THE INITIATION OF MEASURES FOR THE CONTROL OF LEPROSY WITH SPECIAL REFERENCE TO SOUTHERN OGOJA PROVINCE, SOUTH-EAST NIGERIA, AND A COMPARISON OF THE EFFECTS OF TREATMENT WITH THE SULPHONES AND SULPHONAMIDES.

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Introductory.

My appointment as leprologist to the Church of Scotland Mission Leprosy Scheme for Southern Ogoja Province, South-East Nigeria, followed a long period of waiting during which I was engaged largely in general hospital work. Staff shortages and the difficulty in obtaining passages to and from the United Kingdom made it imperative that I remained available for relief work at two of the Mission hospitals during the war years, and the uncertainty of securing additions to the medical staff caused delay on the part of the Mission authorities in accepting the grant offered by the British Empire Leprosy Relief Association which made the appointment possible.

While relieving Dr. Harry Hastings, O.B.E., M.B.Ch.B., D.T.M. & H. at the Church of Scotland Mission Hospital, Uburu, Afikpo, Southern Ogoja Province, between the years 1940 and 1942 and again 1945 to 1946, I was employed part time in supervising the small leprosy work which he had started and wished to develop and extend. For six months between the years 1943 and 1944 I relieved the Medical Superintendent of Uzuakoli Leprosy Settlement in Owerri Province, South-East Nigeria, T.F. Davey, O.B.E., M.Sc., M.D. This brief experience of a Provincial Leprosy Scheme with a Central Leprosy Settlement served to accentuate the necessity of whole time supervision of leprosy work and the advisability of applying similar methods in Southern Ogoja Province. When this became possible by another doctor being appointed to relieve at the Hospital, I took up my appointment as whole time leprologist in May, 1947.

The prolonged delay, inevitably accompanied by a wealth of experience in the ways and sufferings of the kindly indigenous people, was not without its advantages when the opportunity offered for the control of their most widespread and ravaging disease. No one else with sufficient training was ready to take charge: I who was familiar with the tradition was able to maintain and to extend it gradually as occasion arose, adding to the meagre equipment according to the exigencies of the situation and as far as our finances and difficulties and delays in importing allowed; I was acclimatized and was enabled to extend my stay from the prescribed two years to twenty-nine months while waiting for my successor to arrive. By so doing I was able to observe the effects of the sulphones and sulphonamides, and the complete revolution which their administration accomplished not only in the patients concerned, but amongst all the patients in what is now planned to be the Church of Scotland Mission Provincial Leprosy Settlement at Uburu.

I. Historical and General.

1. Origin associated with incidence.

Scott's (1939) History of Tropical Medicine contains the following statement:- "Available historical records are not sufficient to enable us to decide where leprosy originated. Those who have most studied the question incline to the view that its first home was Africa, a country where today the endemicity is greatest. The belt of land extending across central Africa from Nigeria to Abyssinia is still the most severely affected in the world and it is thought that this was the primary home of the disease." From this it would appear that in dealing with the control of leprosy in Southern Nigeria we may be tackling the problem near its source and in an area where there are some of the heaviest rates of infection in the world. Rogers and Muir (1946) point out that, as parts of tropical Africa are sparsely populated, the total number of cases of leprosy there must be " far less than that of leprosy infected India and China," but they make South Nigeria an exception even to these countries.

If high endemicity is associated with origin, facts point, although not conclusively, to Southern Nigeria in the belt of land referred to by Scott. Rogers and Muir (1946) quote estimates of 20 per mille as the leprosy incidence for the whole of Nigeria and only 3.40 per mille for India and Burma and 2.25 per mille for China. Davey's (1942) estimates of leprosy incidence range from 13 to 152 per mille with a mean of 52 per mille in twenty-five villages in Owerri Province, South-East Nigeria. According to the figures given for area and population in Philips' Record Atlas (1941) and for population in the Royal Commission on Population Report (1949), India has a density of population per square mile about four times, and China about twice that of Nigeria taken as a whole. Pitt-Rivers' Problems of Population (1932) records that some parts of India and China have densities of population greater than 400 persons per square mile, and this exceeds the figures recorded for South-East Nigeria in Colonial Reports, Nigeria (1938), Onitsha Province 224, Owerri Province 154 and Ogoja Province only 94 persons per square mile: but Davey (1947) has referred to a "densely populated belt of South eastern Nigeria, where a population density of 1,000 to the square mile is not uncommon"; so, from available statistics it would appear not improbable that endemicity is greatest in South-East Nigeria.

Scott's (1939) suggested route of spread of leprosy, through Egypt and Asia Minor around the Eastern Mediterranean to the Continent of Europe, depends for confirmation on evidences of the presence of leprosy in ancient Egypt. Lowe (1947), adopting "the principle that, in ancient literature the use of a word that might have been used at that time for leprosy is of no value as evidence unless supported by

clinical details definitely suggesting if not clearly indicating leprosy", has shown that references to this effect in early records have not been found to be authentic, and that reports of leprous mutilations in mummies have not been confirmed. Cochrane (1947) admits it is a mere surmise that leprosy spread to the Far East from Africa via India: indeed, if we apply Lowe's criterion and accept his and Dharmendra's statements (1947), it would appear that the earliest authentic descriptions of leprosy are to be found in the ancient literature of India, the Susruth Samhita probably written about 600B.C. Alleged instructions on prophylaxis in the Laws of Manu, regarded variously as having been written between 1300 and 500 B.C., are not considered by Lowe to be conclusive proof of the prevalence of leprosy in India at that time. Early references to the disease in China are also queried by Lowe, who asserts that the first definite clinical descriptions in that country date from the seventh century A.D. - from which time, he says, ostracism was practised - and he quotes authorities who stated that it was described in Japan in the eighth and ninth centuries, A.D. Cochrane (1947) states that "leprosy in Japan was almost certainly introduced from China". Stitt's Tropical Diseases, obviously the "(1942) edition of a standard American book on tropical medicine" referred to by Lowe, dates the first records in Japan at 1250 B.C., which Lowe alters to 1250 A.D., as a copyist's error from another authority. This illustrates the uncertainty and error which surrounds these early records, and the controversy as to whether leprosy originated in the Far East or in Africa.

Scott (1939), Rogers and Muir (1946), Cochrane (1947) and Muir (1948) agree that leprosy was present in Europe in the pre-Christian era, but Stitt's (1942) Tropical Diseases places its introduction "from Egypt at the First Century". The former authorities refer to the possible introduction of leprosy into Greece by the Persian armies from Asia and Africa, pointing to an origin in Africa or the Far East or in both. There seems little doubt that leprosy spread from Greece to Italy, France, Spain and Portugal, Germany, England, Wales, Ireland and Scotland, from which it spread to the Faroe Isles, Iceland and Greenland, and to Norway, Holland, Russia and the Baltic countries. Leprosy was prevalent long before the Crusades (1095 - 1270), but reached its height in Europe during the Middle Ages (1000 - 1400). Taking into account the recently reported increase of cases of leprosy in Great Britain, attributed to "the return of Servicemen and prisoners-of-war from abroad" and other related causes referred to in the British Medical Journal (1949), it would appear likely that the Crusades at least aggravated the prevalence of leprosy at that time. We know that leprosy spread to the Western Hemisphere by the discoverers from Europe before it was taken there from the

West Coast of Africa by the Slave Trade, which, however, is stated by Rogers and Muir (1946) to have been a more important factor. In view of the high incidences of leprosy quoted (page 2) in the region from which many of these slaves came, the Dark Continent must have played a part in the spread of leprosy in this instance at least.

While the assumption that leprosy originated in the 'belt of land' referred to by Scott (1939) rests mostly on its present day high endemicity, it is well to remember that, for the same reason, these regions may have been prominent in present day spread on account of the movement of armies during the Second Great World War. Scott's (1939) statement that, "Fortunately there is now little immigration of the leprosy-infected dark races of Africa," then became inapplicable. With regard to another statement of Scott's (1939) that this region "is likely for many years to come to be a very unfavourable field for both prophylactic and curative measures", I can only comment that it is fortunate that, under the changed conditions referred to, the outlook for both prophylactic and curative measures has changed so profoundly.

2. Biblical Control and Restrictive Measures.

Reference has been made by Stitt's Tropical Diseases (1942) and by Cochrane (1947) to restrictive measures taken in the control of leprosy in Biblical times. According to the former, "these directions regarding leprosy continued in force in the Middle Ages": according to the latter, the "widespread dread of the disease" in European countries "can be traced to the attitude adopted as the result of measures taken against leprosy in Biblical times". But I have been told by aged chiefs of primitive African tribes that a dread of leprosy was present and restrictive measures practised before the Bible was known amongst them, which makes it appear unlikely that Biblical control was the only factor in engendering a fear of leprosy and initiating restrictive measures.

From this there arises the question as to whether leprosy was even known in Biblical times, and whether the disease or diseases, at the control of which restrictive measures were aimed, were, in fact, leprosy as we know it today. Stitt's Tropical Diseases (1942) states that "in Leviticus, Chapters 13 and 14, truly remarkable passages regarding the diagnosis and prevention of leprosy are to be found." This statement has been challenged by Lowe (1947) who writes, "nowhere in the Bible is there any clinical description corresponding to leprosy as we know it today, no mention of numbness and loss of skin sensation, or of manifestations of leprosy of the nodular type such as are found in the ancient literature of India and of some other countries." Lowe concludes: "It appears therefore that the leprosy of Leviticus 13 was not our leprosy, and was much more probably leucoderma." Dharmendra (1947) believes that if the Biblical term Zaraath or Lepra "included leprosy at all, it could have covered only the mild variety, and not the nodular type which was prevalent to a much greater extent."

A perusal of the passages in question left me with the impression that, although other skin diseases besides leucoderma, for example impetigo, tinea, psoriasis and seborrhoea might be indicated in the descriptions, there is no ground for assuming that even the mild type of leprosy is referred to. Regarding prevention, the conception of leprosy being seen to spread on the walls of a house or on clothing appears merely grotesque to our idea, however effective their eventual destruction may have been when these observations had been made. Moreover the control measure advocated is isolation - "he shall dwell alone", Leviticus 13, verse 46 - not segregation among other lepers such as has been in force in the Middle Ages and in recent times.

Previous to reading Muir's (1948) reference to King Uzziah, who, "while he was wroth with the priests, the leprosy even rose up in his forehead" (II Chronicles chapter 26, verse 19) I had recorded in notes on the subject that "the description might well correspond to an early infiltration in a lepromatous case". Muir, the only authority to publish this observation, remarks that "the account given of King Uzziah...is a clear picture of what happens in an early case of the lepromatous type; emotional flushing of the facial capillaries makes the lesions suddenly stand out in relief." Applying Lowe's (1947) criterion, if leprosy is not 'clearly indicated' here, it is at least 'definitely suggested', and Lowe's and Dharmendra's (1947) statements relating to the absence of Biblical references to the more advanced nodular type must be accepted with this reservation. We may conclude that, although no clear clinical description of leprosy nor any really effective measures for its control are given in Leviticus or any other relevant Old Testament passages - Numbers chapter 12, verse 10; II Kings chapter 5; Deuteronomy chapter 24, verse 8 - and the term used for leprosy included a number of other skin diseases, from a reading of II Chronicles chapter 26, verse 19, it appears probable that the writer was familiar with leprosy as we know it today.

3. Effects of Segregation.

In A.D. 600 there are said to have been "hundreds of leper houses in Italy and Germany" (Scott, 1939). The same authority places the foundation of the first Leper Home in England at Nottingham in the seventh century, further defined by Rogers and Muir (1946) and by Cochrane (1947) to between 625 and 638, but Stitt's Tropical Diseases (1942) states that it was at Canterbury in 1096. Weymouth (1938) and Rogers and Muir (1946) agree with the last named authority in reference to a decree issued by Pepin (Stitt's 'Pippin') in France in 757, according to Rogers and Muir, "making the marriage of lepers illegal and the disease a cause for divorce", and Stitt's Tropical Diseases states that it also referred to their segregation. All these sources mention a similar enactment in 950, Stitt's Tropical Diseases ascribing it to England, but Weymouth and Rogers and Muir to Wales. Rogers and Muir

affirm that a leper hospital was established in Ireland in 869 - Cochrane (1947) dates it 809 - that the"first leper house north of the Tweed" was established in 1177, and that the disease was probably carried from Scotland to Norway where a leper hospital was established at Bergen in 1266. Weymouth (1938) gives instances of leprosy laws, some of them depriving lepers of civil rights, others cruel in the extreme, which he says were in force in England up to the fourteenth century. It is evident, then, that leper hospitals were established and laws of segregation in force from an early date.

In the controversy over leper hospitals, their number, size and the type of patients they accommodated, one fact emerges: the weight of opinion is in favour of their value. Only"the non-contagionists such as Hutchinson and Newman" are listed by Rogers and Muir (1946) as denying "any influence of Middle Ages' segregation in reducing leprosy in Western Europe". Influenced mainly by the theories of dietary and hereditary transmission and with no conception of the importance of even modified segregation in reducing leprosy incidence, it was natural that Newman (1895) should advance the objection that Middle Ages' segregation was not strict enough. Scott (1939),however, quotes Munro that the decline was most rapid in England because segregation was more strict there, and he states elsewhere that even stricter measures were applied in Scotland than in England, lepers in the former country not being allowed to attend markets or to beg. Likewise MacLeod (1920) attributes the rapid decline in Europe "to stringent,and too often cruel,methods of isolation which were enforced on lepers, alike by Church and State". Cochrane (1947) states that,"it is felt, however, that the strict laws of segregation, whereby the sufferer was not allowed to come into contact with healthy persons (especially children), were the main factors in controlling the disease". Stitt's Tropical Diseases (1942) states: "As the disease spread far and wide, the advantages of these retreats for the purposes of segregation became apparent, and they turned out to be an important factor in the eventual stamping out of the disease ..... Some idea of the importance which leprosy had reached during the Thirteenth Century may be obtained from a knowledge of the fact that during that century there were 19,000 of these lazar houses, or leprosaria as they were called, 2,000 of which were in France alone!

On the figure 19,000 Lowe (1947) again challenges the "latest book on tropical medicine", explaining that it is a mistake based on a mistranslation, the number of manors administered by the Knights Hospitallers (or the Knights of St. Lazarus) having been apparently assumed to be identical with the number of leper houses. Lowe quotes Ehlers that the number of leper houses was probably not much smaller than the number of manors, and that "there were officially recorded 1,502 leper houses in France and there were probably others also; and that even in 1693 when leprosy had practically disappeared, the order for the closure of the leper houses in France affected 1,133 establishments the income of which was thereafter devoted to

other charitable purposes." The total number of leper houses in Europe listed by Lowe (1947) from various authorities amounts to 2,357. Comparing this with Cochrane's (1947) total of 2,324 for France and Britain alone, we have corroboration of Lowe's (1947) statement that "the number was probably at least several thousands."

Cochrane (1947) records 19 leper houses in Scotland in the Middle Ages, and Spottiswoode (1824) has compiled a list of 28 religious houses in this country at the time of the Reformation, that is, about the year 1534, and he writes that these 'hospitals' "were erected either for the receiving of strangers or for maintaining poor or infirm people." That some, at least, were used for accommodating lepers is evidenced by the fact that in one he numbers eight and in another seven "leprous persons", making a total, however, of only fifteen leper patients for the whole of Scotland at that time. This would appear to indicate that the number of lepers must then have been on the decline or that all had not been recorded. Cochrane (1947) states that "leprosy was apparently not prevalent in Scotland till the fourteenth century", and MacLeod (1920) that:"In the seventeenth century the number of lepers in the Shetland Islands was considerable." There leprosy lingered on until the end of the eighteenth century, segregation being carried out on the Island of Papa Stour. MacLeod also remarks that "...there was a number of these leper houses in the British Isles but it is doubtful if true leprosy ever prevailed to any extent here as the houses seem to have contained all sorts of skin and venereal diseases as well as leprosy." In opposition to this and to similar views quoted by Rogers and Muir (1946) and by himself from Creighton, Lowe (1947) concludes with regard to England,that "nearly all the towns had one, and some two or more leper houses", and that "the number of leper houses in England has not been exaggerated." Some of them, he states, accommodated over fifty patients, and they "were used to a considerable extent for genuine cases of leprosy." He also remarks that the signs which led to a diagnosis of leprosy with consequent segregation were those of advanced cases, but adds that "syphilis was either rare or absent from western Europe" at the time when leprosy was at its height. There would appear, then, to be evidence to the effect that leprosy was prevalent on the continent of Europe and in Britain by the thirteenth century, that local segregation in leper hospitals became established and was retained as the method of dealing with the disease, that a rapid decline took place during the fourteenth and fifteenth centuries and that the disease had almost disappeared from England by the end of the sixteenth century and from Scotland, Ireland and France by the eighteenth century. The reasons for this remarkable decline have been much disputed and are important from the aspect of present day prophylaxis and control. Possible factors will be considered under five heads in the next sub-section.

4. Decline in Western Europe.

(1) Restrictive measures on the liberties of lepers.
(2) The Black Death, 1349.
(3) Improvements in housing, diet, sanitation, hygiene and social conditions generally.
(4) Decreased virulence of the bacillus.
(5) Local segregation of lepers.

Much has been made of the effect of restrictive measures on the liberties of lepers referred to above (pages 4,5 and 6) and the system by which a leper was declared "dead to the world" and so separated from contact with children and susceptible persons (Weymouth,1938; Rogers and Muir,1946; Cochrane, 1947). In order to maintain this view it would have to be established that these measures were actually enforced and that they were enforced effectively. That severe and often cruel methods were adopted during the earlier part of the period when leprosy was prevalent seems beyond doubt, but whether these methods were enforced consistently and effectively is another matter. We have seen (page 6) that Newman (1895) has thrown doubt on the strictness of the measures employed. Weymouth (1938) gives one instance of a leper being deprived of his lands and another of a leper woman "quick with child" being buried alive in England in the fourteenth century. Similar atrocities, as I have been told, have been practised among primitive tribes in Africa, where, as in South-East Nigeria, high rates of infection are found today. The results of severe restrictive measures in modern times, such as the shooting of lepers in China, are quoted by Weymouth (1938) from Leprosy Review (1937) where it is stated that such measures are likely to result in every leper being driven into hiding and lead to "a greatly increased spread of the disease." The failure even of restrained restrictive measures as quoted by Rogers (1946) in reference to compulsory segregation in South Africa and the Philippine Islands, leads us to doubt the efficacy of any of these practices in the control of leprosy in earlier times.

Rogers and Muir (1946) quote MacArthur, who, in England, "found no evidence of the enforcement of the severer measures used in France, for, at any rate subsequent to the Norman Conquest, there has been no law in this country to sanction the divorce of a leper from his wife or to deprive him of his property and civil rights, and he has recorded evidence to the contrary effect." Weymouth (1938) quotes evidence of generosity to lepers in the dietary accorded to them at Sherburne Hospital near Durham and the toll exacted for them at Chester market. This generosity is referred to by MacArthur who is reported in the British Medical Journal (1949) as stating in an address, "If a man did not mind being called a leper his livelihood was assured". It may be that here we have evidence of a changed attitude which took place towards lepers when it was realised that restrictive measures alone were not sufficient, and that segregation had to be made attractive in order to be effective. Weymouth (1938) deplores that, "By the

sixteenth century the vital faith of medieval Christendom had spent itself," and he gives instances of regulations applying to leper hospitals all over England such as that "tainted salmon or pork" be sent to the leper houses. But by this time leprosy was on the decline in England, and, for this reason regulations such as these could not have had a pronounced effect in retarding the progress of prevention.

There appears to me to be insufficient ground for supposing that the Black Death by itself played a part of any considerable importance in the decline of the leprosy epidemic in Europe. Rogers and Muir (1946) suggest that, "not much less than one half of the population" having been destroyed, "the poor helpless lepers must have suffered even more severely than the general population." But leprosy is no respecter of classes in society and it appears doubtful if any were deprived of their property at that period (page 8). Furthermore it is a slowly progressing disease and only a small proportion of lepers are really helpless at a given time. The pneumonic form of the plague might have spread rapidly amongst those who were segregated closely together in hospitals with devastating effect on lepers if segregation had been effectively enforced; but in a population with a relatively high incidence of leprosy - Newman (1895) considered 2.26 per mille too low an estimate - there must have been many incubating the disease who would begin to show signs of leprosy within the following five years, estimated by Rogers (1946) as the maximum usual incubation or latent period of the disease. For this reason the probable duration of the plague is of interest. The Cambridge Medieval History refers to "the terrible year of the Black Death," but adds in reference to Scandinavia that, "this first great plague was followed by others in the course of the same century." Even so, it seems unlikely that a disease so insidious in its onset and of such chronicity would be stamped out by recurring epidemics of plague alone, as indeed it was not, continuing in England for another two hundred years. In my opinion it was the consequences of the plague, not the plague itself, which must have played a part in the decline of leprosy in Western Europe. The Cambridge Medieval History (1936) states that these consequences are much disputed, but that "Economic values, particularly those of land, seem likely to have depreciated through the loss of a large number of the cultivators, and for that reason the wages of the labourers and the conditions of peasants may possibly have improved."

Improved housing conditions with less overcrowding would be an important concomitant of this change. The improved diet of the period and the better sanitation, hygiene and social conditions combined with improved housing conditions may have contributed to the rapid decline of leprosy especially in England, but only indirectly. Rogers and Muir (1946) go too far in stating "improved diet and living conditions may well have been the main factor in the decline and disappearance of leprosy as an indigenous disease from north-western Europe". If we accept the usual assumption that leprosy is an infectious disease,

conveyed most frequently as Rogers (1946) has shown, by prolonged, close contact, we are led to the conclusion that improvements in conditions of living which are accompaniments of a higher degree of civilisation are inimical to the spread of leprosy because they diminish contact. Consequently the improvement most likely to have been concerned in the decline of leprosy in Western Europe was improved housing.

Rogers and Muir (1946) quote Jeanselme "that the retrogression of leprosy in Europe was in large part due to prophylactic measures and not due to acquired immunity or decreased virulence, because the disease continued unabated where no prophylactic measures were carried out". This applies whether it is argued that the epidemic subsided because of increased resistance of the populace or decreased virulence of the bacillus, because the disease still lingers in countries, even in temperate climates, for example Iceland, Norway, Sweden, the Baltic countries and Russia where the lower civilisation encourages close contact or where methods of prophylaxis have been misdirected or insufficient. Nevertheless an attractive theory has been put forward by Chaussinand (1948) who enumerates the causes he has previously put forward for the decline of leprosy in Europe - the Crusades, the Black Death, other epidemics and a progressive improvement in general well being and hygiene - then adds: "Mais l'étude de l'allergie dans la tuberculose et dans la lèpre, entreprise depuis 1939, nous a révélé vraisemblablement la cause majeure responsable du déclin de la lèpre." He goes on to argue that the most important cause of the decline of leprosy in Europe was epidemiological, an increase in prevalence of tuberculosis replacing a decline in prevalence of leprosy; but he admits: "Nous ne pouvons malheureusement avoir recours aux statistiques pour appuyer notre théorie." He concludes: "L'éviction progressive de la lèpre par la tuberculose est le phénomène dominant dû à la prémunition relative croisée de ces deux infections."

Chaussinand affirms that England and Germany, the first two countries in Europe to attain the summit of the epidemiological curve of tuberculosis, were also the first from which leprosy vanished. He also maintains that, although leprosy remained prevalent in Norway until modern times it is now on a marked decline in that country but the prevalence of tuberculosis is increasing, and he gives instances to the same effect from other countries. As he states, it is impossible to prove or to disprove his theory, but in enunciating his hypothesis of reversible immunity he asserts: "En effet, la tuberculose ne constitue généralement une complication fatale de la lèpre que chez les lépreux anergiques. Les lépreux allergiques arrivent d'ordinaire à surmonter facilement la primo-infection tuberculose, qui ne se manifeste le plus souvent que par l'allergie tuberculinique ou quelquefois par des tuberculoses ganglionnaires cervicales." Again, it is impossible to quote statistics, but in our experience at Uburu we have known patients, not clinically anergic, who died of tuberculosis. *

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Chaussinand's theory cannot be ignored. We know, however, that segregation was practised in both England and Norway during the rapid decline of leprosy in both these countries, that it was not abandoned in England, Scotland and France until the disease had almost disappeared in these countries (pages 6 to 9), and has been maintained in Norway in modern times as described by Rogers and Muir (1946). From this it appears unlikely that the decline of leprosy in Western Europe was merely a natural phenomenon, induced by decreased virulence of the bacillus.

There can be no doubt that the establishment of leper hospitals was an advance on the solitary confinement of Biblical times and had, at least, some features in common with village segregation as practised in Africa today. It was a method of local segregation (Lowe, 1947, page 7) one or more hospitals being made to serve a limited area and therefore most likely accommodating patients from its own area. Robert Henryson's poem, The Testament of Cresseid, describes the prompt way in which segregation was effected immediately a diagnosis of leprosy was made, and gives us a glimpse of the kind of community life led by the patients in these institutions, from one who lived in the late fifteenth and early sixteenth centuries when leprosy was still known in Scotland. Efforts to make segregation attractive have already been referred to (page 8) and must have been essential when so little could be offered as regards effective treatment. Stitt's Tropical Diseases (1942) quotes Virchow as referring to the part the leper hospitals played in the "wave of human charity" which swept through Europe, indicating at the same time that there was a rational basis for the change which was also part of "a great social and hygienic prophylactic movement." And I think that the more generous attitude to lepers must have had a utilitarian basis and may have occurred because it was found that the best policy was to be kind to them. Leprosy progresses in a vicious circle: where the leper is treated harshly and made to live in squalor, uncared for except to be ostracised, segregation becomes ineffective because it is unattractive: where, on the other hand, the lot of the leper is improved and only reasonable restrictions are imposed, segregation becomes voluntary and early sufferers come forward; then the disease can be controlled and eventual prevention becomes possible.

