a drawback at first, but when their value had been demonstrated by a few patients the demand rose and has remained. Recently, however, PRICE and RIORDAN have demonstrated at the Schieffelin Leprosy Research Sanatorium shoes similar to a pattern worn by foundry workers in England. Trials with this type are now in progress.

A small number of sandals with rigid soles have been made. The microcellular sole is raised on the inside to support the longitudinal arch and is sewn to a leather sole, beneath which is fixed a stiffener of either steel or wood. Because these are not made on a last and

therefore have not a covered heel, the play permitted by the single heel strap allows some movement at the metatarsal-phalangeal joints. Only a low rocker is therefore required. While we have been examining the whole principle of rigidity we have wished to avoid such a hybrid as this on any large scale, but a number of patients have done well with them and prefer them to the full rigid soled shoe and it may be that this type will be developed when current experiments have shown the degree of rigidity necessary to achieve a marked reduction in shear and thrust. KELLY, in 1958 states that the majority of the cases in his study on neurotrophic ulcers in diabetes mellitus probably owed their origin to poorly fitting shoes in conjunction with anaesthesia. Quite certainly, anaesthetic feet require greater care in fitting than those of the person with skin sensation. It is relevant here therefore to mention some of the hazards associated with shoes and sandals. Friction sores are high on the list of dangers and while it may appear that most patients cannot financially afford socks it may be that medically they cannot afford to be without them. Common sense indicates that shoes should be "worn in" during the first week of wear. There is a practical difficulty however, since few patients will face the need to purchase new shoes before the first pair has completely worn out. Again, the straps on a new shoe are likely to fit very firmly to allow for the inevitable stretching of the leather within the first few days of wear and firmness must not be confused with over-tightness. Occasionally if the sides of the heel covering are made too high, the skin beneath the malleoli will be rubbed. This is easily altered. Claw toes and enlarged joints must be given sufficient room. The mud pyramid sometimes makes its appearances on well used shoes. This term is used to describe the ridge or cone of caked dirt which is liable to form beneath an ulcer which reopens and exudes pus or serum. The dirt, caked hard with this excellent dried gum fits into the ulcer and concentrates pressure in the exact place that it will do most damage. Cleaning the shoes is the clear remedy. Careless and slipshod repairs are major hazards. The thonging sometimes used to bind soles together in country sandals can form pressure points.

But perhaps pride of place should be given to that cobblers' time saver—the nail. The Indian village chappal is a remarkable example and is often a veritable storehouse of iron held together with leather.

Shoes are only second in importance to finding the initial cause of plantar ulceration, and overcoming it. Until such time as that can be done they must take a very important place. There is a great room for improvement in style and lightness over those described. A means of making waterproof shoes for use in field work must be developed, and an adhesive to obviate much of the stitching should not be too difficult to discover. The great number of people in need of footwear,

and their economic situation have to be borne in mind and cost and ease of manufacture have to be taken into consideration.

Summary

The importance of preventing recurrence of ulceration is stated. The mechanical factors of weight, impact, thrust and shear are outlined in relation to ulceration and means suggested of overcoming them. Certain traumatic causes of ulceration are given. Two types of shoe are described, the sandal to prevent initial ulceration and a rigid soled shoe to prevent recurrence. Hazards of shoe wearing are given and suggestions for future advances made.

Acknowledgements

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MACULO-ANAESTHETIC LEPROSY— ITS DIAGNOSIS AND CLASSIFICATION

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Introduction

Flat, hypopigmented; anaesthetic or hypo-aesthetic lesions of leprosy form a distinct clinical entity. They stand apart from the flat lesions of the lepromatous type, and from the residual flat lesions resulting from the subsidence of the thick lesions of the various types of leprosy. Their existence as a distinct form of the disease has long been recognised although different names have been given to them from time to time.

Because of the relative frequency of such lesions in India, they have been studied to a considerable extent and have been recognised as one of the important types of the disease in this country, under the designation "maculo-anaesthetic". In using the label "Maculo-anaesthetic" for such cases, the term "macule" has been used in its true dermatological sense indicating the presence of a circumscribed area of skin showing pigmentary changes but no elevation above the surface of skin.**

A study of the flat hypopigmented patches in leprosy was reported by DHARMENDRA *et al.* (1953), and the features of the maculo-anaesthetic patches were described by DHARMENDRA and CHATTERJEE (1953). However, in view of the apparant lack of understanding on such lesions, the matter is again considered here in detail. It is proposed first to describe the features of these maculo-anaesthetic lesions, to consider the points of differentiation from other macular lesions of leprosy, and then to discuss their nomenclature and place in a system of classification of leprosy.

Features of the Maculo-Anaesthetic Lesions

(1) *Morphological characteristics of the skin lesions.* The skin lesions consist of flat, hypopigmented, anaesthetic or hypo-aesthetic areas of skin, varying in size, number and location. Their morphological characters may be described as under:

Size: There is great variation in the size of the patches.

Number: In number of the patches also there is great variation. There may be a single patch, or there may be several. They

** In leprosy for a long time the term "macule" has been used in a loose manner to indicate all kinds of skin patches including the thick raised patches. The present authors believe that this practice of using the term "macule" in a loose sense is to be discouraged, and that it should be used in a strict dermatological sense.

are, however, not very numerous, not of wide distribution, and not symmetrical.

Location: The patches may be found anywhere, but more commonly on face, lateral or dorsal aspects of extremities, buttocks and scapular region.

Elevation from the surface: The patches are flush with the surface of the skin, without any elevation in any of the lesions or in any part (central, peripheral, or marginal) of an individual lesion.

Colour: The patches are hypopigmented and lighter in colour than the surrounding skin. The loss of pigmentation is only partial, and is not so marked as in the case of leucoderma; the patches are therefore pale as compared to the surrounding skin, and not absolutely white. In some cases hypopigmentation may be masked by erythema or hyperpigmentation and scars caused by application of caustic preparations as local treatment.

Margin: The patches have a well-defined outline; but in the subsiding and subsided patches the margin may sometimes be ill-defined.

Surface: The surface is uniform without any irregularity or pebbling. It is dry due to impairment of sweat and sebacious secretions. Usually there is loss of hair, and those present are stunted and friable.

(2) *Sensory changes.* Loss or diminution in cutaneous sensibility is a prominent feature in this type of lesion except in lesions on the face. Loss or impairment of sensation is most marked in patches on extremities, less marked in patches on the trunk, and least marked in patches on the face. Sensations of light touch, pain, and temperature are affected, the latter two being affected earlier than that of light touch. The resulting anaesthesia and analgesia is more marked at the centre of a patch than at the periphery.

(3) *Thickening of nerves.* Cutaneous nerves supplying the area in which the patches are situated may be thickened, but this is seen less frequently than in case of the tuberculoid patches. Peripheral nerve trunks are sometimes involved, giving rise to polyneuritic changes resulting in the usual sensory, motor, and trophic changes in the peripheral distribution of the affected nerves. Occasionally there may be found a cold abscess in the course of the thickened nerve.

(4) *Results of bacteriological examination.* Results of bacteriological examination by the routine "slit and scrape" method of the patch are usually negative for leprosy bacilli. In cases with active

disease, a small number of bacilli may sometimes be found specially by the concentration method of examination.

(5) *Histological characteristics.* The histological characters in this type of lesion present the picture of a banal or non-specific infiltration mostly with small round cells which is found around the blood vessels, nerves, hair follicles and sweat and sebaceous glands. In this histological picture there is nothing characteristic of leprosy, except some occasional endoneural infiltration.

The infiltrating granuloma consists of a collection of the small round cells, arranged mostly in perivascular and perineural foci, as also around other skin appendages. A small number of epithelioid cells may also be present, but usually there is no localisation to form a follicle, and no giant cells of Langhan's type. Occasionally nerves may show slight endoneural infiltration and a few leprosy bacilli may be found inside the nerves specially on examining serial sections. A few leprosy bacilli may also be found in other parts of the section, outside the nerves.

(6) *Lepromin reaction.* The lepromin reaction is usually positive though only moderately so in most cases.

(7) *Evolution.* This form of the disease is essentially benign, slowly progressive and the lesions are relatively stable. In a vast majority of cases, the patches undergo subsidence after remaining stationary for varying periods, or after increase in size and/or number without becoming thick; after subsidence they usually leave behind some residual loss of sensation and/or slight pigmentary change. In a small number of cases, prior to subsidence there may be increase in activity with thickening to varying degrees, whereby the patches take on the characters of the tuberculoid type. In a few cases the disease progresses into the more serious lepromatous type with erythematous, ill-defined, shiny, bacillated lesions.

Differentiation from other Macular Lesions of Leprosy

Above have been described the distinctive characters of the lesions designated as maculo-anaesthetic. The lesion is essentially a macule (in the true dermatological sense) consisting of a well-defined hypopigmented area showing no elevation. Flat lesions are seen in other forms of leprosy also, and they have to be differentiated from the maculo-anaesthetic lesions described above. These other flat lesions of leprosy are: (i) Macular lesions of the lepromatous type, (ii) Macular lesions of the "Indeterminate Group", and (iii) Residual lesions resulting from the subsidence of thick patches of the tuberculoid, lepromatous, and borderline types. The distinguishing features of the various types of the flat lesions seen in leprosy are given in the accompanying table. Some clarification appears

necessary regarding the macular lesions of the "Indeterminate" group since this term appears to have been used with different meanings.* Here we have used this term in the distinctive sense as applied by Wade and ourselves to denote macules which differ from the maculo-anaesthetic lesions in several important respects as shown in the accompanying table. Compared to the maculo-anaesthetic lesions, the macules in the Indeterminate group are usually (*a*) more numerous and of wider distribution, (*b*) smaller in size, and (*c*) ill-defined with hazy outline. Sensory changes may be slight or absent; not infrequently, of the several patches, only a few may show loss of sensation. Thickening of cutaneous nerves is not common, and involvement of nerve trunks with consequent polyneuritic changes are not seen. On bacteriological examination the routine "slit and scrape" smears from some of the patches, usually show a small to moderate number of leprosy bacilli, may be in some of the patches only, but sometimes all the smears may be negative. With more elaborate methods of examination, bacilli will be found even in the cases with negative smears, specially some bacilli inside the nerves, as also in other places in the skin sections. Finally, from the point of view of evolution of the disease, these lesions are very unstable, and a large proportion of them may pass on to the lepromatous type.

Classification of the Maculo-Anaesthetic Lesions

The existence of the form of leprosy described in this paper as maculo-anaesthetic is recognised on all hands, though there may be regional differences in the frequency and therefore in the relative importance of this type of lesion. There are however some differences regarding the nomenclature applied to this form, and its exact place in a system of classification of leprosy. It is proposed to discuss the matter here.

The existing differences. The differences in this respect are exemplified by the differences regarding this form in the classification adopted at the Madrid Congress (1953), and the Indian Classification. According to the Madrid Classification these lesions are included in the Tuberculoid polar type, and are designated as macular tuberculoid. On the other hand the Indian Classification, because of their distinctive clinical entity, places them in a separate

* It was first used at the Havana Congress to replace the term "Uncharacteristic" which had been used in the South American Classification. The "Uncharacteristic" lesions of the South American Classification were defined as macules which may be erythematous or hypochromic or combine these appearances and sometimes they may present distinct elevation of skin. At the Havana Congress these "Uncharacteristic" patches were called "Indeterminate" and defined as "flat macules, either hypochromic, erythemato-hypochromic, or erythematous". At the subsequent Congresses (Madrid and Tokyo) the same definitions were retained. The "Uncharacteristic" or "Indeterminate" lesions were supposed to include the "Maculo-anaesthetic" lesions described in the present paper, and the fact was definitely stated in the first W.H.O. Expert Committee on Leprosy (1952). Wade (1953) and Dharmendra and Chatterjee (*loc. cit.*) brought out the differentiation in the maculo-anaesthetic and the other flat lesions included in the "Indeterminate" group, and suggested two different groups—Maculo-anaesthetic and Indeterminate.

category, and designates them by the term "Maculo-anaesthetic". This question was inconclusively considered by the Classification Committee of the International Congress, Tokyo (1958), and the Committee decided to leave a decision with reference to this matter to individual leprologists.*

Before discussing this matter any further, we would like to stress that this difference in the nomenclature of the lesions concerned is a minor one, and that the difference should not be magnified as is often done.

In order to make it absolutely clear what the Indian Leprologists refer to when they speak about the maculo-anaesthetic lesions, the various features of these patches have been described in detail in the present article. From the description given it will be clear that though sometimes this form of the disease has been considered as conforming to the "uncharacteristic" or "indeterminate" form of the South American and Havana-Madrid classifications respectively, it really conforms to the macular sub-type of the tuberculoid type as defined in these classifications, for which the term "macular-tuberculoid" was coined at the Madrid Congress. This narrows down the issue at discussion. Essentially two points come up for consideration: firstly, whether the term "maculo-anaesthetic" or the term "macular-tuberculoid" is more appropriate; and secondly, how best the relationship of this entity to the tuberculoid type can be indicated.

Criteria for primary classification. To facilitate discussion on these two points we would like to start with enunciating the criteria of primary classification, which have been universally accepted. At its first session the W.H.O. Expert Committee on Leprosy clearly stated its unanimously agreed decision "that the basic criteria of primary classification should be clinical comprising the morphology of skin lesions and neurological manifestations. Indispensable in connection with the clinical criteria is the bacteriological examination of smears of the skin lesions and the nasal mucosa". These views have been endorsed by almost everybody, and highlighted at the two International Congresses on Leprosy (Madrid and Tokyo) that have been held since then. At its second meeting the W.H.O. Expert Committee (1960) has once again expressed emphatically "that in classification priority should be given, as in the past, to the clinical criteria (including the bacteriological findings when that examination can be made".

* The only other difference between the two systems of classification is in connection with the pure polyneuritic lesions without any cutaneous lesions. Because of their importance as a clinical entity the Indian Classification places them in a separate group (Polyneuritic); on the other hand in the Madrid Classification there is no such separate group, but such cases are split up into tuberculoid, indeterminate and possibly lepromatous types. In this matter also the classification Committee at the Tokyo Congress had no specific recommendation to make, and the decision on the matter was left to individual leprologists. In the present discussions we will confine ourselves to the maculo-anaesthetic lesions and will not deal with those pure "polyneuritic" lesions.

Application of these criteria. Let us try to examine the question of nomenclature and classification of these flat anaesthetic lesions with this background of generally accepted criteria for primary classification of leprosy.

Regarding the first point, i.e., the nomenclature, it should be quite apparent that from the clinical point of view, the term maculo-anaesthetic very aptly describes the lesion; it indicates the morphology of the lesion and the main characteristic feature of it—a macule in the true dermatological sense, and the presence of anaesthesia. On the other hand the term macular-tuberculoid does not describe the clinical character of the lesion. Moreover, it is an anomaly from the clinical point of view as it is a strange and confusing mixture of two terms having different clinical significance, one indicating a flat lesion, and the other an elevated lesion.* This term was coined at the Madrid Congress evidently to justify the continued inclusion of the type of lesion concerned in the Tuberculoid type. However, one of the members (WADE) of the Classification Committee at that Congress had appended a note of dissent to the report of this Committee expressing the inadvisability of including the "simple" flat macules with the thick, red and elevated "tuberculoid" lesions, and stressing the confusion in terminology likely to be caused by the term "macular-tuberculoid". It may be stated that these views of Wade are in complete accord with those of the Indian Leprologists.

Regarding the second point, i.e., the relationship of these "simple" flat lesions to the "tuberculoid" lesions, it is agreed by all that from the immunological and prognostic points of view they are closely allied, both being of benign nature. It is also unanimously agreed that this relationship should be appropriately indicated in the classification of the disease. One obvious way of achieving this object is to include both types of lesions in one broad group, and that is what has been actually done in both the Madrid and the Indian Classifications, though different terms have been used for the broad group in the two systems. In the Madrid Classification the flat lesions (designated as macular tuberculoid) and the thick elevated lesions (designated as minor and major-tuberculoid) are classified together under the "Tuberculoid" type. In the Indian Classification the flat lesions (designated as maculo-anaesthetic) and the thick elevated lesions (designated as minor and major-tuberculoid) are included in a broad group "Non-lepromatous", in contrast to the "Lepromatous" which includes the malign forms of the disease. The present authors consider that the term "tuberculoid" which may be suitable for the thick and elevated lesions, is not suitable for the group containing both the thick elevated and the "simple" flat lesions, for reasons

* Even from the histological point of view the term is not apt, as in most of these flat lesions the histological picture is that of chronic banal infiltration, and not of the tuberculoid nature.

already stated earlier in this paper. On the other hand the term "Non-lepromatous" is considered very suitable for the benign forms of the disease as against "lepromatous" for the malignant forms. They are however aware of the objections raised against the use of the term non-lepromatous for this purpose. To meet these objections though may be given to finding out some more suitable term to be used in place of or as a synonym of the term "Non-lepromatous".