Rogers and Muir (1946) quote Jeanselme in reference to a letter of 1371 "that lepers circulated with impunity in town and country in spite of injunctions and threats of the authorities", and their reference to the opinions of Hutchinson and Newman already cited (page 6) affirms that "not all the lepers were isolated and that they were allowed to beg in towns, so the conditions were not such as would prevent the spread of a contagious disease." I feel that these opinions ignore the factor of prolonged, close contact, the importance of which has been shown by Rogers (1946), and I think that it is not improbable that conditions were consistent with those which would have

prevented the spread of a contagious disease like leprosy. In modern times a system of selective segregation of infectious cases from contact with susceptible persons has been found to simplify and lessen the problem of leprosy control considerably (Davey, 1942, 1943, 1945, 1947; Rogers and Muir, 1946; Rogers, 1946; Cochrane, 1947; Muir, 1948), and Cochrane (1947) considers that segregation of this nature, especially at night when opportunities for close contact are greatest, may prove to be sufficient. Accordingly I am not surprised that leprosy, as an endemic disease, disappeared from Western Europe and most rapidly from England under the modified conditions of segregation that were imposed, believing as I do that it was not a matter of great importance that some lepers circulated with impunity in the towns or begged in the markets.

For similar reasons Rogers and Muir (1946) state that enforced residence of the few infective cases outside a town or village must have played some part in the reduction of new infections", and under conditions where residence was not only enforced but also made attractive, a greater part would be played by these measures. According to Cochrane (1947), "Priests must have had a fair knowledge of leprosy and the easier diagnosis in the light skin made the recognition of the disease simpler and probably only a small proportion were missed." If this were the case, taking into account that I have found African chiefs in the Oso Edda area of Afikpo Division, Ogoja Province, South-East Nigeria, who were able from observations based on their own experience of leprosy to differentiate roughly between the infective or lepromatous and the less- or non-infective tuberculoid types, it seems not without the bounds of possibility that eventually, in medieval Europe, most of the infective cases were effectively segregated. The special injunctions quoted by Cochrane (1947), not only that prohibiting a leper to touch a child, but more especially the one requiring the leper to return to his cabin every night, must have been of importance in the control and prevention of leprosy. It may well have been, then, that precautions taken which aimed at reducing the chances of contact with lepers, and a system which considered the interests of the diseased and the healthy alike, were factors operating in the decline of the leprosy epidemic in Western Europe, especially in those countries where the decline was most rapid and most successful.

5. Control from the Nineteenth Century.

The history of the control of leprosy from the beginning of the nineteenth century may be divided roughly into four main periods:-

(1) A period of uncertainty as to aetiology when a vacillating policy of imperfect compulsory segregation was carried out previous to the discovery of the bacillus of leprosy by Hansen between 1871 and 1873, and his report on his discovery in 1874.

(2) When the significance of this discovery was realised there ensued a period of attempted compulsory segregation in Main Territorial Settlements or Leper Asylums which merged into the next period.

(3) Following the introduction of improved methods of treatment by the injection of preparations of chaulmoogra and hydnocarpus oil and the activities of the British Empire Leprosy Relief Association in the nineteen twenties, the emphasis was on treatment as a means of control. Leprosy clinics were advocated, and segregation, mostly voluntary in Leper Colonies was practised.

(4) The fourth period started in the nineteen thirties and is apparent in directions for provincial leprosy control by the Cairo Conference in 1938, and in publications like those of Davey (1942, 1943, 1945) stressing the importance of epidemiological work and of village segregation. This has been followed by a renewed interest in the possibilities of treatment by the sulphones from 1943.

During the first period there are said to have been many lepers in Norway and Iceland, and some in Portugal, Spain, Italy, Sicily, Crete and New Zealand; and leprosy was known to be prevalent in India, China, Japan and the West Indies (Weymouth, 1938) and must have been prevalent, although not reported on in Africa. A leper hospital was established in Calcutta in 1811, and the Cape Colony Robbin Island Settlement was started in 1817 with little effect on the control of the disease, for, as Rogers(1946) points out, yearly admissions to the latter averaged 21 between 1845 and 1852, and 100.7 between 1894 and 1905. The hereditary theory of origin of leprosy propounded by Danielssen and Boeck held sway, and is stated by Weymouth (1938) and Rogers and Muir (1946) to have influenced the Danish Government in closing the four leper hospitals in Iceland in 1848, and to have delayed control measures in Sweden, where, however, a leper asylum was opened in 1864. "Hospitals or sanatoria for leprosy patients with a minimum of compulsion", are stated by Rogers (1946) to have been provided in Norway in 1856, and "led to a great reduction of the disease during the next seventy years." The hereditary theory of origin of leprosy was supported by a report of a committee of the Royal College of Physicians in London in 1867 (Weymouth, 1938) but it was soon to be eclipsed: the discovery of the bacillus of leprosy by Hansen in Norway, given variously as in 1871 to 1873, and his report on his findings in 1874 put the control of leprosy on a new foundation by establishing contagion as an accepted fact.

This became evident at the First International Congress at Berlin in 1897 where Hansen presented a paper and a committee of twenty was appointed to enquire into the aetiology of the disease. At the International Conference at Bergen in 1909 leprosy was accepted as contagious, and when Jonathan Hutchinson put forward his theory that it was caused by eating bad or half-cured fish, he was in a minority of one (Weymouth, 1938); lepers were to be'isolated', excluded from certain occupations, and children removed from leprous parents and contacts examined. Although leprosy was considered to be 'not incurable', no certain remedy was described (Scott, 1939). Unna (1928) remarks on the changing attitude to methods of segregation at the three early conferences, stating that whereas at the first compulsory segregation was advocated, at the second milder methods were favoured, while at the Third International Conference at Strasbourg in 1923 it was decided that measures should be suited to different countries, and that treatment, not 'isolation' is necessary.

Attempts were made to impose compulsory segregation in most countries where leprosy was prevalent during the second period I have defined,without success except in Norway where the modification 'minimum compulsion' has already been noted (page 13), in the relatively small community of Iceland, and in South Africa where the entire system had to be altered before real success was achieved. In Norway the number of lepers was reduced from 1377 in 1885 to only 68 in 1931; in Iceland the number of lepers was reduced from 140 in 1894 to less than half in ten years; in South Africa the Government of the Dominion formed in 1909 reported a decrease of eleven percent in relation to the total population in the number of lepers during the eight years previous to 1919, when segregation had been more effectively enforced, (Weymouth, 1938). Future developments showed that the leprosy problem still remained unsolved in South Africa as was also the case in India where only 4.7 percent of lepers were accommodated in asylums in 1911, and 7.7 percent in 1921. Village segregation is mentioned as having been practised in New Caledonia in 1901 and in German East Africa in 1912, but no indication is given as to the results achieved. Selective segregation is mentioned in connection with Iceland in 1909 when all 'tubercular' - new classification, 'lepromatous' - cases were to be segregated. The continued rapid decline in that country to 25 lepers, mostly of the benign anaesthetic form in 1932 (Rogers and Muir, 1946), is of interest. In contrast to this achievement, laws passed in Jamaica in 1896 and in British Guiana in 1905 in connection with the compulsory segregation of vagrant lepers, and with the compulsory segregation of lepers in Ceylon where funds were lacking to put the ordinance into practice, could not be expected to have much effect on the control of leprosy in these countries (Weymouth, 1938). In 1906 the great Culeon Settlement in the Philippine Islands was established, but, as has been shown by Rogers (1946), "In 1930 5,000 cases were segregated, yet the number of yearly admissions remained as high as at first."

The third period which I have defined was initiated by the introduction in 1916 by Sir Leonard Rogers of an improved method of administering the ancient Indian remedy, Chaulmoogra oil, until then given orally. Rogers used "a soluble sodium salt or soap in the form of gynocardate of soda" by subcutaneous or intravenous injections, and Muir later used pure Hydnocarpus oil with an antiseptic which became generally adopted as the standard treatment for leprosy. About 1922 Rogers formed a plan for the control of leprosy, the principles of which may be summarised from the British Medical Journal (1946) as follows:-

(1) Leprosy is mainly a house infection.
(2) Children are far more susceptible than adults.
(3) The incubation or latent period is rarely over five years.
(4) The 'neural' - new classification 'tuberculoid' - or non-infective cases, which constitute three fourths to four fifths of the sufferers in most countries, are little if at all infective, so these need not be 'isolated'.
(5) Close contacts of all discovered cases of leprosy should be examined at least every six months for five or more years to enable the great majority of new infections to be traced in a very early and, for the most part, recoverable stage.

Rogers' difficulty was in putting his plan into operation under the system of compulsory segregation which was prevalent at that time, for, "early cases suitable for treatment were all hidden for fear of imprisonment for life." He published a preliminary account of his epidemiological researches in 1922 and his system was adopted in South Africa with effective results (Rogers, 1946). One third of the 2,501 compulsorily 'isolated' cases was released as non-infective in that country in 1925, and this, "with the provision of agricultural colonies and improved treatment soon resulted in most of the admissions being early voluntary cases. In twenty-five years 4,502 patients - two thirds of the known total - had been released recovered, and three fifths of them had remained free from active symptoms for five years and upwards." (British Medical Journal, 1946).

Similar experiences have been recorded from Nauru Island where selective segregation of infective cases was in force; from the Anglo-Egyptian Sudan where all infective cases were segregated in agricultural colonies; from British Guiana where clinics and surveys were employed; from Ceylon where a provincial leprosy control system was adopted with settlements, surveys, propaganda and clinics; and from Nigeria, where, in addition to the provincial leprosy scheme detailed for Ceylon, within the past ten years great popularity has attended the extension and development of local segregation of patients in model villages (Rogers, 1946). This system, started by the lepers themselves and favoured by the healthy community, commends itself particularly to South-East Nigeria where a clan system of local government is in force. It was first encouraged by Dr. Hastings from Uburu Hospital who started a treatment clinic at Oso in the Edda

district of Afikpo Division, Ogoja Province, in 1933, and served six of these segregation villages. Dr. Davey, working at Uzuakoli in the neighbouring Owerri Province, found the same system in operation and likewise encouraged it, making it one of the main activities in his scheme for control and eventual prevention of leprosy. It has since been adopted by the Nigerian Government as an important element in its Proposals for the organisation and development of Leprosy Control in Nigeria (1943).

These activities in widely separated parts of the British Empire required a central organisation for co-ordination and development. This was forthcoming at an early date in the third period I have mentioned with the foundation of the British Empire Leprosy Relief Association in 1924, an event of the greatest importance in the history of leprosy control (Scott, 1939). The functions of BELRA, as it is called, may be summarised from the same authority as follows:-

(1) To encourage the application of improved methods of treatment.
(2) Lepers were to be segregated and sound schemes under this head supported.
(3) The latest information on leprosy was to be dispersed.
(4) Information and statistics were to be collected and further research work supported.

The success with which these efforts have been attended can be judged by the results achieved in the countries mentioned above and further detailed by Rogers (1946). In Nauru Island where 30 percent of the population was infected with leprosy in 1925 and 189 infective cases were segregated in 1928, about one third of that number were segregated by 1937; 11 percent of the infective nodular cases had been released as bacteriologically negative, and, further to illustrate the value of treatment combined with segregation, the number of those suffering from the severer infective forms of the disease had diminished. In the Anglo-Egyptian Sudan where, from a total of 6,500 cases, 4,800 infective, mainly early types had been segregated between 1927 and 1930, 3,679 or 52 percent of the total had been cleared of their symptoms by 1934, and there were few new cases. In British Guiana where, in 1923 only 267 advanced cases had been segregated, 747 were in residence in 1932; 71.2 percent became arrested in 15 years and only 400 patients were in residence at the end of that period. In Ceylon, following the suspension of the Compulsory Leprosy Ordinance under which 577 cases were segregated in 1921, 3,618 cases were known in 1939, 1,031 of them infective,and 71 percent had been discovered at surveys; the numbers started to decline from the year 1941. Rogers (1946) has also recorded the opening of the large Leper Colony under the Church of Scotland Mission at Itu, Calabar Province, South-East Nigeria in 1926, which accommodated some 2,400 patients in 1943; the Leprosy Settlement at Oji River, Onitsha Province in 1936 with 1,187 patients in residence and another 13,000 being treated at satellite clinics about the year 1946; the Leprosy Settlement at Uzuakoli, Owerri Province which, in 1938 had only 1,100 patients in residence (Davey, 1940), but about 1946 had 1,255 resident cases and 11,548 being treated

at 43 outlying clinics. The voluntary segregation and treatment of advanced infective cases in 34 villages in connection with this scheme is also mentioned by Rogers (1946), who records that, in a survey of "7,000 in one tribe not a single advanced case was found; but 40 very early ones detected which should nearly all clear up with out-patient treatment."

The Leper Colony, Itu, is of the Main Territorial type operating on the system described by Muir (1948) as Centripetal; until recently when village segregation was inaugurated, a central settlement at Oji River with clinics, each serving an area within a fifteen miles' radius combined with supposed compound isolation was in vogue in Onitsha Province (Money, 1941,1944); the provincial leprosy system in force at Uzuakoli with a central settlement, clinics and segregation villages has been referred to above (pages 16 and 17). Whatever the merits or demerits of each system, it is apparent that in Nigeria where, in 1931 only about 6,000 cases were under treatment (Rogers, 1946), by 1946 there were 29,390 receiving treatment in these three provinces in the South eastern region alone, where also 4,842 were segregated. For this achievement the assistance of BELRA to the Missions concerned must receive a considerable share of the credit. I have personal knowledge of the value of BELRA in supplying literature, doctors and lay staff and funds for the carrying on of leprosy work of all types in Nigeria. The most important aspect of its work in Southern Ogoja Province was that, in its distribution of Government funds, it enabled the limited activities of the Church of Scotland Mission in treating lepers at Uburu and Edda in Afikpo Division to be developed and expanded into a provincial leprosy scheme on the lines of that in Owerri Province, centred at Uzuakoli. As Uzuakoli is within sixty miles from Uburu by road, it has been possible to maintain contact with the epidemiological activities carried out by Dr. Davey, and later with the research on the sulphone drugs carried out by Dr. Lowe and Mr. Michael Smith, Biochemist, at the BELRA Research Unit there.

The activities of BELRA led up to the Cairo Conference in 1938 with the inauguration of a new classification and its emphasis on segregation and epidemiological work, full data being given for the carrying out of surveys on the lines later followed by Davey. Perhaps the most notable feature of this fourth period which I have defined was the waning stress on treatment as a means of control, noted as predominant at the previous Strasbourg Conference in 1923 (page 14). Hydnocarpus oil and its esters remained "the most efficacious drugs for the special treatment of leprosy" (Rogers and Muir,1946), and as regards aetiology little advance had been made on Hansen's discovery, it being recorded that "the problems of the <u>in vitro</u> growth of the causative agent of leprosy have not yet been solved satisfactorily"(Cochrane, 1947). Cochrane (1947) ascribes the diminished

faith in treatment alone as a means of eradicating leprosy to disappointed hopes on the part of BELRA, including Sir Leonard Rogers and others, when it became apparent that out-patient clinics were not sufficiently effective to this end. It has been shown, however, that Rogers' plan laid stress on selective segregation of lepromatous cases (page 15,(4)), the theory of which is sound enough although open to abuse if not practised carefully. Nevertheless, Cochrane (British Medical Journal, 1947) sounds a timely warning to those who would be over enthusiastic with regard to similar potentialities on the part of the sulphones. Treatment must still be combined with segregation.

As regards classification, the Leonard Wood Memorial Conference at Manila in 1931 altered the older division of types of leprosy from tubercular (or nodular), maculo-anaesthetic and mixed, to cutaneous and neural. The Cairo Conference altered the nomenclature of these two main types to lepromatous and neural, designated by the symbols 'L' and 'N' respectively. An important subclassification was also introduced by this conference, an elaboration, too, of the findings of the 1931 conference, with respect to stage or degree of advancement of the disease, using the symbols referred to and the numerals 1,2 and 3. As nerve involvement is frequently observed in lepromatous cases, the South or Pan-American Classification, decided at the conference held at Rio de Janeiro in 1946, is more rational. By this classification leprosy is divided into two polar forms, lepromatous and tuberculoid with an intermediate group termed "uncharacteristic". Cochrane (1946) points out that this"is a step in the right direction in that they have based their classification on a pathological concept, and linked up the only test that we have which indicates an effective tissue response - the Lepromin Test." The Classification Committee of the Fifth International Leprosy Congress held at Havana, Cuba in 1948, held to the principles of this classification on the grounds mentioned above, clinical, histopathological, immunological and also that it is bacteriologically more perfect, the infective and relatively non-infective types being separated. The last distinction should prove useful in co-relating the findings of epidemiological research workers in various parts of the world and applying them to the control of leprosy. The Cuba Congress retained the symbol 'L' for lepromatous but introduced the symbol 'T' for tuberculoid, and changed the term 'uncharacteristic' to'indeterminate', designated by the symbol 'I'. (Leprosy Review, 1946; 1948).

Two points raised in criticism of the report of the Committee on Epidemiology and Control at the Havana Congress deserve emphasis: first, that it "has little to add to the recommendations of the Cairo Congress", and second, that "No mention is made of the increasing importance of special forms of control, such as village segregation and night segregation". It is otherwise with the report of the Committee on Therapy. Reports from the Rio de Janeiro Conference regarding the value of the sulphones were confirmed, it being affirmed "that the sulphones are the present drugs of election for the treatment of leprosy", and, "The importance of further investigation of

chemotherapeutic agents and methods is stressed." (Leprosy Review,1948).

Having reached this point of progress in the control of leprosy in countries where it is known to be endemic, it is appropriate that we take a parting glimpse at the situation in Great Britain where it is recorded in the British Medical Journal (1949) that, in answer to a question asked in Parliament "Mr. Bevan said he was considering making leprosy notifiable ..... There was one leper hospital in England, run by a voluntary body, which could accommodate 13 cases and had 12 there now. Arrangements were being made to supplement this by another provided as part of the National Health Service."

II. Control.

1. The Plan.

In 1943 the Government presented its Proposals for the organisation and development of Leprosy Control in Nigeria. These were based on Rogers' plan of 1922, on Muir's Report of 1936 and on Davey's practice in Owerri Province. The Proposals stated that the general policy would be that of the Executive Committee of BELRA and that control would be developed on a provincial basis under a Provincial Leprosy Board in each province. A minimum of 200,000 lepers in Nigeria was estimated of whom some 6,000 only were 'isolated'. It should be noted that Muir (1948) has since estimated the number of lepers in Nigeria as 400,000. It was pointed out that the 'isolation' of all lepers in institutions was not a practical proposition, and that it had been necessary to seek an approach which was "less perfect in theory but more possible of achievement."

Other main points in the Proposals may be summarised as follows:-

Settlements were to be organised on a provincial basis. Propaganda and education would be directed to encourage
(1) the voluntary segregation of infected persons with treatment provided;
(2) the granting of land for provincial settlements, daughter settlements, villages, clinics and dispensaries; and
(3) local funds for their support and maintenance.
A Central Leprosy Unit was to be formed with a Senior Leprosy Officer and small staff. These would be under the direction of the Colonial Government in the person of the Director of Medical Services in consultation with the Nigerian Executive Committee of BELRA. The Central Leprosy Unit would control and co-ordinate the activities of the Provincial Organisations in the three provinces, Onitsha, Owerri and Benin. These provinces had been selected to come under the Nigerian Leprosy Service because, it was stated, leprosy work there had been carried out on a provincial basis and had then reached a stage when a division of activities could be contemplated. The Missions which, until then, with the aid of BELRA and Native Administration funds had been responsible for the carrying out of leprosy work in these provinces would continue to be responsible for social, educational and welfare work, and the Government and Native Administrations would be responsible for medical and preventive work administered through or by settlements, industries, clinics and villages. Initially proposed as part of a Five Years' Plan to start in the financial year 1944 to 1945, this organisation was designed eventually to be put on a permanent basis and extended to other provinces. The activities of the Missions in the provinces not included in the Five Years' Plan would remain under the control of a Provincial Leprosy Board in each province, but the object would be to bring them under the Government Scheme.

While it is not specifically stated in these proposals that provinces like Ogoja, excluded from the Five Years' Plan because the work had not then been developed on a provincial basis would come under the Central Leprosy Unit, it should be understood that, as the work was to be financed by Government grants distributed through the Nigerian Executive Committee of BELRA, the policy of BELRA had to be followed according to one of the terms of the Mission's agreement with Government. The Nigerian Executive Committee of BELRA worked in close association with the Nigerian Government in assessing the amount of Government grant which each Mission was to receive, reserving the right to adjust the amount applied for through the Provincial Leprosy Board: the Senior Leprosy Officer, through whom the application was also submitted, had thus some control over the method in which the grant was spent.

In order to indicate what was expected of the Church of Scotland Mission in the area which was eventually allotted to it, at this point it seems advisable to give an account of what would constitute a provincial leprosy scheme. Institutions would comprise a provincial leprosy settlement with, where necessary, daughter settlements, on the construction of which the Leprologist in charge of the area - in provinces under the Nigerian Leprosy Service called the Area Superintendent - would consult with the Director of Public Works and the Senior Leprosy Officer. The Provincial Leprosy Settlement would be the centre for treatment, training, administration and control in the area. As regards treatment, the Government Proposals stated that preference would be given to hopeful cases likely to respond to treatment and so enhance the popularity of the new institution: later, lepromatous types would be admitted and those with other diseases requiring special treatment and hospitalisation; or women in pregnancy, mothers and the newborn uninfected children of leprous parents. Clinics would be established throughout the Province in each clan with the purpose of serving primarily as centres for propaganda and the treatment of non-infective cases. Patients attending these clinics would form a nucleus for the formation of clan segregation villages. These are vital for the purpose of control. The aims of these villages would be the segregation of infective cases, treatment at a clinic in or near the village and the construction of villages which would be a model in sanitation, hygiene and housing. Surveys would be carried out by the Leprologist, assisted by his trained staff, as a means to ascertain the incidence of leprosy in each area and with the purpose of examining contacts, discovering cases of leprosy and encouraging them to come to the clinic. These surveys would be repeated at frequent intervals by leprosy inspectors, well educated Africans trained at the Settlement, one of whom would be stationed in each clan. Leprosy inspectors would also be concerned with the supervision of treatment at the clinic where one of them would be in full charge in the absence of the touring unit from the Settlement. Admission of new patients would be the responsibility of the doctor at the Settlement or with the touring unit, but the doctor, or leprologist, would be relieved of routine duties in the matter of control by these devolving on the leprosy inspectors. These duties would include

securing regular attendance of patients at the clinic, the follow up of patients on parole and other preventive work and propaganda in the clan. Training would include instruction and supervision of the activities of healthy African staff and intelligent and educated patients employed as assistants. The former would comprise a permanent cadre of nurses, interpreters, clerks, laboratory assistants, leprosy inspectors and supervisors of agricultural and other activities of the patients, employed on standard terms of service: the latter would comprise a temporary cadre of nurses, clerks, cleaners, ward servants and labourers, receiving a maintenance allowance. Administration would include the supervision of all the activities of the Scheme and the carrying out of research. These activities would be gradually introduced and developed by the Missions in provinces such as Ogoja, and all these activities, including also social educational and welfare work, would remain the responsibility of these Missions for the duration of the Five Years' Plan at least. Social, educational and welfare activities would include the foundation and management of homes for helpless and incurable lepers, homes for new born uninfected children of leprous parents, and homes and schools for uninfected children of leprous parents with no relatives to assume the responsibility of caring for these children.

The Missions remaining outside the Nigerian Leprosy Service were, in Calabar Province the Church of Scotland Mission and the Qua Iboe Missionary Society and in Ogoja Province the Church of Scotland Mission and the Roman Catholic Mission. Leprosy work had not been started on a provincial basis in Calabar Province, there being two settlements of the Main Territorial type operating on the system which Muir (1948) has designated centripetal, that is, they admitted patients from far and near for treatment, no other efforts being made to control or prevent the disease. These settlements are the Leper Colony, Itu, on the Cross River and the Leper Colony, Etinan in the south-west of the Province, under the auspices of the Church of Scotland Mission and the Qua Iboe Missionary Society respectively. The position with regard to Ogoja Province was different. In Afikpo Division leprosy work had been started under the Church of Scotland Mission by Dr. Hastings in a small settlement or leper camp at Uburu in 1927. A few acres of land had been secured about a mile from the Mission Hospital where the patients built little 'bee-hive' huts with round mud walls and grass roofs of the type common in the district, and in 1933 a treatment and dispensary building of permanent materials was constructed with the assistance of funds provided by BELRA. Finding that lepers had segregated themselves in a village in the Edda area Dr. Hastings opened a clinic for them at Oso Edda also in 1933. This clinic eventually served six segregation villages in the surrounding district and another clinic was started in one of these segregation villages in 1943. The village in which this new clinic was started is called the Owerri Edda Segregation Village, a name apt to be confused with the neighbouring Owerri Province with which it has no connection whatsoever apart from the similarity of methods of leprosy control which were applied. Dr. Davey's example in transforming these leprosy segregat-

ion villages into models of sanitation, hygiene and housing in Owerri Province had, however, stimulated us in our efforts to open up communications into these villages in Ogoja Province with the same end in view. Other advantages in more intensive supervision, and increased facilities for treatment especially of ill and disabled patients are apparent. In 1944 clinics were opened at Okposi, Akeze and Afikpo, but the last had to be closed in 1945, the patients then attending at Owerri Edda, because the additional clinic was too much for the doctor to undertake single handed along with the ever increasing work of the general hospital at Uburu. Before the acceptance of the grant from BELRA in the financial year 1946 to 1947, a nominal fee was charged from each patient when treatment by hydnocarpus oil or novarsenobillon was administered, otherwise the cost of African staff's salaries, transport and all accessary treatment was covered by profits from the general hospital. Since the acceptance of the grant no charge for any of the amenities of the service has been made from patients. Leprosy work in Ogoja Province, then, had already been started on a provincial basis, but development was limited by the fact that the doctor in charge was primarily responsible for the general hospital, and no increase in the leprosy work could be contemplated until a whole time leprologist had been appointed. Large waiting lists of patients who could not be admitted until this objective was accomplished, the advent of treatment having greatly encouraged the popularity of village segregation, made it increasingly urgent of attainment. The fact that such encouragement by treatment had first been given in this area, but that development had lagged behind that in other provinces where increased staffing had been available although commended by Muir (1936), tended to the same end. Declaring the impossibility of "the effective isolation of all infectious cases in a central provincial settlement," Muir, following a visit to the Oso Edda Clinic remarked that, "the clan settlements established some years ago in the neighbourhood of Afikpo seem to point to a possible solution."