Criticism of the Indian Classification. After stating our position regarding the nomenclature and classification of the "simple" flat lesions of the benign kind, we would like to refer to the criticisms made of this point of view by those who do not agree with the Indian Classification. This brings us to the recent article of CHAUSSINAND (1961).

It appears that CHAUSSINAND'S objections to the Indian Classification are mainly three: (i) the nomenclature and position of the "simple" flat benign lesions which are the subject of discussion of the present paper, (ii) the inclusion of Borderline and Indeterminate forms in a broad group called "Intermediate", and (iii) creation of a separate form "Polyneuritic" for the clinical entity of pure polyneuritic cases without any skin lesions. He also indicates his preference for the benign-malignant nomenclature to the non-lepromatous—lepromatous conception, and also voices his opposition to the use of the terms "open" and "closed" for administrative classification to indicate the "infectious" and "non-infectious" cases respectively. Since the present paper is concerned only with the "simple" flat lesions, we will deal with his objections with reference to only these lesions. In passing we may however say a few words in connection with the other two main objections. Regarding the inclusion of "Borderline" and "Indeterminate" in a broad group designated as "Intermediate" (between the lepromatous and non-lepromatous), we have made it perfectly clear in our publications that this arrangement is suggested only for the convenience of certain types of workers, and that this is not an essential feature of the Indian Classification. Regarding the use of a clinical term (Polyneuritic) to designate a clinical entity, CHAUSSINAND says "it is inconceivable this group should be given a place in the primary classification, since the classification has the precise object of defining the principal forms of the disease with a view to orderly scientific classification of patients". To this our only reply is that in view of the unanimous agreement of the leprologists "that the basic criteria of primary classification should be clinical", it is inconceivable to split up a definite clinical entity into different groups or types on the basis of actual or likely histological and immunological findings. If it is done, it will be a mockery of the idea of the primary classification being based on clinical criteria.

We will now deal with CHAUSSINAND's criticism against the use of the term "maculo-anaesthetic". According to CHAUSSINAND "It would be unfortunate to use, as the Indian Leprologists wish to do, histological definitions for the tuberculoid and lepromatous forms and the clinical definition of maculo-anaesthetic leprosy for the indeterminate form". We are amused to read that the Indian leprologists wish to use histological definitions for the tuberculoid and the lepromatous forms, and clinical definitions of maculo-anaesthetic leprosy for the indeterminate form. We do not know what is the source of his information, and whether he is depending on hearsay, since in the list of references attached to his paper under discussion there is included not a single reference to the papers by the Indian workers. For his information, and for the information of others of his way of thinking, we may say here that the Indian leprologists would like to use *clinical definition* for *all* the forms of leprosy. They are aware that the terms "tuberculoid" and "lepromatous" are based on, and have their origin in, the histological findings made in the active cases of the respective forms. But it does not necessarily mean that this fact imposes a ban on the use of any term other than histological to designate any of the forms of leprosy, and that the terminology of all forms of leprosy must necessarily be histological. We have reasons to believe that in this stand we have the support of many workers who advocate the use of the Madrid Classification in entirety, and who say that though the terms used therein are histological they are used in a clinical sense. It is on this basis that these workers justify the use of the term "tuberculoid" for the lesions which do not have a tuberculoid histology, and that is how the term macular-tuberculoid has been coined. CHAUSSINAND's suggestion to use the term "atypical tuberculoid" for such lesions would itself indicate such a position and the desire to somehow retain the term tuberculoid for the entire group including the form where there is even no tuberculoid histology.

Use of the term tuberculoid. The term "tuberculoid" and "lepromatous" have now been well established in leprosy by long usage, since 1931 in the case of "lepromatous", and since 1945 in the case of "tuberculoid". The Indian Classification has adopted these terms for the forms of leprosy where the respective histological pictures are generally found at least in the active lesions; this means the adoption of "lepromatous" in its entirety, and "tuberculoid" with the exclusion of the "simple" flat patches. It would be better to explain our position regarding the use of the term "tuberculoid". In infective granulomatous diseases other than leprosy, for example, in syphilis and dermal leishmaniasis, there exist in the skin both flat lesions and thick elevated lesions, the latter with tuberculoid histology; however nobody uses the term "tuberculoid" with reference to these thick

elevated lesions of these diseases with tuberculoid histology. Why should then anybody insist on the use of the term "tuberculoid" with reference to such lesion in leprosy. All the same, because of the term having been in popular use for some time now, we are not against the use of the term as applied to thick and raised benign lesions of leprosy which generally have a tuberculoid histology. However, we cannot understand and support the extension of this term to the "simple" flat benign lesions, which are tuberculoid neither clinically (not elevated) nor histologically. In order to somehow include such lesions in the "tuberculoid" category, confusing nomenclature such as macular-tuberculoid has been coined, or it is suggested to resort to such terms as "atypical tuberculoid" for this purpose.* To use CHAUSSINAND's own expression we will say "It would be unfortunate to use, as CHAUSSINAND wishes to do, the term atypical tuberculoid for the 'simple' flat lesions which are not tuberculoid either from the clinical or from the histological point of view".

Conclusions

We fully share CHAUSSINAND's regret that "leprologists are not yet able or willing to agree on one classification that might at least be adopted by all". We also fully share his views expressed in the concluding remarks of his paper that "An acceptable classification of leprosy could be rapidly decided on if leprologists would agree to remove from consideration certain regional or personal preferences, to which it is hard to attach any real importance. And this result could be achieved easily since no doctrinal differences exist in clinical, immunological or histological aspects". We sincerely wish that any regional and specially any personal preferences do not stand in the way of arriving at a generally acceptable classification of leprosy. We feel that this would be possible only if the general principles unanimously accepted and often repeated regarding the criteria of primary classification are faithfully followed. As we have already stated it has been repeatedly agreed and stressed that the criteria for primary classification should be clinical including the results of bacteriological examination of lesions. However when the question of practical application of these principles arises, actually the histological considerations loom large in the minds of many workers. In our opinion it is this dual concept—clinical criteria in principle and histological criteria in practice—that is mostly responsible for the differences that are seen amongst the various groups of workers on this important matter of classification of leprosy. It may be said that the Indian Classification conforms strictly to the principle that "the basic criteria for primary classification should be clinical".

* The use of the term atypical tuberculoid may be in order in case of the thick raised "tuberculoid" lesions with some atypical feature in the tuberculoid histology.

We would like once again to stress that the differences in the points of view of the Indian and Madrid Classifications are only slight, and that these differences should not be unnecessarily magnified. What is really necessary is to try to understand each other's point of view. This should, however, be mutual and not expected to be one-sided only. We will conclude with the hope that some method may be found to reconcile the minor differences. However, till such solution is found and till the use of two different terms are continued, at least two things should be done to avoid or minimise confusion.* Firstly, it should be clearly understood that the term macular-tuberculoid (of the Madrid Classification) and maculo-anaesthetic (of the Indian Classification) refer to one and the same type of lesion. Secondly, the the purposes of special investigations and for collecting data for subsequent analysis, macular-tuberculoid or maculo-anaesthetic, as the case may be, should be listed separately from the other components of the Tuberculoid type (in the case of the Madrid Classification) or the Non-lepromatous group (in the case of the Indian Classification) respectively. This is essential because of the differences in the so-called macular-tuberculoid and the other components of the Tuberculoid type regarding such matters as the extent of nerve involvement and consequent deformities, the evolution of the lesion and prognosis of the disease, and the response to treatment. We feel that with due attention to this little matter of detail, data could be collected from different countries which could be comparable even without making any change in the nomenclature and the system of classification that is being followed in the different countries at present.

Summary

1. The flat hypopigmented anaesthetic patches of leprosy constitute a distinct clinical entity in leprosy. In the Indian Classification such lesions are designated as "Maculo-anaesthetic".

2. A detailed description is given of these lesions which are macular in the true dermatological sense, being flat hypopigmented areas of skin, without any elevation but with clearly defined margins, with definite sensory changes, a rough dry surface, bacteriologically usually negative, histologically showing usually only simple banal infiltration, and having a benign course.

3. Differentiation of these maculo-anaesthetic lesions is considered from other macular lesions in leprosy, such as the macular lesions of lepromatous and indeterminate forms and residual flat lesions remaining after the subsidence of the thick raised patches of the tuberculoid, lepromatous and borderline types.

* The present paper refers only to the "simple" flat benign lesions of leprosy and comments on the subject have therefore been limited mainly to cover this type of lesion.

Particulars of the flat patches of various kinds seen in leprosy

	Maculo anaesthetic macule	*Indeterminate macule*	*Lepromatous macule*	*Subsided tuberculoid patches*	*Subsided infiltrated lepromatous and borderline patches*
1. History of elevation of the lesion.	All along flat.	All along flat.	All along flat.	Originally red and raised from the surface of skin.	Originally red and raised from the surface of skin.
2. Morphology of the patch.	Hypopigmented; in treated cases the centre may be hyperpigmented. Dry surface.	Hypopigmented or erythematous. Surface not dry.	Hypopigmented or erythematous. Surface smooth and shiny.	Hypopigmented, the centre may be normal looking or hyperpigmented. Surface dry and shows wrinkling due to subsidence.	Hypopigmented, the centre may be hyperpigmented. Surface smooth and shows wrinkling due to subsidence.
3. Anaesthesia to light touch.	Anaesthesia is a prominent feature.	Anaesthesia is not a constant feature. If present, it is comparatively slight and may be found in only some of the patches.	Not anaesthetic.	Anaesthetic.	Lesions of extremities may sometimes be anaesthetic. Others are non-anaesthetic.
4. Thickening of the associated nerves.	Usually present.	Usually absent. If present, there is only slight thickening.	Absent.	Usually present.	Usually absent.
5. Bacteriological examination by the routine "slit and scrape" method.	Usually negative. A few bacilli may be found in a small number of cases.	Usually positive slightly. Scanty to moderate number of bacilli are usually present at least in some of the lesions. Sometimes smears are negative.	Moderately or strongly positive.	Negative.	Usually positive for a considerable time after subsidence.
6. Lepromin reaction.	Usually positive though moderately.	Usually negative or weakly positive.	Negative.	Moderately positive.	Negative.
7. Histological picture.	Non-specific round cell and epithelioid cell infiltration around blood vessels, nerves and other skin appendages without tuberculoid foci. Some endoneural infiltration usually present.	As in the maculo-anaesthetic macule. Usually no endoneural infiltration, but bacilli may be present, inside the cutaneous nerves.	Loose focal granuloma usually with presence of foam cells; in early cases well developed foam cells may be absent. No endoneural infiltration.	Mainly non-specific cell infiltration. Tuberculoid foci may be found in some places, nerves infiltrated, some may be badly damaged beyond recognition.	Mainly non-specific infiltration but foam cells persist for long after subsidence. No endoneural infiltration, may be marked perineural infiltration.
8. Evolution.	Benign and relatively stable. A vast majority remain true to type, and in due course undergo subsidence but there may remain, some residual loss of sensation and/or slight pigmentary change. A small number may become thickened and pass on to the tuberculoid type; while a few may pass on to the lepromatous type.	Very unstable, and quite a large proportion of them pass on to the lepromatous type in course of time.	In time other lesions of the lepromatous type such as diffuse infiltration, thickened patches, and sometimes nodules appear, and the case becomes a typical lepromatous one.	Usually remain subsided. In case of relapse or activity they again become tuberculoid.	May relapse, and then usually the activity is of the lepromatous type.

4. The maculo-anaesthetic form is a benign form allied to the Tuberculoid type from the prognostic point of view. However, it is not tuberculoid, either from the histological or the wider clinical point of view—neither having a definite tuberculoid histology, nor being thick and elevated.

5. The maculo-anaesthetic lesions of the Indian Classification are designated as macular-tuberculoid in the Madrid Classification. Besides this slight difference in the nomenclature of this form of leprosy in the two systems of classification, there is some difference in its grouping also. In the Indian Classification they are included as a separate type, their close relationship to the tuberculoid type being indicated by including both of them in the broad group of benign (non-lepromatous) leprosy. In the Madrid Classification these flat lesions are included as a variety of the Tuberculoid type (the other varieties being minor and major tuberculoid).

6. The above differences in the terminology and grouping of these flat hypopigmented benign lesions in the two systems of classification are considered to be only minor. A plea is made that these differences should not be unnecessarily magnified, and that efforts should be made to understand the two different points of view.

7. It is hoped that with mutual understanding it should be possible to evolve a unanimously agreed classification since there are no basic differences involved.

8. Till such agreement is reached, even with the existing differences it is possible to collect data for comparative studies from different countries without any difficulty. The Tuberculoid type of the Madrid Classification may be considered identical with the "Non-lepromatous" group of the Indian Classification; and the macular-tuberculoid component of the Tuberculoid type (Madrid) identical with the maculo-anaesthetic component of the Non-lepromatous group (Indian).

It would be better and more informative if for the purpose of collecting certain data in both the systems of classification the flat patches are separated out from the thick and raised patches in the Type or Group as the case may be. Thus in countries using the Indian Classification data should be collected separately for the maculo-anaesthetic and the Tuberculoid lesions, and in countries using the Madrid Classification it should be collected separately for the macular-tuberculoid and the other components (minor and major) of the Tuberculoid type. This is essential because of the differences in the so-called macular-tuberculoid and the other components of tuberculoid type regarding the extent of nerve involvement and consequent deformities, the evolution of the lesions and prognosis of the disease, and the response to treatment.

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A CLASSIFICATION OF LEPROSY FOR RESEARCH PURPOSES

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Accepted systems of classifying leprosy, being based on the need to achieve the widest possible agreement and to serve a variety of purposes, do not provide the detail which is sometimes desired for research. This paper has the limited object of describing a classification which has been adopted for certain therapeutic trials and other projects. The scheme contains few important departures from accepted ideas.

It was assumed that, underlying the various differences between tuberculoid and lepromatous leprosy, the question of resistance by patient to infection was fundamental. The object of classification was to assess prognosis and expected response to treatment, which depend to a considerable extent on a patient's resistance. It was assumed further that every degree of resistance may on occasion be encountered; but for convenience an attempt was made to define 5 grades or groups by reference to the clinical, histological, bacteriological and immunological patterns which have been found by experience to have a bearing on a patient's resistance and prognosis.

The procedure therefore was to construct a skeleton scheme of classification in 5 groups (Table 1), the two "poles" of which were tuberculoid and lepromatous defined by the strictest orthodox criteria; and subsequently to determine the characteristics of the intervening groups by correlating various characteristics with the outcome of a follow-up study after treatment.

Method

For several years we had attempted to classify new patients at the Jordan Hospital as precisely as possible in the "spectrum" between tuberculoid and lepromatous and in due course the "5 group TT–LL" classification evolved. The response to treatment was followed in several ways. Close clinical observation was supported by photographs. Bacteriological progress was assessed by routine serial biopsies (RIDLEY, 1958), using biopsies of 2 lesions every 6 months; large but representative lesions or areas of diffuse involvement, which provided a number of consecutive biopsies were selected; where the lesions were all small, comparable lesions suitable for future biopsy were marked on a chart. Skin smears also were examined. Recently a granularity index for bacilli was introduced but the

results, being incomplete, are omitted from the analysis. Lepromin testing was undertaken as a routine. The various criteria we had used in classification were then evaluated in the light of the follow-up study. The analysis, based on 35 cases, was retrospective. In 1958 we were given the opportunity to examine a large group of new patients at Sungei Buloh Settlement, Malaya, and subsequently to observe the bacteriological progress of 47 suitable cases in the same manner as for the Jordan Hospital patients. It was thus possible to check our retrospective conclusions, and where necessary to revise them, in the light of a non-retrospective trial.

The patients at the Jordan Hospital were of many races, those at Sungei Buloh were predominently Chinese. All those with an initial biopsy index of 1.0 or more were accepted for a follow-up analysis. (The maximum score was 6.0; 1.0 would be the score of a lesion occupying 1/5th of the dermis in which the bacterial index was 5 +). This qualification allowed the inclusion of an occasional BT case, the majority of BB cases and nearly all BL and LL cases. All the patients who were included in the analysis were on sulphone treatment except for 4 who received Ciba 1906. Reactions were disregarded in the bacteriological analysis unless they were sufficiently severe to cause an interruption of treatment for a month or more, or to cause an alteration in the patient's classification, in which case the patient was rejected from the analysis. All the 82 patients in the combined analysis were followed for at least 12 months, except for 6 (all BT or BB) in whom bacilli became too scanty to assess after 6 months; 35 were followed up for two years or more.

Results

Clinical classification. Clinically the characteristics of tuberculoid and lepromatous leprosy merge from one to the other through the intervening sub-divisions. Clinical classification therefore was based on an estimate of the general trend or pattern of the lesions. It was possible to judge the value of this classification by the subsequent course of the infection, but not to evaluate individual charactertisics on which it was based. The principal features of the clinical assessment were as follows.

Clinical features which differentiate borderline leprosy from the lepromatous and tuberculoid types. Skin lesions of borderline leprosy are not as numerous or as small as in the lepromatous type nor as few or as large as in the tuberculoid type; their distribution is not as symmetrical on the two sides of the body as in the lepromatous type nor as markedly asymmetrical as in the tuberculoid type; their surface is not as smooth and shiny as in the lepromatous type nor as irregular and dry-looking as in the tuberculoid type; they have neither the absence of anaesthesia which is a feature of lepromatous

leprosy nor the marked sensory loss of tuberculoid leprosy; macules and plaques have neither the vague and ill-defined edges characteristic of lepromatous lesions nor the sharp, clearly-defined edges of tuberculoid lesions.

Annular lesions are common in borderline leprosy and often take the form of a roughly oval area of hypopigmented skin surrounded by a slightly raised lesion which has a raised and well-defined *inner* edge, giving a punched-out appearance. In contrast, annular lesions are not a feature of lepromatous leprosy, and in tuberculoid leprosy they have raised and clear-cut *outer* borders with flattening towards the centre.

Palpable thickening of peripheral nerves, if present, may help in making a diagnosis of borderline leprosy, for the number of affected nerves is likely to be greater than in tuberculoid leprosy and they are less thick and irregular; their number and thickness is also likely to be more than in lepromatous leprosy with a comparable length of history. Additional points of distinction from lepromatous leprosy are: the skin between lesions appears normal, not thickened (this applies especially to the face); there are no mucosal changes; the eyes are free from keratitis or iritis; the eyebrows are not deficient (unless a plaque is actually situated on part of an eyebrow); lymphadenopathy is not a feature of borderline leprosy.

Clinical features of lepromatous leprosy which has evolved from the borderline types. These patients have unmistakable evidence of lepromatous leprosy but careful examination reveals one or more of the following:

(1) One or more plaques or annular lesions possessing the characteristics of borderline lesions—see above.

(2) Peripheral nerve thickening in excess of that which would be expected in pure lepromatous leprosy with the same length of history, and not completely bilaterally symmetrical.

(3) Less involvement of eyes, mucosa and eyebrows than would be expected in pure lepromatous leprosy with a similar length of history.

These clinical criteria are summarized in Table 2.

Follow-up Study. The above clinical criteria were applied to patients both in England and in Malaya. In view of the distance separating the two groups of patients it was not possible to make a clinical comparison of progress under treatment. Progress was assessed by means of the biopsy index, which is a bacteriological index, but which takes into account the size of lesions; its value depended of course on clinical judgement in the selection of lesions.

It was desired to select those criteria which would divide patients as accurately as possible between groups with distinctly different

TABLE 1

Skeleton Scheme of Classification

General Usage	*Modified Categories*	*Characteristics*		
		Clinical and Histological	*Bacilli**	*Lepromin*
Tuberculoid	Tuberculoid TT	Full tuberculoid	Nil	Positive, 2 or 3+
	Borderline-tuberculoid BT	Near tuberculoid	Nil, 1 or 2+	Weak positive (1+) or negative
Borderline (Dimorphous)	Borderline BB	Borderline	2 to 5+	Negative
Lepromatous	Borderline-lepromatous BL	Near lepromatous or atypical	4 or 5+	Negative
	Lepromatous LL	Full lepromatous	5 or 6+	Negative.
Indeterminate	Indeterminate	Not classifiable on TT–LL scale.	Nil	Weak positive or negative.

* The bacterial indices here referred to are based on a logarithmic scale (Maximum 6+) applied to skin smears.

The clinical and histological criteria of classification are given in the text.

TABLE 2

Clinical Criteria for Subdividing Borderline Leprosy

Lesions	*Type of Leprosy*	
Skin	*Borderline, nearer lepromatous (BL)*	*Borderline, nearer tuberculoid (BT)*
Number	Becoming more numerous the nearer to lepromatous.	Becoming less numerous the nearer to tuberculoid.
Size	Smaller on average.	Larger on average.
Distribution	Tendency towards bilateral symmetry.	Asymmetrical.
Surface	Smoother, shinier, more hairy.	Rougher, drier, less hairy.
Pain, temperature and touch sensation	Slight impairment.	More pronounced impairment.
Thickened Nerves		
Number	More numerous.	Less numerous.
Character	Smooth.	May be slightly irregular.
Distribution	Tendency to bilateral symmetry.	Asymmetrical.

rates of fall in this bacteriological index in response to chemotherapy. From this point of view the clinical assessment of patients in the first trial was eminently successful; in one case classified as BT, 3 as BB, 10 as BL and 21 as LL the mean fall in the biopsy index for each period of 6 months was BT 100%, BB 96%, BL 51% and LL 29%. There was a very good demarcation of groups in terms of progress rates.

The histological criteria to be tested included the finding in significant numbers of Langhans's giant cells, epithelioid cells, histiocytes, foam cells, globi, foreign body giant cells, lymphocytes and plasma cells; and the presence of fibrosis, of a clear sub-epidermal zone, and of neural infiltration or perineural cuffing.

When an attempt was made to choose the criteria which would give the best differentiation of progress rates it was found that granulomata in which epithelioid cells were present gave a mean rate of fall in the index of 98%; those in which epithelioid cells were absent but lymphocytes numerous gave a rate of 57%, those in which foam cells and globi were the only prominent cells, 31%. These figures are very close to those for the BB, BL and LL clinical groups. The other criteria which were considered proved to be of secondary importance and they are discussed later.

The same clinical and histological criteria were applied in the second trial at Sungei Buloh. The attempt to forecast clinically the rate of fall in the index under treatment was less successful than before; BB 70%, BL 39%, LL 33%. There was no definite separation of BL and LL groups. To some extent this could be attributed to the fact that the second trial, unlike the first, was non-retrospective. To a greater extent it was probably due to the fact that the time available was insufficient for thorough clinical examinations.

Histologically the second trial necessitated some modification of the circumstances under which lymphocytes were to be considered as indicative of a BL classification (see below). When this revision was made the progress rates for the three categories were much the same as before: 89%, 58% and 33%.

Histological classification. The mean progress rate for each of the histological criteria referred to above was calculated. After analysis of the results it was concluded that the typical features of the 5 groups were as follows. The descriptions refer to the fully developed lesions.

TT Focalized epithelioid cells, often with Langhans's giant cells, encompassed by zones of lymphocytes and extending up to the epidermis. Nerves within the granuloma infiltrated and often unrecognizable.

BT Epithelioid cells either focalized or accompanied by Langhans's giant cells or both. There is a narrow clear zone beneath the epidermis at least in some places. Lymphocytic infiltration

sometimes heavy. Nerves often very swollen by infiltrate but usually they are discernible.

BB Diffuse epithelioid cell granuloma with little or no focalization and usually no Langhans's giant cells. Lymphocytes variable. Usually some nerve damage and possibly cuffing or infiltration.

BL (1) Histiocytes showing a tendency to epithelioid cell development. Lymphocytes scanty.
(2) More commonly, histiocytes loaded with bacilli and perhaps some foamy degeneration but no large globi. Dense clumps of lymphocytes present (*a*) as peri-neural cuffs or (*b*) occupying whole segments of the granuloma.

LL Histiocytes typically show foamy degeneration and globus formation, but this may not exceed that of BL. Multinucleate globi, if present, are diagnostic. Lymphocytes diffuse or scanty especially in untreated cases.

The number of patients in the BT class with a sufficiently high index to justify follow-up was too low to be significant and in the TT class there was of course none. It was impossible therefore to assess the characteristics of these two classes separately in the follow-up study. The histological features referred to above are those which appeared to correlate best with the clinical findings, the lepromin test and the apparent stability of the patients.

The most striking correlation between bacteriological progress and a histological characteristic was in the case of the epithelioid cell. In 7 patients whose biopsies showed definite epithelioid cells the lowest fall in biopsy index in the first year of treatment was 88%, the mean 96%.

The main problem in the selection of patients for therapeutic trials was the definition of the BL and LL groups. In this matter the degree of cellular infiltration of the sub-epidermal zone was seldom helpful. Heavy infiltration was rare in LL cases but was also unusual in BL; minor degrees of infiltration showed no correlation with progress rates. Cellular infiltration of nerves was absent. Cuffing of small nerve trunks by lymphocytes however was a definite characteristic of the BL group. Damage to these nerves was of little significance; one presumed that it might have occurred during an earlier phase of the disease and the same applied to destruction of sweat glands. Silver impregnation of axons had some advantage over routine staining methods, but less for classification than for diagnosis. The presence of plasma cells or fibrosis had no correlation with rate of progress. Lymphocytes were significant either when present as peri-neural cuffs, or when they infiltrated densely an entire focus or segment of granuloma, in which case they were indicative of BL status. Diffuse relatively thin infiltration by lymphocytes, or clumps of these cells surrounded by foamy cells were quite consistent with

LL classification, and lymphocytes could be numerous in ENL lesions. But lymphocytes were often the only histological indication that a patient was in the BL group; on occasion the decision between BL and LL could be difficult or impossible.

The BL group presents two alternative histological pictures according to whether the predominant cell is the lymphocyte or a degraded epithelioid cell. Lymphocytes are the predominant cell in early and indeterminate leprosy and it is possible that some of the BL cases in which lymphocytes predominate (and epithelioid cells are absent) are still in an early stage in the evolution of the infection. This type of case has been seen occasionally in Eurasians, Indians and Chinese, but it is most frequent and characteristic in some of the African races.

Giant multinucleate globi were indicative in all cases of the LL group.

Fat stains were carried out in some cases. We agree with DAVISON, KOOIJ and WAINWRIGHT (1960) that, although in general the more fat there is the nearer the lesion is to leproma, the test can be misleading in cases in which its help is most wanted. Its small value does not seem to justify the technical complication of undertaking fat stains for routine purposes.

Bacterial index. There is a broad correlation between the value of the bacterial index of smears (the density of bacilli in the granuloma) and the subsequent rate of fall in the biopsy index. The mean progress rates for the various indices were 2+, 97%; 3+, 74%; 4+, 81%; 5+, 41%; 6+, 30%.

Discrepancies between clinical and histological findings. There was agreement on the exact classification of 56 out of the 82 cases. Minor disagreements usually concerned the decision whether a patient was to be classified BL or LL; in such cases the follow-up results usually supported the opinion in favour of LL unless the opposite opinion, whether clinical or histological, was unusually emphatic. There was serious disagreement as to whether the patient was BB or LL in 5 cases. Subsequent progress provided definite support for the clinical findings in 3 of them and for the histology in the other 2.

Occasionally the clinician diagnoses a borderline condition when the histology appears to be lepromatous, and often in such cases the clinical judgement is proved correct by the follow-up test of progress, but not invariably. ALONSO AND AZULAY (1959) make the same comment. Sometimes the histological picture of these cases is masked by considerable oedema. As already stated, epithelioid cells when present are conclusive evidence of a considerable degree of resistance irrespective of the clinical findings.

In the final analysis a reasonably satisfactory classification was

TABLE 3

Final classification of 82 cases according to clinical and histological assessments, and their progress rates.

Assessment: Clinical	Histological	*Final* Classification	*% Fall in Biopsy Index per 6 months treatment — Number of Cases* 0–9%	10–19%	20–29%	30–39%	40–49%	50–59%	60–69%	70–79%	80–89%	90–100%	*Total No. of Cases*	*Mean % Progress Rate per 6 months*
LL	LL	LL	2	9	15	17	9	2	0	0	0	0	41	28
LL	BL												5	30
BL	LL												8	33
													54	30%
BL	BL	BL	0	0	2	2	0	4	2	3	2	2	10	60
BB	BL												7	66
													17	64%
LL	BB	BB	0	0	0	0	0	0	0	0	1	5	1	93
BL	BB												0	—
BB	BB												5	96
													6	95%
BB	LL	?	0	1	0	0	0	0	0	2	0	1	4	—

1 case classified BT is omitted from the Table. Progress rate 100%.

obtained for 78 out of the 82 cases, as shown in Table 3, which also records their progress rates.

Reactions. Cases with severe reactions have been excluded from this analysis at the time of the reaction and subsequently; figures therefore cannot be quoted. But our experience is that, although the borderline state is well recognized to be unstable when untreated, with treatment the great majority of cases respond predictably without alteration of classification, although on occasion alterations occur as a result of reactions. Cases undergoing a borderline reaction tend to show discrepancies between their clinical, histological and bacteriological patterns fairly frequently.

BL cases appear to be suitable for therapeutic trials, although their rate of progress is less predictable than that of BB or LL cases. Occasionally they react, and move to BB, even though their previous progress may have been slow. They differ from LL cases in that erythema nodosum leprosum never occurs in them.

Racial differences. The available results suggest that there are no differences in rate of bacteriological improvement for any particular category (BB, BL or LL) among Europeans, Eurasians, Negroes, Indians, Malayans and Chinese. The only differences detected concern the distribution of cases between the classification groups, to which reference has already been made.

Discussion

The application of a classification such as the one described will be strictly limited. There is however nothing incompatible between a strictly defined scheme of classification and a looser and simpler classification which would be of more general use—all that is required is that there should be available a loose and flexible terminology such as the one in current use besides another more strictly defined set of terms such as the TT–LL grouping (Table 1). The definition of criteria would be the same for both sets of terms. But whereas classification in the field would be mainly clinical and would employ the general terminology, a classification based on clinical, histological and other evidence would employ the precise terminology.

There is however little hope that agreement would be reached on the definition of groups unless there was prior agreement on the object of classification. If, because clinical examination is the most feasible means, the object is to be clinical description, then there will need to be as many groups as there are clinical varieties of patient; but their significance will be in doubt. If the object is to assess the patient's resistance and prognosis by reference to all observable characteristics then the matter can be put to the test.

Summary

The paper attempts to define a 5 group classification of leprosy in which the groups represent 5 grades of resistance by patient to infection.

The definition was made by assessing the significance of clinical, histological and other characteristics by reference to the bacteriological response to treatment.

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SOME BIOCHEMICAL ASPECTS OF THE LEPROMIN REACTION PATTERN EVOKED BY NORMAL LIVER PREPARATIONS

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Introduction

Many attempts have been made to develop a diagnostic skin reaction for leprosy, analogous to the tuberculin reaction for tuberculosis. Although not suitable for diagnostic purposes, the reaction described by MITSUDA (1919, 1953) is now universally used for the classification of leprosy. MITSUDA used antigens prepared from leproma's, now called "Lepromin". He observed the reactions during the first few days and subsequent weeks and thus found the marked difference of results in lepromatous and in tuberculoid cases of leprosy. Since the reaction is often found to be positive in healthy people, no absolute value for the diagnosis of leprosy could be ascribed to the test.

The above-mentioned late reaction is called the "Mitsuda reaction" and has found world-wide application. Its maximal intensity is usually reached between the third and fourth week after injection. Apart from the late reaction an earlier reaction can be observed between 48 and 72 hours. At first this reaction was regarded as non-specific, but FERNANDEZ (1940) stated that this early reaction ("Fernandez reaction") coincides in its results with the late reaction in the majority of cases.