To consider the possibility of expansion of leprosy work under the Church of Scotland Mission in Ogoja Province an unofficial meeting was held at Uburu in 1944, attended by the Church of Scotland Mission doctor at Uburu, Government administrative officials in the Province and the nearest Government Medical Officer. This was followed by the first meeting of the Ogoja Provincial Leprosy Board at Abakaliki in January, 1945. The Provincial Leprosy Board is in charge of initiation, siting, development and co-ordination of leprosy work in a province, besides deciding the amount of grant to be applied for to the Nigerian Executive of BELRA in the case of each Mission. The Resident of the province presides at the meeting and on the Board there are also two representatives from each Mission engaged in leprosy work in the Province, all district officers and medical officers in the province,

a representative of the Agricultural Department and the Provincial Engineer. Until the year 1943 the only Mission engaged in leprosy work in the Province had been the Church of Scotland Mission at Uburu and Edda in Afikpo Division. About that time the Roman Catholic Mission commenced activities in the northern part of the Province and had continued to operate in that area. At this first meeting of the Provincial Leprosy Board it was decided to divide the Province of Ogoja into two areas for purposes of leprosy treatment and control and in so doing to hold to administrative boundaries between the north and the south; the Roman Catholic Mission being granted the Divisions of Abakaliki and Ogoja and the District of Obudu in the north and the Church of Scotland Mission being granted the Divisions of Afikpo, Obubra and Ikom in the south. These proposals were accepted by the Nigerian Executive Committee of BELRA on 23rd. March, 1945. In May, 1945, Dr. Hastings submitted a Report which outlined the policy to be adopted by the Church of Scotland Mission and detailed the basic equipment required. This was followed by a request from Government for financial estimates which was submitted on 7th. January, 1946. A modification of these estimates offering a capital grant of £120 for clinic equipment and a recurrent grant of £950 annually for medical and general expenditure excluding the cost of European staff, was accepted by the Church of Scotland Mission Council in October, 1946, and at the same meeting I was located as leprologist. This location was confirmed by the Foreign Mission Committee in Edinburgh in December, 1946.

I discussed plans for the development of the Ogoja Leprosy Scheme with Dr. Muir, then the Medical Secretary of BELRA in London. In Lagos I interviewed the Director of Medical Services for Nigeria. For the greater part of my period in charge of the Scheme I have benefitted by the advice and co-operation of Dr. Hastings, who, with his long experience as pioneer in leprosy work in Afikpo Division and in his capacity as Honorary Medical Adviser to the Ogoja Provincial Leprosy Board, is in a position to assist greatly in directing the campaign for leprosy control. Each of these three advised me to make the development of the Settlement a primary concern. The Director of Medical Services encouraged me to present plans and estimates for a capital grant for buildings in the Settlement and granted immediate permission to acquire a kitcar for the Scheme for which a grant of £500 had already been received from Government. Presentation of plans and estimates resulted in the first instalment of a capital grant to the amount of £2,000 being given in the financial year 1947 to 1948. An annual grant for transport amounting to £220 was secured in the same year from the Native Administrations of the three Divisions concerned. The annual grant from BELRA of £950 was raised to £1,250 in the financial year 1949 to 1950.

2. Development and extension of Existing Work.

Within three months of taking up my appointment as Leprologist I had visited the Native Authorities of all the clans in Afikpo Division, two in Obubra Division and the Group Council of Ikom Town. From all these I received offers of land. This, from chiefs who hold land as in sacred trust from their ancestors, parting with it always reluctantly and only for the most pressing reasons, is sufficient proof of the demand for this work. That being so, it is also understandable that some have found it impossible to maintain their offers owing to disputes with local or neighbouring landowners. Others have not agreed to comply with the terms of our agreement with Government (1946) regarding the construction of clinic buildings and patients' quarters, "by the patients concerned and/or the local Native Authority," and in areas where patients have not yet come forward this is a real difficulty. The number of clinics has been increased from five to eleven since I took charge. Seven new clinics have been started, the one at Oso Edda having been closed to form three others in or near the villages it had served; and the new clinics have, in their early stages, required close direct personal supervision which, with the others, has entailed travelling on five days in the week. Much time is consumed in this way, and until the European staff can be increased, additions made to the existing African staff and those already employed more intensively trained, it would be inadvisable to increase the work by opening other centres for segregation and treatment. I consider that when this is done it will also entail devolving more of the routine work on African staff and initiating a system of less frequent but efficient supervision by the European staff.

Cochrane (1947) has pointed out that the early hopes, following the introduction of treatment of leprosy by injections of Hydnocarpus oil and its esters, that treatment would control the disease have not been fulfilled. He concludes, "It was later gradually accepted that the newer methods of treatment were not producing the results anticipated and that the out-patient clinic would fail to control the disease unless associated with schemes of segregation. Thus arose the idea (which has never been completely worked out) of village segregation." My experience of clinics without village segregation closely associated with them confirms this statement. They are a danger to the community in that they encourage infective patients to attend from their homes and the effect of the treatment referred to above is too uncertain and at best too slow to allow us to consider control by this means alone. Neither is treatment at clinics satisfactory because the requirements of ill or disabled patients, who are unable to walk the distance to the clinics, are neglected. Holding as I do that it is the working out of the idea of village segregation which the Ogoja Leprosy Scheme has set out to achieve and that control must be centred in a provincial leprosy settlement for which early plans must be made, I found myself at variance with a ruling of the Provincial Leprosy

Board, Minutes (1944). The minute referred to states: "The Board recommend that the policy of the new leprologist should be to set up clinics as his first consideration, and when the latter were established they would consider the best sites for settlements in the north and south of the Province." At the Provincial Leprosy Board meeting in July, 1947, with the support of the Honorary Medical Adviser, I stressed the importance of the foundation of the Settlement as a first priority, and this was then agreed. I also suggested that in starting clinics, preference should be given to those clans which had already offered segregation village sites, and this was accepted. (Minutes, 1947). I deplore the system already referred to (page 17) as in vogue in Onitsha Province (Money, 1941) whereby reliance is placed on the Settlement and clinics alone to control leprosy, and welcome the introduction of the principle of village segregation in a later publication (Money, 1944) in reference to the same Province. For, in dealing with a problem so vast as that of the control of leprosy in South-East Nigeria, settlements without local village segregation are likely also to prove a failure. Again to quote Cochrane (1947): "It is impossible to state very definitely how far either institutions or out-patient clinics have helped to control the disease. Out-patient clinics, treating a few dozen or a few hundred cases, but not connected with scientific work, contribute little or nothing towards the control of leprosy. Institutions, in so far as they segregate infective cases and act as centres of training and propaganda are undoubtedly of great value in the general anti-leprosy campaign, but, apart from this, it is doubtful whether they can make any adequate contribution to the eradication of leprosy unless they are linked with a comprehensive scheme of prevention."

From this it would appear that the Provincial Leprosy Scheme is the solution he envisages, and, from his conclusion quoted previously, that the idea of village segregation has presented itself as an alternative to reliance on treatment alone which is at least worthy of experiment in the problem of control. The aim of Ogoja Leprosy Scheme is the control and eventual prevention of leprosy in Southern Ogoja Province. If the experiment is successful it might be anticipated that a precedent would have been set for work under similar conditions elsewhere and other far reaching results, besides the prevention of leprosy might follow. In these the function of segregation villages as models in sanitation, hygiene and housing becomes apparent, for, as Davey has acknowledged (1942), "Leprosy control is a key problem, with which are bound up all those sanitary and economic problems the solution of which seems so remote in Southern Nigeria." Crocker (1947) has maintained that, "Starting from the base of the self-subsistent peasant you set all your departments going on the essential tasks!" The patients in segregation villages are self-supporting farmers and agricultural workers, so it would appear that in starting with them - and they are much more ready to follow instruction than healthy villagers - we have administrative as well as medical grounds for making the practice of village segregation the essential element in

our scheme for control.

The British system of administration in South-East Nigeria makes the Clan or village group the administrative unit in native affairs. By carrying out segregation on a clan basis we are thus in a position to co-ordinate our activities with those of the administration while reaping the advantage of operating within a self-contained native unit, aiming at a system of local control in a limited area where, as in the matter of segregation, compulsion comes from within the clan itself. The clan must be enlightened on the reasons for our activities, so the method of approach to the clans in Afikpo Division was as follows: it was first ascertained from patients in the settlement where a demand for local treatment and segregation was likely to exist. The Clerk of the Native Court of the clan chosen was then written to and a meeting with the Clan Council arranged. At this meeting it was explained to those present how we think leprosy is conveyed and how it can be controlled, this being a useful opportunity for propaganda; then offers of land for a clinic and a segregation village were solicited and requests for surveys were considered. With those clans which were able to maintain their offers of land and build a clinic, I made a point of insisting that land be offered for a segregation village before treatment was started at the clinic.

The first new clinic to be opened was at Ukawu, where, on the same site, land was secured for a segregation village and building of houses has started. The second was at Oshiri and the third at Itigidi, all these clinics being started between April and August, 1948. At Oshiri land surrounding the clinic building was given for a segregation village and on this land the building of patients' houses has now been started. At Itigidi only a clinic site was secured initially. Land for a segregation village for the Agbo area which includes Itigidi had already been given on the Agbo side east of the pontoon crossing of the Eastern Aboyne and beside the River, but this site was found to be too far removed from the majority of the Clan. A site nearer to Itigidi has since been offered.

Early in 1949 a new segregation village was opened at Apojo between Akpoha and Afikpo. This was primarily due to a break away of one division of the Amaseri Clan from Owerri Segregation Village where they had been segregated along with Edda people, and this was welcomed because the Owerri Clinic had enrolled 428 patients who were attending for treatment and staying in the village in December, 1948. 248 patients remained at Owerri in August, 1949, so there is now room to increase the numbers there again, up to 300 patients being a manageable number at a clinic. The new segregation village was also welcomed because there had been difficulty in obtaining a site for a clinic and segregation village for the Afikpo Clan, and the Akpoha Clan had previously expressed itself willing to combine with another clan: now these three clans proposed to combine in forming a segregation village on the Apojo site. Here village planning could be started from the beginning, and full advantage can now be taken of the fine natural amenities of the site to make the Apojo Segregation Village a model in sanitation,

hygiene and housing in accordance with the Government's Proposals(1943).

One task remained before I could consider that we had reached the limit of our present resources for development and extension of the existing work. It was one which had occurred to me when, in my early years at Uburu I had deplored the backward condition of the segregation villages of Ndi Chuku, Ama Oso, Ezi Edda and Ndi Iba in the Edda area, and which had urged me in 1946 to enlist the assistance of the District Officer, Afikpo, who made Native Administration funds and supervisors available, the patients acting as labourers, to start the work of making roads into these villages. Work was resumed on these roads, one leading to Ndi Chuku on the north and the other to the three villages on the south of the main Afikpo road, the construction of bridges and culverts of temporary materials being especially aimed at in 1948; the patients eagerly complied and the task was accomplished early in 1949. Three new clinics were built by the patients, one in Ndi Chuku, one in Ama Oso and one between the villages of Ezi Edda and Ndi Iba to serve both villages. In this way the Oso Edda Clinic which, at the end of 1948 had 498 patients, was divided into three clinics of reasonable size with room for new admissions. Situated at the side of the main Afikpo road, the Oso Edda Clinic had been a convenient centre for six segregation villages,each within a radius of about three miles; before communications were opened up, numbers were manageable and supervision had to be carried out by the doctor in the time available from his responsibilities at the Uburu general hospital. A treatment clinic had been started in Owerri Edda Segregation Village as described (page 22), and another small village from which patients used to attend had been closed, the patients finding accommodation in one of the four remaining villages which have since been 'opened up'. The importance of this process will be realised from what has been stated in connection with the Owerri Edda and Apojo Segregation Villages (pages 23 and 27) the aim being to intensify supervision of segregation and treatment and create model villages. On our present system all clinics are visited weekly by the touring unit from the Settlement, the Leprologist accompanying it as frequently as possible, usually weekly, but in the case of the four villages referred to, on alternate weeks during the rainy season. The reason for this difference is that the roads to these villages are not yet in a passable condition for motor traffic in the height of the rainy season when they are often soft and flooded. Then the villages have to be visited on bicycle, the motor lorry being left on the main road; and one large clinic on the north and the other two on the south of the main road have to be supervised fortnightly by the Leprologist, experienced African staff carrying on the work when he is not there. It should be added that Government grants have been applied for with a view to constructing roads with improved surfacing and culverts of more permanent materials. Assistance has already been given by Government to improve conditions in these four segregation villages: the Rural Water Supply Authorities are digging and constructwells in them so that an adequate supply of pure water even in the dry season will be assured, solving what was formerly a serious problem and a source of contention between the healthy villagers and the patients.

Other sites in Afikpo Division have been offered as follows:- At Ikun five miles north of the Native Court and near the main road for a segregation village; in the Enna district, near the main road and one mile north of the market place for a clinic, a previous site offered for a village and clinic having been considered to be unsuitable; at Ndi Okam about three miles north of the road between Unwana and Ebo-Unwana, three miles from Ebo-Unwana, for a segregation village to serve the Unwana, Ebo-Unwana and Ebara Edda Clans; for the Ishiago Clan, near to and on the east of the railway, about one mile south of Ndeaboh Station; at Akeze where a clinic is already in operation, a site for a segregation village about five miles north of the clinic and an alternative site about two miles north of the clinic. The former site is difficult of access and the latter is considered to be too near healthy peoples' dwellings, so somewhere between the two sites might suffice. In three clans only, Isu, Onicha and Ugulangu, has it not been possible to secure a permanent offer of a suitable site for a clinic or segregation village in Afikpo Division. The Settlement at Uburu accommodates many from these clans as in-patients, and others are near enough and of suitable type to have been allowed to attend the Settlement Clinic as out-patients, there being no marked geographical, administrative or ethnological barriers. It is doubtful therefore, if leprosy control would be made more effective by local treatment and segregation in these areas.

There remains the problem of leprosy control in Obubra and Ikom Divisions. In considering this I think it is important that we bear in mind that no leprosy work has yet been done in either of these areas, and what has taken twenty-two years to accomplish in Afikpo Division is not likely to take much less than half that time, even with a doctor whole time as leprologist in Obubra and Ikom. Again, taking into account the wide distances to be covered owing to the insuperable natural barriers of rivers and mountains between Ikom and Obubra and, to a less extent between Obubra and Afikpo, nothing short of separate daughter settlements for Obubra and Ikom Divisions in accordance with the Government's Proposals (1943), would be satisfactory as centres of leprosy control in these two areas. Although on account of staffing and financial difficulties this ideal might be difficult to attain, it is nevertheless something to be aimed at, and an effort should be made to arrive at some measure of control in these divisions within the next ten years however remote that prospect seems at present, and repeated representations should be made to Government with this in view.

In the meantime my proposals for Obubra Division would envisage a start being made on the site offered at Adun on the Cross River where a considerable area of land has been offered on what is a peninsula in the dry season and an island when the river rises in the rainy season. I would suggest that one or both of the well educated patients from that Division whom we are training as nurses at Uburu be sent to Adun when a clinic and segregation village can be started

there, and that as much supervision as possible be given from Uburu. The approach by road from Uburu to Itigidi and over the pontoon crossing to Ediba, Ugep and Adun Rest House would mean the touring unit staying there over night. An alternative route is from Abomege by Ikwo and Imogo, and this route will be shortened by the completion of a road already partly constructed between Abomege and Ikwo, thus avoiding the detour by the Abakaliki road to Ikwo: the journey, then, to Imogo and by canoe to Adun and back, need not occupy more than one day. This would allow of supervision at least once a month which, with an intelligent, well trained and educated staff in residence, would be the best that can be done in the circumstances and might prove to be sufficient. Thus a start could be made in Obubra Division.

The position with regard to Ikom Division, more urgently than in Obubra Division, is that another doctor is required to start a settlement and carry out provincial leprosy work there. In default of this, that is, presuming as seems likely that staff shortage continues and funds for the construction of a settlement at Ikom are not forthcoming within the next five years, the only possibility of a start being made would lie in the location to Ikom of a trained and experienced member of the African, non-patient Uburu staff, to supervise the construction of a central segregation village and the administration of treatment there. The site already offered at Ikom would be a suitable one for this purpose. As Ikom is 154 miles from Uburu by the shortest route, only occasional supervision could be given under our present system in Afikpo Division and with our present resources of European and African staff and transport facilities, and careful consideration would have to be given to the question as to whether supervision of this nature would be effective and fair to the patients. With an intelligent and trustworthy man, whom I have in mind, placed in charge at Ikom, I think this might suffice, and this proposal is certainly the best that can be contemplated meantime.

3. Development of the Settlement.

I consider that the Nigerian Government's apology contained in its Proposals (1943) to the effect that the Provincial Leprosy System is less perfect in theory than the Main Territorial System is unnecessary. I have referred to Rogers' plan (page 18) as sound in theory"although open to abuse if not practised carefully". It has also been shown that Rogers' plan which enjoins the selective segregation of lepromatous cases has been applied to Nigeria in the Government Proposals (1943),(page 20). If "three fourths to four fifths of the sufferers in most countries"are non-infective (page 15, (4)), surely it is more perfect in theory not to segregate them. If all should be segregated surely it is as perfect in theory to segregate some in villages and reserve the Settlement for special cases. It might be asserted that segregation in villages near the patients' homes is less perfect in theory, but if it is acknowledged, as seems likely, that leprosy is most frequently conveyed by prolonged, close contact (Rogers, 1946), opportunities for which are possibly most abundant at night (Cochrane, 1947), then this argument can hardly be maintained without reference to difficulties in practice.

Assuming that the majority of patients in the tuberculoid group are non-infective, the fact that four fifths of the sufferers are in this state is borne out by my findings on survey in the Agbo Clan, Afikpo Division, where the proportion of the types had not been modified by treatment. * Approximately 81 percent of 112 lepers were found to have tuberculoid, 16 percent lepromatous and 3 percent indeterminate types of leprosy. No exact figures for the population of Afikpo Division are available, but, in correspondence with the District Officer, Afikpo (1949), I have ascertained that, from the number of taxable males in the Division, the population may be calculated to be approximately 180,000. I regard my estimate of leprosy incidence in the Agbo Clan of 36.8 per mille among a total of 3039 persons † examined as representing a minimum for Afikpo Division as a whole. That this is likely to be the case is confirmed by my estimate on survey in the Oso Edda Clan of 90.2 per mille among a total of 1064 †† persons examined and where most lepers are known and segregated, and by the estimates quoted by Davey (1942) for the neighbouring Owerri Province already referred to (page 2). Making an estimate of 40 per mille there would be 7,200 lepers in Afikpo Division of whom 1,440 might be infective and would have to be segregated. Were it possible to persuade all these infective cases to come into a settlement, I would still regard it as inadvisable to deal with such large numbers in a limited area for reasons to be given. The idea of segregating all of 7,200 lepers in a settlement is, from my experience of the habits of the people, the difficulty of acquiring land and finance,

* Table IX, page 76. † Table VIII, page 76. †† Table XII, page 77.

entirely out of the question. I therefore cannot agree that the Provincial Leprosy System is "less perfect in theory" than the Main Territorial System, but heartily corroborate that it is "more possible of achievement."

Muir (1948) has designated the two main systems of dealing with leprosy Centripetal and Centrifugal. The advantages of the former, featuring the Main Territorial type of settlement, over the older type of institution in which sometimes only a few hopeless cases were segregated, is recognised. A leper with any type of the disease from anywhere in the country or in neighbouring countries can come for admission to a settlement of this type. There he receives treatment and engages in various activities for his own benefit and for the good of the settlement community. While in the settlement he is segregated and if he is of the infective type this is of advantage to the community from which he comes. "Cured" lepers return to their homes and enhance the popularity of the settlement, but it is difficult to imagine how, in a primitive community such as Nigeria with 400,000 lepers (Muir, 1948), even a great number of these settlements accommodating up to 5,000 patients of all types but waiting on infective patients to infiltrate from a wide area could ever tackle successfully the problem of leprosy control. While even a few infective cases remain in their homes they are a danger to the community.

Objections to the Main Territorial type of settlement may then be stated as follows:-

(1) It attempts too much: settlements accommodating over 1,000 and up to 5,000 patients, apart from economic problems, become unwieldy, and then their main advantage of continuous individual supervision of patients lessens. The enforcement of effective segregation becomes difficult, and what Muir (1948) has described as a "diffuse margin" is set up, "merging with the outside area which tends to have unusually high endemicity and incidence." My findings on survey in the Oso Edda Clan where local segregation in several villages was carried out, encouraged only by treatment at a communal clinic over a period of sixteen years, demonstrate that in this instance and under these circumstances no "diffuse margin" of the nature above referred to was found. On the contrary, in seven villages of this Clan, two within three miles of these segregation villages and the others nearer, I found among 1064 persons examined only one definite case of tuberculoid leprosy in a woman who had come recently to the district and not a single case of the infective or lepromatous type. (p.p. 74 and 77).

(2) Infective patients come from a wide area and may infect others on the way. Muir (1948) has elaborated this point, stating that the leper "travelling through areas where he is unknown is a greater danger to his possible contacts than when he remains within his home." Rogers' (1946) conclusions from an analysis of 700 cases that leprosy is a house infection conveyed most frequently by prolonged, close contact has already been referred to (pages 11, 15 and 31). I have made a similar analysis of 100 cases of patients who admitted contact

of any kind from a series of 384 cases interogated. 90 of these 100 cases had contact with a leper relative, usually a close relative staying in the same compound according to the local custom; 5 had been in contact with a leper who stayed in the same compound, and of the remaining five, two had been in contact with a friend and neighbour in the same village, one had an uncle a leper who died before his birth, one had worn a leper's clothes and one had bathed in a pool where a leper also bathed. The high percentage of relatives involved where contact is admitted makes it appear likely that long, close contact as staying in the same compound as a leper is an important factor in transmission of leprosy, but there remains a large number of cases, 284 in my series, where no contact is admitted and where contact with infective cases not suspected of having leprosy may have taken place. Accordingly, this must be acknowledged as a possible disadvantage of the Main Territorial Settlement, as must also another disadvantage presented by Muir (1948) that, "there is a tendency for patients to settle more or less permanently in the neighbourhood of a leprosarium." Here, then, we have another argument for local segregation.

(3) It does not deal with the problem of leprosy control in a defined area, the emphasis being on the treatment of those who are admitted without discrimination as to type of the disease to the neglect of those infective cases who remain at large and are a danger to the community. This, I think, is the most important objection of all, and to it might be added the criticism that segregation is not effective, patients returning to their homes for varying periods on vacation when they again become a danger which should not exist if adequate facilities were provided for local, especially night segregation. Furthermore, patients are sent home with certificates stating that they have been found to be "symptom free", and where homes are at a distance from the settlement there is little tendency to regular re-examination and renewal of these certificates, as a result of which the disease may have recurred for some time before it is suspected. In contrast to Macdonald's (1948) description of "Rehabilitation" in a Leper Colony other objections which arise under the same head would include the change of environment away from tribal and, in the case of children, parental control; the futility of Europeanizing the patients in their recreations and interests; the training of patients in specialised, for example electrical engineering activities which they cannot practise when they return home, demonstrating a disregard for the important period of rehabilitation when they go back to their farms.

The disadvantages of the Provincial Leprosy Scheme or Centrifugal System with a central provincial Leprosy Settlement have emerged in my discussion of the development and extension of existing work, the main disadvantage being the distances to be covered in supervising work that involves many clinics and villages scattered over a wide area. It is believed, however, that with sufficient staff and moderate funds these difficulties can be surmounted, and that the

results of organised scientific work will justify the effort. To those who might, with misguided enthusiasm, proceed to apply this system to other continents or even in other parts of Africa, it may be fitting to recall Muir's (1948) reservation, "that the Eastern Nigerian system is dependent for its success upon the integrating power of the tribal system, and the remoteness of the region from large industries and other influences which would cause considerable movement of population and break down the power of the chiefs and elders over their tribesmen." This statement also may be taken to emphasise the importance of proceeding with this system, favourable as it appears in the campaign to control leprosy, with a view to prevention of the disease before these unfavourable influences assert themselves.

At the Fifth International Congress in 1948 it was decided that the word "leper" be abandoned and that a person suffering from leprosy be designated "leprosy patient". Underlying the change is the idea of stigma attaching to the word as applied to a person without at the same time recognising that he is suffering from a disease and under treatment. In the absence of treatment, presumably "leprosy case" would be the term of choice; but the distinction between "leper" and "leprosy" appears to me to be fine, and one the elaboration of which has doubtful advantages. Because of the opprobium attached to the word "leper" in English and in native dialects, it is, however, more kindly to avoid it where it can be dispensed with as in the term used to designate an institution for these sufferers, the use of which would be a constant reminder to them of their hard fate. The terms most commonly used in Nigeria are "Leper Colony" and "Leprosy Settlement". I prefer the term "Leprosy Settlement" used in the Nigerian Government's Proposals (1943), and which unlike Muir (1948) I do not associate with the word "Penal" but rather with "Community", suggest- as it does to me a willingness to settle in a community and adapt our methods to the ways of the people. The word "Colony" suggests the opposite. The qualifying word should, of course, be "leprosy"; for it is a settlement dealing with a disease not a leper as in "Leper Colony", a term which could only be justified from long misusage. The awkward hybrid "Leprosarium" recommended by Muir (1948) and "Leprosy Sanatorium" used in connection with the Institution in Chingleput, South India, are terms which would not be likely to come into general use in a community which is mostly illiterate: for this reason and because it omits reference even to the disease, the abbreviated form "Settlement" should be most acceptable locally.

4. The Site at Uburu.

At a meeting of the Ogoja Provincial Leprosy Board (Minutes, 1947) I presented my plans and proposals for a leprosy settlement at Uburu. These were accepted. The advantages of the site at Uburu are as follows:-

(1) It is healthy as has been proved by its use as a site for a leper camp for the past twenty-two years.

(2) A substantial treatment and dispensary building has already been erected on the site, representing a saving of some hundreds of pounds in the construction of settlement buildings.

(3) Proximity to the Uburu general hospital allows of supervision of the Settlement by one of the doctors there in an emergency, especially acceptable when there is only one doctor at the Settlement.

(4) It is near to but not on the main road, and the nearest point on the land offered for a settlement is at least a mile from the Uburu town market. There are pontoon crossings over rivers on each of the three roads leading out of the area, but it is near enough to both rail (twenty miles) and Cross River (27 miles) to ensure that transport charges will be reasonable; being quite well situated in this respect. No part of Afikpo Division is further than fifty miles distant by road. Uburu is also situated at a reasonable distance from the Roman Catholic Mission Leprosy Settlement at Abakaliki.