As lepromin is composed of dead leprosy bacilli and human tissue from the host it is of the utmost importance to know which role is played by the bacilli and (or) the tissue elements in the lepromin reaction. A few workers have attempted to isolate the antigenic fraction of fractions from lepromin. RABELLO, THIERS AND VILLELA (1938) reported the isolation from lepromatous tissue of an active non-lipid substance, probably of protein nature. DHARMENDRA (1948) expressed his doubts as to whether the above antigenic

Present Addresses

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fraction contains protein of the bacilli. PARAS (1943) isolated the major lipid components of lepromatous nodules and HENDERSON (1940) isolated proteins from lepromatous spleen. Tests were carried out with these preparations and only weak Fernandez reactions were seen.

DHARMENDRA (1948) reported a detailed study on this subject. He isolated various chemical fractions and tested the protein, polysaccharide, glyceride, phosphatide and wax substances. He concluded:

(1) That in the lepromatous nodule, only the bacillary matter is antigenic.

(2) The bacilli produce both the Fernandez and Mitsuda reactions.

(3) The lipids from the nodule showed slight activity, but this is believed to be caused by traces of bacillary matter.

(4) The nodular tissue freed from bacilli is not antigenically active.

(5) Of all the fractions isolated from the bacilli, only the protein fraction is positive, producing only the Fernandez reaction.

Other workers have postulated the existence of two different substances, one for the Fernandez and the other for the Mitsuda reaction. From the above it is clear that the findings of the various investigators are very contradictory.

KOOIJ AND GERRITSEN (1956, 1958) showed that positive lepromin-like reactions could be evoked with a suspension prepared from normal tissue not containing leprosy bacilli.

In Table A some of their results are shown.

Kooij and Gerritsen who chiefly concerned themselves with the Mitsuda reaction, assume that the presence of particles is essential for this reaction. For further particulars see KOOIJ *et al* (1956, 1958, 1959). This lepromin-like activity of normal tissue suspensions was recently confirmed by DAVEY AND DREWETT (1958).

One must distinguish between two types of epithelioid cell reactions. The first which gives epithelioid cell reactions in both the lepromatous type and tuberculoid type of leprosy as was shown by Kooij and Pepler (in press) for BCG. The second produces only an epithelioid cell reaction in tuberculoid leprosy and no reaction or only very weak in lepromatous leprosy. The latter we call the lepromin reaction pattern, which can be evoked by lepromin, and by certain suspensions of normal tissue and by Kveim antigen.

Purpose of the Investigation

The aim of the present investigation was (*a*) to find the active constituent in normal human liver which produced the lepromin

TABLE A

Average readings in mm. with various preparations from normal human liver.

TUBERCULOID LEPROSY

Prep.	48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
N (19)*	1.9	1.7	1.9	0.9	0.6
O (15)	4.3	3.0	1.9	1.7	1.6
V (20)	3.6	7.1	7.1	5.0	3.7
W (15)	8.0	7.0	6.9	8.5	8.9

LEPROMATOUS LEPROSY

N (10)	3.8	2.5	1.7	1.4	0.4
O (16)	5.0	2.9	1.7	1.2	0.6
V (15)	2.6	2.1	0.7	0.3	0.1
W (16)	3.9	3.5	2.1	2.2	1.2

N = Mitsuda-Wade preparation from normal liver.
O = Preparation N: 12 x concentrated.
V = Dharmendra preparation from normal liver.
W = Preparation V: 25 x concentrated.
* The numbers between ( ) show the number of patients, tested with that particular preparation.

pattern of reaction, (*b*) to investigate the hypothesis of Kooij and Gerritsen that the presence of particles and their size might be of importance and that in the Mitsuda reaction we are dealing with a kind of foreign body reaction.

The investigations described in this paper were conducted with a suspension prepared from normal human liver in the same manner as lepromin from lepromatous tissue. As Kooij and Gerritsen obtained the strongest reactions with suspensions of normal liver prepared by the Dharmendra method, we also used this method.

Experimental Procedure

Preparation of normal tissue suspensions: (Dharmendra method).

Normal human liver was autoclaved in a 0.9% sodium chloride solution at 120°C. and 15 lbs. per sq. inch for 20 minutes.

One hundred grams of the autoclaved liver were thoroughly blended and extracted with 200 ml. of chloroform in a Waring blender and filtered through a thick layer of cheese cloth. The residue was subjected to three successive extractions with 200 ml. of chloroform and the extracts combined. The chloroform was removed by distillation under reduced pressure and the syrupy residue was extracted with ether to remove the ether soluble lipids. After each extraction the particles were separated by centrifugation for 10

minutes at 3,000 r.p.m. and finally dried at 40°C. for a few minutes. It should be noted that after the final washing the ether layer must be colourless and transparent, indicating that all ether soluble lipids have been removed. The average yield of the lepromin thus prepared, was 1.5 gm. from 100 gms. of liver. The particles were suspended in 0.9% sodium chloride 0.5% phenol solution and 0.1 cc. was intradermally injected in Bantu patients with tuberculoid and lepromatous leprosy.

Experiment 1: To prepare a suspension which is able to produce satisfactory reactions, various concentrations of the tissue suspensions were made in 10 ml. 0.9% sodium chloride 0.5% phenol solution.

The results of the average readings are shown in Table 1 and Fig. 1.

TABLE 1

Average readings in mm. of various concentrations Dharmendra normal tissue suspension.

TUBERCULOID LEPROSY

Prep.	48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
A (15)*	2.4	—	—	—	.8
B (15)	3.3	3.1	2.5	2.8	2.8
C (18)	4.4	3.5	—	3.5	3.5
D (15)	5.2	4.3	3.9	3.9	3.9
E (11)	5.5	5.2	5.2	5.2	5.2

LEPROMATOUS LEPROSY

Prep.	48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
A (15)	.6	—	—	—	0
B (15)	1.9	1.3	1.0	0.6	0.5
C (10)	3.9	3.0	—	2.0	1.4
D (15)	3.5	2.5	2.1	2.0	2.0
E (15)	5.2	4.4	3.3	3.2	3.2

A = 100 mg./10 ml.
B = 200 mg./10 ml.
C = 400 mg./10 ml.
D = 600 mg./10 ml.
E = 800 mg./10 ml.
* See note Table A.

We confine ourselves in this article to the Mitsuda reaction read after 28 days. The results of this experiment show that the reactions produced by preparation A and B were too weak and could thus not be used. Preparations C and D successfully produced positive Mitsuda reactions in tuberculoid leprosy. Preparation D produced too strong a reaction in lepromatous cases and was thus omitted as a suitable suspension. We could not succeed in producing such

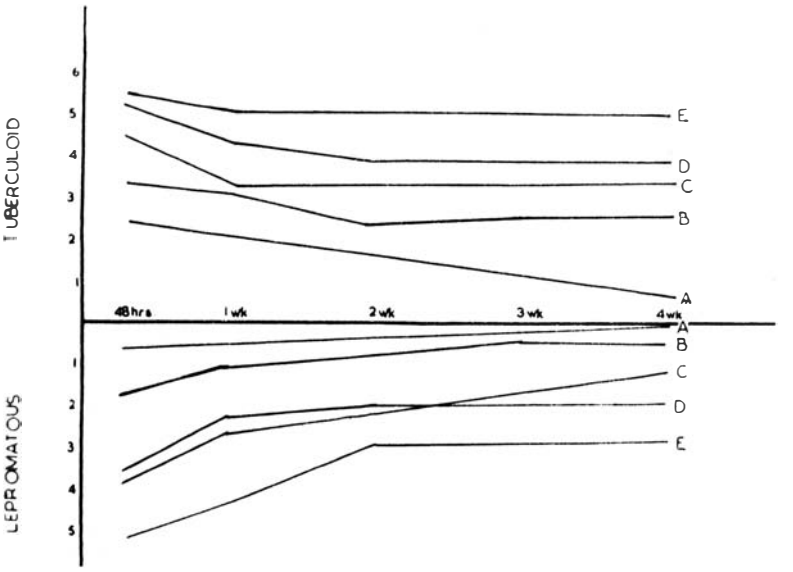

Fig. 1. Average readings in mm. of various concentrations Dharmendra tissue suspension. For explanations see Table 1, Experiment 1.

strong reactions, as was reported by KOOIJ AND GERRITSEN (1958) who used 80 mg./10 ml. suspension (Prep. W in the "introduction"). See "Discussion". Preparation C was used by us as the most suitable suspension. Preparation E also evoked too strong reactions in the lepromatous leprosy and these reactions also tended to ulcerate.

Experiment 2: To investigate the influence of the particles and particle size, the following attempts were made to annihilate them.

(*a*) Four-hundred milligrams Dharmendra tissue suspension in 10 ml. of phenol saline solution were irradiated with ultrasonic waves for 20 minutes and then injected as before.

(*b*) Two-hundred milligrams were hydrolysed for 12 hours with 6 N H_2SO_4 to break up the proteins, polysaccharides etc. in their fundamental compounds and thus removing them. The residue was washed until free from acid, suspended in 5 ml. and injected.

(*c*) A suspension of 200 mg. silica (particle size about 5 μ compared to the 3–4 μ of the tissue particle size) in 5 ml. saline phenol solution, diluted to facilitate administration, was injected. It should be noted that this was not a colloidal silica preparation as was used by SHELLEY AND HURLEY (1960).

(*d*) The particles were digested by means of the proteolytic enzyme, trypsin. In order to obtain the optimum pH of 8 for Trypsin action, 200 mg. of normal tissue suspension were

mixed with 2 ml. 1% trypsin and 2 ml. of 0.5% sodium carbonate. One control preparation was also made and the two reaction mixtures incubated for 3 hours at 37°C. Subsequently, after inactivating the enzyme by heating in a boiling waterbath for 30 minutes, the pH was adjusted to 7.4.

The results of the average readings are shown in Table 2 and Fig. 2.

TABLE 2

Average readings in mm. of the various preparations tested in Experiment 2.

TUBERCULOID LEPROSY

Prep.	48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
A (18)*	3.4	3.0	—	2.8	2.7
B (12)	4.1	4.0	—	4.2	3.0
C (15)	1.1	0.9	0.5	0.1	0
D (15)	1.1	1.1	0.9	0.1	0.1
E (15)	1.1	1	0.6	0.1	0.1

LEPROMATOUS LEPROSY

Prep.	48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
A (10)	3.1	1.9	—	1.5	1.5
B (6)	1.7	1.7	—	1.7	1.7
C (14)	0.5	0.3	0.2	0.2	0
D (14)	0	0	0	0	0
E (14)	0	0	0	0	0

A = 400 mg./10 ml. Irradiated by ultrasonic waves.
B = 200 mg./5 ml. Hydrolysed by 6 N H_2SO_4.
C = 200 mg. silica/5 ml.
D = 200 mg. in approx. 5 ml. solution. Digested by trypsin.
E = Trypsin control.
* See note Table A.

Preparation A, which was irradiated by ultrasonic waves, in an attempt to destroy or break them up in smaller fragments, evoked a slightly weaker reaction than the equivalent, which was not irradiated (See Experiment 1, Prep. C). It was, however, impossible to destroy the particles completely by ultrasonic waves. The residue which contained particles of unknown composition after the hydrolysis with 6 N H_2SO_4 (Preparation B) showed positive lepromin-like reactions and it could be concluded that the active principle was not destroyed. As a further method, the particles were treated with the enzyme, trypsin. The results show that the latter preparation, where the proteins of the particles were broken down to their fundamental amino acids and peptides, reacted negative in both the lepromatous and tuberculoid leprosy. It could be assumed that this preparation

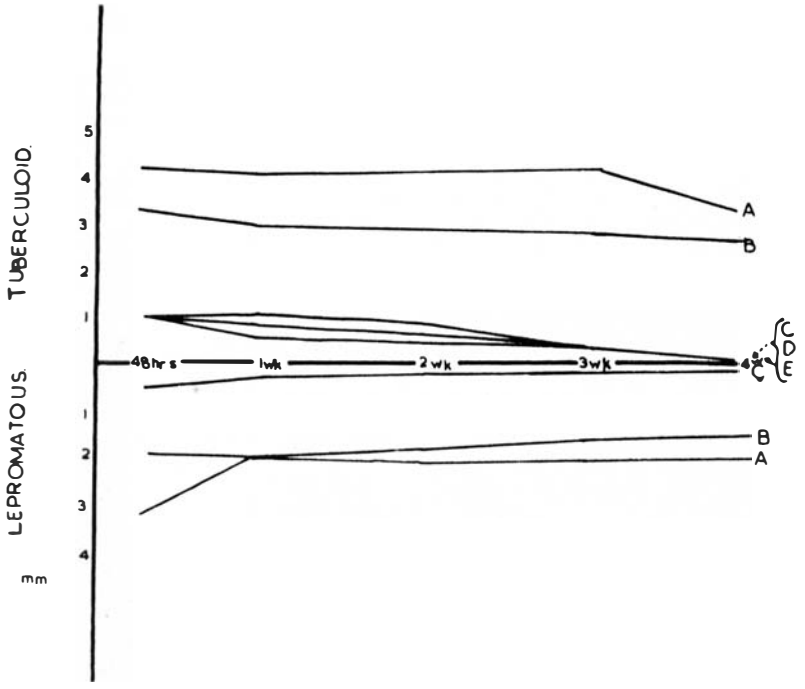

Fig. 2. Average readings in mm. of the various preparations tested in experiment 2. For explanation see Table 2.

did not contain any perceptible macroparticles. It seems also that the proteins are not responsible for this reaction, although it might have some influence. Preparation C showed only negative results.

The results of this experiment indicate that the presence of tissue particles might be of importance for the lepromin reaction pattern evoked by normal tissue preparations, but also that not every particle does it. (Preparation C).

Experiment 3: In order to investigate the action of the ether insoluble lipids, a chloroform extract of the Dharmendra normal tissue preparations was tested. Four-hundred milligrams were extracted in a micro-soxhlett apparatus with 50 ml. of chloroform for 8 hours.

After evaporation of the chloroform under reduced pressure the 25 mg. fatty extract was emulsified in 2 ml. of phenol saline solution. The residue after chloroform extraction was also suspended in 10 ml. of phenol saline solution, and tested.

Chromatographic examination of the lipid fraction was carried out according to ASSELINEAU (1952) and BEVAN *et al* (1951). As solvent, a chloroform:ethanol:water (80:20:2.5, by vol.) system was used. Ten microliters of a 1% solution of the fatty extract was applied on Whatman No. 1 paper and the chromatogram developed for

6 hours. To locate the position of the lipid, the paper was dried at 100°C. in an oven and then treated with a 1% solution of Phosphomolybdic acid in a mixture of equal parts of chloroform and ethanol, and dried again at 100°C. A yellow spot, R_f value 0.9, was found which corresponds with the sphingomyelin group of the phospholipids. Ninhydrin treatment showed in one chromatogram a very faint purple spot, due to cephalin, but this could not be confirmed by further chromatography.

The average readings in 5 patients with tuberculoid leprosy and 4 patients with lepromatous leprosy injected with the above preparation, as well as the lipid-free preparation, were as follows. See Table 3 and Fig. 3. No histological investigation of the reaction papules was carried out.

TABLE 3

Average readings in mm. of the lipid, lipid-free and control preparations.

Prep.	48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
TUBERCULOID LEPROSY					
A (5)*	6.5	5.2	5.4	5.4	5.0
B (15)	3.5	2.5	2.3	2.1	1.8
C (18)	4.4	3.5	—	3.5	3.5
LEPROMATOUS LEPROSY					
A (4)	6.0	3.0	3.0	1.0	1.0
B (15)	3.3	1.7	1.4	0.9	0.6
C (10)	3.9	3.0	—	2.0	1.4

A = Lipid fraction.
B = Lipid-free fraction.
C = Prep. C: Experiment 1.
* See note Table A.

There seems to be a tendency for this lipid fraction to follow the lepromin pattern of reaction. However, the number of patients tested was small and further investigation was necessary. The absolute lipid-free fraction (B) showed positive results although weaker than the control preparation (Preparation C).

The lipid extract of the same concentration as in the earlier experiment was then injected in 15 patients with tuberculoid leprosy, and in 14 patients with lepromatous leprosy. In half of the tuberculoid cases and half of the lepromatous cases the reaction papule was excised 3 weeks after injection and the reaction papules of the remaining patients were excised after 4 weeks and examined histologically.

The average readings are shown in Table 4.

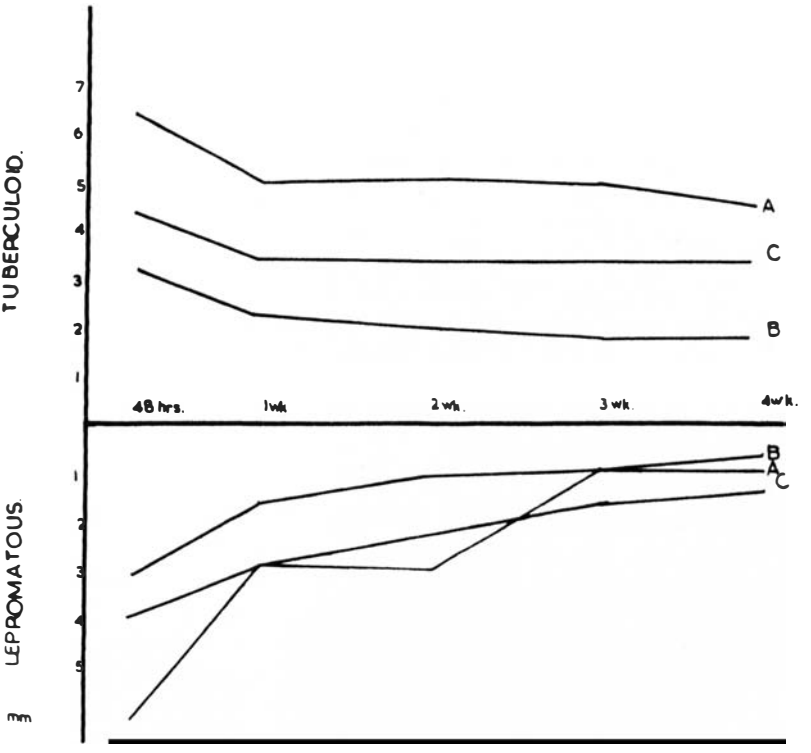

Fig. 3. Average readings in mm. of the lipid, lipid-free and control preparations. For explanation see Table 3.

From these experiments it was evident that the lipid extract produced reactions in both tuberculoid and lepromatous cases, although weaker in the latter type. The absolute lipid-free preparations (Table 3, Prep. B) evoked weaker reactions than the control preparation (Table 3, Prep. C), probably because some active principle was removed.

Although the average readings of the reaction papules in the lepromatous cases after 3 and 4 weeks are somewhat lower than those of tuberculoid cases, the general pattern cannot be called the lepromin pattern of reaction. The readings are therefore too high

TABLE 4

Average readings in mm. of the lipid fraction.

		TUBERCULOID		
48 *hrs.*	1 *week*	2 *weeks*	3 *weeks*	4 *weeks*
6.1	5.9	5.6	5.3	4.9
		LEPROMATOUS		
6.0	4.2	4.3	3.7	3.1

in the lepromatous cases. Histologically the lipid fraction evoked an epithelioid cell reaction in several cases. This was only slight and did *not* occur in the lepromatous cases. However, compared to an active normal tissue suspension the epithelioid cell reaction was very weak and did not occur in sufficient cases of tuberculoid leprosy.

Discussion

Although we could confirm the results of KOOIJ AND GERRITSEN, the reactions obtained with our preparations from normal liver were considerably weaker in evoking the lepromin reaction pattern. Probably the composition of the livers used for the preparation of the tissue suspensions was not the same due to age, unknown diseases, etc. In preparing these tissue suspensions, attention should be given to these conditions.

Irradiation by ultrasonic waves and also breaking down of the proteins and other hydrolysable compounds by 6 N H_2SO_4 did not decrease the activity of the normal tissue preparation much. Both preparations still contained particles. Complete destruction of the particles by the enzyme, trypsin, lead to a preparation which was inactive. The influence of the lipid fraction was probably eliminated by the higher degree of dilution. KOOIJ AND GERRITSEN (1958) also found that bacterial filtrates of normal liver suspensions were inactive. This indicates that the particles and probably their size are of great importance if not essential for eliciting the lepromin pattern of reaction by a normal tissue suspension. That a special particulate state can be of importance for producing an epithelioid cell reaction was recently shown by SHELLEY AND HURLEY (1960) who demonstrated that epithelioid silica granulomas could be evoked regularly in any individual by intradermal injection of colloidal silica and that the phenomenon is dependent on the colloidal nature of the silica. It is not known yet how colloidal silica reacts in lepromatous leprosy. This problem is under investigation.

In addition, a certain chemical composition of the particles seems essential because not every particle evokes the reaction. The reactions produced by the isolated lipid fraction (Exp. 3, Prep. A) were stronger than those of the control (Exp. 3, Prep. C), however, the readings in lepromatous leprosy were rather high. This does not resemble the lepromin reaction pattern. Histologically, the lipid fraction produced a very weak epithelioid cell reaction in several tuberculoid cases but none in lepromatous cases. On the contrary the lipid free preparation containing particles (Exp. 3, Prep. B) showed weaker reactions than the control, but more the typical lepromin reaction pattern. Unfortunately no histological examination of the reaction papules were carried out. It should be stressed that in future research in this field histological examination is necessary.

Although the lipid fraction did not elicit the typical lepromin type of reaction it is still of interest that a substance can be isolated from normal liver tissue which produces epithelioid cell reactions. It is possible that this or a similar substance was responsible for the histological sarcoid reaction which SONES *et al* (1955) obtained with filtrates of a Kveim antigen prepared from sarcoid lymph nodes. If this explanation is correct it does not support the view that the Kviem reaction in sarcoidosis is a response to the introduction of a specific antigen.

As the normal tissue suspension contains both particles and the isolated lipid fraction it is possible that they co-operate in evoking the lepromin pattern of reactions.

Summary

1. We could confirm the results found by Kooij and Gerritsen, but were unable to produce such strong reactions reported by them. This deflection might probably be due to a difference in age, unknown diseases, etc. of the individual.

2. Annihilation of the particles by ultrasonic waves was unsuccessful. Preparations of normal liver tissue irradiated with ultrasonic waves, as well as an absolute lipid free suspension and the residue after 6 N H_2SO_4 hydrolysis still showed the lepromin pattern of reaction. By means of trypsin an inactive preparation was obtained which failed to produce the lepromin pattern of reaction. Therefore it is assumed that the particulate state is of importance, if not essential.

3. A lipid substance, sphingomyelin, was isolated from normal liver preparations which was able to produce epithelioid cell reactions but not the typical lepromin pattern of reaction. This finding is not in favour of the view that the Kveim antigen contains an antigen specific for sarcoidosis.

4. It is possible that the particles and the isolated lipid fraction co-operate in producing the lepromin pattern of reaction evoked by normal liver suspensions.

Acknowledgement

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A REVIEW OF LEPROSY WORK IN ETHIOPIA, UGANDA, N. RHODESIA AND TANGANYIKA

Report of a Brief Tour made by
DR. N. D. FRASER
Medical Secretary of The Mission to Lepers in May-June 1961

Review of Leprosy Situation in Ethiopia

A valuable survey undertaken by Dr. K. F. Schaller, Chief of Leprosy Control Service of Ethiopia and Medical Director of the Princess Zenebework Memorial Hospital indicates that there may be as many as 200,000, or even more people suffering from leprosy in Ethiopia. The survey shows the distribution in the various provinces, and the incidence, which varies from 5 to 140 per 1,000 of the population.

Provision for treatment is available at certain hospitals, segregation villages and out-patient clinics, and 30,000 patients are listed as having received some treatment.

In the Shoa Province. The Princess Zenebework Memorial Hospital provides 1,250 beds. At Akaki, a segregation village looks after 270 patients, and at 4 Government O.P. Clinics the patients registered number 8,570.

In the Arussi Province. The Sudan Interior Mission's Shashemane Leprosarium is listed as providing 240 beds, and the S.I.M. Shashemane Segregation village as providing 413 beds, while out-patients registered number 8,500.

In the Wollo Province. The Selassie S.I.M. Leprosarium near Dessie is listed as having 600 patients in a segregation village with 1,500 out-patients on the register.

In the Haran Province a Roman Catholic Hospital provides accommodation for 208 patients, with 300 in a segregation village and 2,000 registered as out-patients.

In the Kaffa Province the Government Princess Tsahai Hospital at Jimma provides 30 beds for leprosy patients, while 100 are housed in a Government Segregation Village and 100 are listed as out-patients.

In the Gojjam Province 7 Government Clinics are listed with 5,600 patients registered.

In the Begemeder Province the Ethiopian Church is caring for 70 patients in a segregation village at Mandeba, while a Government clinic lists 217 registered at Gondar.

These figures were reported to a National Leprosy Conference in 1959. Though not completely up-to-date they are significant and give an indication of the size of the problem and of the interest it has aroused.

From Dr. Larsen I learned of a project now being carried out. The Swedish Government is financing the building of a poly-clinic in the Gojjam Province. The cost is in the neighbourhood of U.S. $140,000. It is to include 4 Leprosy Clinics and a 40 bed Leprosy Hospital. It is eventually to be staffed by Ethiopians who have been trained at Addis Ababa.

The Ethiopian Government has put a proposition before 4 Missions—the Sudan Interior Mission, the Moravian Mission, the American Baptist Convention and the Roman Catholic Mission. It involves the establishment by each Mission of a Leprosarium for 500 patients to which Government would have the right to transfer 250 patients from the Central Leprosarium at Addis Ababa. The aim is to reduce the number of patients who have been found begging in the streets of Addis Ababa, and if possible to close down the Central Leprosarium. Government is prepared to pay U.S. $10,000 to the Mission as soon as the contract is signed. Each Mission is asked to put U.S. $30,000 into the project for buildings over a 5-year period. Land is offered in each of the areas concerned. Government will accept responsibility for a maintenance grant on a per capita basis of U.S. 20 cents a day, up to 500 patients. The Mission will have full freedom for religious work, and will have the right to dismiss any patient who fails to co-operate. Government maintain the right to see that no patient remains who should be discharged.

Rev. D. S. Sensenig of the Moravian Mission gave me these details and showed me on the map the site of their Mission work and of the proposed new leprosarium. It is in Harar Province at Deder near Dire Dawa. At present they have an O.P. Clinic there attended by some 70–80 patients.

Dr. Schenck of the Baptist General Conference informed me that his mission is signing an agreement to go forward with the establishment of a new leprosarium for 500 patients in the Arribo district of the Shoa Province some 50 miles west, and 60 miles north of Addis Ababa. Dr. Schenck is planning to undertake orthopaedic surgery, while Dr. Rupert develops the General Medical programme.

The Swedish Ambassador reported that Swedish friends, having seen the leprosy situation in Ethiopia returned to their country and began an appeal which raised over £1,000,000 (one million pounds, sterling) within 12 months. This has, I gather, been turned over to the "Save the Children Fund" for use in leprosy work.

Impressions of the S.I.M. Selassie Leprosarium near Dessie, 240 miles north of Addis Ababa. The site is an excellent one with a good water supply and plenty of land for gardens and agricultural

development. The Rev. F. E. Estelle is in charge of the agricultural work and is doing a splendid job.

There were more than 200 patients in the leprosarium. 100 had just recently been transferred by Government from Addis Ababa of whom 25 had refused to stay—but more patients were to be admitted from the O.P. Clinic. It is planned to increase the accommodation by repairing huts in the "Segregation Village" adjacent to the leprosarium, and bringing them under the full control of the leprosarium.

In addition to the O.P. Clinic held at the leprosarium there are two other clinics, one 50 miles to the North and the other 50 miles to the South at which patients are seen once a month. Because many patients have to travel several days journey to attend these clinics tablets are given to cover a period of three months—and when the heavy rainy season is approaching even five months! The regularity with which patients return is evidence that very considerable good work is being done by this bold treatment. Over 6,000 have been entered in the out-patient register.

There is no doctor at the Selassie Leprosarium, the treatment of the patients being under the control of Mrs. M. M. Fishwick, R.N., R.M. with the assistance of "dressers"—patients who have been trained in the work. The level of education of all the patients is, however, very low and the best are not very reliable. In spite of the size of the work and the difficulties of finding suitable assistants from among the patients, excellent work was being done.

The Rev. P. E. Entz, the Superintendent, arranges for all patients to spend half the day at school and half the day working in the gardens or on the farm. No patient is allowed to be idle. One or two patients were weaving cloth.

Hospital Buildings and Equipment. These were of the simplest, but were being put to good use.

Mission to Lepers Grant. The grant from the Government covers the cost of the patients' food, clothing and pocket money. The Mission to Lepers grant covers the upkeep of the huts, the replacement of huts too old to repair, and the cost of medical supplies.

Invaluable work is being done by the staff of the leprosarium but the appointment of a doctor is urgent. One with experience of eyes would be most valuable, as there is a general clinic held in a separate building at the entrance to the leprosarium to which many patients with eye conditions come. The S.I.M. are well aware of the need for a doctor—in fact are on the look-out for at least three doctors.

Impressions of the Shashemane Leprosarium, 150 miles South of Addis Ababa. The excellent agricultural work being done in this leprosarium needs no detailed comment. Mr. B. H. Bond is making very good use of the land available.

The Leprosy Hospital, planned to provide accommodation for 25 patients, had 54 patients in it at the time of my visit. The so-called "hospital area" is a long row of 50 huts which provide accommodation for single women, for married couples and for men, to a total of 200 patients. Government grant covers cost of food for these patients. The segregation village provides further huts for the accommodation of 300 patients. Others have occupied land outside the leprosarium on the banks of the stream which brings water through the leprosarium to the Staff Compound. Treatment is provided for approximately 1,200 patients in addition to those who attend as out-patients and who now number some 7,500 on the register.

Dr. Margaret Fitzherbert and her colleagues are doing a wonderful piece of work. In addition to the leprosy work there is a General Clinic, attended by approximately 100 patients a day, to which is attached a ward unit of 12 beds. Mr. R. D. Nagel, R.N., carried a very large part of this responsibility, but it inevitably adds to Dr. Fitzherbert's burden.

The work the nurses are doing in the hospital is beyond praise, but the conditions in which they are working are so bad that steps should be taken as a matter of urgency to improve them. The hospital should be enlarged to provide 50 beds. My suggestion would be (1) to increase the ward accommodation from 25 to 50 beds. (2) Build a new operating theatre. (3) Provide a "clean-room" for the use of healthy staff only.

Government's proposal to support a further 500 patients at Shashemane is giving the S.I.M. some concern, and they are giving the whole matter very careful consideration. It is, I think, already realised that the leprosarium is not only attracting too many patients, but that patients are camping round about. No centrifugal action has been developed, and discussions were held as to what further expenditure might be incurred in the training of patient-staff to undertake mobile clinic work and later to staff outlying dispensaries; support for such developments, if needed, might well be sought from The Mission to Lepers.

Leprosy in Uganda

In 1955 Dr. J. A. Kinnear Brown, Government Leprosy Specialist, estimated that there were some 80,000 persons suffering from leprosy spread over a population of more than 5,000,000 and an area of 93,000 sq. miles. In 5 voluntary settlements it was possible to accommodate rather less than 2,500 patients.

Since then treatment has been made available to more than 60,000 patients, and it has been clearly demonstrated that a co-ordinated leprosy programme can be developed in which Govern-

ment Medical Services, Medical Missions and Local Authorities each carry a share of responsibility.

This outstanding achievement is the result of careful preparation and planning, including conference with County Councils and district teams, with a persistent and consistent follow-up programme. Over a period of $2\frac{1}{2}$ years more than 60 surveys were undertaken with the co-operation of the administrative and medical staff of the country and with the goodwill of the people.

Two points were consistently emphasised—the need for continuity of treatment over long periods of time, and the need for the segregation of those suffering from the contagious form of the disease. It was suggested that the community should, in each area, provide small treatment villages within reach of rural medical units. The work was undertaken as a form of communal labour. In one area the local population cleared a site, made a road 2 miles long and provided accommodation for patients all within a matter of a few weeks; and within 3 weeks of its opening 400 patients were admitted and treatment begun. In another area 6,000 workers turned out and within 3 days cleared a site and completed the building of a village and treatment centre.

In the first year 3 such leprosy treatment villages were built; in the next 8 and the next 11. Year by year the number increased until today there are some 80 leprosy villages throughout Uganda, which, with facilities available in clinics and rural medical units for non-contagious patients, provide treatment for some 30,000 patients.