(5) The tradition of successful treatment at Uburu makes the enlargement of the existing settlement a wise choice. Leprosy patients in Afikpo Division already regard it as the centre for special treatment, training and administration. It is in the heart of an area where leprosy is known to be prevalent and where leprosy consciousness and confidence in the methods of treatment and control are present from long use. My experience in visiting the Clan Councils in Afikpo Division has confirmed me in the opinion that here, where the method of segregation in clan village settlements originated, has become so popular and proved such an unqualified success, a phenomenal opportunity presents itself for demonstrating that leprosy can be controlled and eventually eradicated by this method.

Possible objections to the site are these:-

(1) The site is not central for the Divisions of Ikom and Obubra. But it is central for Afikpo Division where the most active and concentrated efforts towards leprosy control and prevention are likely to be made in the near future. Separate daughter settlements are envisaged for the other two Divisions (page 29),, the central Settlement at Uburu being the centre for initiation, development and co-ordination of leprosy control in Southern Ogoja Province.

(2) Wood and water are not abundant and the latter is in short supply in the dry season. With the co-operation of the Government Agricultural Department arrangements have been made for the planting of Gmelina arborea which should be ready for cutting for firewood in six years. There is also a dense forest of wide extent on the south bank of the Asu River two miles from the Settlement where an ample supply of

firewood is available. Water from the central stream which runs through the Settlement land might be conserved and form a reliable source of supply even in the dry season. With the assistance of the Government Rural Water Supply Authorities a well has been dug in the Settlement near the treatment building, and it will be completed when materials for lining and covering are available. The digging of another well nearer to the proposed African and European staff quarters is planned.

(3) Land offered for the Settlement belongs to two Clans, Uburu on the west and Okposi on the east side, between which a boundary dispute has existed for a long time. But representatives of both Clans have offered to give a portion of the land in dispute for use as a leprosy settlement; the Resident, Ogoja Province, has made a decision regarding the boundary dispute, and this decision has been upheld by the Commissioner for the Eastern Provinces: the Resident has advised us to await the outcome of an appeal in connection with a similar dispute between members of the Okposi Clan, when, he writes, "a final decision can be reached." A definite offer of at least 363 acres of land has been made by the Uburu Clan, and, in view of the Resident's encouragement it seems probable that most of the area originally offered to us and estimated by the Native Administration Surveyor at 872 acres may be negotiated for when formalities have been completed.

5. Settlement Buildings and Activities.

While waiting on the outcome of these negotiations which must precede the signing of the lease, the permission of the landowners has been obtained for the erection of essential temporary structures, expenditure on which has, of necessity, been kept to the minimum. These structures include a house for the Leprologist, built in native style but more commodious than the patients' houses with kitchen and boys' house, a watchman's house and three latrines, one for each of the dwellings, situated to leeward of the dwellings. Apart from the exigency of economy, it was hoped that by planning this compound on simple hygienic and sanitary principles and using native materials for building, to set an example which could be easily followed by patients and by healthy villagers. Latrines are holes dug ten to twelve feet deep and three to four feet wide, covered with cut tree branches and mud moulded before dry to leave an orifice about one foot in diameter; surrounded by mud walls and with a roof of palm or bamboo sticks covered with grass thatch or woven palm branches with leaves. Patients' latrines are similar in structure except that they are arranged in rows of four all covered by the same roof, with mud walls dividing one compartment from the other. In planning new houses for the patients I have also thought it wise to preserve the 'bee-hive' type of structure to which they are accustomed and for which materials are readily available locally. This type of house has also been found to be more economical and more resistant to the weather than the oblong type of house popular in some of our segregation villages. The

Government specifications for houses of patients living in leprosy settlements or villages are 60 square feet of floor space to each patient with windows one eighth of the floor space and walls eight feet in height. Leaving a reasonable margin outwith these specifications, a round house for two patients is planned with a diameter of 14 feet and two windows each 3½ feet square. The original huts were built in streets, but the compound arrangement is more acceptable locally, and this plan is proposed for patients' houses, having already been followed by Dr. Hastings in the erection of a women's compound: this consists of a quadrangle of ten houses joined by walls and with a door which can be closed at night, the compound in this instance communicating by a narrow walled passage with a two hole latrine of the type I have described.

Patients are encouraged to practise any crafts commonly useful in their villages. One of my staff was trained as a carpenter before being employed as a medical orderly, and he has been useful as an instructor. A set of carpenter's tools has been provided with a view to the construction of doors and windows for the patients' houses and other necessary equipment for the Settlement. The principal occupation is work on about twelve miles of the main road between Okposi and Mpu, and for this work the Native Administration pays £264 annually. This amount is divided among the patients who receive payment at the rate of about sixpence daily for working five hours on four days of the week. Besides the routine work of keeping the main road in repair, a new road has been constructed into the Settlement, about three miles in length, to join the main road on the Okposi side as this is the most convenient approach.

The question has not yet arisen whether Uburu shall become a large agricultural settlement which aims at being at least partially self-supporting on a communal basis. Davey (1942) deplores this system on the ground that, "There can be no room for highly infectious cases weakened by their disease, for deformed cases, or for representative numbers of women and children." I agree on similar grounds that such a system might be conducive to the exploitation of patients' labour in an effort to cover expenditure, an aim which, if not achieved as on the failure of crops, might end in disaster, an issue not unlikely in connection with institutions where no great capital is available. Consequently I would recommend the system already in force whereby each patient is encouraged to farm a portion of land allotted to him for his partial support and use as food, and to supplement this by work on the roads or other paid work in the Settlement, or by hiring himself out to till the soil for neighbouring farmers. Patients give one day weekly to communal work in the Settlement which carries no remuneration, and on this day, as the need arises, certain of them labour on the allotments of those who, through incapacity, are unable to work for themselves. So far this system has proved adequate.

Certain activities started with the assistance of the Government Agricultural Department should enhance the value of the

Settlement land and encourage the patients to grow new crops the products of which can be divided equally or given to necessitous patients without leading to exploitation or undue economic problems. The planting of Gmelina seed has already been referred to (page 35). Seven hundred palm seedlings have been planted in the Uburu Nursery, and four hundred of them have now been planted out in the Settlement. Arrangements have been made for the planting of Nigerian Orange seedlings. Mangoes were offered but have not been accepted owing to the myriads of flies which gather on the fallen fruit. Two hundred pounds of rice seed was planted in a nursery in the Settlement and the seedlings planted out in the early rains, some in the Settlement and the rest in segregation villages. Attempts to grow Hydnocarpus wightiana in the Settlement have been disappointing, but it has flourished in Owerri Segregation Village reaching a height of eight to ten feet in two years. Intensive and skilled supervision of these activities would be required to make them a success, and for this purpose a member of the African staff has been sent for a course of training in Agriculture.

The following estimates for essential permanent buildings in the Settlement have been presented with our application for lease of land:-

Three Europeans' houses, permanent BELRA type, each £1,700	£5,100
Six African staff's houses, each £300	£1,800
Thirty patients' houses, each £16	£ 480
Two twenty bed hospital wards, each £900	£1,800
Garage and store	£ 500
Operating theatre	£ 450
Sanitary annexes, each £450	£ 900
Administration block	£1,100
Total	£12,130.

Plans for these structures were drawn, according to Government specifications where indicated, by the BELRA draftsman at Uzuakoli. In accordance with the Government Proposals (1943), provision would require to be made at a later stage for the erection of the following:-
(a) Homes for helpless and incurable lepers.
(b) Uninfected babies' crèches.
(c) Homes and schools for uninfected children of leprous parents with no relatives to assume the responsibility of caring for them. To these I would add another, now indispensable in the use of the sulphone drugs, (d) a laboratory. Arrangements would also have to be made for the erection of places of worship for the predominant religious sects among the patients. A school for children who are patients on the lines already followed in Owerri Segregation Village would have to be started at an early date, but a simple building of temporary materials would suffice. A recreation room in which physical therapy could also be carried out would be another project for consideration in the future.

With regard to homes for incurable and helpless lepers, it is to be hoped that, as more patients are treated in the early stages and as a more effective treatment can be used on a wider scale, numbers of these will lessen. As the majority of these patients are in the arrested or non-infective stage of the disease, expenditure on the part of the Mission should be limited to those who are really necessitous:many of them are, and some can continue to be cared for by relatives without danger to the community. The Mission provides a limited sum for the care of these patients, and with the taking over of medical and control activities by the Nigerian Leprosy Service as is proposed, greater resources might be made available. I would still advise caution in the distribution of these funds for the erection of institutions and the relief of indigent cases, thorough investigation followed by recommendation by a welfare officer being desirable, lest we rob these people of their responsibilities and independence.

The care of uninfected infants of leprous parents presents a problem which has not been solved in South-East Nigeria. Various expedients have been attempted in the settlements where I have worked and which I have visited, the most popular being the establishment of crèches where the babies are cared for by African nurses. The mothers attend at feeding times, wash, don a clean white linen gown with the arms closed over the hands and holes through which each breast protrudes. The breasts are cleansed with a mild antiseptic and the child is suckled. In reference to precautions which should be taken when in contact with or proximity of severe lepromatous cases, Muir (1948) has stated: "Reliance should not be placed on antiseptics (we do not know what will kill leprosy bacillus) ..." and we can understand that as this refers to medical attendants in leprosy settlements, a baby sucking repeatedly at an infected breast must run a considerable risk of infection. I have found no statistics as to results of this method and doubt if it is worth the cost and effort involved. The rearing of infants confined together in institutions presents problems in tropical Africa which are not met with to the same degree elsewhere. Infections spread rapidly and the mortality among these infants is high. Continuous European supervision to a degree which is impracticable would be required in order to attain anything like the efficiency on the part of nurses which is accepted as normal elsewhere. If we recognise that only infective mothers require these precautions the extent of the problem is lessened, but even so it is not a method which can be applied to all infective mothers in a primitive community, where it is impossible to persuade all to come into the Settlement.

Graver objections apply if it is proposed to separate the babies from their mothers at birth. Because they are confined together in institutions and must be fed on preserved milk - for the foster-mother, owing to native beliefs, is almost unknown in South-East Nigeria - these infants are even more difficult to rear, and the cost of attempting to do this on a large scale is prohibitive. Weymouth (1938) refers to a babies' house in connection with one Nigerian

settlement where each baby costs £50 to rear. He quotes the Medical Superintendent as estimating that he could segregate seventy-five infectious lepers for that amount. In any case, he comments, the children go out from these institutions to homes where leprosy is often rife; a problem which, incidentally, only the Provincial Leprosy Scheme with its repeated surveys can tackle. Weymouth concludes: "Is it not better to let the babies run the risk of staying with their parents callous as it may seem ? " In considering this problem it should be stated that, in my series of cases who admitted contact, 14 percent acknowledged a mother with leprosy and that involves 3.6 percent of the series interrogated.* Infections from other relatives would then appear to be more frequent, women in another series of mine including 1007 cases being shown to suffer in lower proportion than men from the infective lepromatous type of leprosy, 14 percent women as opposed to 26 percent men, and the separation of infants from their infective mothers at birth would appear not to be the main problem in the control of leprosy.+ It remains a problem for which a solution must be sought and the results of repeated examinations of the children of infective mothers under treatment with the sulphone drugs while these children were suckled as infants will be awaited with interest. Meantime, in default of a better method, babies in the Settlement and in segregation villages in the Ogoja Leprosy Scheme stay with their mothers until they are weaned, when they are removed to the care of healthy relatives. I conclude that caution should be observed before committing the Mission to expense in this matter also.

The same conclusion applies to the third proposal (c). The Mission already provides schools for healthy children throughout the district where leprosy work is being carried out and is planned to start. According to native law in these parts even a relative not closely related may be made to assume responsibility for a child, failing which some other suitable person is usually willing to do so. In the rare instance where none can be found the Native Administration should be responsible for the cost of rearing the child and the Mission might provide the limited accommodation necessary.

There is no need to comment further on the need for a laboratory except to add that equipment and reagents having been recently assimilated in connection with bacteriological work and the investigations necessary for the administration of the sulphone drugs, available space in the dispensary where this work is carried out being limited, the need for more spacious and suitable accommodation is clamant.

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* p.p. 32 & 33. + Table I, page 52.

6. Aetiology and Transmission.

It is important that our method of control be in accordance with what knowledge we have of how leprosy is conveyed. The hereditary theory and Hutchinson's 'fish' theory have already been referred to (pages 6,13 and 14) where it has been shown that these theories were superceded by Hansen's discovery. While Hansen's bacillus is widely accepted as the causal organism of leprosy, absolute scientific proof of this assumption is still lacking, attempts at culturing or inoculating the human form of the disease into experimental animals not having been established as successful (Cochrane, 1947). It remains that no alternative causal agent has been established, and the frequency with which large numbers of the Mycobacterium leprae are found in active lesions of cases belonging to the lepromatous type which we associate with high contagion and in active lesions of the tuberculoid type suggests, at least, that this is the organism concerned. Rogers' (1946) theory of prolonged close contact as the principal factor in transmission is based on this belief and has not been successfully challenged. Such a means of transmission is strongly suggested by my own findings (pages 32 and 33) and has received wide support from contemporary authorities, Lowe (1946), Cochrane (1947) and Muir (1948). Lowe emphasises "bad housing necessitating close and intimate contact" with an infective case of leprosy and Rogers, Cochrane and Muir stress the susceptibility of children and young persons to infection under circumstances such as these.

Another suggestion as to the mode of transmission which has aroused interest in recent times deserves mention. Moiser (1945, 1947) denies Rogers' theory: having found acid fast oval bodies and bacilli of Hansen in cockroaches from his leprosy hospital and native kralls he asserts that these insects have, from ancient times, played a role in the transmission of the disease either occasionally by biting or from contact with dried faeces , and he hopes that further investigation may produce evidence to this effect. He acknowledges that leprosy is a house or family disease, but cites the failure of inoculation experiments and the paucity of clear case histories of contagion in support of his contention. Davey (1947a) queries the inoculation of the organism in the act of biting and points out that much more substantial evidence would have to be forthcoming. Dungal (1947) affirms that cockroaches did not exist in Iceland until a decade or two ago and that they are even still practically unknown in the countryside where leprosy has had its origin. Regarding Moiser's contention in reference to the failure of inoculation experiments I would comment that, although absolute proof of direct inoculation as a means of transmission is still lacking, instances where this seems likely to have occurred are forthcoming from cases reported in recent times. There is the case of Lagoudaky (1937) who apparently successfully inoculated himself, subsequently dying with the disease. Porritt and Oslin (1948) have recorded two cases of men serving in the United

States Marine Corps who were tattooed by the same man on the same day in Australia in 1943 and both developed leprosy in their tattoos within what is assumed to be the usual incubation period of leprosy, showing signs of the disease in the first half of 1946. That cases of this type are rare and that casual contact seldom conveys leprosy where reasonable precautions are observed, appears to me to point to prolonged, close contact as the principle factor in transmission. I have noted, however, that the person with whom contact is admitted, when known to me, is not always an infective case, from which I conclude that there must be occasional infectivity of tuberculoid types especially in acute exacerbations. I have, in one case, obtained a history of the disease starting on the spot where the patient had been bitten by a cockroach.

Following on this there arises the question as to whether leprosy first shows itself where inoculated, or whether, as Cochrane (1947) postulates, bacilli on inoculation reach some unknown focus in the body - skin, nerves or reticulo-endothelial system - from which they later spread to the lesion in the skin where the disease must be anchored; otherwise the reticulo-endothelial system becomes invaded. Andrews (1946) refers to a reticulo-endothelial system in the skin, and it has occurred to me that this might account for the unknown focus where the organism lurks, following upon which the immunity of the individual, associated with allergy, condition its spread and effects, that is, whether the lepromatous or tuberculoid type appears. From a series of 181 cases interrogated by me 170 acknowledged an initial lesion. These initial lesions were plotted on a body chart (Figure I), a few of them coinciding, where it was shown that sites where many points were aggregated were consistent with the assumption that friction and pressure at night might be considered as a contributory factor, situated as they were on the parts most likely to be exposed to these processes in the characteristic African attitude in repose. It should be explained that the African usually sleeps with his head on his left flexed forearm, the right arm being free to defend himself in haste should the need arise. It is unlikely that scratching with the resulting abrasions could have induced the lesions on the middle of the back chest where many points were aggregated, and the distribution there and on the limbs did not suggest scabies as a contributory factor. I consider that abrasions must be a more important factor than droplet infection in involvement of the mucous membrane of the nose as in picking with nails imbued with infected material, perhaps from elsewhere on the body, the nasal lesions being most pronounced in accessible parts as on the septum. Few initial lesions are seen on the face, but spread from the centre of the face is common at a later stage. Conversely, in resolution, definite regression towards the centre of the face is common, being noticeable in all cases under treatment with the sulphones and sulphonamides in which subsidence took place peripherally first, regression towards the centre being observed in those where the response was marked. (1 - 20). It would appear to be worthy of speculation, then, that initial

lesions may sometimes be associated with points of friction and pressure at night and that the organism may gain entrance at these points. That the second lesion noted often arises on a widely removed part of the body, as evidenced by the case histories of patients treated with the sulphones and sulphonamides with the exception of cases numbers 6, 10 and 16, accords with my experience in dealing with other allergic skin manifestations and does not contradict the first appearance of the disease on the site of inoculation.

With regard to the susceptibility of children and young persons, statistics from patients in the Ogoja Leprosy Scheme indicate a later onset of leprosy than in childhood and adolescence. Assessment of age is difficult in Nigeria and never exact among the illiterate, but with experience a fair approximation can be attained. The average age at onset was estimated by me among 578 cases to be 31 years. Of these cases 50 were under 10 years, 112 between 10 and 20 years, 303 between 20 and 40 years and 113 over 40 years of age when the disease was said to have started. If we deduct 5 years as the usual maximum incubation or latent period (page 15, (3)) we find that only 162 patients were likely to have been in childhood or adolescence when infection took place. Other factors besides age estimations, such as forgetfulness on the part of the patients as to when their disease started or a longer latent period than is usually estimated as the maximum might be considered in drawing conclusions from these statistics, but, on the whole, they accord with my experience that leprosy in this part of Nigeria is a disease which attacks men and women in the prime of life and that onset after middle life is not uncommon. It should be noted that the marriageable age falling between 15 and 20 years when the mode of life frequently changes has been taken as the limit of adolescence; this may partly account for differences of opinion on this point, but it is clear from these statistics that leprosy in Southern Ogoja Province is not principally a disease of childhood.

Factors of less importance in the spread of leprosy may include diet. The theory put forward by Oberdörffer (1938) that a diet rich in cocoyam (Collocasia antiquorum) may be a predisposing agent in infection with leprosy has been modified by Davey and Ross (1944) who carried out the experiment of feeding a group of children on this diet. No deleterious effect on the disease in these patients was observed and it was concluded that the sapotoxin of the cocoyam "is but one among many factors predisposing to infection with leprosy in Nigeria." Cochrane (1947) fed this tuber to a splenectomised monkey infected with leprosy and observed an erythematous moist rash in which he found acid fast bacilli, which, however, he decided was an acid fast saprophyte. Cocoyam constitutes one of the articles of diet but never the sole item in the diet of the people of Afikpo Division among whom my work has been carried on. Their food supply is fairly plentiful except for a month or two in the early summer when, the resources of the previous year's harvest becoming exhausted and the new crops not then being ripe there is frequently a scarcity.

Exacerbations of lepra reaction have been noted at that period, but, apart from this, diet is not considered to have much effect on the disease.

Similar considerations apply to nutrition generally and to the influence of other diseases in reference to which I am in agreement with Cochrane (1947) that too much has been made of these as predisposing factors. I have noted on general observation that, not infrequently, the well-developed and well-nourished patient is found to be suffering from the more infective or lepromatous form of the disease. This fact is borne out by the records of 'development', which includes nutrition in the lepromatous cases numbers 1 to 20 under treatment with the sulphones and sulphonamides. Of these only three, numbers 4,9 and 13 are classified as 'fair', four, numbers 6,11,14 and 19 as'fairly good' and the rest as 'good'. Similarly with other diseases: yaws is mentioned in four cases, numbers 1,9,13 and 17, as a predisposing factor; other complaints which may have been associated with the first manifestations of leprosy are mentioned, swellings thrice, numbers 5,6 and 18, pains once, number 12, and fever once, number 14, whereas in the remaining 11 cases no mention is made of such factors. This accords with my experience and I have also noted that other diseases are sometimes mentioned as predisposing factors but that the treatment of these diseases has little or no effect on leprosy. I am therefore in agreement with Cochrane (1947) that, although dietetic deficiencies should be corrected and other diseases remedied where found, no great reliance should be placed on these measures in dealing with the control of leprosy as, at most, they are only indirect factors in its causation and transmission.

In contrast to these factors of age, diet, nutrition and other diseases,the importance of the type of the disease and type of contact with associated housing conditions stands out in marked relief. These housing conditions in South-East Nigeria at the present time must approximate to and exceed in overcrowding those obtaining in medieval Britain when leprosy was rife there. The natives lie huddled together on the floors of their huts,only the more privileged members of the family occupying mud beds and the head man of the compound a house of his own. When an infective leper is amongst them opportunities for transference of the disease must be numerous. I found on survey in the Agbo area that the majority of the lepromatous cases were aggregated in two compounds in Anong Village, the disease being of the less severe tuberculoid type or absent in neighbouring compounds where these compounds were completely separate. Where, however, the compounds communicated with one another as in Itigeve Village, the disease was more generalised throughout the village, although here also the active lepromatous cases living at home were in one compound. These facts appear to me to corroborate the assumption that the lepromatous type of case is the most infectious, that close association with this type of case tends to produce the lepromatous form of the disease, that leprosy is a compound or house infection and that spread takes place most frequently at night when opportunities for close

contact are greatest.

Bearing these facts and conclusions in mind it is of interest to discuss an experiment carried out by Cochrane (1947), for the purpose of which selective, local, night segregation was made attractive by the provision of an evening meal. The experiment, accompanied by surveys, involved four villages, two others being used as controls, and it extended over a period of five years between 1939 and 1945. In two of the villages where night segregation was carried out Cochrane reported a striking drop in the gross incidence of leprosy, whereas in the control villages the gross incidence of leprosy increased more than twice in one, and one and a half times in the other. He noted a marked decrease in the open or infective case rate in three out of the four villages where night segregation was adopted, but this he has also recorded in the case of both controls. A consistent and definite fall in the child rate also noted, took place in all four villages and one of the controls. Without drawing any definite conclusions, Cochrane feels that the over all picture "shows a downward trend, indicating a possible favourable turn in the epidemicity of leprosy in these villages." The results of this experiment have been commented on by Muir (1948) who states that Cochrane's "reported figures of surveys in four night segregation villages in 1939 and repeated in 1945 do not reveal any greater improvement than in two control villages where there was no separation." This comment does not apply in relation to the gross incidence of leprosy recorded by Cochrane.

Further evidence of the importance of the lepromatous state in the transmission of leprosy and more definite and encouraging results from village segregation have been recorded by Davey (1947). Davey conducted an experiment over a period of six and a quarter years, carrying out intensive surveys in March, 1941 and again in January and July, 1947, to assess the significance of changes which took place in the incidence of leprosy in a group of seven villages, Ndi Oji Abam, in the Bende Division of Owerri Province, South-East Nigeria. Control from the Central Settlement at Uzuakoli with African staff in charge of treatment, leprosy inspectors instituting propaganda and carrying out intervening surveys by themselves, with voluntary, selective day and night segregation in villages on the lines described by Muir (1948) who called this the Eastern Nigerian System, came into force following the first survey in 1941. Other factors which might have influenced the course of the leprosy epidemic remained relatively constant: there was no significant change in the climate or in the habits and living conditions of the people; no comparable improvement took place in six control cases who failed to attend for treatment nor in 118 untreated cases in a distant village. The intensive survey in 1941 revealed a leprosy incidence of 361 persons affected in a population of 3,063 or 117 per mille. By July, 1947, cases of active leprosy had declined to 134, a decline of 62.9 percent in six and a quarter years. Lepromatous cases had declined from 34 in 1941 to 12 in July, 1947.

Davey's main conclusions are as follows:-
(1)"The principal factor in the decline of leprosy was the segregation of all lepromatous and advanced cases which was complete by the end of 1941.
(2) By arresting the disease in its early stages, treatment was of great importance in inhibiting the development of the lepromatous state.
(3) It was possible to achieve the drastic decline in the leprosy epidemic only because of the excellent co-operation given by the people, both healthy and patients. Where this is given it is possible in relatively few years to control a relatively heavy infection of leprosy in a rural community by suitable local measures with supervision from a central Settlement."

7.Diagnosis of Clinical Types and Sub-types.

For the purpose of leprosy control it would be convenient to divide cases of leprosy into two main types, infective and non-infective, hence the apparent advantage of the South American (1946) and Havana Congress (1948) classifications (page 18), postulating two main polar types, lepromatous and tuberculoid. I have observed, however, that tuberculoid cases sometimes show positive nasal smears on admission and in the early stages of treatment and that the infectivity of skin smears varies with the activity of some tuberculoid lesions. Change of type from tuberculoid to lepromatous, if it takes place, would also vitiate the assumption that the two polar types referred to always correspond to infective and non-infective states unless repeated clinical and bacteriological estimations were made in each case. In my experience I have not known a case where a degenerative change of this nature was suspected in which bacteriological evidence was also forthcoming to prove that the non-infective had actually changed to the infective state and it is my opinion that such a change, if it occurs at all, must be exceedingly rare. Statements to the effect that this change has taken place unless accompanied by bacteriological proof should thus be disregarded. I have, however observed cases where a change in the reverse direction from lepromatous to tuberculoid type appeared to be taking place in one of which a negative result was obtained on all smears.* Differentiation between the early lepromatous and indeterminate types is difficult unless confirmed by a strongly positive smear in the former case; but the fact remains that in much routine and in most field work such as is carried out in the Ogoja Leprosy Scheme, reliance must be placed on clinical diagnosis in hundreds of cases, and for practical purposes the assumption that the clinically lepromatous case is infective and the tuberculoid and indeterminate cases relatively non-infective is sufficiently accurate.

* Case no. 26.

I have adopted the following sub-classification based on that in use at Uzuakoli, modified by my experience at Uburu and amplified to correspond with the most recent sub-classification introduced by Muir (1948), no sub-classification having been forthcoming from the Havana Congress in 1948:-

Tuberculoid. Minor tuberculoid, symbol m.t.,
Major tuberculoid, symbol M.T.,

Lepromatous. Lepromatous macules and diffuse lepromatous macules,
Lepromatous infiltration and diffuse lepromatous infiltration, symbols d.l.m. and d.l.i. only being used,
Lepromatous nodules and papules and
Ulcerating lepromatous nodules.