The part the Mission Leprosaria play in this comprehensive programme is to provide special facilities for the investigation and treatment of those patients who do not respond to routine treatment; to train medical assistants, leprosy dressers, welfare workers and others to assist in the treatment of patients in the leprosy villages and in rural clinics; to undertake research in occupational therapy and in the training of patients to acquire skills within the limitations imposed by their disabilities; and when skilled surgery and physiotherapy is available to undertake the plastic and orthopaedic operations for the correction of deformities, contractures and paralyses.

In addition to this medical and surgical care for the body there are wonderful opportunities for the education of the patients, and for presenting to them the Good News of One who died for them and promised a Life more Abundant and indeed Life Everlasting to those who believe.

Leprosaria in Uganda

(1) Kumi and Ongino
(2) Kuluva
(3) Lake Bunyonyi
(4) Bulubu
(5) Nyenga

Impressions of the work at Ongino and Kumi, and in the leprosy villages. One's first impression was of well-cared-for grounds both at the Kumi School, and at the Ongino Leprosarium. Bush had been cleared, playing fields and gardens laid out, and wide tracts of lands brought under cultivation. Flowering shrubs and bushes brought colour into the scenery; and a flourishing honey-producing industry was attracting a lot of interest.

The school with 300 pupils was winning prizes for competitions open to all schools in the district; I saw the physical drill, and a football match, and found the spirit of the work excellent.

In the leprosarium with 400 patients under treatment everything seemed very well organised. Miss Neville's research into suitable handwork for crippled patients was meeting with real success and had already attracted a great deal of interest.

The most immediate need was for new dormitories for the school and better housing for the African Staff.

A visit to one of the leprosy villages interested me very much indeed. Built by communal effort, and controlled by the Chief of the district, the segregated patients were well cared for, and supervision was sufficient to encourage them to maintain their huts in good shape and the grounds in good condition. District officers, agricultural officers and health officers all helped in the supervision and development of the villages, and treatment was given by a medical assistant, or leprosy dresser under the supervision of one of the members of the staff of the leprosarium. This made it possible to provide segregation and treatment for those patients suffering from the contagious form of the disease at very little cost and without removing them hundreds of miles from their families and normal environment. In fact relatives (but not children) were encouraged to visit members of their family in the villages and to bring them food, etc., in so doing maintaining contact with them throughout the period of their treatment.

Dr. Kinnear Brown's B.C.G. Research Programme. Under the direction of the Medical Research Council Dr. Kinnear Brown with the assistance of Miss Stone, S.R.N. of the Kumi and Ongino Leprosarium has begun a research project to test the effect of BCG vaccination on children, and to show whether or not such vaccination in any way protects children from infection with the leprosy bacillus.

Dr. Brown is contacting the children of patients attending the leprosy out-patient clinics and those of patients in the leprosy villages, is testing every child with tuberculin, and is inoculating alternate tuberculin negative reactors with BCG Vaccine. Dr. Brown hopes to deal with some 12,000 children in this way. and in due course to show whether there is a greater incidence of leprosy amongst those not protected by BCG Vaccine than amongst those so protected.

Leprosy in Northern Rhodesia

A detailed list of Leprosaria in Northern Rhodesia is to be found in the *International Leprosy Journal*, Vol. 29, No. 3.

Although a number of surveys have been undertaken in Northern Rhodesia (R. G. COCHRANE in 1932, E. MUIR, 1940, ROSS INNES, 1950, J. WORSFOLD, 1957), the full extent of the problem has never been clearly revealed. Figures vary from 10 per 1,000 to 25.6 per 1,000 for different provinces. Dr. Worsfold indicates that his 1957 survey in the Balovale region reveals a decline in the incidence of leprosy there. The Health Department reports some 44,000 cases of leprosy in the Federation, with some 14,000 receiving care or treatment.

The figure of 3,000 estimated for the Copper-belt is apparently based on records showing 300 patients registered and attending out-patient clinics or rural health centres for treatment. At the Fiwale Hill Hospital all those suspected to be suffering from leprosy are referred to Ndola and only those sent back with a diagnosis of non-contagious leprosy are registered and given treatment, the contagious patients being sent to Luapula.

Since January, 1961, 60 patients have been registered; while at the Kafulafuta S.A.B.M.S. Hospital, 40 patients are attending for treatment.

The patients were advised that Dr. Currant, Leprosy Specialist for the Federation, would be visiting the Fiwale Hill Hospital on June 14th, and were asked to attend so that he could review their progress. In addition to 20 patients already on the register, 10 new patients appeared. For 3 of these Dr. Currant, made special arrangements for rail transport to Liteta so that he could admit them for special treatment of reaction conditions.

The main purpose of my visit to Northern Rhodesia was to meet the Rev. Wilfred Edmunds, Missionary Director of the S.A.B.M.S., and to discuss with him a proposal for the establishment, with the support of The Mission to Lepers, of new work at Fiwale Hill. This proposal had been brought to the attention of the S.A.B.M.S. by the Health Department of the Northern Rhodesian Government which meantime has to send leprosy patients in need of segregation either to the Government leprosarium at Liteta, 120 miles to the South, or to Luapula 270 miles to the North.

Our visit to the proposed site showed us a dirt road which was just passable, but which could easily be improved, leading to a good tract of land lying between the junction of two rivers. Thick bush covers the site at present but this could be cleared without difficulty.

We were joined by Dr. E. J. Currant, Leprosy Specialist for the Federation and by Mr. Densham representing the Provincial Medical Officer to discuss the matter in more detail.

Dr. Currant confirmed Government's desire to see established in the Copper-belt area a leprosarium to which patients in need of

segregation could be admitted, so as to avoid the necessity of sending them to Luapula 270 miles to the North. It was, however, realised that while leprosy villages might be developed by the Africans who were living in the bush on sites near their homes, there would be difficulties in developing such villages for those living in the urban and suburban regions of the Copper-belt. Fiwale Hill is, however, close to the railway and a model leprosy village built near the leprosy centre could provide the accommodation needed, and would still be within access of family and friends.

Leprosy in Tanganyika

Having completed my discussions at Fiwale Hill I travelled by air to Mbeya in Southern Tanganyika and was able to visit the Makete Leprosarium on the following day, June 15th, through the kindness of Dr. Eckart who arranged transport for me to Tukuyu. At the Tukuyu Government Hospital I met Dr. Carson and Sister Macnamara and accompanied them on a routine visit to the leprosarium. Dr. Wheate, formerly Medical Superintendent had been transferred to Ghazi; Mr. Powell, a BLRA worker had resigned to take up work for the blind; Sister Pedersen was on leave, and a new African Medical Assistant had just recently taken up his duties. There are 650 patients under treatment, with hospital beds for 36. Twelve out-patient clinics attend to some 3,000 patients. In spite of serious staff shortages the work seemed to be well maintained. Dr. Carson, who was to retire at the end of the month, saw all the patients in the wards and showed me over the leprosarium, including the new Church, which is a very attractive building.

The leprosarium has some 5 sq. miles of land for cultivation. The Minister of Health at Dar-es-Salaam, however, feels it is a mistake for the Medical Department to be responsible for agricultural developments and it looks as if part of this land may be taken over for other use.

The major problem is one of staff shortage, which is affecting nearly all the medical work in Tanganyika.

From Mbeya I flew to Tabora and was most kindly received by Dr. Runciman, Provincial Medical Officer, Tabora. Dr. Runciman took me by road to visit the Sikonge Leprosarium where I met and was entertained by Mr. and Mrs. Jorgensen, by Dr. (Mrs.) Petersen, Sister Martha Pedersen, and by Dr. and Mrs. Andersen. Dr. Andersen had just arrived to assist Dr. Petersen in the heavy responsibilities she was carrying in both the General Hospital and the leprosarium. The work at Sikonge was well organised in every department, medical work, education and occupational activities, but the need for yet more to be undertaken was appreciated.

From Tabora I took the train to Itigi where Dr. S. Moris of

American Lutheran Mission, kindly met me and motored me to the Iambi Leprosarium. This new venture has been established on 5,000 acres of high-lying land, falling away on one side to the site of the new reservoir and on the other to land reclaimed from the bush.

In addition to Dr. and Mrs. Moris, the staff consists of Mr. Renner, Administrative Superintendent who is bringing more and more land under cultivation. Str. V. Hult, Str. Lois Bernhardson who has had training in laboratory work and Miss Ois Heidel, an Occupational Therapist with Physiotherapy training.

Four-hundred and forty patients have been admitted. There are excellent wards for 35 male patients with accommodation for 45 more in "weak" lines (i.e. the hospital annexe). Eight out-patient clinics have been developed by the Mission. Many patients attend Government rural health clinics.

The need for a women's ward is recognised, as well as accommodation for healthy children, and nearby for their mothers while they are nursing them.

The majority of patients live in wattle and mud huts built by themselves and sited near the cultivated land, one and one-third acres of which is allocated to each patient who is fit to work it.

Disabled patients are helped in preparing their ground for growing crops.

The arrangement by which patients farm their own plot is one which allows the patient freedom to do the work in his own way and in his own time. This has advantages, but where a skilled agricultural supervisor is available, and the aim is to encourage patients to stay only as long as may be necessary, even better results should be possible of achievement by employing communal methods; or possibly by a combination of both.

Makutupora. Dr. Moris accompanied me by road to Kilimatinde where I received a warm welcome from Dr. and Mrs. Wellesley Hannah, and to Makutupora where Miss Preston and Mr. and Mrs. Leach entertained us.

It took me some time to grasp the size and extent of the problem here. Miss Preston is grappling, with assistance from Dr. Hannah, and strongly supported by Mr. and Mrs. Leach, with some 1.200 patients.

There were 16 women in the 6 bed women's ward; 10 men in the men's ward with 3 more on the verandah; 12 with ulcerated feet in special cottages nearby. There were 40 in the women's lines, 110 in the men's lines, 30 boys and 30 girls.

These figures include 23 men and women who support themselves at Sukamahela, a mile away, on land which they can farm. There they have built themselves a wattle Church, which was kept clean and tidy and to which come many of the 200 former patients who have established themselves beyond Sukamahela. There are in

addition some 300 former patients who have settled down in the Rift Valley where they are farming the land.

In addition to these 500 former in-patients, who now attend as out-patients, and of whom a number have relapsed and appear to be resistant to further DDS treatment, there are some 300 of their children who come to Miss Preston for general treatment, and so come under her observation. A further 150 healthy partners of patients or former patients also turn to Miss Preston for help. Many of these people are already in need of food supplies, as the rains practically failed and crops have consequently been very poor. On account of a water supply which has proved quite inadequate, it is planned to transfer all in-patients to a new leprosarium at Hombolo near Dodoma.

On June 23rd Mr. J. Denton, Dr. Hannah and I flew over the site of the new Hombolo dam and reservoir, in a Missionary Aviation Fellowship 'plane to view the land allocated for the new leprosarium. The reservoir came into view within a few minutes of climbing to flying height, and the intervening 20 miles soon slipped away below us. We got a good view of the dam, of the reservoir, built to protect a main road from damage during heavy rains, and of the thick bush (said to harbour elephants and rhinoceros) allocated for the leprosarium. Breaks had been cut through the bush marking boundaries of the 200 acres, and these we were able to identify. From the air the land seemed flat and unattractive, but when in the afternoon Bishop Stanway accompanied us on another visit by road we got a different impression. The huge size of the dam was appreciated, and the tremendous amount of work that had gone into its construction, damming the river for 2–3 miles in its course; and the ground seemed much more fertile; while the bush was found in some parts to be quite impenetrable.

Work on the construction of the dam has now been completed, and arrangements have been made for carrying a 3 in. pipe-line from a sump below the dam to a pump house, from which water will be led to the site providing 80,000 gallons a day. All other outstanding difficulties have been overcome, and the work can proceed as soon as this piping is completed.

The first stage will involve clearing of the bush, then work on buildings can begin.

The need for new developments in Western Tanganyika. At Dodoma both Archdeacon Pearson and Bishop Wiggins spoke to me about the need for new work to be developed in the Western regions of Tanganyika.

Bishop Wiggins is responsible for the Lake Provinces, bordering the Southern half of Lake Victoria on the East, South and West sides. There has been delay in considering what should be attempted pending information as to plans for leprosy work to be undertaken

by the Swedish Lutheran Mission, and by a Swedish Save the Children's Fund Grant. These efforts, it now appears, will be concentrated in the tip of Western Tanganyika where it impinges on the Ruandi Urundi and Uganda borders. This leaves wide areas to the South and to the East of the Lake where no leprosy work is being done.

Archdeacon Pearson is responsible for the Uha Province which lies along a part of the Ruanda Urundi border to the North of Kagoma, and along the shores of Lake Tanganyika to the South. Kibondo, 150 miles to the North East of Kagoma would be a possible centre from which to develop new work.

While it is known that there is a leprosy problem in these regions there is not sufficient information to give a clear picture of the extent and nature of the problem. The people are primitive and suspicious. One WHO Yaws survey group had to be evacuated hurriedly for their own safety, as the taking of blood for examination had become associated with the bottle of tomato sauce on the group's dining table, and with the lipstick used by some of the nurses.

The most important step to be taken is to make contact with and gain the confidence of the leaders of the people; then by patient and persistent teaching and demonstrations to show the value of modern treatment of such simple conditions as yaws, malaria and worm infections. When once confidence has been gained then some measure of co-operation can be looked for and the establishments of a chain of health centres begun.

This is a process which will take time and will depend on the appointment of staff, able to talk to the people in their own language, and prepared to travel extensively throughout the district, making themselves known, and accomplishing as much as can be done successfully with limited facilities during brief visits.

A survey alone tends to bring out into the open problems which are best left undisturbed if nothing further is to be done about them; a survey that established treatment centres and is followed up by regular visitation could lead to the development of a widespread public health service which include leprosy within its purview.

I was assured that the co-operation of District Officers and Health Officials would be forthcoming, and felt that developments along the lines of those achieved by Dr. Kinnear Brown in Uganda might be undertaken; the most important step is to find the right personnel for the project, and then to give them sufficient experience to make a good start. A visit to Uganda might be invaluable, followed by a tour of the districts, combining a health survey with health talks, films and demonstrations, and with the treatment of simple conditions; and with a well-planned follow-up programme.

I travelled by train from Dodoma to Morogoro, where I was met by Dr. J. S. Meredith, Medical Specialist for Tanganyika, and

by Mr. G. Cooper, BLRA worker at the Chazi Government Leprosarium. Dr. L. E. B. Delany, Provincial Medical Officer, had kindly arranged for us all to stay with him in his home where we were welcomed by Mrs. Delany.

Dr. Meredith had come from Dar-es-Salaam especially to join us in a visit to the Chazi Leprosarium; as indeed had Mr. Cooper who, with his family had already reached Dar-es-Salaam on the first stage of their journey to England.

On June 27th Dr. Delany took us all in his car by road, first to a Health Centre some miles beyond Chazi, and then back to the Chazi Leprosarium. It was the day for the treatment of leprosy patients at the Health Centre and so we were able to review a number of men and women who were making very satisfactory progress under the care of the African staff.

The Chazi Leprosarium was, at the time of our visit, rather understaffed. Dr. H. W. Wheate was on leave; Mr. and Mrs. Cooper had left to go on furlough and were not returning; and while Mr. Cooper was being replaced, his successor, Mr. Waters had only had 3 months in which to acquire the rudiments of the language, and the details of his responsibilities; further Mrs. Cooper had been in charge of nursing work, and her duties had been taken over by an African nurse.

The work was, however, being well maintained in good buildings and nicely laid out grounds. We saw a glimpse of the farming activities, of the school classes, of the Church for which funds had been given by The Mission to Lepers, and visited all the patients in the wards.

One need was recognised and it was hoped would be met in the near future—the provision of accommodation for all grades of workers to come to the leprosarium for experience and for teaching in various aspects of the problem of treating leprosy patients. Dr. Wheate's return in the autumn of 1961 may help to develop this new side to the work at Chazi.

After visiting the Morogoro Hospital and speaking to the African staff about new developments in leprosy work, I was motored by Dr. Meredith to Dar-es-Salaam. In Dar-es-Salaam I called on the Permanent Secretary to the Ministry of Health and Labour to thank him for the arrangements that had been made by Provincial Medical Officers for my tour. Dr. Meredith also took me on a tour of the hospitals, introduced me and gave me an opportunity of speaking to the staff of the training centre at the modern Princess Margaret Hospital.