Indeterminate. Pale flat macules, symbol p.f.m. (undifferentiated, initial, terminal and intermediate or transitional).

It is my opinion that the majority of cases start in the type to which they ultimately belong, the sub-type varying with the severity of the disease and the reaction of the patient's tissues, but that, in resolving, the tuberculoid and lepromatous types frequently pass into the indeterminate type. From early cases of the tuberculoid type which I have seen on survey, I think that this type usually starts as a tuberculoid papule and that more papules arise which spread and fuse into tuberculoid macules, usually asymmetrical in distribution.* The axillae, groins, palms and soles are not usually involved as sites of macules in the tuberculoid type, but I have seen macules on other 'immune' areas as the eyelids and scalp, usually of the major tuberculoid type. Tuberculoid macules always show a raised edge, the degree to which the edge is raised or the whole macule raised being the criterion chosen in differentiating between the major and minor tuberculoid sub-types. This may appear an arbitrary distinction, but marked reaction in tuberculoid macules is not common in South-East Nigeria and, with a little experience, it is not difficult to attain a reasonable measure of uniformity in delegating the few cases involved to this sub-type. The differentiation is useful in estimating the 'resistance' of the patient's tissues, and the major tuberculoid sub-type may also be associated with occasional infectivity, a shorter duration of active disease but otherwise a worse prognosis regarding mutilations and deformities. The typical lepride with central flattening described by Muir (1948) is the configuration most commonly observed, macules like this being either major or minor tuberculoid as defined above regardless of extent, although major tuberculoid macules of this configuration are sometimes also of great extent. Muir's (1948) second and third varieties of lepride with thin and broad red edge but no tubercles are definitely of the minor tuberculoid sub-type: his fourth variety, the uniformly raised lepride, is major tuberculoid, but his fifth or multiple leprides may be either major or minor tuberculoid.

Tuberculoid macules, then, are raised and infiltrated with granular papules in minor, and larger perifollicular papules in major

* Case no 22

tuberculoid sub-types in pebble formation most noticeable at the edge and hypopigmented. In the reactive state these macules have a reddish tinge which is more marked in those Africans whose skin is not deeply pigmented, and it fades on resolution of the reactive state with desquamation. The characteristic healing centre is, of course, dark in the African. Spread of the macules is indicated by a serrated edge with, sometimes, colonial macules or papules close to or at some little distance from the edge. Anaesthesia to light touch is tested for with a teased out piece of cotton wool mounted on a small stick, the patient being told to close the eyes under the observation of an assistant; or the eyelids are held down by one finger and the thumb of the left hand while the other explores areas of anaesthesia. Response to tactile exploration varies greatly in minor tuberculoid macules of the trunk where anaesthesia is frequently not detected, and it is seldom detected on the face; but it is usually present in minor tuberculoid macules of the limbs, and almost invariably so in major tuberculoid macules on the trunk and limbs. Its detection can be relied upon in the latter when these are grossly infiltrated plaques. Thermal anaesthesia of limbs has been detected before the presence of tactile anaesthesia, but this test has not been employed as a routine. Muir's (1948) two pin test for analgesia has been found more useful, the patient indicating which of two identical pins is the sharper, the point of one pin being placed on a macule and the other on a corresponding point of normal skin on the other side of the body. One advantage of this test is that it has been found to be positive in all minor and major tuberculoid macules even on the face.

Lepromatous leprosy appears to start in the macular and progress to the infiltrative and then to the nodular sub-types. In a few cases nodules have been mentioned as initial lesions, as, for example, numbers 9,17 and 6 - in the last a papule - on the sulphones' and sulphonamides' series, and in number 16 infiltration is mentioned. Early lepromatous macules and even infiltration as on the back of the chest are, however, difficult to detect in a diffuse light, and could easily be missed unless specifically looked for by a trained observer. Lepromatous lesions may occur on any part of the body except that the 'immune' areas referred to (page 47) are usually spared, predilection being given to the forehead, face and ears in nodular and infiltrative lesions. I have sub-divided macular lepromatous lesions into macules which are usually small, reddish, multiple, symmetrically placed and not anaesthetic to light touch; and diffuse macules when these coalesce, expressed also by 'diffuse hypopigmentation' when erythema is absent, but when erythema is present this is stated. 'Lepromatous infiltration' and 'diffuse lepromatous infiltration' indicates that there is some thickening of the skin and subcutaneous tissues appreciable on observation or on picking up the skin between a finger and thumb. 'Papules' when lepromatous are deep seated but of smaller size than nodules, which

may show ulceration as defined in the sub-classification. All these lesions are always bacteriologically positive, if active and especially when nodular, markedly so.

As opposed to the tuberculoid macule which is sometimes called a 'raised macule', lepromatous and indeterminate macules are true macules in the dermatological sense, that is, they are not raised above the level of the surrounding skin. To mark a distinction from the tuberculoid macule, chronic, undifferentiated lesions of the indeterminate type are designated 'pale flat macules'. These are usually small, multiple and frequently symmetrical in distribution, having a pale, hypopigmented café au lait tint, and they are not usually anaesthetic to light touch. I have found these macules to be associated with diffuse hypopigmentation and slight puffiness or thickening of the face and ears, when differentiation from an early lepromatous case is difficult (page 46) clinically, but can easily be made by strongly positive nasal and skin smears in the latter case, for smears from an indeterminate type of case are only weakly positive or negative * especially as regards skin lesions. Evidence from histological examination is not quoted in dealing with any of these types or sub-types, because facilities for this were not available in the Ogoja Leprosy Scheme, specimens for biopsy in cases where diagnosis was in doubt being sent to the Medical Research Institute, Yaba, near Lagos, necessitating a delay of some weeks before confirmation was received. It may be stated, however, that little assistance can be anticipated from histological reports in making a diagnosis in cases of the undifferentiated indeterminate sub-type, where reliance must be placed on clinical and bacteriological examination. Clinical examination is paramount in cases with negative smears in which it cannot be too strongly emphasised that, unless other signs of leprosy are present such as nerve thickening or anaesthesia of limbs, it is better not to make a diagnosis of leprosy but to tell the patient to report for re-examination in three months' time. Cases of leprosy showing pale flat macules alone which remain in this state for a long period without showing other signs of the disease, must, in my opinion, be exceedingly rare, and reports that numbers of such cases have been found in Nigeria should provoke the query as to whether the disease in question was, in fact, leprosy. I can recollect only one suspected case of this type in an adult from another area in which, for that reason, I have not been able to ascertain whether other symptoms and signs of leprosy arose. Cases with pale flat macules alone are sometimes seen in children, and in these I have found it best not to start treatment unless there is a history of close contact with a case of leprosy; otherwise it is more prudent to await developments, delay in starting treatment not being vital to the patient suffering from a disease of such chronicity, and, as he is non-infective and not likely to become so, there is very little risk to the community in his not being segregated, provided he attends for re-examination in the period stated. Other varieties of the indeterminate type designated by Muir (1948) 'initial','terminal' and

* Case no 23.

'transitional'or'indeterminate' are stages of the lesion above described, before, at the end of or in progression towards another type, in which case some of the characteristics of the other type may be present. In the terminal sub-type of the indeterminate type where the resolving lesion has been a uniformly enlarged tuberculoid macule, irregular, mottled hyperpigmentation appears and marked and extensive anaesthesia of macules may remain; the ringed tuberculoid macule with healing centre also retains anaesthesia if present, the ring becoming flat and a pale red then an orange colour and fading while pigment returns. Lepromatous macules become more defined, then smaller, losing their reddish tinge, but retaining their characteristics of multiplicity and absence of anaesthesia. 'Initial' and 'transitional' macules, included for the sake of completeness must remain theoretical for the purpose of this description, owing to lack of information on the progression of cases from or through the indeterminate type, but I think that cases like this without some evidence of the characteristics of other types must be rare.

Some signs of nerve involvement are usually present in all types and are thus an important aid to diagnosis in the indeterminate variety. These nerve signs include thickening, and tenderness in reaction, of nerves in limbs where the nerve can be palpated over a bony point, anaesthesia and trophic signs. The nerves in which these signs are detected are the ulnar at the elbow, the superficial peroneal behind the head of the fibula, the radial in the forearm and the medial calcaneal at the internal aspect of the heel. Other nerves where thickening can be observed are the great auricular, cervical cutaneous and supraclaviculars, and the medial antibrachial cutaneous. These nerves are involved in lepromatous and in tuberculoid leprosy in South-East Nigeria where greater thickening of nerves, especially the ulnars, superficial peroneals and medial calcaneals is frequently found in lepromatous than in tuberculoid leprosy. Marked thickening is noted in tuberculoid leprosy where these or other nerves mentioned are associated with sensation in an area where a major tuberculoid macule is situated, but I have not observed corresponding thickening of small cutaneous nerves of the trunk. Segmental anaesthesia of varying extent is usually present in both polar types, sometimes of the heels or fifth finger only or extending to higher levels until the whole limb is involved, being present, but usually to a lesser extent in the undifferentiated indeterminate sub-type. The upper level of segmental anaesthesia is usually symmetrical in distribution on corresponding limbs except in the tuberculoid type where the upper level inclines to vary with the existence of tuberculoid macules, present or resolved. This upper level where macules are not or have not been present in the tuberculoid type and in other types is usually found to slope downwards and outwards on the upper and downwards and inwards on the lower limbs.

Trophic signs include ulceration following the blisters of burns or other injuries, the lesions of epidermophytosis being a frequent contributory cause in initiating ulceration of the feet. If

allowed to extend, ulceration is followed by septic infection with consequent necrosis of bone. Deformities resulting from nerve involvement include ankylosis of joints of phalanges in flexion with the production of claw hand and hammer toes; absorption of bone with shrinking of phalanges, a vestige of the nail remaining at the extremity of finger or toe; atrophy of muscles producing flattening of thenar and hypothenar eminences; paresis and paralysis following acute neuritis evidenced by facial paralysis, drop wrist and drop foot. On the face lagophthalmos with flaccid lips is a common sign in both polar types, producing the typical 'mask face'. Parakeratosis is present over resolving macules but especially over the legs where segmental anaesthesia is present, and hyperkeratosis is sometimes present on the soles. Depilation especially of the outer eyebrows is common in the lepromatous type where a generalised 'moth eaten' alopecia of the scalp is usual in severe cases, and a similar condition over tuberculoid macules of the scalp has been noted. Depilation is also present over macules on the trunk and limbs and in the areas of distribution of segmental anaesthesia on the limbs. Anhydrosis is likewise present on limbs and macules with compensatory hyperhidrosis on unaffected parts of the trunk. Before leaving the subject of nerve involvement it should be mentioned that as regards 'neural anaesthetic' or pure nerve leprosy (Cochrane, 1947) I have only seen one case where there was thickening of the superficial peroneal nerve with some parakeratosis of the leg and anaesthesia in a man where no macules had appeared. Secondary neural signs as those described above are, however, common in cases where macules have resolved which are also bacteriologically negative, when the case is termed 'arrested'.

Affection of mucous membranes as of the accessible parts of the nose can be present in all types but is most frequent and severe in the lepromatous type where infiltration, nodulation and ulceration may be found. The nasal septum sometimes becomes necrosed with flattening of the nose, but affection of less accessible parts of the mucous membranes is rarely severe. In this connection it is interesting to note that laryngeal involvement, although evinced by hoarseness, has never been observed by me to advance to a serious stage requiring operative interference; a complication which must therefore be rare in South-East Nigeria. Nerve abscess is another complication which I have not observed. Corneal ulceration, keratitis and iritis are not very common and seldom severe, complete blindness from leprosy being, in my experience, unknown.

7 (a). Type Incidence and Sex Distribution.

In an analysis of 1,007 cases of leprosy staying in the Settlement at Uburu and in four segregation villages, I found the following type incidence and sex distribution:-

Table I. Type Incidence and Sex Distribution.

Case type	Patients	Percent	Males	Percent	Females	Percent
Minor tuberculoid	463	46	216	41.6	247	50.6
Indeterminate	216	21	95	18.3	121	25
Lepromatous	204	20	135	26	69	14
Arrested	117	12	68	13.1	49	10
Major tuberculoid	7	1	5	1	2	0.4
Totals	1007	100	519	100	488	100

Table I typifies a regular finding of mine in Nigeria that relatively non-infective types constitute about four fifths of the total cases (80%). The presence of a fairly large indeterminate group is of interest, and can probably be accounted for by the fact that the majority of the cases under consideration have been under treatment for some years. Comparison with table IX* shows that this group was much smaller where no treatment had been carried out as in the Agbo Clan, 2.7 percent as compared with 21 percent above. The tuberculoid sub-types are included to illustrate the small percentage of major tuberculoid cases (1%) and the consequent absence of marked resistance in the tuberculoid type. The relatively higher percentage of mild types in females is also noteworthy; minor tuberculoid and indeterminate forms total 75.6 percent in females as opposed to 59.9 percent in males: then, following on this the lower percentage of the more severe and infective lepromatous type in females (14%) as opposed to males (26%). Arrested cases include some disabled patients but mostly those who could be discharged but are unwilling to leave.

7 (b). Mutation of Types.

I have noted that leprosy, although a disease of great chronicity, is characterised by rapid changes often accomplished in the phase of acute lepra reaction. The possibility of change from one type to another, especially if this were accompanied by transition from the non-infective to the infective state, is therefore of importance, but it could only be assessed conclusively in a large series of cases where careful records of clinical, bacteriological and histological findings had been made over a period of five or more years. Detailed work of this nature has not yet been possible at Uburu, but I have been able to follow up a series of 47 cases, all examined clinically and all but six bacteriologically between the years 1941 and 1942, and all examined clinically and bacteriologically between the years 1947 and 1949. Of these 47 cases, 30 were assigned to the

* Page 76.

minor tuberculoid sub-type, 13 to the lepromatous and 4 to the indeterminate types. 30 cases, including, of course, all the lepromatous ones, showed definitely positive smears at the beginning of the period, and one minor tuberculoid case showed a positive scanty smear, making a total of 31 positive smears in a group of 47 patients. At the end of a minimum period of five years, in some cases up to eight years, only three cases all belonging to the lepromatous type remained bacteriologically positive. In none of the ten cases negative at the beginning had a positive smear developed, nor were any of the six cases, assessed clinically as of mild type and likely to be relatively non-infective at the beginning, bacteriologically positive at the end. While no definite conclusions can be drawn from so small a series of cases, certain features of interest may be remarked upon, such as the number of cases (17) of relatively mild and non-infective type showing definitely positive smears (all of them nasal smears) at the beginning, that all these together with one mildly positive case and ten out of thirteen lepromatous cases became negative during treatment with hydnocarpus oil injections extending from five to eight years, and that none of the sixteen clinically mild or negative cases became bacteriologically positive. Mutation of types was as follows:-

15 minor tuberculoid cases became indeterminate
5 minor tuberculoid cases became arrested
3 minor tuberculoid cases resolved
7 minor tuberculoid cases remained minor tuberculoid
9 lepromatous cases became indeterminate
1 lepromatous case became minor tuberculoid
3 lepromatous cases remained lepromatous
3 indeterminate cases became arrested and
1 indeterminate case remained indeterminate.

The complete absence of clinical retrogression to a severer type is the marked feature of these changes, the majority of the tuberculoid and lepromatous cases becoming indeterminate, resolved and arrested and the majority of indeterminate cases becoming arrested. One lepromatous case actually became minor tuberculoid. No control series of cases not receiving treatment has been possible to arrange, but it should be stated that the majority of these 47 patients were attending weekly at an out-patient clinic where regular supervision was given by a doctor, and to this the favourable trend in most cases might be attributed. Improvement in the general condition of most cases is evidenced by a marked decrease in the erythrocyte sedimentation index in 30 out of 36 patients in whom this was performed at the beginning and end of the period; of the remainder four became slightly reduced and two increased.

8. Differential Diagnosis.

The differential diagnosis of leprosy is not difficult in cases where macules such as I have described are present along with one or more of the three cardinal signs, a positive smear, nerve thickening with or without tenderness and anaesthesia. Difficulty arises in a few tuberculoid and some indeterminate cases where these signs have not appeared, a matter which has been discussed in reference to the latter (page 49) and which can be dealt with by repeated re-examination in the latter and is often confirmed by a histological report in the former. As leprosy consciousness increases and more patients come forward or are discovered at survey in early stages of the disease, occasions for the exclusion of other skin diseases common in West Africa may become more frequent. Only these most likely to cause confusion are dealt with here, a preference being given to those in which differentiation has commonly been required. It should be mentioned that case histories in leprosy are often not reliable and symptoms few and of little value in early cases. One symptom which I have not found recorded elsewhere, itching or tingling, is common in early skin lesions, and localised or generalised pains are most commonly complained of at a later stage.

Syphilis is not encountered as an indigenous disease in Southern Ogoja Province, and for routine purposes in this area its secondary manifestations need not be considered as a possible source of confusion with leprosy. Yaws, however, is probably the most common condition requiring to be excluded. The perifollicular papular rash sometimes following on yaws lesions of the more florid secondary type bears some resemblance to tuberculoid leprosy in the elements or papules with which it is composed, but not in the distribution of these elements. These may be arranged in patterns like grouped syphilides, annular, serpiginous and corymbose, or, more commonly distributed uniformly but not aggregated closely as in leprosy. In cases of doubt as in children without other signs of leprosy but where, from the history or appearance of the lesions yaws seems likely, one injection of novarsenobillon will exclude yaws because its lesions rapidly disappear thereafter. Crab yaws on the foot or hand often requires to be differentiated in treating cases of leprosy in which the concomitant presence of yaws is suspected. The hyperkeratosis of yaws and leprosy might be expected to give rise to some difficulty, but in yaws a multiple pitted appearance is a frequent accompaniment, and where crab yaws is present the radiating cracks or fissures from a tender, frequently nodular central eminence differentiates the condition from the more uniform thickening seen in leprosy. Where pitting or ulceration is present in yaws there is a definite angular, punched out edge as opposed to the round, conical configuration of the leprotic ulcer when overhanging epithelium has been removed.

Tinea is the next common condition requiring exclusion, especially tinea corporis and tinea flava, the latter being found

to co-exist frequently with leprosy. Neither of these conditions is difficult to differentiate from leprosy, the distinct vesicles of the former set in a true circle or covering a round area of normal skin being unlike the raised, irregular, confluent papular edge of the tuberculoid macule with infiltration tapering to healing areas and beyond the spreading edge. Tinea flava with its characteristic yellow colour more vivid against the dark skin involving wide areas or localised to multiple small macules, superficial in appearance with an irregular coalescing semilunar margin, is not likely to be confused with the café au lait indeterminate macule. Likewise vitiligo need never be confused with leprosy if it is recognised that the characteristic of the former is depigmentation whereas that of the latter is hypopigmentation. Psoriasis is more difficult to differentiate from leprosy, especially the multiple leprides of the major tuberculoid sub-type when these are desquamating following the reactive state. One case of this type in which there was no nerve thickening and only slight anaesthesia of one foot and where slight bleeding was observed on removal of scales, had to be confirmed, as regards a diagnosis of leprosy, by histological examination.* In this connection it should be noted that a diagnosis of leprosy from a small area of anaesthesia where the appearance of the macules is not typical is not advised, findings in this respect being somewhat subjective and inclined to vary. It should also be added that psoriasis is not commonly seen in South-East Nigeria. Lupus vulgaris can be diagnosed by the presence of the typical 'apple jelly' nodules, and, when this disease has spread to any extent, corresponding leprous lesions would be accompanied by nerve enlargement and possibly anaesthesia.

Nutritional deficiency diseases with skin manifestations are more difficult to differentiate from leprosy, where diffuse and localised hypopigmentation occurs and appears to be associated with these conditions especially in children. I have noted that phrynoderma is a frequent accompaniment in these cases and is not seen in leprosy, advice as to diet , and, where there is any doubt, to report for re-examination being indicated. The characteristic lesions of pellagra with distribution on exposed surfaces are not difficult to differentiate because they are hyperpigmented. Hypopigmented cutaneous nævi are frequently seen in children in whom leprosy as a causative factor has to be excluded, but where the history of presence from birth, inactive appearance and lack of other signs over a period of observation if considered necessary, should be sufficient. In dealing with the lichens the different configuration of the papules and usually less confluent nature of the lesions should assist in differentiating from leprosy as with two cases of lichen spinulosis brought to me for this purpose. Scars from native caustics used to conceal macules are a considerable source of difficulty in making a diagnosis of leprosy where no other signs are present, histological examination sometimes being necessary as when the macule is completely covered. Applied to the centre of a flat macule the caustic scar may simulate

* Case no 25.

superficially the healing centre of a resolving tuberculoid macule, but when there is spread of a macule beyond the edge of a caustic scar the purpose of concealment is usually in little doubt and a diagnosis of leprosy likely to be confirmed. With the exception of one case of nerve injury with trophic ulceration of the sole of the foot I have not encountered any cases with signs that might be confused with the secondary neural manifestations of leprosy, and it is obvious that in cases where mutilations and deformities occur other cardinal signs of leprosy would be apparent. Not many other conditions simulate lepromatous leprosy in the infiltrative and nodular types, but I have seen one case of dermal leishmaniasis presenting ulcerating papules aggregated on the right cheek and one on the right shoulder in which the lesions presented some similarity but the distribution contraindicated leprosy. For the same reason, cases of neurofibroma which I have seen are not likely to be confused with leprosy. In differentiating all these conditions clinical aspects have been dealt with because of the difficulty of obtaining other confirmation in routine field work.

9. Treatment.

Because of the important part it plays in the scheme for the control of leprosy, a few notes on treatment are appropriate. The principal routine treatment in the Ogoja Leprosy Scheme has been, and is likely for some time to remain, subcutaneous and intramuscular injections of sterilised Hydnocarpus oil and 4 percent creosote. Formerly the crude oil was processed and the creosote added in the Hospital operating theatre, but since January, 1949, sealed bottles of the complete preparation, processed in Britain, have been imported and distributed by the Nigerian Government. Throughout my period of supervision the abscess rate has remained low, being 0.31 percent per attendance for injection for the year 1948 and 0.5 percent per attendance for injection between January and August, 1949. Administration of the injections is mainly the responsibility of trained patients licensed by the Director of Medical Services for that purpose, and they are supervised in the Settlement and at clinics by experienced African Staff, the doctor being also present whenever possible. It is obvious that the routine employed must be of the simplest and safest, and a system of this nature, devised by Dr. Hastings, has been retained. Intradermal injections have not been introduced because of the hideous scarring I have seen resulting from this method when the administration has not been in expert hands.

The maximum number of injections given to any one patient at one session is three, not more than 3 c.c's being injected at any one site and the needle is partly withdrawn and re-inserted in another direction then entirely withdrawn, 1½ c.c's being injected each time while the needle is being withdrawn in subcutaneous injections. Intramuscular injections are employed in the buttocks. Injections are administered in a cycle as follows:- one to each side of the back of the chest and one in the right, or alternatively left calf at one

session ; followed by one in each thigh and one in the right buttock at the next; and one in each arm and one in the left buttock at the third session, extensor or outer surfaces of the limbs being employed. The skin is previously cleansed with tinc. Iodi mitis. On the assumption that lepra reaction may sometimes be induced by large doses of the drug administered at the beginning of treatment, dosage is always started at ½ c.c. which is continued for four sessions then increased by ½ c.c., the same period intervening before the next increase. The maximum dosage is regulated according to a rough estimation of weight and tolerance, according to the age of the patient and whether any complications are present. The maximum dose administered is 7½ c.c's. Patients in pregnancy and the puerperium have their doses reduced from the maximum to 6 c.c's. In lepra reaction of the lepromatous type I have found it advisable to reduce the dose to ½ c.c. and raise again as described, but in reactions of the tuberculoid and indeterminate types, especially when these are mild, reduction of dosage is not necessary. Weekly injections are given, no greater frequency or increase beyond the present maximum dosage having been attempted since shortage of the drug necessitated twice weekly injections and a maximum dosage of 9 c.c's at each session being abandoned in the Settlement in 1942. Increasing numbers of patients and a continued need to conserve the amount of the drug available for distribution have been contributory factors in this economy.

A satisfactory response to treatment in all early cases and many more advanced cases of the tuberculoid type is usually observed, the majority starting to improve in three or four months and some showing resolution of macules in a year or eighteen months, but progress to complete freedom from active symptoms is slow, and recurrence both during and after the cessation of treatment is frequent. When, by bacteriological and clinical tests the patient is assessed to be 'symptom free' , no macules having been observed and negative smears having been obtained over a period of at least three months in tuberculoid cases and six months in indeterminate and lepromatous cases, no other evidences of active disease being present, the patient is paroled for three months with a certificate to this effect. If no recurrence is noted at the end of this period the parole is renewed for a further period of three months, increasing after a year to four or six months, until, at the end of five years no renewal is considered necessary. Owing to the chronicity and uncertain outcome of the disease under the present treatment and the fact that many of the patients are living normal lives in segregation villages, large numbers of discharges on parole have not been aimed at. I have not discharged any patient before two years' treatment has been completed, few are discharged then and the majority have to continue treatment for many years.

A pharmacopoeia containing a list of standard prescriptions for accessory treatment has been compiled but will not be detailed here. Reference will be made to the treatment of trophic ulcers and acute neuritis because these are among the most distressing of the

complications complained of by the patients. Removal of the epithelium of blisters or from around ulcers is, of course, essential before dressings are applied. The routine treatment for ulcers consists of Acriflavine 1 - 1000 applied on surgical lint, bandaged and the dressing changed daily. If sepsis is present Eusol is similarly applied, the lint having been previously pressed in the dresser's hand to avoid excessive moistness of the skin with consequent sloughing of epithelium. Eusol dressings may have to be changed more frequently, but, unless some deep source of the sepsis as from necrosed bone has remained undetected, the dressing can usually be changed to Acriflavine in one week. Indolent ulcers where no sepsis is present frequently respond to an application recommended by Ryrie (1940) as being rich in vitamin A. The following is a modification of Ryrie's prescription which became very popular in the Ogoja Leprosy Scheme:-

℞ Red Palm Oil 4 parts
Cod Liver Oil 4 parts
Eucalyptus Oil 1 part
Hydnocarpus Oil 2 parts
Pulv. Zinc Ox., native starch or chalk q.s. to make a paste.

Applications of Sulphanilamide, whole or in a 15 percent powder, have also recently proved successful in these cases or in cases following operation where necrosed bone has been removed. Injections of Hydnocarpus oil and 4 percent creosote around and beneath trophic ulcers of the sole has been followed by improvement and healing in some cases, which, however, has not always been maintained.

In neuritis, severe and unremitting, where other analgesics have failed and sleep is still being lost, I have tried injections of a few c.c's of 2 percent 'Planocaine' into the thickened ulnar and superficial peroneal nerves with some success. In one case of this type the pain subsided and has not recurred, the superficial peroneal nerve subsequently reduced in thickness and no adverse effects were observed. Relief of pain has been accomplished by this method in other patients, for example, case number 19 of the sulphones' and sulphonamides' series. In cases of less severe pain acetyl salicylic acid in the form of tablets or in a mixture with potassium citrate is the routine treatment and it is distributed liberally.

9 (a). Lepra Reaction.

Because it may be a manifestation of aggravation of the disease in the lepromatous type and of infectivity in the tuberculoid type of leprosy, lepra reaction deserves mention. Important signs of this state include renewed activity of existing lesions and the appearance of fresh lesions; fever, swellings and tenderness of nerves are not present in all cases. I have confirmed that it appears to be precipitated by a number of factors, drugs, for example Hydnocarpus oil especially in high dosage and iodides, the latter being now omitted

from all internal medication for that reason; other diseases, for example, malaria fever and gonorrhoea, also septic complications such as ulcers; vaccination; hormonal,as in pregnancy and the puerperium; emotional, as in a domestic crisis; and following operation. Often no precipitating factor can be detected the phenomenon appearing as if it were in the nature of the disease itself; even those I have mentioned are only possible precipitating factors, but in an analysis of twenty cases the main ones I have mentioned, drugs, other diseases, septic complications and pregnancy revealed themselves as fairly evenly distributed among the three types of leprosy, and the reaction might be attributed to one or other of these conditions in every case except one.

I have found lepra reaction to occur in the indeterminate as well as in the lepromatous and tuberculoid types of the disease, and I have likewise observed a response to the anti-histamine drug "Benadryl" (B-dimethylaminoethyl benzhydryl ether hydrochloride) in all types, possibly indicating an allergic condition in other than the tuberculoid type of reaction. The cost of the drug prohibited its use in a large series of cases, but four tuberculoid, one indeterminate and two lepromatous cases all showed some favourable response in less activity of their lesions. "Benadryl" was administered in capsules each containing 50 m.g. taken twice daily, the total dosage varying from 400 m.g. in the case of a boy to 750 m.g. in the case of two of the adults. In four patients, two tuberculoid, one indeterminate and one lepromatous type, this treatment had to be supplemented with Antimony Tartarate because the effect of "Benadryl", in the dosage administered, was not sufficiently pronounced. 'Antimony Tartarate' † given intravenously in a dose of two grains dissolved in five c.c's of sterile water, repeated at weekly intervals up to a total of four or six injections is the best treatment in my experience for acute lepra reaction in all types of the disease. Expense also limited supplies of penicillin for experimental purposes, but in one tuberculoid and two lepromatous cases of lepra reaction some favourable response appeared to take place to 62,000 i.u. of penicillin in oil administered twice daily for four to six doses. Less activity was noted in skin lesions of all cases and subsidence of swelling in one lepromatous case, the erythrocyte sedimentation index becoming reduced in one lepromatous case but increased in the other two, but in none was the improvement maintained. The response of lepra reaction to drugs is difficult to assess, for it often exacerbates and remits and may last from three weeks to three months or, with remissions, for a number of years. Possible effects on organisms other than the Mycobacterium leprae which may play a part in the reactive state, must also be taken into account.

I was not able to observe the response of an acute exacerbation of lepra reaction to the sulphones, because the supplies available and the accessory premedication and investigations considered necessary caused these drugs to be reserved for the series of cases dealt with in

† Antimonii et Potassii Tartras gr ii (0.12 gm.)

the Third Section of this Thesis, some of whom were in sub-acute, chronic or localised conditions of the reactive state.

The prognosis in leprosy generally is so closely bound up with whether or not the reactive state develops, and the intensity and frequency with which it is manifested when it does develop, that an investigation of the prognosis in lepra reaction was considered to be of importance. In December, 1948, I was able to follow up the case histories of twenty-three patients all of whom I had examined in acute lepra reaction at the end of 1943 and the beginning of 1944 at the Uzuakoli Leprosy Settlement. These comprised 13 lepromatous, 7 indeterminate, 1 major tuberculoid and 2 minor tuberculoid cases. Of the lepromatous cases only three (23%) had become negative after five years' treatment with Hydnocarpus oil, but three had been transferred to the BELRA Nigerian Research Unit, and one of these cases estimated bacteriologically as 'positive scanty' had become negative after six months' treatment on the sulphones between May and November, 1948. Of the other two transferred patients, one was still strongly positive after sixteen months' treatment, and the other had remained 'one plus' after four months' treatment with the sulphones. Of the remaining seven lepromatous cases two had gone away, one had died, one had been dismissed and three were still in the active and infective state but continuing Hydnocarpus oil treatment, two having been found not suitable for, and one having refused the sulphones. The prognosis for this small series of cases suffering from acute lepromatous reaction in 1943 to 1944 is thus seen to have been unfavourable under treatment with Hydnocarpus oil in 77 percent of cases, some of whom persisted with treatment, but an equal number to those rendered negative returned to their homes to spread infection.

Of the 7 indeterminate cases, one had become minor tuberculoid, four had been discharged negative, one was waiting and considered fit for discharge and one had died. The single major tuberculoid case had been discharged as had also the two minor tuberculoid cases. The high discharge rate and the transition to a benign, resistent type illustrates the better prognosis in these cases of indeterminate and tuberculoid types, in which reaction appears to be associated with elimination of the disease. The fact that reaction in tuberculoid cases is sometimes followed by ulceration and deformities should, however, be kept in mind in assessing the outlook for these patients and treatment regulated to avoid reaction if possible, because if it occurs severely and frequently it is not always of good portent.*

* Case no. 21.

10. Staff.

Patients are the best leprosy workers and full use should be made of those who, whether discharged or still under treatment, are suitably qualified and show interest and ability. It is imperative that all patients be given something to do which is in accordance with their aptitude and training, and when this work justifies the payment of a small sum from the funds of the scheme it contributes towards their support, although these earnings should be considered as merely supplementary to individual agricultural activities in which all able bodied patients should engage (page 37). The sharing of certain activities between patients and healthy African staff relieves the latter of various less important tasks which would otherwise occupy their time, and the employment of patients as nurses presents actual advantages over the employment of healthy staff for these duties in which the question of risk of infection from long, close contact might arise. Other advantages are that lepers can be made to take a special interest in the disease from which they are suffering; they reside in the Settlement or villages and can be readily summoned by day and by night; they are amenable to discipline and a small maintenance allowance amounting to ten shillings a month for each of them has been found to be sufficient for their essential requirements in Afikpo Division. Many are still voluntary workers, but it is hoped to extend the system of making small payments to nurses in segregation villages when funds for that purpose are made available by the Nigerian Government. The 'patient' staff of the Ogoja Leprosy Scheme in September, 1949 was as follows:-

24 patients licensed as injectors and assisted by others trained to boil and sterilise and handle needles and other equipment and to apply antiseptics, all acting on a voluntary basis.
3 nurses in the Settlement on a maintenance allowance.
1 nurse in Owerri Edda Segregation Village on a maintenance allowance.
5 nurses in other segregation villages on a voluntary basis.
1 evangelist on a maintenance allowance from Mission funds.
1 night watchman in the Settlement on a maintenance allowance.
3 sweepers for Settlement buildings on a maintenance allowance.
A varying number of road labourers, usually about 80, divided into two gangs, one composed of able bodied men and the other of men with some disability and boys detailed for lighter duties remunerated as already indicated (page 37); also a varying number of Settlement labourers for building and for initiating various agricultural activities.

'Patient' staff are so termed to avoid the word 'leper': healthy staff are termed African staff.

African staff was composed as follows:-

2 experienced medical orderlies both with several years' general hospital training. Both can supervise treatment at clinics, labour, crafts and agricultural activities, and one has considerable experience

in survey work. We have an ex-service man undergoing a years' training at the Government Experimental Farm at Abakaliki, who, when he returns, should be able to give the necessary supervision to agricultural activities. This man has had experience of general hospital and clerical work also, and may have to turn his hand to these as the occasion arises. There are two young medical orderlies in training. One has had two months' training in the common tests required in connection with the administration of the sulphones, haematological and bacteriological work at the BELRA Research Unit at Uzuakoli, and he has also had an introduction to compiling statistics and the keeping of records. The other young medical orderly has concentrated on the supervision of clinics and is available for general work such as business at the post office and railway station which would otherwise occupy the time of the more experienced men. One general 'transport assistant', another ex-service man, supervises labour on the roads and is responsible for the cleaning and lesser repairs to cars, cycles and the autocycle. He also assists the driver-mechanic, the most recent addition to the staff, in larger repairs.

Lectures have been given to the two experienced medical orderlies and to certain of the 'patient' staff. Most of the latter have fairly simple duties to perform, but a little theoretical knowledge is useful for the nurses. In the early part of their training the young medical orderlies benefit most from practical work under the direct supervision of one of the senior orderlies or the doctor. Later they will benefit more from lectures and reading in preparation for examinations. One examination was held for the two senior medical orderlies in which both did exceptionally well; one, in particular, had grasped the principles of control and scored high marks in the differentiation of case types.

The medical orderly trained in laboratory work is reserved for this and for statistical work in the Settlement and he also tours the clinics to take smears. He will be required to relieve the other medical orderlies and supervise clinics when they are on holiday. Each of the three other medical orderlies has a number of clinics for which he is responsible and which are also supervised by the doctor at least once every three weeks. All clinics are still supervised by the touring unit from the Settlement, not more than three being attempted in a day, and I have found it more profitable to concentrate my own activities on one clinic on these occasions for the purpose of calling the names of patients on the register, examining them and adjusting dosage where necessary, typing and admitting new patients, ensuring that the sterilisation of instruments and the technique of administering injections is being properly carried out, administering special injections myself, dealing with medical and administrative complaints, planning new houses and supervising village life and negotiating with chiefs who are patients and head men in these segregation villages and healthy chiefs of adjacent villages about the acquiring of land and other administrative matters concerning them both. If time is available

one or both of the other clinics where injections have by then been administered may be supervised by the doctor on the same day and some of the activities mentioned may be carried out. All the clinics at present in operation are in Afikpo Division and within a thirty miles' radius of the Settlement and so within reach by bicycle and motor lorry, making this frequent and detailed supervision possible.

The question arises, what will happen when more clinics are opened, some of them at a greater distance ? And there is also the more immediate problem of how the routine work can be devolved in such a way that it will be carried out satisfactorily and yet leave the doctor time to concentrate on essential activities like the development of the Settlement, special treatment as with the sulphone drugs, administration and the organisation of control activities and the carrying out of research. The answer is that more educated patients will have to be trained as nurses and leprosy inspectors will have to be employed on the lines laid down in the Government Proposals (1943) and practised at Uzuakoli (pages 21 and 22). Nurses for the proposed centre in Obubra Division are already in training and it is to be hoped that more educated patients will be attracted to the Settlement with the improved amenities following on its development, by improved treatment, and sufficient funds to cover their salaries. When sufficiently trained,a nurse could be stationed in the area from which he comes. Provided he showed sufficient ability and was non-infective there could be no objection to his handling records and being primarily responsible for the carrying out of treatment at the clinic. These nurses would have to be carefully chosen as regards character because temptations to yield to bribery are great, and supervision by the touring unit at least once a month would be essential. More of the patients requiring special treatment and more advanced infective cases would have to be encouraged to come to the Settlement as it is obvious that only those likely to respond to routine treatment with Hydnocarpus oil and those with ulcers requiring simple dressings and some with minor complications and other conditions could be satisfactorily dealt with by this system. The position with regard to leprosy inspectors is that our present funds are fully allocated and and although provision may be made for the salaries of this type of staff from Native Administration funds at a later date, negotiations have not yet been started to this end. Material assistance from leprosy inspectors cannot therefore be contemplated in the near future. When funds are available a few of these men should be trained and located to clans where control activities are in progress and in the maintenance of these, especially of propaganda and the carrying out of repeated surveys they should prove invaluable. I hold, however, that no great reliance should be placed on them as substitutes for regular and frequent visits of the touring unit from the Settlement in the supervision of treatment at clinics. Under the Uzuakoli system the nurse administers treatment, but with our system of voluntary injectors at clinics this could be modified and the nurse become responsible for supervision under the touring unit.

11. Development of the Scheme.

Nigeria is divided into four main regions from south to north by its vegetation. There is the costal region of mangrove swamp stretching up to fifty miles inland at some parts, followed by a region of palm and deciduous forests extending up to about a hundred miles from the coast. From there the region of savannah or grass country occupies the greater part of Nigeria and merges in the north into the regions bordering on the Sahara Desert. Afikpo Division of Ogoja Province lies partly in the region of palm and deciduous forests and partly in the savannah or grass country, a transition which is defined enough to be noticeable on crossing the Asu River between Amaseri and Okposi. Situated in undulating country between seventy and one hundred and twenty miles from the coast, this area where most of my work has been carried out and where methods of leprosy control are likely to be applied in the near future, is largely on a subsoil part lateritised sandstone and part clay (Geological Survey Department, 1950). It is bounded roughly by the Ngusu hills to the south of the Edda area, the Mpu hills west of Uburu, the Cross River to the east and a wide plain to the north. Rainfall at Afikpo was recorded as 80.24 inches in 1947, a moderate rainfall for Nigeria. The seasons are well marked, a hot dry season between October and February alternating with a cool rainy season between March and September. The Division stretches at its widest points about forty miles east to west and about fifty miles north to south. The density of population for Ogoja province is given (Nigeria, 1938) as 94 per square mile. No recorded estimates for Southern Ogoja Province or for Afikpo Division have been obtainable, but if the same applies as for the Province as a whole there should be no land shortage, except that much of the land is not, and some of it cannot be used for agricultural purposes. The predominant occupations are farming and trading, the palm oil industry being of major importance.

Of the various methods of controlling leprosy none is more suited to this locality and none is more likely to be effective than that chosen by the people themselves. The Provincial Leprosy Scheme for the control of leprosy with administration, treatment and training of staff centred in a settlement and backed by clinics, surveys and propaganda in the clans which are the administrative unit and the core of compulsion, with local village segregation as the most important element in the scheme for control, has already been referred to (pages 25 and 26). There it has been stated why it would be inadvisable to attempt to deal with the problem by clinics alone or even by a combination of clinics and a central settlement: elsewhere the disadvantages and ineffectiveness of the Settlement alone in attempts at control have been dealt with (pages 31,32 and 33). Isolation of a patient in his own compound might not be effective under the conditions of overcrowding which prevail, and if it were efficiently practised would have a depressing effect on the patient. Incidentally, I object to the word 'isolation' being applied to the control of leprosy by

settlements and villages because it savours of solitary confinement, but is correctly used in the term 'compound isolation'. Clan chiefs in Edda have told me that compound isolation was in force there before the advent of civilisation when Nigeria came under British protection, and some also stated that the number of lepers has increased since this method was abandoned. That leprosy might increase with the progress of civilisation is conceivable, but I was also told that terrible cruelties were perpetrated towards lepers at that time and a return to such measures is unthinkable. It seems doubtful whether lepers were actually put to death by being buried alive, but one chief modified a statement to this effect by declaring that they frequently committed suicide when ostracized and driven into the 'bush'. It may have been, then, that because of these cruel measures few lepers were known, the majority concealing their condition in the early stages and remaining a danger to the community, but whatever occurred the measures employed were not effective. * Table XII shows an incidence of 90.2 per mille in this community: allowing for the fact that estimation of the total population is difficult and that not all were examined, there were 96 lepers in 7 villages where now most lepers are known and segregated. And here is the answer to the possible objection I have already raised (page 31) that segregation of patients in villages near their homes might be less perfect in theory and in practice as compared with segregation in a distant settlement: for when compulsion comes from within the enlightened community itself, cruel methods are abandoned and segregation being made attractive becomes effective.

It is proposed, then, to encourage and develop schemes for village segregation where these already exist and to extend them to other clans. The preponderant demand in Afikpo Division for village segregation is sufficient evidence of the popularity of this method. Of the eight offers of land which have been maintained in this Division, seven are for segregation villages and only one - from the Enna Clan - for a clinic alone; that is, seven clans offered land of sufficient extent to accommodate their lepers under reasonable living conditions with facilities for water supply, transport and agricultural development. The reason for this is undoubtedly the popularity and success of the system in the Edda area. The response of the patients is also of interest as an indication of the development of the scheme generally and with reference to village segregation in particular as evidenced by the following tables:-

Table II. Increase of patients on registers, 1941 to 1949.

1941	1942	1943	1944	1945	1946	1947	1948	1949
640	704	907	1111	1047	1232	1608	1972	2116

* Page 77.

Table III. Increase of patients segregated in villages, numbers of females exceeding males.

Clinic.	December, 1945	May, 1947	December, 1948
Oso Edda.	Males 190	200	238
	Females 217	242	260
	Totals 407	442	498
Owerri	Males 115	165	206
Edda.	Females 109	167	222
	Totals 224	332	428

Table IV. Patients not segregated attending two clinics; numbers of females not exceeding males or increase not maintained.

Clinic.	December, 1945	May, 1947	December, 1948
Okposi.	Males 51	78	97
	Females 27	53	79
	Totals 78	131	176
Akeze.	Males 61	85	101
	Females 29	136	85
	Totals 90	221	186

Table V. Numbers of patients at all clinics in August, 1949.

Clinic	Numbers	Remarks
Settlement	321	In-patients, 145; out-patients, 176.
Owerri Edda	248	Segregation Village. Divided to Apojo,1949
Afikpo	12	11 out-patients, 1 segregated at Owerri.
Akeze	138	Clinic. Land for village being sought.
Okposi	167	Clinic. Clan offered Settlement land.
Oshiri	166	Clinic. Adjacent land for village.
Itigidi	144	Clinic. Nearby land for village.
Ukawu	200	Clinic. Adjacent land for village.
Ndi Chuku	249	Seg. Village. Divided from Oso Clinic.
Ndi Iba & Ezi Edda	139	Seg. Village. Divided from Oso Clinic.
Ama Oso	124	Seg. Village. Divided from Oso Clinic.
Apojo	208	Seg. Village. Divided from Owerri Edda.
Total	2116	Number segregated 1114.

Table II shows the numbers of patients attending for treatment at the end of each statistical period being December of each year except 1949 when statistics were compiled in August. An increase could not be maintained between 1944 and 1945 because the work had reached a stage when admissions of new patients had to be curtailed. With the prospect of my appointment as Leprologist more patients were admitted in 1946 and since then the increase has been marked. There seems to be every prospect that, as additions are made to the staff and new clinics are opened this increase will continue and that as

more patients are segregated the control of leprosy will become possible. That some progress has already been made to this end in the Edda Clan in Afikpo Division appears to me to be indicated by tables III and IV where it is shown that increasing numbers of patients have been segregated since 1945, and that the numbers of females has continued to exceed males in Oso Edda and risen to exceed males in Owerri Edda. Davey (1947) found that when all the lepers were known in a community as on his surveys at Ndi Oji Abam (pages 45 and 46), the incidence of leprosy was higher in females than males although females showed no greater tendency to develop serious types; indeed, the incidence of lepromatous types was less in females than in males. I confirmed the latter finding in my series of 1007 cases (page 52) although in this instance the total number of males was greater than females due to the fact that more males were segregated in the Settlement. Table IV illustrates that the number of males usually exceeds females at clinics, and when the number of females exceeds males as at Akeze in May, 1947, this increase is transitory. This confirms my opinion that clinics are not a satisfactory means of dealing with leprosy treatment or control (page 25), while the fact that the sexes are both attracted to segregation villages where they continue to reside and attend for treatment makes it appear that the problem is being tackled in the community by this method which is acceptable to the people and therefore likely to succeed.

Table V shows the numbers of patients at all clinics in August, 1949. The notable features are that all the clinics are in or associated with land for segregation villages with the exceptions of Akeze where land for this purpose is being sought and Okposi where the Clan has offered land for the Settlement, and that in none are there more than 300 patients with the exception of the Settlement Clinic which is divided into in-patient and out-patient clinics. The Afikpo Clinic is included separately although it meets at Owerri Edda Segregation Village where 11 out-patients still attend and one is segregated, these patients being unwilling to change to staying in Apojo Segregation Village as I have recommended. 1,114 patients or more than half the total are segregated, but infective cases are still attending at clinics where village segregation has not been established and this number includes many non-infective cases who are segregated in the Settlement and segregation villages, no organised attempt at selective segregation having yet been made. In the Edda Clan where village segregation has been in operation and in the Amaseri Clan which has been co-operating with them at Owerri Edda and initiated the new segregation village at Apojo it is accepted that all types of leprosy require segregation. I have not attempted to change this system in these areas because it appears to be working satisfactorily and to present less risk from the occasional infectivity of tuberculoid types for the regular estimation of which bacteriological facilities have not been sufficient. My assumption that degenerative

changes as from the tuberculoid to the lepromatous type seldom take place (page 46) is borne out by my findings in 47 cases (page 53) and has been confirmed by the opinions of African and 'patient' staff and one segregation village chief who all assert that such a change has not been known in their experience. The statement might be modified to the effect that under careful treatment regularly supervised, changes of this nature have not been observed, and so the principle of selective segregation of lepromatous and extensive or active tuberculoid cases and 'indeterminate' cases with some lepromatous characteristics (page 50) remains a sound one. In clans where it has been difficult to urge all patients to segregate themselves I have attempted to persuade the lepromatous cases to segregate themselves first, and I have found it useful to make a distinction between usually non-infective and infective types in explaining to the chiefs of clans how we think leprosy is conveyed and in the hope that it may induce their co-operation when control by selective segregation is introduced. Table I illustrates that only about one fifth of cases of leprosy are lepromatous and therefore definitely infective, and from this it is clear that, where difficulty is experienced in segregating all lepers, the problem could be considerably reduced by concentrating our activities to these lepromatous cases and those in stages of the other types mentioned above. For this reason I consider that, under these conditions, selective segregation should be aimed at in framing our future policy, and in instituting propaganda.

Among a population which is largely illiterate propaganda by books and posters is not likely to be very effective. It is true that with the rapid spread of education an ever increasing proportion of the populace is learning to read, but until more are able to take advantage of these facilities literature is not likely to prove a very effective channel for propaganda about leprosy. It is important first to influence the chiefs of clans and the village and compound head men many of whom are autonomous in their own domain. Our method of approach to the Clan through the Clerk of the Native Court then speaking to the Clan Council and discussing the question of leprosy control in the Native Court and later with village and compound heads on survey, has proved an effective method of propaganda as well as a means of initiating control and treatment in an area where no previous work of this type had been done. Because of his official status and intimate association with Native Authorities the District Officer is in a particularly favourable position to spread information about facilities for the control of leprosy and to encourage the clans to put our measures into effect, and we have been fortunate in enjoying the co-operation of all the District Officers who have been stationed at Afikpo. Recent legislation enforced by the District Officer to the effect that only lepers staying in segregation villages shall be exempt from paying tax has done much to encourage the Akeze Clan to look for a site for a segregation village. Successful clinics and segregation

villages are important factors in bringing forward new patients and in demonstrating the means whereby leprosy can be controlled, but where both have been in operation in Afikpo Division for sixteen years it is only now that their effects are becoming apparent. These, by themselves, are too gradual a method of disseminating propaganda planned to be effective within a reasonable period of years, and they must be combined with surveys which I consider to be the most effective propaganda because they carry the practice of the system into the heart of village life.

Surveys have been defined by Rogers and Muir (1946) as of two types, extensive or general and intensive or particular. The former "may be based upon the incidental examination of known cases of leprosy by officials and others, or upon the examination of certain groups, as for example, school children, prisoners, conscripts, or upon the examination of contacts of known cases." With regard to the latter, the same authorities state: "An intensive survey depends upon the complete examination of the entire population by a trained personnel. In reports of such surveys it should be stated whether the examinations were conducted in the clinic or in the persons' own homes."
My original plan for the control of leprosy in Afikpo Division (Logan, 1948) envisaged a scheme in accordance with Rogers' plan initiated by extensive surveys of all school children and possibly Church members, to ascertain in which clans the incidence of leprosy is highest. When this was discovered intensive measures for leprosy control were to be applied in each of eight sectors of the Division over a period of ten years, starting with those in which the problem is most acute. Rogers (1946) enjoins the segregation of infectious cases and the repeated examination of contacts over a period of five to ten years, combined with treatment by Hydnocarpus oil injections, by which means the disease would be prevented from spreading and those already infected would be discovered at a very early stage and some ninety percent of them cleared of their symptoms. Rogers assumes that segregation applied over a period of ten years would be effective because, "lepromatous cases that have reached a stage unamenable to treatment live only for an average of eight to ten years, as shown by reliable U.S.A. records;" and the incubation period of leprosy being invariably less than five years, at the end of ten years all infective cases would have been segregated for that period at least, advanced cases would have died, the majority of patients treated in the early stages would be cleared of their symptoms, prevented from going on to the infective stage, and renewal of the epidemic would become impossible. This simple theory was to be explained to the native authorities of all the clans in Afikpo Division, put into operation during the whole term of lease of the Settlement or ninety-nine years if necessary and applied when possible to Obubra and Ikom Divisions.