Some minor inconvenience caused by the loss of my suitcase at the beginning of my travels was the only difficulty that was encountered in the course of my journeying. I am most grateful to all who helped to make the journey so easy and so interesting; in some

parts it was not much more than a glimpse of a very active and widespread piece of work, but it was sufficient to enable me to appreciate the tasks that were being undertaken, and the problems that were being tackled. Other opportunities presented themselves for detailed discussions of future developments and I hope these will, under God's guidance, bear fruit.

Finally I would like to record my warm appreciation of the welcome which I received, as a representative of The Mission to Lepers, from missionary colleagues and from Government officials.

I found courtesy, kindness and consideration wherever I went, and was given every opportunity of seeing the work that was being done, and of coming to a clearer understanding of the complexity of the problems, and of the patient persistence that is needed to overcome them.

As a result of recommendations to the Council of The Mission to Lepers generous grants have been made to help develop the work of the S.I.M. Shashemane Leprosarium, Ethiopia, to the Kumi–Ongino Leprosy Centre, Uganda, and towards the establishment of the new Leprosarium at Hombolo in Tanganyika. The South African Baptist Missionary Society is exploring the situation at Fiwale Hill in Northern Rhodesia and will receive generous support for any development it can undertake there.

LETTER TO THE EDITOR

DUNLOP CHEMICAL PRODUCTS DIVISION,
BIRMINGHAM 24

Dear Sir,

We have read with interest the article "Etiology and Treatment of Plantar Ulcers" by W. F. Ross which you published in your January, 1962, issue.

The use of a specially prepared latex compound is mentioned (Appendix 2) for the preparation of the Karigiri Boot and, as a result of this, we have already had one enquiry. It may be that some of your readers engaged in similar work overseas would appreciate having fuller details of the material.

Although the material was originally prepared to an outline specification given to us by Dr. Ross, in view of the likely interest we have decided to include it in our range for general supply under the code number AL.1002. AL.1002 is basically a prevulcanised natural latex, which means, that, on drying in air, it will give a fully vulcanised rubber. Among the compounding ingredients used are stabilizers to give the desired characteristics in preparation of the Boot and antioxidant and antiozonant materials to ensure satisfactory service life of the finished Boot. The compound has a Specific Gravity of 0.968 and a Total Solids content of $57 \pm 1\%$.

We suggest that the most convenient method of supply is in 5-gallon non-returnable drums. The price of the material will vary somewhat depending on the current price of rubber, but at present we would charge 23s. 0d. per gallon free-on-board to which would be added 1s. 0d. to 2s. 0d. per gallon depending on quantity and distance for carriage, insurance and freight paid by us. Any import duties would be paid by the purchaser at port of entry into the country concerned.

The Company frequently undertakes non-commercial developments for medical work and it gives all concerned great pleasure and satisfaction when, as happens here, a piece of work results in something which can have such a wide application in reducing human suffering. Our thanks are due to Dr. Ross for giving us this opportunity and to your Journal for the widespread publication of the result he has obtained.

Yours faithfully

R. R. STAPLETON
For Dunlop Chemical Products Division.

ABSTRACTS

Lepra bubalorum: report on transmissional experiments; A. A. RESSANG and SUTARJO (Part 1) and A. A. RESSANG (Part 2). Communicationes Veterinariae Sept. 1961, 5, No. 2, pp. 89–106, Bogor, Indonesia.

An account is given of attempts at transmission of buffalo leprosy to experimental animals, namely guinea-pig, mouse, white rat, rabbit, calf, heifer, horse, sheep, goat, dog, cat, monkey and alligator. Pretreatment with cortisone or total body irradiation was used in some of the animals in order to lower their resistance. The material was injected or transplanted in various ways. The only positive result was in 1 heifer in which a subcutaneous transplant produced a growth after 7 months, and a second passage from this nodule produced a new growth smaller in size. In Part 2 RESSANG describes a case of buffalo leprosy with intracutaneous, subcutaneous, and hitherto unrecorded intramuscular, periarterial, and perineural distribution of leprosy nodules. It was found that nerve bundles and arteries which were embedded in or attached to the granulomatous tissue were unaffected. No growth was observed within the perineurium or within the wall of an artery lumen (5 figs. are given).

Leprosy lesions of internal viscera, with special reference to borderline leprosy and lepromatous reaction: WU LITI'IEN, CH'IN KUANG-YU, and LIU TZE-CHUN. Chinese Medical Journal, **81,** 1: Jan. 1962, pp. 30–38, 8 figs.

The authors made a study of tuberculoid and lepromatous lesions in the various organs in 2 cases of borderline leprosy and describe their findings in detail. No lepra cells were seen in the kidneys, myocardium, and lungs, central nervous system, pituitary, thyroid, thymus, oesophagus, stomach, intestine, pancreas and ovaries, in other cases varying in number from 2 to 23. In lepromatous leprosy (2 cases) histological changes were found in the nasal mucosa, eyeballs, nerves, cervical sympathetic ganglion, spleen, and testis. These changes are described by the authors.

REPORTS

The Hyderabad Conference. By Dr. E. MUIR.

The VIIIth All India Workers' Conference and Vth Meeting of the Indian Association of Leprologists met in Hyderabad from January 4th to 8th, 1962, the "Workers" meetings following on those of the "Leprologists". An empty school provided ample accommodation for the meetings in its large hall, and dormitories for most of the delegates. The VIP's were luxuriously accommodated in an ex-palace of the Nizam. All the arrangements, both social and technical were excellently planned and executed, and it was the opinion of all that the meetings were in every way a great success. Hyderabad was an ideal site, with its salubrious climate at an elevation of 1,700 ft., its historic buildings, and its central position. Here, in the fifth largest city of India, the Capital of the Andhra State, one saw a unique combination of the old and the new, on the one hand the ancient bazaars exhibiting all kinds of handicrafts, and in contrast wide roads with modern colleges and research institutes.

The President of the Conference was Rajkumari Amrit Kaur, who as Health Minister of India has done so much to advance the public health of the country. In the opening meeting, presided over by the Governor of Andhra Pradesh, Rajkumari emphasised that "there is no longer any justification for treating leprosy in separate hospitals and separate clinics", but at the same time she gave the caution that "while we should do everything to destroy every vestige of the old ostracising attitude to leprosy patients—we may never forget or ignore preventive measures".

Drs. Dharmendra and Ramanujam gave a paper on Chemoprophylaxis of the Healthy Child Contacts with Sulphones. Their results showed that 9.5% of 116 contacts of the prophylaxis group, and 10.5% of the 110 contacts of control group contracted leprosy within the 3 years of the experiment. It was therefore concluded that under the circumstances of the experiment, and with the dosage of DDS used (10 to 50 mgm. orally twice weekly) the incidence of leprosy has been about the same. However a more extensive, better controlled, 5-year experiment is being planned in a population of 80,000 with a prevalence rate of 2% and a lepromatous rate of 20%.

Dr. Doull's paper stressed the importance of field observations on leprosy with the following objectives: to obtain full knowledge of the nature and frequency of the disease; to follow over a considerable period clinically recognised cases, to discover the possible role of non-lepromatous cases in the spread of infection, to investigate the portal of entry of the bacillus, to use new techniques such as the inoculation of the mouse footpad in discovering the possible role

of insects, to investigate the nature of resistance by studies of attack rates in comparable groups.

Under *Prevention and Correction of Deformities*, Dr. Anderson read a paper on Deformities of the Foot and their Prevention, and Dr. Antia read one on Prevention and Correction of Deformities of the Face.

At the third technical session there were papers on the Physiotherapy of Leprosy by Dr. Namasivavan, and on the Use of Splints in Treatment of Deformed Hands in Leprosy by Dr. Selvapandian and N. Palani.

The fourth technical session was devoted to Chemotherapy, and most interest centred round the use of Etisul. A paper by Drs. Dharmendra and Noordin described a trial in 93 cases, 60 having been given Etisul with or without DDS and 33 DDS alone. After treatment for 5 to 7 months improvement was more or less the same in both groups. They added "It is difficult to explain the discrepancy in our results with Etisul as compared with those reported by Davey in Nigeria". In the discussion various workers reported that the results varied much in different patients, and that more thorough and prolonged trial is called for before a final judgement can be pronounced on the usefulness of this drug.

Dr. Vellut gave an assessment of the value of DDS treatment of out-patients between 1955 and 1959. Of these 43.4% had been discharged. Of 150 lepromatous cases taking regular treatment 80% became bacteriologically negative, while of 44 attending irregularly only 38% became negative. Drs. Mukherji and Ghoshal recorded that of 71 lepromatous cases on DDS orally, 38 continued treatment for 7 years, and of these 55% became negative. The remaining 33 patients continued treatment for less than 7 years. The reduction in positivity in smears was marked up to the end of the second year of treatment: thereafter it slowed down and became more or less steady after treatment for 5 years. The study indicates that a hundred per cent may be expected to be negative after treatment for 12 to 14 years.

Drs. Bose and Haldar found combined treatment with DDS orally and hydnocarpus oil intradermally and subcutaneously gave quicker results than DDS alone.

In the fifth technical session Drs. Dharmendra and Chatterji described maculo-anaesthetic leprosy and the classification adopted by Indian leprologists as compared with the Madrid classification. "The tuberculoid type of the Madrid classification should be considered identical with the non-lepromatous group of the Indian classification, and the macular tubercular component of the tuberculoid type identical with the maculo-anaesthetic component of the non-lepromatous group".

Dr. Chakravarti read a paper on aggravations in leprosy during

and after pregnancy. He found that leprosy patches get red during the menstrual period. Out of 82 pregnancies there was aggravation in 35 instances.

In the sixth session Dr. Wardekar gave a paper on Criteria of Arrest of the Disease. A case in which all signs of "activity" are absent for a period of one year should be considered "inactive", and after the signs of activity have been absent for 2 years "arrested". Signs of activity were described as: increase or decrease in the size or number of lesions, increase or decrease in anaesthesia, erythema and infiltration, tenderness and thickening of nerves, presence of bacilli by standard method of examination. It was pointed out in discussion that where the disease has proceeded rapidly to negativity the occurrence of arrest is likely also to be rapid; but that in "dimorphous leprosy", though the bacillary index generally becomes rapidly negative, there is special danger of relapse if treatment is stopped too soon.

The Leprosy Workers' Conference began on the afternoon of January 6th with the inaugural session followed by an At Home given by the Governor. At the first working session Dr. Subrahmanyam (after referring to the first two plans) described the Third Five-year Plan for the Control and Eradication of Leprosy from India. A sum of 434 lakhs of rupees (the equivalent of about $3\frac{1}{4}$ million pounds) has been provided for the following programmes: establishment of 50 Leprosy Control Units and 10 training centres; appointment of 1,000 para-medical workers for study education and treatment (SET) centres, and of 15 Assistant Leprosy Officers; research in leprosy; aid to voluntary organisations; rehabilitation programme, health education programme; establishment of Survey and Assessment Teams for States. Also international assistance for leprosy control would be available from WHO/UNICEF. During the discussion which followed the opinion was expressed, notably by Rajkumari Amrit Kaur who presided, that too ambitious a programme had been envisaged, and that the chief deterrent would be the scarcity of doctors and para-medical workers with the necessary public health outlook and the right spirit of devotion without which success could not be accomplished. Many considered that it would be better to begin on a smaller scale, learning by tentative measures, and gradually extending as experience was gained and the right type of workers became available.

Dr. Wardekar, who under the Gandhi Memorial Fund has taken a lead in the first two 5-year periods, spoke on the Leprosy Campaign —Retrospect and Prospect. He described the vastness of the problem in India. There are about 2 million leprosy patients, of whom 4 hundred thousand are infectious and an equal number have deformities, while about one hundred thousand have already become beggars. Several hundred thousand children continue to stay with

their infectious parents. "As against this the achievements are meagre; even the fringe of the problem has not yet been touched. The number of in-patient institutions is about 200 and the total accommodation with them 20,000 and about 250,000 are being treated in out-patient departments".—"Among the difficulties in the way are poverty, non-availability of doctors and lack of co-ordination. The first can be met by dealing with only one or two facets in the first instance. The second can be met by using available doctors only for supervisory, organisational and special medical work and entrusting the routine work to para-medical personnel". He also emphasised the need of satisfactory emoluments for medical men, and the need for all leprosy workers to agree on a common goal and a common method of approach. "The objective should be to tackle only selected facets of the problem at any one time. Balanced planning implies an understanding of the inter-relationship of various facets. In that context, therefore, for some time to come, case-detecting and out-patient treatment must become the common objective. This does not count out the existing in-patient institutions. They can be upgraded as hospitals for needy cases. But the great value which sulphones possess should not be ignored. If all workers adopt the above objective and method of approach, a co-ordinated effort can be made. In the present situation, the problem is how to do this".

In the second working session, Health Education and Publicity were discussed. Several papers were read, and among them that of Dr. Kapoor was of particular interest. Dr. Kapoor spoke of his experience in rural areas in Maharastra (Bombay State). He said: "Propaganda from the level of the leprosy workers may enlighten the patients but it will not achieve what is wanted. But if a few enlightened people and social workers are given the proper education, and if it can be coupled with demonstration of the benefits of treatment of known cases, and if their knowledge is harnessed to education of the patients and general masses, the chances of achieving what we want is great. Actual work on these lines has been started in Maharastra for the last three years, and the results are very encouraging. The education is given in the beginning to the known patients, their relations and the enlightened few who have either administrative powers or social influence on the patients and masses. A few of them are then constituted into a village leprosy committee to help carry the work further. The main functions of the village leprosy committee are: help in giving massage, help in getting the village surveyed, help in bringing absentee patients under regular treatment, help in the removal of local harassment to the patients and their dependents or contacts, removal of the present stigma, rehabilitation of local patients. The advantages of these village leprosy committees are that a higher percentage of people are

examined during the survey and a larger number of patients attend regularly for treatment; rehabilitation does not arise or can be locally solved". In using these committees the initiative must be taken by leprosy workers, and these should be trained in the science of health education, and particularly in the arrangement and management of group talks in health education.

At the third working session, Social Aspects and Rehabilitation were considered. Miss Surty, describing her rehabilitation work in the City of Bombay, said that annually an average of 600 leprosy patients are certified fit for reinstatement. Of these 25% find it difficult to regain their posts in spite of certificates. The Medical Social Workers are successful in the majority of cases in getting them reinstated. A Pilot Project for a craft training centre and sheltered workshop will be commenced at the Akworth Leprosy Home.

Dr. Vaidyanathan mentioned that in the rural area of Polambakam, where the incidence of leprosy is 4%, the percentage of deformity varied from 13.6 to 52.2 in different localities. "Facial disfigurement was not found to create a great social problem in such areas. Patients are more concerned with functional recovery of their hands and feet. For reconstructive surgery, practical considerations should be taken into account such as age, sex, occupation, social position, economic and marital status, and it is considered to be of more importance to the young than old, to women than men, to city dwellers than rural population.

Dr. Muir read a paper on Leprosy in Other Countries, giving special reference to Norway, the West Indies, Brazil and Nigeria, and pointing out lessons which might be learned from other lands. "Three main requirements are necessary in an effective scheme for leprosy relief and control. These are money, wise planning, and intelligent well-trained personnel. But all-important, and without which these three requirements will be wasted, is the spirit which inspires the worker, the spirit which inspired Father Damien and Mahatma Gandhi; and above all the spirit of Him who inspired these two great Mahatmas, and who Himself, we are told healed those with leprosy with His healing touch."

Among the resolutions, passed unanimously by the Conference, were the following. "Rehabilitation should be an attempt to keep in, or send back the patient to, his own normal environment. Attempts to give work and shelter to patients in a secluded environment, however worthy, result in strengthening prejudice against leprosy". "The patient should be prepared for rehabilitation right from the beginning of his treatment by suitable advice and physiotherapy, craft training and building up of morale".