Further consideration and subsequent experience led me to modify my plan and abandon the idea of preliminary extensive surveys, and to conclude that it is better to start with intensive surveys in a clan where facilities for treatment and, preferably, segregation also, are already available. These intensive surveys should be carried out in each compound when they are likely to be more exhaustive than if conducted in a clinic, central building or open space between the compounds. At Oshiri Church of Scotland Mission School 78 pupils, their ages varying from 5 to 16 years were examined and no cases of leprosy found although there are now 166 lepers attending for treatment at the Clinic there. At Itigidi I had a similar experience, and here there were some suspected cases. I then realised that Cochrane's (1947) proviso, that school attendance has to be compulsory, must apply before preliminary extensive surveys become "the most practical method of estimating the relative importance of leprosy in a district." Where, as in Afikpo Division, school attendance is confined mainly to selected children of more prosperous parents who can afford to pay fees, an extensive survey yields information of little value with regard to the incidence of leprosy in a community. Furthermore, it is better that suspected cases found on these surveys be discovered in the presence of their parents or senior members of their families than in the presence of the schoolmaster who would normally be present when his pupils are being examined. It is easier to explain to relatives that the child, if a suspected case and non-infective, need not be excluded from attendance at school, but should report for re-examination in three months when a definite diagnosis may be arrived at. Similar considerations might apply to Church members, but the enlistment of the co-operation of these and of teachers, pastors and evangelists as agents in the leprosy control campaign, and the retention of the school which is also in many cases the Church as the place of residence overnight and the centre of these activities as in my original proposals, remains a sound idea. Officials in Church and school have been found to give intelligent and thorough assistance: they usually know where a focus of infection exists and, being in a position of trust in the community, are able to advise on how an approach should be made to dealing with the problem humanely and effectively. The assistance of scholars has been enlisted as interpreters of local dialects and as carriers of the equipment necessary for a survey, collapsible table, a chair, basin for washing hands, rubber gloves, soap and disinfectant. Their association with the anti-leprosy campaign in this way is also a useful means of propaganda among the younger generation. This work may later be devolved on leprosy inspectors and hired labourers, but in the absence of these such assistance is invaluable. I would advocate, then, the Propaganda-Treatment-Survey method of Muir (1948) applied to all clans willing to co-operate, with repeated surveys and examination of contacts in the clan and facilities for treatment and village segregation available within the limits of our resources.

The difficulties of puting Rogers' plan into practice in a primitive community are aggravated by the fact that treatment by injections of Hydnocarpus oil, while often contributing little to improve advanced nodular and diffusely infiltrated lepromatous cases and nothing to render them non-infective, appears to prolong life indefinitely as evidenced by the records of patients, for example cases numbers 4,15 and 16. The fact that less than 10 percent of cases showing positive smears at the beginning of a period of five to eight years may belong to this group at the end of that period (3 out of 31 cases in my series of 47, page 53),and that these cases may not constitute more than 6.4 percent of all cases is offset by the experience of Davey (1947) who traced 31 new infections to 8 lepromatous cases only. It has been shown that some cases like these grow tired of ineffective treatment and return to their homes or have to be dismissed for one reason or another, and this is not surprising (page 60), and the absolute segregation of these cases over a number of years must, under any circumstances, present difficulties.

Accordingly treatment with the sulphone drugs which presents promise of rendering infective cases non-infective within a shorter period and appears, at least, to be more effective in advanced lepromatous cases (Cochrane, 1949), must be considered as an adjunct to the methods of control which I have described. Faget (1947), using promin, diasone and promizole reports that,"after 4 years of continuous intensive treatment the incidence of negative reports exceeds 50 per cent." Lowe (1948) using diasone and sulphetrone reports that, "23 (68%) out of 34 cases have become bacteriologically negative", treated over two years, mostly 32 months. Muir (1947) points out the advantages offered by the use of the sulphone drugs for earlier segregation and more effective treatment of infective cases, cutting off the danger of infection at its source. In a later publication Muir (1948a) states:"There is reason to hope that the whole question of the control of leprosy will be considerably modified by the introduction of sulphone therapy." He suggests a prospect that the more effective treatment of leprosy with the sulphones may justify a radical change in policy, at least in places where leprosy is of low endemicity, such as the abolition of leprosy asylums, intensive training of specialists and periodic examinations of new arrivals and contacts as sufficient to control the disease; but he considers that, where the incidence is higher, "it would be a mistake at the present stage to abolish institutions for isolation." Lowe (1948a) predicts"increased demands for sulphone treatment and for admission to institutions using it. An increased discharge rate of healed lepromatous cases may be expected, which may necessitate increased staff and facilities for supervision and re-examination of discharged cases." Like Muir he suggests, "the need for the modification of the types of leprosy institutions and methods of work, since more patients should be effectively treated and discharged, and fewer patients will remain indefinitely and finally die in leprosy

institutions." Cochrane (1947a) stresses the danger of treatment receiving precedence over prevention and the toxicity of the sulphones promin and diasone; sulphetrone, he asserts, is the least toxic. His warning regarding the neglect of prevention is countered by Lowe (1948a) who asserts that, "any improvement in treatment is potentially an aid to prevention," but he cautiously adds, "It remains to be seen whether sulphone treatment is, or can be made, sufficiently effective to afford this aid to preventive work which is so much needed."

My experience of the sulphones is too limited for me to draw definite conclusions as to what is likely to be their ultimate value in the control of leprosy, but the results I have seen are encouraging, and I have formed the opinion that the future of these drugs regarding use on a wide scale with consequent effects on control and prevention may well depend on the factors of cost and toxicity. Diamino-diphenyl-sulphone is heralded by Cochrane (1949) as the most effective anti-leprosy remedy he and his co-workers have used, but they have not formed conclusions as to its toxicity. Lowe (1948) in a preliminary report on the use of this drug asserts that, "Six weeks' treatment, continuous in most cases has produced no toxic effects of consequence. Oral administration is preferred to injection....This method of treatment, if effective, should prove most economical in drug, staff, labour and equipment." If this drug were proved to be of low toxicity and available in large quantities at a low cost it might become an effective adjunct to other measures in the control of leprosy, apart from the possibility of the development of a resistent strain of the organism. Further research into the potentialities of this and other drugs with a view to the synthesis of other compounds if necessary is therefore indicated.

12. Surveys.

It was considered that useful information might be obtained by comparison of the results of intensive surveys in two areas, the Agbo Clan where no measures for the control of leprosy had been applied and the Oso division of the Edda Clan where village segregation had been in practice for a long time and encouraged by treatment for the past sixteen years. The primary purpose of the survey in the Agbo Clan was to initiate measures for the control of leprosy, and at Oso to estimate the effects of village segregation and treatment, no other control activities having been applied. It should be emphasised that these are preliminary surveys only and that a satisfactory response is not likely to be attained until repeated surveys have been made. An exact estimation of the population is impossible, but the number of taxable males in each village is recorded. This number is usually multiplied by three to form a rough estimation of the population of a village, and this makes the discrepancy between the number of persons examined and the possible population apparent in most villages and in the totals for each area. The results, however, present features of interest which, taken along with my experience of the people and in consideration of the satisfactory response in some villages, form a basis from which certain conclusions can be drawn.

In the Agbo Clan all persons were examined in their compounds except in Itigidi Village where a central clinic building was used. Examination was facilitated by the fact that little clothing is worn, the men wearing a towel tied round the waist and the women a narrow cloth or kappa drawn between the legs and suspended round the waist. Women were examined in a separate part of the compound from the men or one by one at the clinic, a senior or educated woman being present to ensure that local ideas of modesty were complied with. In the Edda area where few of these taboos apply all persons were examined in an open space between the compounds or in a central building. Children up to the age of puberty are usually unclothed. 3039 persons out of a possible population of 6507 were examined in the Agbo Clan and 1064 out of a possible population of 3012 in the Oso area. In the former I was informed that there were many absentee lepers but in the latter that only three cases suspected by the tribe as possibly suffering from leprosy were absent when the examinations took place. There are no significant differences in ethnological and social groupings among the majority of persons examined and climate and geological features are also similar, being as for Afikpo Division (page 64). The two areas are not more than twenty miles apart by road and are both in the area of palm and deciduous forests, the Agbo Clan being nearer to the Cross River where this area extends further north. Most of the Agbo Clan are pagans, but the Church of Scotland and the Roman Catholic Missions exert an influence which is extending. The Church of Scotland Mission influence is pronounced in the Edda

Clan, throughout which churches and schools have been established for a long time. Economic conditions are poor in the Agbo Clan being only slightly better in the river village of Itigidi, and poor or, at most only moderately good in the Oso Edda area. The staple diet, yams, cassava and maize with palm oil and sometimes a little meat, and fish in the river areas, varies little between Agbo and Oso Edda. Housing conditions are poor with marked overcrowding in both areas, the compound arrangement being also common to both. Sanitation is poor throughout Agbo and Oso Edda, open latrines being used situated in the 'bush' beside the villages. Except beside the Cross River there is a great scarcity of water in the dry season, with the consequent lack of pure drinking water and adequate washing facilities. The predominant occupations are as for Afikpo Division (page 64) with fishing added at Itigidi on the Cross River. Prevalent diseases other than leprosy were, in order of frequency in the Agbo area, molluscum contagiosum, vitiligo, guineaworm, septic wounds, abscesses, osteomyelitis, tropical ulcers, tinea corporis and flava, filaria with its common accompaniment, hydrocele, sclerodactylia; malaria is prevalent everywhere, there was an epidemic of whooping cough among the children and adults showed evidence of previous epidemics of smallpox with facial pitting. In the Edda area secondary and tertiary manifestations of yaws was most commonly observed, followed by tinea corporis, capitis and flava, sclerodactylia, naevi, tropical ulcers, molluscum contagiosum, septic hands, abscesses, knee, and joint infections elsewhere, malaria, 'rheumatic' pains and dysentery; whooping cough was present and sporadic epidemics of cerebrospinal fever and smallpox occur from time to time with devastating effect on the population who are, on the whole more severely affected by these and other diseases than the Agbo Clan. Migration in search of work is more common in the Edda than in the Agbo Clan, and in Edda there is also a changing population of workers engaged in 'tapping' palm trees for wine, which may partly explain the greater discrepancy between actual population examined and possible population in this area. The survey in Agbo was conducted between November and February, 1947 to 1948, and the survey in the Edda Clan between March and July, 1949.

The main differences, then, were the methods in which the surveys were conducted, and the more pronounced civilising influence in the Edda Clan. Had the compound method of examination been carried out in Oso Edda it is probable that more persons would have been examined, and for this reason I would recommend this method for future surveys. The civilising influence in Oso was evidenced by the belief among the village head men that leprosy was conveyed by contact, two of them being able to differentiate roughly between infective and non-infective types. Where a good response was obtained in Oso, as at Ndi Obasi, no lepers were found at large in the community and where a fair response was obtained as at Ndi Ubo, only one tuberculoid leper woman who had recently come to the district was detected on survey, all the others being segregated, which contrasts markedly with the numbers of lepers at large in the community in villages where a good response

was obtained in the Agbo area as at Itigeve and Akarafo Igbo, and even in villages where the response was not considered to be so good, as at Itigidi and Anong and Anong Ede. The greatest numbers of lepromatous lepers were found in this last group of villages, Anong and Anong Ede in the north of the Agbo area, the other lepromatous cases found on survey being all in the south of the area near the Cross River at Itigidi, Adadama and Itigeve, but it would be unwise to make generalisations about the spread of infection from these two foci throughout the Clan, because it is my opinion that not all infective cases were found on survey. In Oso Edda, on the other hand, where I believe all infective cases are now known and segregated, it appears from table XI that lepromatous cases are more evenly distributed throughout the villages, and this, I consider, is a more accurate picture of what actually occurs.

The main factor in the control of leprosy in Oso Edda was, undoubtedly, the establishment of the Oso Clinic in 1933 which popularised the system of village segregation already in force. This, continued over a period of sixteen years is now showing results in that, among a population which would appear to have a higher incidence of leprosy even in relation to the possible population and certainly in relation to the population examined - 90.2 per mille in Oso and 36.8 per mille in Agbo - nearly all the lepers are segregated including, apparently, all the infective ones. The presence of a high proportion of indeterminate cases (29.1%) in Oso where treatment and segregation have been in force is interesting compared with the low proportion in the Agbo Clan (2.7%) as recorded in tables IX and XIII. Perhaps we may assume that about one third of these cases have been lepromatous as illustrated by my findings (page 53) that 9 out of 25 cases of the indeterminate type had been lepromatous five to eight years previously. In that case, although the frank lepromatous rate is higher in the Agbo Clan (16.1%) than in Oso Edda (12.5%), the actual lepromatous rate may have been higher in Oso Edda (one third of 29.1 added to 12.5, 22.2%), and we have one of Muir's (1948) two main signs that leprosy is diminishing in a community. With regard to Muir's other sign, a low child rate, this is recorded as 15.2 percent in the Agbo Clan and 6.2 percent in Oso Edda for children between the ages of 0 - 10 years, and I consider that this finding is of definite significance as indicating a higher rate of infection among young children where no organised methods of control were in force. Age estimations are mere approximations in these communities, so no great significance should be attached to the fact that the 0 - 10 and not the 0 - 14 group as recommended by Muir has been chosen: the total percentage under 18 years is still a little higher in the Agbo area (19.7%) as compared to the Edda area (16.6%), but the percentage in the 11 - 18 group is higher in the Edda Clan (10.4% compared with 4.5% in Agbo). There may then have been a higher child rate in Oso before village segregation was popularised. These and other findings are recorded in the following tables:-

Table VI. Preliminary Survey in Agbo Clan: population examined.

Villages	Males	Females	Total	Taxable Males	Remarks.
Anong and Anong Ede	177	177	354	269	Distant village not surveyed.
Itigidi	195	165	360	300	Survey in clinic.
Adadama	180	67	247	581	Survey stopped.
Ngerabi Igbo	119	80	199	162	Unsatis. response.
Ekurikunta	174	177	351	217	Unsatis. response.
Akarafo Igbo	309	328	637	226	Good response.
Umonekpo	92	89	181	70	Good response.
Agbara Igbo	261	204	465	268	Fair response.
Ogborenyi Akarafor	54	61	115	39	Good response.
Itigeve	50	80	130	37	Very good response.
Totals	1611	1428	3039	2169	Possible pop.6507.

Table VII. Preliminary Survey in Agbo Clan: persons with leprosy.

Villages	Types: Tuberculoid	Lepromatous	Indeterminate	Total.
Anong and Anong Ede	8	10	1	19
Itigidi	17	3	-	20
Adadama	5	2	-	7
Ngerabi Igbo	2	-	-	2
Ekurikunta	7	1	-	8
Akarafo Igbo	13	-	2	15
Umonekpo	6	-	-	6
Agbara Igbo	15	-	-	15
Ogborenyi Akarafor	2	-	-	2
Itigeve	16	2	-	18
Totals	91	18	3	112

There were in addition 47 suspected and 5 arrested cases seen on survey.

Table VIII. Preliminary Survey in Agbo Clan: incidence of leprosy.

Sex	Population examined.	Cases of active leprosy examined. Tuberculoid	Lepromatous	Indeterminate	Total.	Incidence, per mille.
Males	1611	47	14	1	62	
Females	1428	44	4	2	50	
Totals	3039	91	18	3	112	36.8.

Table IX. Analysis of cases by type and age.

Age group.	Tuberculoid	%	Lepromat.	%	Indeterm.	%	Total for age group.	% total cases.
0 - 10 yrs.	16	14.3	1	0.9	-	-	17	15.2
11 - 18 yrs.	2	1.8	3	2.7	-	-	5	4.5
18 - yrs.	73	65.1	14	12.5	3	2.7	90	80.3
Totals	91	81.2	18	16.1	3	2.7	112	100.0

Table X. Preliminary Survey in Oso Edda Clan: population examined.

Villages	Males	Females	Total	Taxable males	Remarks.
Ndi Ikpo	43	21	64	85	Unsatisfactory.
Ndi Uche	70	65	135	92	Unsatisfactory.
Ama Oso Nta	81	42	123	177	Unsatisfactory.
Ndi Ubo	84	86	170	94	Fair response.
Ndi Nnachi	51	41	92	89	Unsatisfactory.
Ndi Okpo	91	68	159	294	Unsatisfactory.
Ndi Obasi	146	175	321	173	Good response.
Totals	566	498	1064	1004	Possible pop. 3012.

Table XI. Preliminary Survey in Oso Edda Clan: persons with leprosy.

Villages Types:	Tuberculoid	Lepromatous	Indeterminate	Total.
Ndi Ikpo	5	2	-	7
Ndi Uche	7	1	2	10
Ama Oso Nta	8	3	9	20
Ndi Ubo	10	2	3	15
Ndi Nnachi	7	1	2	10
Ndi Okpo	16	2	10	28
Ndi Obasi	3	1	2	6
Totals	56	12	28	96

There were in addition 9 suspected cases, 19 arrested cases and 11 cases in segregation villages not classified.

Table XII. Preliminary Survey in Oso Edda Clan: incidence of leprosy.

Sex	Population examined.	Cases of active leprosy examined. Tuberculoid	Lepromatous	Indeterminate	Total.	Incidence per mille.
Males	566	27	7	11	45	
Females	498	29	5	17	51	
Totals	1064	56	12	28	96	90.2

Table XIII. Analysis of cases by type and age.

Age group.	Tuberculoid	%	Lepromat.	%	Indeterm.	%	Total for age group.	% total cases.
0 - 10 yrs.	5	5.2	-	-	1	1.0	6	6.2
11 - 18 yrs.	5	5.2	-	-	5	5.2	10	10.4
18 - yrs.	46	48.0	12	12.5	22	22.9	80	83.4
Totals	56	58.4	12	12.5	28	29.1	96	100.0

III. A Comparison of the effects of Treatment with the Sulphones and Sulphonamides.

Similarities in Structure and Properties.

It was suggested to me by Mr. Michael Smith (1949) that, the sulphones and sulphonamides belonging to the same chemical family, the latter might also be worthy of trial as chemotherapeutic agents in leprosy. As Biochemist to the BELRA Research Unit at Uzuakoli, Mr. Smith was in a position to advise on this matter, and he also made available for my perusal some literature on the subject which corroborated that a clinical trial was justified. Mr. Smith pointed out that it is possible that the action of the sulphones is similar to that of the sulphonamides in substituting for para-aminobenzoic acid as a growth factor in bacteria which cannot synthesise this compound for themselves and therefore attempt to metabolise sulphonamides which have a similar chemical structure but are not suitable for bacterial metabolism, with consequent degeneration of the organism concerned. He also affirmed that it was possible that similar considerations would apply to any chemotherapeutic action of these drugs on the Mycobacterium leprae or the tubercle bacillus. Feldman (1946) has dealt with the derivation of the sulphones and sulphonamides from aryl-sulphonic acids, the common feature being an amine group in the para position with which he associated the therapeutic efficacy of the compounds he studied (Figure 2). Feldman has also confirmed the results of others, notably Rich and Follis (1938) and Follis and Rich (1939), and summarised the results of his own experiments with the sulphonamides in experimental animals as follows: "Sulfanilamide and a few of its derivatives are capable under certain specified experimental conditions of exerting a limited but definite retarding effect on experimental tuberculosis ... the degree of efficacy is striking in certain sites of predilection, but, at the most, the inhibitory effect was definitely circumscribed." With regard to the effect of the sulphones, Feldman records that they are capable of "modifying the morphological aspects of experimental tuberculosis profoundly," but he refers to their toxic properties as rendering them "unpromising."

This failure of the sulphones to be established as suitable in the clinical sphere in tuberculosis has not applied to their use in leprosy. The sulphones are all derivatives of diaminodiphenlysulphone, the parent compound, those commonly in use being promin, diasone, promizole and sulphetrone. Favourable reports on the use of one or other of these compounds have been submitted by the following:- Faget et alia (1943, 1947), promin; Faget et Pogge (1945, 1947), promin and promizole; Wharton (1946, 1947), promin and sulphetrone; Mom (1947), promin; Muir (1946, 1947), diasone; Fernandez and Carboni (1947), diasone; Fite and Gemar (1947), promin; Johansen and Erickson (1947),

promizole; Lowe (1948), diasone, sulphetrone and diaminodiphenylsulphone: Cochrane (1947a) warns regarding the toxicity of promin and diasone and recommends sulphetrone as the least toxic, but, in a later publication he and his co-workers (Cochrane et alia, 1949) report favourably on diasone, sulphetrone and diaminodiphenylsulphone.

In contrast to this wide unanimity on the value of the sulphones in leprosy, reports on the use of the sulphonamides are few, vary in their conclusions and, where favourable, have not been adequately confirmed. Dharmendra and Bose (1943) recorded that sulphanilamide and sulphapyridine in a dilution of 1 - 1000 possessed a bactericidal effect in vitro on Mycobacterium leprae muris if allowed to act on the organism at 37°C. for 48 hours. Krakower et alia (1943) reported that in rats and mice experimentally infected with a virulent strain of lepra bacilli, a diet containing 1 percent of sulphanilamide given for one year completely inhibited growth and development of leproma at the site of inoculation and prevented the occurrence of distant metastases. Control animals were not affected, and sulphathiazole, 1 percent in a single trial gave corresponding results. Krakower concluded that these drugs were definitely bacteriostatic for this mouse strain of the lepra bacillus and explained the modified results in tuberculosis by the greater vascularity of experimental leprous lesions. Dharmendra and Makherji (1944) failed to confirm the results of this experiment: using sulphapyridine in a 1 to 2 percent suspension for the treatment of leprosy in rats, they noted that the survival time of the treated rats was greater than any of the control rats, but concluded that sulphapyridine had failed to modify the course of experimental rat leprosy and that the drug did not appear to have any inhibitory effect in vivo. Faget, Johansen and Ross (1942) using large doses of sulphanilamide in 20 cases of humans with leprosy and producing blood concentrations between 5 and 9 mg. percent, noted pronounced toxic symptoms and signs; febrile reactions in most and anaemia and leucocytosis in many. They concluded that although the drug was useful for secondary infections it was not a curative remedy for leprous lesions. The 1943 Report of the Leprosy Research Department of the School of Tropical Medicine, Calcutta (1945) recorded that the injection of gr. ii (0.12 gm.) of sulphanilamide in 2 c.c. of Arachis oil into bacteriologically positive macules had no effect on the bacilli. The 1944 Annual Report of the Indian Council of BELRA recorded that sulphapyridine had not proved of value in the treatment of rat leprosy (1945). Chorine and Chabaud (1945) are reported as having made an attempt as early as 1936 to treat rat leprosy with sulphanilamide in doses of 10 mg. two or three times a week without any effect in retarding the progress of the disease. Negative results were again recorded by these workers in a later (1943) experiment in which larger doses were employed, and they are reported as having undertaken a subsequent trial in a case of human leprosy, resulting

in the conclusion "that the bacillus of Hansen is sensible to the action if sufficently high doses are injected directly into the diseased tissues, but it is not effective in any feasible oral doses." No direct lethal action on rat leprosy bacilli was detected when they were exposed to 2 percent saline solution of the same drug up to 72 hours. Again, Chorine and Chabaud (1945a) made a comparison of the action of sulphanilamide and acetamide septoplix in large doses in rats for 117 days, reporting that both drugs caused a reduction in the local lesions at the sites of infection but were no better simultaneously.

Only one successful attempt to treat leprosy in humans with the sulphonamides has been recorded. Lima and Cerqueira (1945, 1946) tried a complex sulphonamide, soluthiazamide, in the treatment of 50 early and 50 severe lepromatous cases over a period of eight months, starting with a dose of 0.2 gm. raised in adults to 2 gms. Results obtained are stated to have been: cicatrisation of lepromatous ulcers and conglomerate lepromata; the disappearance of lepromatous infiltrations and the softening of subcutaneous nodules; occasional improvement in perforating ulcers of soles; ocular symptoms after a brief period of exacerbation showed considerable amelioration and had not relapsed and nose blocking was relieved. The only other long term trial which I have encountered in the literature on the subject was by Cochrane (1947) who employed sulphapyridine in nine patients over a period of six months. Cochrane started with a dose of 2 gms. and increased it to 3 gms. but found that nausea and vomiting occurred: he then reduced the dose to 1.5 gm. and 2 gms., and maintained this until a reaction was precipitated. He concludes that, "The sulphonamides appear to have no influence on leprosy and should not be used unless there are specific indications for its use."

The Experiment.

Another clinical trial using a different sulphonamide in small dosage over a period of six months with accessory medication as for the sulphones, preliminary tests and regular haemoglobin estimations, under conditions in which a small series of cases could be compared with a similar series treated with the sulphones, appeared to be justified. Apart from the inhibitory effect on experimental animals with tuberculosis as recorded by Feldman, the sulphonamides had been recorded as having a bactericidal effect *in vitro* by Dharmendra and Bose, a bacteriostatic effect by Krakower *in vivo*, and had been claimed to be effective clinically by Lima and Cerqueira in leprosy. The sulphones had been found by Feldman to modify experimental tuberculosis profoundly and had subsequently been shown to be effective in leprosy in man: it seemed not unlikely, then, that in spite of the unfavourable reports recorded above, the sulphonamides might also have some effect on leprosy in man and the one favourable report to this effect might be confirmed. It was considered that this confirmation, if forthcoming,

might be a source of useful information on the action of the drugs and for future use in the synthesis of new compounds with repercussions on leprosy treatment and control. The experiment was also acceptable because of the scarcity and expense of the only sulphone available, sulphetrone, leading to a demand for its use which considerably exceeded the supply.

The compound first suggested to me as suitable for a clinical trial in leprosy was sulphamerazine, but I chose sulphamezathine * because of its lower toxicity and relative freedom from liability to crystalluria and renal damage reported by the manufacturers as due to the"high solubility of the free drug and also of its acetyl derivative" (Imperial Chemical -Pharmaceuticals - Ltd., current literature), and also because of its lower cost. It was decided to commence treatment with a daily dose of 0.5 gm. administered on alternate days for the first three doses, then every day with one week's rest for every three weeks' administration. It was originally proposed to raise the dose to 1.0 gm. daily in the fourth week of administration, but owing to 0.5 gm. daily producing the blood concentration expected with 1.0 gm. the larger dose was not administered except to two patients at a later stage of treatment. Besides Lima and Cerqueira above referred to as setting a precedent for the long term administration of the sulphonamides in small doses, Barclay and King (1945) have reviewed reports on similar trials in the prophylaxis of rheumatic fever. Asserting that these reports are"so promising as to encourage the promotion of similar trials in this country," these authors recommend sulphamezathine as "the least toxic of the sulphonamide drugs so far used over here", that is, in Britain. Reporting only one death which was from agranulocytosis among many thousands of cases recorded, these authors conclude that"the statistical danger from toxic manifestations is very small." Smith (1949) having suggested that as leprosy is caused by a lowly pathogen an agent interfering with bacterial metabolism or one that renders the bacilli susceptible to the action of the phagocytes would be successful, it was considered that low dosage as above detailed might be effective. The dosage of sulphetrone † was started at 1 gm. daily continued for a week, raised by one gram each week to a maximum of 4 gms. in certain cases varying according to weight - roughly 0.5 gm. per stone being aimed at - and apparent toleration. Full details regarding dosage are given for each case on sulphetrone and sulphamezathine, numbers 1 to 20. The course of sulphetrone was started on 1st. March, 1949 and finished on 31st. August, 1949: the course of sulphamezathine was started two weeks later, on 15th. March, 1949, and so finished on 15th. September, 1949.