"In view of the fact that a large number of voluntary leprosy institutions in the country are in a position to play an increasingly active role in leprosy control, the Conference strongly urges that

the Government should make adequate budgetary provision for encouraging with suitable grants the active participation of voluntary agencies in leprosy control programmes. In endorsing the following resolution of the Indian Association of Leprologists the All India Leprosy Workers Conference wish to emphasise that, while expanding the leprosy control programme, due care should be taken to ensure that centres are suitably located, and that a high standard of work is achieved by proper preparation for the work, provision of suitable staff, and provision of adequate supervision". The resolution is as follows: "This Association places on record its deep appreciation of the action of the Government of India and State Governments in implementing the National Leprosy Control Programme, and assures the Government of its whole-hearted support and co-operation in the execution of its control programme. However the Association wishes to invite the attention of the Government that there is need for improving the standard of work and the administrative set-up in the control programme."

Second National Leprosy Conference—Addis Ababa 1961. By Dr. K. F. SCHALLER.

The Second National Leprosy Conference of Ethiopia was held at the Princess Zenebework Memorial Hospital, Addis Ababa, from November 30th to December 2nd, 1961, under the patronage of HIS IMPERIAL MAJESTY HAILE SELASSIE I, EMPEROR OF ETHIOPIA. The venue of the Conference was the Princess Zenebework Memorial Hospital, which harbours the Head Office of the Leprosy Control Service of Ethiopia. It was opened in the presence of a distinguished gathering consisting of:

H.E. ATO ABEBE RETTA—Minister of Public Health.
H.E. ATO YOHANNES TSIGE—Vice-Minister of Public Health.
MR. AYLEN—United Nations Technical Assistance Representative.
DR. P. DESCOEUDRES—WHO Area Representative.
DR. P. CHASLES—WHO Senior Adviser.
MR. EHRENSTRALE—UNICEF Resident Representative.
ATO ABERRA DJAMBERE—Acting Director-General Haile Selassie I Foundation.
DR. KRAUS—Adviser to the Haile Selassie I Foundation.
DR. PRINCE—Director of the United States Technical Assistance Programme.
PROF. D. ALLBROOK—Makerere University College, Kampala, Uganda.
MR. F. H. LUNN—Makerere University College, Kampala, Uganda.
DR. G. KLINGMUELLER—Professor of Dermatology at the University of Wuerzburg.

High officials of the Ministry of Public Health.
The Directors and Administrators of the various hospitals, Addis Ababa.
The Directors of Leprosaria in the provinces.
Provincial Medical Officers of Health.
Representatives of Mission Leprosaria in the provinces.
Physicians from Addis Ababa.

The Conference was officially opened by the Minister of Public Health, His Excellency ATO ABEBE RETTA and he was followed in the Inaugurating Session by the undermentioned speakers:

DR. HYLANDER—Principal Adviser to the Ministry of Public Health.
"Role of basic public health services with special reference to leprosy control".

MR. AYLEN—Resident Representative of the United Nations Technical Assistance Board.
"Aid available under the United Nations Technical Assistance Programme".

DR. DESCOEUDRES—WHO Area Representative.
"Greetings and best wishes from Dr. Taba, WHO Regional Director for the Eastern Mediterranean for a successful conference".

DR. CHASLES—WHO Senior Adviser.
"Role played by the World Health Organisation in leprosy control".

MR. EHRENSTRALE—UNICEF Area Representative—.
"UNICEF's role in the struggle against leprosy".

DR. KRAUS—Adviser to the Haile Selassie I Foundation Welfare Trust.
"Need for a uniform doctrine".

DR. SÉRIÉ—Director of the Pasteur Institute of Ethiopia.
"Latest modern achievements in the field of laboratory work on leprosy".

Finally the Inaugurating Session closed with an address by DR. SCHALLER, Chief of Leprosy Control, on leprosy control in East and West Africa.

First Working Session. Chairman: His Excellency ATO YOHANNES TSIGE.

This was opened by His Excellency ATO YOHANNES TSIGE, Vice-Minister of Public Health. Under his Chairmanship, the Chairmen of the various Working Sessions were elected and also the following members of the Steering Committee:

DR. SCHALLER, ATO HAILU SEBSIBIE, DR. TAUSJOE, MR. JOHNSON.

DR. SCHALLER introduced the programme and outlined the objectives of the Conference as follows:

To assess the extent of the leprosy problem in Ethiopia;
To study and agree on the most suitable methods for controlling leprosy;
To learn about progress in the laboratory and to introduce methods which could be applied in the field;
To discuss the choice of treatment in mass campaigns, to gather information about new leprosy drugs, and to agree on methods of testing new drugs;
To study the problem of leprosy reactions;
To exchange experiences in the field of leprosy surgery and to make recommendations on the rehabilitation of leprosy patients;
To discuss problems of health education, legislation and vocational rehabilitation in respect of leprosy.

Second Working Session. "Epidemiology of Leprosy". Chairman: DR. GREPPI—Asmara.

This Session served the purpose of gathering more information about the problems of leprosy in the various provinces of the Empire. The following speakers contributed:

DR. FERON, Director St. Antoine, Harrar, talked about the history of leprosy control in Harrar Province.
DR. GREPPI, Chief of Leprosy Control in Eritrea, told the members of the Conference about leprosy in Eritrea.
DR. BALZER'S paper on leprosy and its control in Wollo Province was read in his absence by DR. FITZHERBERT.
DR. FITZHERBERT who is in charge of the Shashemane Leprosarium gave a report on leprosy and its control in Arussi Province.
DR. SCHAEUFFELE, Director of the Clinomobile Service, talked on leprosy in the Ogaden.
DR. TAUSJOE, Provincial Medical Officer of Health, described the situation in Sidamo Province with regard to leprosy.
DR. HOGGEVEIT submitted a paper on leprosy in Camo Gofu.
DR. REMEDIOS spoke on leprosy in Illubabor Province.
ATO ZERIHUN DESTA, Health Officer, read papers on leprosy and its control in Godjam and Shoa Provinces.
Finally DR. SCHALLER gave a report on leprosy in Ethiopia.

Third Working Session. Control of Leprosy. Chairman: DR. CHASLES.

In this session the problem of BCG and leprosy was one of the main topics. DR. CHASLES read papers on the tuberculin test and

BCG vaccination in connection with leprosy control in Ethiopia. He concluded that BCG vaccination was harmless and, furthermore, useful against T.B.; it should, therefore, be adopted for leprosy patients and leprosy contacts.

It was emphasised that the type of campaign should be adapted to the characteristics of each country or region. In the case of Ethiopia the static integrated services were the choice, out-patient clinics being the main weapon. Treatment villages could be used in certain areas especially if they were linked to leprosaria. It was recognised that compulsory and indiscriminate segregation was an obstacle to the development of mass campaigns.

DR. TIEDEMAN submitted a paper on "Integrated-Specialised Services".

Fourth Working Session. Laboratory Work in Leprosy. Chairman: DR. SÉRIÉ.

DR. SÉRIÉ gave a complete lecture on the bacteriology, histopathology and immunology of leprosy. DR. CHASLES recommended a new, simpler method of staining leprosy bacteria. Agreement was reached in estimating numbers of bacteria in smears and reading lepromin reactions.

Fifth Working Session. Therapy of Leprosy. Chairman: DR. FITZHERBERT.

MR. HACKETT reviewed the leprosy drugs. DR. LANGUILLON submitted a paper on new Sulphonamides for leprosy which was read by DR. SÉRIÉ, who, in his turn, reported on his research with CIBA 1906 carried out in conjunction with the Ethiopian Leprosy Control Service. The Health Officer, ATO ZERIHUN DESTA reported on the findings of a research study made with Vadrine, and DR. SCHALLER gave an account of the experiments made with Etilfarm, Etisul and DDS in the Princess Zenebework Memorial Hospital. DR. HOFVANDER in his paper reported on cases suffering from DDS intoxication, and DR. KLINGMUELLER gave a summary of the various leprosy reactions.

The members of the Conference agreed that for mass campaigns the methods recommended by WHO at the Brazzaville Conference 1959 in the case of weekly treatment shall be adopted. Hospitals and leprosaria would give individual treatment according to the needs of the patient, and in the case of research into new drugs the recommendations made by WHO would be adhered to. The testing of new drugs in Ethiopia had become possible owing to the good co-operation between the Pasteur Institute of Ethiopia and the Leprosy Control Service in Ethiopia.

Sixth and Seventh Working Sessions. Surgical Treatment and Medical Rehabilitation in Leprosy. Chairman: MR. BARRY.

DRS. DIALER, FITZHERBERT and SCHENCK, surgeons, gave an account of their past successes in the surgical treatment of leprosy complications. After the lecture on ulcers given by MR. H. LUNN, the treatment of trophic ulcers in leprosy was discussed at length and recommendations for the prevention of ulcers were made.

MR. BARRY read his paper on "The Effect of Leprosy on Locomotion" and showed orthopaedic shoes made in Ethiopia for leprosy patients. He reviewed the plaster of paris technique for treating plantar ulcers as used in the Princess Zenebework Hospital and discussed some of the problems associated with the generally accepted views on plantar ulceration.

The problem of rehabilitating leprosy patients was another topic of discussion and the Conference stressed the necessity of giving adequate attention to rehabilitation in the treatment of leprosy.

The Session ended with a talk by DR. DOBROVIC on eye complications in leprosy.

Eighth Working Session. Chairman: ATO HAILU SEBSIBE.

Professor ALLBROOK gave a lecture and showed slides of his research using the electronic microscope on muscle growth.

This was followed by DR. SCHALLER's film on leprosy, and a professional film made by the United States Public Health Service on the Management of the Leprosy Patient. MR. BARRY showed a cine film relating to his foregoing lecture on the foot of leprosy patients in walking.

Slides on differential diagnosis of leprosy were shown by MR. LUNN and DR. SCHALLER.

The Chairman, ATO HAILU SEBSIBE, closed the meeting by commenting on the standard of the material contributed and stressed the importance of good documentation in public health.

Ninth Working Session. Health Education in Leprosy. Chairman: ATO HAILU SEBSIBE.

ATO HAILU SEBSIBE gave a comprehensive report on problems of health education with regard to the condition extant in Ethiopia. DR. ERNERT gave a talk on legislation affecting leprosy control and MR. MARLAND treated the question of vocational rehabilitation and social work in leprosy control. In the presence of the permanent members of the Conference and the social workers of Addis Ababa a lively discussion took place. The importance of vocational rehabilitation was emphasized; health education in leprosy control should be handled carefully. Finally it was agreed that no specific legislation was required in leprosy control.

Ad hoc Session. Chairman: DR. SCHALLER.

At the request of the participants an extraordinary session was held in order to comply with the wish of the participants to discuss the problem of leprosy control which arose out of the Conference. Questions of diagnosis and treatment were discussed at length; a joint control service against T.B. and leprosy was another item of discussion. Control problems of local importance were brought to the attention of the gathering and experiences were exchanged.

Tenth and Final Session. Chairman: ATO HAILU SEBSIBE.

Conclusions and resolutions were read. On behalf of the participants in the Conference DR. TAUSJOE thanked the Minister of Public Health and the Ethiopian Leprosy Control Service for having arranged this, in his opinion, most successful Conference. The wish was expressed that such Conference be made a permanent institution of the Ministry of Public Health. DR. SCHALLER reviewed the work carried out in the various sessions and thanked the Chairmen and all the participants for the most useful contributions.

His Excellency ATO YOHANNES TSIGE finally closed the Conference by thanking all those who took part in its deliberations and promised that the Ministry of Public Health would do its share in effecting the recommendations arising out of the Conference.

The Ethiopian Medical Association held on December 2nd, 1961, following the Conference. President: DR. HYLANDER. Secretary: DR. F. BARRY.

The President of the Ethiopian Medical Association, DR. HYLANDER, commented on the past activities of leprosy control in Ethiopia and referred to the resolution of the First National Leprosy Conference held in Addis Ababa in 1957 according to which, he said, the Ethiopian Leprosy Association should be established. After DR. SCHALLER'S Report, the members of the Ethiopian Medical Association established the Ethiopian Leprosy Association as a branch of the Ethiopian Medical Association. It was the unanimous opinion to have this Association affiliated to the International Leprosy Association.

Annual Report of the Ministry of Health, Uganda Protectorate, 1959–1960 describes leprosy control work on pp. 13 and 14. This is of great interest and is here transcribed.

Leprosy

As the 1959 census showed a considerable increase in the population, the estimate of the number of persons suffering from leprosy, based on sample surveys, has had to be adjusted to a figure nearer 80,000. This includes those who have been adequately treated and

those still under treatment, as well as those who have not yet registered at a treatment centre.

The campaign to bring the disease under control began in 1951. Since then 60,000 patients have been treated, 20,000 have become symptom-free and 30,000 are under treatment at the present time, leaving a balance of 10,000 which includes those who, during the nine years, have ceased to attend and have not yet been traced. A proportion of these no doubt have died, some have ceased attending because they themselves were satisfied that they were cured and have presumably not relapsed, whilst others have been prevented from travelling to clinics by distance, extreme age or disability. The general level of attendance is improving, especially in those areas where it has been possible to establish satellite clinics based on a treatment village.

As many as 9,000 patients have been seen for the first time in a year, especially in the earlier years of the campaign; 18% of all new patients are children, and 47% are males.

There are 85 leprosy treatment villages with accommodation for 4,000 patients, as well as 5 leprosy settlements having hospital or dormitory accommodation for 1,750 in-patients. The latter include amongst their staff expatriates from missionary societies and the British Leprosy Relief Association. The settlements take in the most infectious patients, children whose education can be continued in the settlement schools and those who are in need of some particular medical or surgical care. The settlements at Buluba, Nyenga and Kumi-Ongino are concentrating increasingly on disability and deformity and an occupational therapy unit has been opened at the latter. The total number of clinics, including those at the settlements and villages, is 211. The co-operation of the settlement staffs in the clinical supervision of the villages and clinics is producing better attendance and helps to get the right type of patient into the settlements.

Surveys have been held to determine the disability rate in different areas and to trace those who have ceased to attend. Investigations have continued into the use of the depot lepromin test and the leprosy/tuberculosis relationship. Most of the immunological work has been carried out in eastern Uganda with Kumi-Ongino as a base.

The links with World Health Organisation and UNICEF have been maintained. Doctors of many nationalities with World Health Organisation fellowships have paid visits to Uganda to see the methods of control used. The Specialist Leprologist attended the All-Africa Leprosy Conference at Brazzaville and later acted as rapporteur for the second World Health Organisation Expert Committee on Leprosy in Geneva. UNICEF has continued its assistance on the same scale as hitherto.

The missionary societies and the British Leprosy Relief Association have maintained their contributions in staff and funds as in previous years; it is a pleasure to record appreciation of their co-operation and of the service of those whom they have sent to Uganda.

Annual Report of the Director of Medical Services for the year 1959, *for British Guiana.*

The population of British Guiana is about half a million. Listed among the special hospitals is Mahaica Hospital for Leprosy, of 405 beds. The number of cases registered in 1957 was 128, 76 in 1958, and 56 in 1959, with a lepromatous type percentage of 11, 31 and 9 respectively. The Medical Staff of Mahaica Hospital is Dr. A. Abdurahman as medical superintendent (acting) to November 30th, 1959 and Dr. F. A. Chandra from December 1st, 1959. Dr. F. A. Chandra was awarded a WHO Fellowship for training in leprosy work. He visited Venezuela, Surinam and Brazil. In Mahaica Hospital 114 patients were admitted in 1959 and 107 patients discharged (this from Table 19) but in Table 20 the distribution of patients and contacts is given as 55 in infirmaries, 99 in cottages, 36 in private rooms, 39 in a new hospital, 21 in the Bishop Galton Home for infected children and 32 in the Lady Denham Home for children of patients, to a toal of 282 persons. In Table 21 the treatment of patients is given as 216 under treatment with DDS, DPT, etc. and 70 patients had positive smears at the end of the year. The Report states that 65 discharged patients were allowed to remain in the institution and doles were given to 117 discharged patients to the total amount of $5,313.00. Clinics are mentioned as being held in several parts of the country and visited by the medical superintendent. School surveys were carried out. In Demerara 36,213 children were seen and 24 cases of leprosy found; in Berbice 11,341 and 13, in Essequibo 5,356 and 2 (totals 52,910 examined and 39 cases found).

REVIEW

The True Facts about Leprosy by DR. I. A. SUSMAN, Medical Officer, Ghana Leprosy Service.

This pamphlet of 25 pages with 15 illustrations in a simple, sensible and accurate way deals with leprosy in a country like Ghana and incidentally gives much information as to how the problem has been tackled in Ghana with such success to date. This pamphlet is much to be recommended.