In medical selection of cases preference was given to the most severe and advanced nodular lepromatous sub-types, infiltrative and macular sub-types to form a representative picture of the lepromatous type in two roughly parallel series of cases. All the cases

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* Structural formula, figure 3. † Structural formula, figure 4.

chosen were clinically of the lepromatous type and showed positive smears at the beginning of treatment. Haemoglobin estimations were carried out when medical selection was made and ferrous sulphate in pill form at doses varying from gr. 5 to gr. 15 daily (0.32 gm. to 0.97 gm.) was administered for four weeks before administration started to all cases on the sulphetrone series except numbers 9 and 10 who had it for three weeks. All cases in this series received medicinal yeast (D.C.L.) in doses of 4 drs. daily for the child (number 9) and 6 drs. daily for adults (15.55 gm. and 23.32 gm.) for three weeks before administration started. Only those patients who showed a haemoglobin estimation of 60 percent or over were chosen for sulphetrone administration and consequently numbers 11 to 14, started on sulphamezathine two weeks later were rejects from the sulphetrone series whose haemoglobin percentages had risen in the interval to the required level. All other cases on the sulphamezathine series were given similar medication for varying periods previous to administration, number 15 for four weeks, number 16 for 17 days and numbers 18, 19 and 20 for 12 days. During administration sulphetrone was given twice daily, morning and evening, and usually in equally divided doses, ferrous sulphate and yeast being similarly administered. In the sulphamezathine series 0.5 gm. or less was administered at one session, usually in the morning, ferrous sulphate being given concurrently and also at the evening session in equally divided doses. When 1 gm. of sulphamezathine was given it was divided into equal doses administered at the morning and evening sessions. The usual dose of ferrous sulphate during administration was gr. 10 daily (0.64 gm.), but this dose was increased in cases where the percentage of haemoglobin fell below 60 when proprietary liver extracts were also administered as in cases numbers 10, 11 and 12 in whom this was experienced during the long rest period accorded to all the patients between 28th. April and 23rd. May, 1949, resumption of administration being delayed as regards sulphetrone and sulphamezathine for the same reason. Ferrous sulphate crystals, ground down and dissolved in water were used in the dosage stated above to replace the pill form during part of the period of administration, and in this case it was found that the mixture had to be prepared freshly before each session because oxidised mixtures were useless. With the exception of case number 19 in whom special benefit appeared to accrue, the dose of medicinal yeast was reduced to 2 drs. daily (7.774 gm.) during the second month of administration. All the patients were living in the Settlement and were under my direct supervision at all sessions when any of these drugs were administered: they all led an active life, and it was not found necessary to impose any restrictions apart from advising rest during reactions.

Various investigations and estimations were carried out in the course of the experiment, but only those performed by myself at the commencement and at or towards the end of the six months' period in each series are recorded here. Routine monthly haemoglobin

estimations were performed to detect the appearance of hypochromic anaemia and were found to be sufficient for this purpose. Some of these were performed by myself and others by my African assistants, but are not included here; neither are those tests for liver function, estimations of blood concentrations or bacterial counts, the last being assessed on a different system than the one I employed, which were carried out by Mr. Smith or the BELRA Research Unit at Uzuakoli. It may be stated that histological examinations of material taken for biopsy about the middle of the experimental period from all cases in both series and sent to the Medical Research Institute, Yaba, confirmed that the sulphetrone and sulphamezathine series were roughly parallel in pathological as in clinical aspects, further details being omitted. Differential leucocyte counts performed on cases with fever in the early weeks of treatment revealed no marked deviation in the relative percentages of polymorphonuclear leucocytes and lymphocytes: Barclay and King (1945) having recorded that agranulocytosis is only to be expected between the 14th. and 49th. days, these investigations were not considered necessary in the later weeks, and no case of agranulocytosis occurred. Young (1949) has pointed out that," no evidence has been found that serial leucocyte counts during the administration of agranulocytosis-producing drugs either prevent agranulocytosis or reduce case mortality," and he suggests that a sore throat or fever be reported by a patient under prolonged sulphonamide administration. With patients in a settlement having temperatures recorded twice daily on charts and under direct medical supervision it was considered that time consuming laboratory work if not strictly essential could be dispensed with and that observation of the precautions which Young suggests would be sufficient. Frequent clinical examinations were carried out on all patients, in more detailed form at the beginning and end of treatment, the results being recorded on body charts. A record of dosage of sulphetrone and sulphamezathine was kept together with a note of any complaints made by the patients or any adverse signs all of which were carefully investigated. Investigations and estimations were dealt with as follows:-

Haemoglobin percentage: monthly, or where a low percentage indicated frequent repetition.

Red Blood Cell or erythrocyte counts: at beginning and end only required

White Blood Cell or leucocyte counts: at beginning and end only required

Thin blood film: as considered necessary.

Erythrocyte sedimentation index: three monthly; three times performed.

Bacterial counts: two monthly; four times performed.

Stools: ol. chenopodii m. viii to the boy, number 9,and adults m xv,to all patients for hookworm to prevent anaemia at the beginning and during administration of sulphetrone and sulphamezathine where necessary.

Urine: the heat test for albumen, acetic acid being added if a a white cloud developed; Schlesinger's test for haemolysis and liver damage, at beginning and end or when considered necessary.

Blood: Fouchet test for increased bilirubin in serum; at beginning and end of administration only required. Blood sulphone and sulphonamide concentrations were estimated by Mr. Smith of the BELRA Research Unit, Uzuakoli and by myself towards the end of the experiment.
Lepromin: not available.
Patients' weights: at beginning and end and three times throughout.

Where necessary these are further detailed as under:-

Bacterial counts. Two smears were taken from the nose, one from each nostril, by scraping the septum with a narrow bladed scalpel previously smeared with methylated spirits and flamed; one from the lobe of one ear by the slit method - a wound 2 to 3 mm. deep, the tissue scraped from the bottom - and four or five from the skin, usually the forehead, cheeks or chin, affected parts of the trunk and the buttocks. Smears are fixed by holding over a flame until the heat is just bearable when the slide is held against the back of the hand. Blotting paper cut to cover all the smears is placed over each slide, concentrated carbol fuchsin applied to cover the blotting paper and the slide heated gently over a flame until the steam rises, then left for 10 minutes. The slide is then washed in water and 10 percent sulphuric acid is applied, washed again and the acid reapplied if necessary to obtain a pale pink colour, washed again, then if a pale pink or colourless treated with methylated spirits for about 15 seconds, washed, and finally treated with watery methylene blue for two to three minutes then washed and dried by setting up on a stand or with blotting paper. In staining leprosy bacilli methylated spirits may be omitted or applied at the end, washing before and after, which method I prefer as I consider that thereby a clearer smear is obtained. Muir's (1948) method of estimating the numbers of bacilli or the degree of positivity of a smear or group of smears was adopted, † (one plus) indicating bacilli present but not more than ten in one field - when bacilli are scanty indicated by †s - and no globi in the whole of any smear: †† (2†) indicates one or more globi in the whole of any smear and/or more than ten bacilli in any one field: ††† (3†) indicates more than 10 globi in the whole of any smear. At least 30 fields were examined in each smear where bacilli were not abundant and at least 100 fields each of nasal, ear and skin smears, representative fields of the last, including the buttocks being investigated before a slide was declared negative, indicated by the sign'-ve'. Nevertheless, the arbitrary nature and limited scope of these estimations deserves emphasis, results being influenced by such factors as thickness of a smear and a few, sometimes degenerating globi in one smear only, bringing the degree of positivity into the second or even the third category. Cochrane et alia (1949) have recently introduced a better system of estimating the degree of positivity by a bacteriologic index which serves to eliminate this error by taking into account all the smears on a slide, a method which should be followed in future work of this nature.

Urine. In no case was albumen discovered at any stage after the preliminary medical selection of cases. Schlesinger's test for urobilin was applied by adding 3 drops of tinc. iodi mitis to 5 c.c's of urine in a test tube. 0.5 gms. of zinc acetate and 5 c.c's of absolute alcohol were placed in another test tube. The two were mixed and poured repeatedly from one tube to the other until most of the zinc acetate was dissolved, filtered, and the filtrate examined against a dark background. Only in one case, number 4 at the end of treatment with the sulphones, did a slight green fluorescence appear; no evidence of raised plasma bilirubin was observed in this case who will nevertheless have to be watched for evidences of liver damage if treatment with the sulphones is continued.

Blood. The serum Fouchet test for raised bilirubin was applied by taking one drop of serum on a white tile and adding to it one drop of Fouchet's reagent. In no case in either series of cases at the beginning or end of treatment did a green precipitate develop. Blood sulphone and sulphonamide concentrations were estimated by the method of Bratton and Marshall, standards for comparison being made up in dilutions between 1 and 10 mg. percent from tablets of both drugs dissolved in water and, in the case of sulphamezathine, acidified with hydrochloric acid; one tablet of sulphetrone or sulphamezathine or 0.5 gm. dissolved in 500 c.c's giving a dilution of 100 mg. percent and 1 c.c. of this dilution further diluted to 100 giving a dilution of 1 mg. percent, and so on. In carrying out the test, 0.5 c.c. of blood was added to 10 c.c's of N/1 HCl., mixed, then 4 c.c's of 12 percent aqueous trichloracetic acid solution added; filtered through a Whatman no. 1 (rapid) paper and the filtrate repassed if necessary to give a bright solution. To 3 c.c's of the filtrate was added 2 drops of 0.3 percent sodium nitrite solution; this was shaken and allowed to stand for 3 minutes. There was then added 2 drops of 1.5 percent ammonium sulphamate solution which was mixed well and allowed to stand 2 minutes. Finally there was added two drops of 0.1 N-(1-naphthyl) ethylene diamine dihydrochloride reagent and the colour was allowed to develop for 10 minutes before being compared with the standards already referred to on which similar procedures had been carried out.

Discussion of Results.

A perusal of the results of clinical examination in cases 1 to 10 and a glance at the signs of clinical improvement in the sulphones' series of cases in table 1 is sufficient to establish that favourable results reported from the use of the sulphones in leprosy have been confirmed in this series of ten lepromatous cases treated by the oral administration of sulphetrone over a period of six months. Reference to details of the cases referred to and also to the sulphones' series of cases in table 2 demonstrates that in every case with the exception of number 4, administration was accompanied by some possible toxic effects; and case number 4 has been referred to above as developing a reaction to Schlesinger's test at the end of treatment. Severe

acute reactions to the drug were noted in two cases, transient in case number 1 and recurrent in case number 9. In spite, then, of every precaution being observed in medical selection, the administration of ferrous sulphate before administration for four weeks, yeast for three weeks and both ferrous sulphate and yeast concurrently during the whole course; and in spite of the fact that continuous personal medical supervision was given and the drug suspended when adverse effects were observed, sulphetrone has been shown to have toxic properties which would prohibit its use other than in a settlement where adequate supervision is available. The fact that most of these toxic effects were minor and transient does not contraindicate this conclusion, because their neglect might have led to more serious manifestations. The oral administration of sulphamezathine was maintained throughout a course of the same duration, similar effects in clinical improvement noted, and toxic effects which were not widely dissimilar (cases numbers 11 to 20; sulphonamides' cases, tables 1 and 2); and so the results reported by Lima and Cerqueira (1945) on the effects of another sulphonamide in leprosy have been confirmed by this small series of 10 lepromatous cases treated over a period of six months. Lima and Cerqueira employed injections of soluthiazamide, so that my experiment would appear to be the first successful trial of oral administration of the sulphonamides in leprosy. In contrast to the unsuccessful trials which I have recorded, I consider that this demonstration of the activity of the sulphonamides in leprosy has been made possible by the choice of a suitable sulphonamide, sulphamezathine, administered in small dosage carefully supervised, with regular rest periods, and the concurrent administration of iron and yeast supplemented where necessary by liver extract. Lima and Cerqueira observed similar precautions, using erythrocyte counts in place of haemoglobin estimations as used by me to ascertain when supplementary administration was necessary. It was not possible to arrange for a control series of untreated cases or of cases on Hydnocarpus oil medication to be observed concurrently, but as far as adequacy and accessibility of patients' records allowed a note was made in each case (1 to 20) of the duration of treatment with Hydnocarpus oil and whether any improvement had been observed. From these notes it is evident that no comparable improvement took place within a similar or, usually, much longer period on Hydnocarpus oil therapy to that which has been recorded in all cases under treatment with sulphetrone and sulphamezathine over a period of six months. It should be added, however, that adverse effects of Hydnocarpus oil administration in the dosage I have described (pages 56 and 57) over a similar or longer period in a like series of cases, reasonable precautions being observed, might be expected to be negligible or very small.

Regarding a comparison of the clinical effects of the sulphones and sulphonamides, it is obvious that records of the number of patients showing clinical improvement in each group of signs are not

an indication of degree of improvement, and similar considerations apply to the degree of severity of toxic effects; some idea of both these factors may, however, be gathered from the case records. In these they are more detailed, others are included which have been omitted from the tables as of lesser importance, and, as with fever in case number 10, some have been recorded where the effect was apparently not due to the drug, and for this reason have been omitted from the table. Even where some have been included as in the case of catarrh, gingivitis and diarrhoea, they are only possible toxic effects. Although the series were roughly parallel with regard to lepromatous sub-types and stage of the disease they could not be exactly parallel regarding the presence of other clinical signs; and it is found, for example, that where 7 patients showed subsidence of infiltration of the nasal mucous membrane in the sulphones' series, only 5 showed similar improvement in the sulphonamides' series: but only 7 patients were recorded as showing infiltration of nasal mucosa in the sulphones' series at the beginning of treatment, and only 5 in the sulphonamides' series had it then also, so that all patients showing this particular sign improved, although the total numbers in each series differ. Nevertheless, it is considered that some idea of the comparative effects of the sulphones and sulphonamides in leprosy may be gathered from tables 1 and 2 in which it is obvious that a remarkable correspondence exists between the higher groups in each series; a correspondence which would appear to be beyond coincidence. Owing to imperfections already referred to, it would be unwise to press numerical relationships too far, but it may be remarked that the average number of patients showing signs of clinical improvement in each group of signs in the sulphones' as compared with the sulphonamides' series is in proportion to the average number of patients showing possible toxic effects in each group of possible toxic effects in the sulphones' as compared with the sulphonamides' series of cases, both being in a proportion of 1.3 to 1.0 (4.6:3.4 and 3.4:2.6, tables 1 and 2). Taking into account the proportion between the blood sulphone and sulphonamide concentrations towards and at the end of the experiment (averages 3.5:2, table 3) which is 1.75 to 1.0, which may be taken as representative of the whole experiment, or, if any difference exists, a little low as regards blood sulphone concentration, it would appear that similarities exist between the two drugs in clinical activity and toxic properties which are not unfavourable as regards the sulphonamides. As I have indicated above, too much reliance should not be placed on these figures, and my clinical experience has led me to prefer the use of the sulphones as affording a greater margin of safety in adjusting dosage, a more uniform and definite degree of improvement in each patient without complications, for example, the flattening without the bursting of nodules, and as showing more favourable results in haemoglobin estimations, erythrocyte counts, erythrocyte sedimentation rates and patients' weights (tables 4,5,7 and 8). From these tests it would appear that the sulphonamides as represented by sulphamezathine are actually more toxic than the sulphones as represented by sulphetrone under the conditions of this experiment.

Other facts which should be recorded as points of similarity include symptoms not dealt with in the case records or tables. All patients in both series experienced marked bulimia in the early weeks of treatment, lessening later: all likewise experienced relief of pains which they associated with the disease, an increased feeling of well being and increased ability to work. Naso-pharyngeal blocking was relieved in six patients in each series; numbers 1,4,6,8,9,10 in the sulphones' and numbers 11,12,14,15,19 and 20 in the sulphonamides' series. Growth of hair was stated to have been stimulated in five patients, numbers 1,2,6,8,9 in the sulphones' and in all ten of the sulphonamides' series. Two patients in the latter series demonstrated to me that healthier tow nails were growing since treatment started. Another point not indicated in table 2 is with regard to swellings which were confined to extremities or were subcutaneous in the sulphonamides' series but were seen in the genitalia, subcutaneous and an extremity in the sulphones' series. As is indicated in the table referred to, headache and epigastric and abdominal pains appeared more commonly among those treated by the sulphone, but pains in bones or nodules, and it should be added that these were mostly localised to the bones, for example, the anterior tibiae, appeared more commonly among those treated with the sulphonamide, all these patients complaining as opposed to eight of the sulphones' series.

Differences in blood concentrations of both drugs may be remarked upon, a variety of results being apparent in different patients not always corresponding to the dosage employed: in number 15 a larger and in number 20 a smaller dose than the average produced the same blood concentration, both patients being adults. Case number 1 who had been on a dosage of 3 gms. sulphetrone daily showed a blood concentration of 2 mg. percent one week after the drug had been suspended for reaction, and the boy, number 9, who showed the high level of 5 mg. percent concentration on a daily dose of 1.5 gms. developed reaction 2 days later. These facts possibly indicate a relationship between reaction and high blood concentrations, and confirm the importance of regular estimations, which, with a trained African assistant, should now be assured in the Ogoja Leprosy Scheme. Six estimations in the sulphetrone series show what is commonly experienced with this drug that the dose in grams. is approximately equal to the blood concentration in mg. percent: with sulphamezathine the blood concentration (mg.%) appears to be about four times as great as the dose in grams.

It should also be recorded that administration of the drug concerned had to be suspended in one patient in each series, numbers 9 and 20, in which cases it could not be re-administered without signs of reaction, a development of sensitivity which might make these cases unfit for further treatment of this nature. In two others, numbers 1 and 17, desensitation was apparently achieved by the administration of small, gradually increasing doses. Effects on secondary neural signs were not anticipated, but one patient on sulphamezathine revealed, at the end of treatment, free movements of formerly ankylosed joints of the second, third and fourth fingers of the right hand (case no. 18).

A reduction in haemoglobin percentage was more frequent in the sulphonamides' than in the sulphones' series, being manifest in four cases of the former as opposed to two of the latter, but case number 9 in the sulphones' series showed the severest reduction, 20 percent at the end of six months (table 4). Cases showing a marked reduction in haemoglobin percentage - numbers 9,16 and 20 - showed a reduction in the erythrocyte count as did also cases numbers 2,11,12 and 19, five in the sulphonamides' as opposed to only two in the sulphones' series, possibly indicating greater haemolytic properties of the former drugs. In only one case, number 9 of the sulphones' series, did the erythrocyte count fall below 3,500,000; but this case has been shown to be unsatisfactory in attendance for treatment and general nutrition (case record). The risk of glandular fever as a complication of the administration of the sulphones having been raised by Lowe (1948), evidences of this were carefully watched for in the early weeks especially. It is interesting to note in reference to table 6 that no marked leukopenia or leucocytosis was observed. In case number 9, the only patient who showed evidence of adenitis and fever - and this occurred at the end of the course - the leukocyte count was not significantly raised. 5 patients showed an increased leukocyte count in the sulphones' as opposed to six in the sulphonamides' series, but in no case was the difference regarded as a significant variation from the normal.

The erythrocyte sedimentation index (table 7) became reduced in all cases in the sulphones' series except number 9. This we may regard as evidence of improvement in their general condition, and it may be considered as confirmatory evidence of the greater suitability of these drugs in leprosy and of their lower toxicity. For 6 cases, numbers 11 to 16, on sulphamezathine showed an increase in erythrocyte sedimentation index, but the remaining four (numbers 17 to 20)showed a definite reduction including number 20 in which case toxic signs were present. Case number 17 also suffered from reaction from which he recovered. Still, by the only test we have which indicates general improvement, sulphetrone has been shown to be more suitable than sulphamezathine. A reduction in weight was found in most cases in both series, six in each, and this should not be surprising considering that the 'famine' season intervened. There was, however, a marked reduction in weight, 11 lbs. each, in cases numbers 16 and 20 of the sulphonamides' series. As mentioned above, number 20 suffered from severe reaction and number 16 became almost emaciated in appearance although still protesting that he experienced an enhanced sense of well being. It is interesting to note that case number 9 of the sulphones' series, while he suffered reactions, gained 3 lbs. in weight, but he was a boy previously poorly nourished who was admitted to and cared for in the Settlement. The total weight lost in the sulphones' series was considerably less than was lost in the sulphonamides' series of cases, which again adds to the evidence of greater toxicity and less suitability of the sulphonamides in treatment.

I have referred to the difficulty in accurate assessment of bacteriology by the standard method employed (page 84), where it has also been emphasised that maximum counts are recorded. As would be expected in so short a period, the majority of these bacillary counts remained the same, but a definite decrease was demonstrated in case number 5 on the sulphones' series, whose clinical condition correspondingly improved; but so rapid was the decrease that the uniformity of the original count was called in question. Similarly with case number 18 on the sulphonamides' series who was actually found negative on repeated examinations of smears. Another case, number 13 on the sulphonamides' series, estimated at the commencement as 3+ became 2+, and case number 19 on the same series estimated as 2+ became 3+; but, owing to the vagaries of the method of assessment already referred to, a difference of 1+ should not be regarded as significant, in the latter case being found in one field only. As far as these records can be relied on, then, the effects of the sulphones and sulphonamides on bacillary counts would appear to be comparable. (Table 9).

Clinical improvement as symbolised by the Leonard Wood and Cairo Conferences' estimations of stage of the disease is interesting in that it corroborates the roughly parallel nature of the series and the clinical improvement of the lepromatous condition in eight members of each series; each of these passing from an L3 or L2 group to an L2 or L1 group. Corresponding improvement in neural signs was not to be expected: in case number 3 appearance of anaesthesia caused an increase in stage of the disease from N1 to N2; in number 5 anaesthesia receding caused the stage N2 to be decreased to N1, whereas number 17 was degraded from N3 to N2 because of the healing of ulcers. Those patients numbers 9,10,15 and 20 remaining in the same stage were all extensively involved advanced lepromatous types where improvement in degree without concomitant regression in extent of the lesions could not be indicated by the symbols employed. (Table 10).

Summary and Conclusions from preceding Sections.

In the course of a discussion on the historical and general aspects of the control of leprosy with special reference to recent literature on the subject, the effects of local segregation, improved housing conditions and a liberal and sympathetic attitude to lepers are stressed. Reasons are given why these appear to have been important factors in the control and prevention of leprosy as an endemic disease in Western Europe and particularly in Britain where the disease was prevalent in the Middle Ages. Measures for the control of leprosy in various parts of the world from the beginning of the nineteenth century to the present day are summarised, predominant factors being the failure of compulsory segregation in leper asylums followed by voluntary segregation in agricultural colonies, reliance being placed on treatment there or at clinics in an attempt to control the disease. In supporting and encouraging these activities the British Empire Leprosy Relief Association is shown to have played a leading role, as also in supporting more recent attempts to control leprosy by village segregation in South-East Nigeria where village segregation has become an essential element in the anti-leprosy campaign with its provincial leprosy schemes. The findings of various conferences on leprosy are referred to, culminating in the Cuba Congress, 1948, with its renewed interest in the possibilities of treatment following the advent of the sulphones on which favourable comments were made. Evidences of the increase of cases of leprosy in Great Britain are referred to.

In dealing with the initiation of measures for the control of leprosy in Southern Ogoja Province, South-East Nigeria, the Nigerian Government's Proposals, particularly as affecting the Church of Scotland Mission's Ogoja Leprosy Scheme are dealt with. A description is given of how these proposals are being put into practice under our present system and the modifications required for future developments in Afikpo Division, for extending the work to Obubra and Ikom Divisions and for initiating a comprehensive scheme for leprosy control. The Settlement is considered to be of primary importance in the Provincial Leprosy Scheme and reasons are given why it should not be of the Main Territorial Type, the Provincial Settlement, not essentially self-supporting on a communal basis, but individually agricultural and operating on the Centrifugal System being preferable. Reliance should not be placed on the Settlement or clinics alone in the control of leprosy, but these should be combined with propaganda, surveys and village segregation, the last being considered at least worthy of experiment as the main element in the scheme for control. Opinions are given on the aetiology and transmission of leprosy and confirmatory evidence quoted to the effect that it is most usually caused by prolonged, close contact with an infective case and that transmission is facilitated by overcrowding

under unsuitable housing conditions; hence the importance of segregation villages as models in housing, sanitation and hygiene. The diagnosis of clinical types and sub-types is dealt with, a classification being given and a description of these,mostly in their active stages,with a note on resolution and a description of secondary neural manifestations. Statistics on type incidence and sex distribution are presented, it being shown that the indeterminate type is more common where treatment has been carried out and that females are prone to develop the milder types of leprosy. The mutation of types in a series of 47 cases over a period of five to eight years is investigated, resulting in the conclusion that,under treatment at a clinic, no case of retrogression to a severer or infective type occurred. Notes on differential diagnosis, treatment and lepra reaction are given, including a reference to prognosis in that condition. The composition of the existing'patient' and 'African' staff is detailed and future developments regarding these is discussed: some devolution of activities on Africans is considered necessary, but should not replace regular and thorough supervision of clinics and villages by the touring unit from the Settlement.

A description is given of the topographical features of Afikpo Division which is the sphere for present activities and developments in the near future. Progress of the Scheme, the success of Village Segregation and the method in which this principle is being applied are illustrated by statistics. Future policy is defined as aiming at the selective segregation of known or potentially infective cases under conditions in which segregation is made attractive and the co-operation of clan chiefs, village and compound head men and others in the clan has been secured to ensure that it is being effectively carried out. A plan for the control of leprosy in Afikpo Division based on a publication of Rogers' is discussed and modifications indicated. The importance of surveys as a means of propaganda having been stressed and types of surveys defined, the Propaganda-Treatment-Survey method of Muir is recommended with intensive surveys in each clan where co-operation is secured and other methods applied within the limits of our resources. Opinions on the possible effects of the sulphone treatment of leprosy on control are stated and certain limitations indicated as making further research advisable. Details of preliminary surveys, one in an area where no methods of control had been in force and the other where village segregation had been encouraged by treatment at a clinic for sixteen years, are recorded. Despite an inadequate response in most villages in both areas, it is considered that the low child rate accompanied by a high indeterminate case rate with consequently a possibly higher past lepromatous case rate in the latter area may indicate a diminishing leprosy incidence in the population. The fact that all infective cases were segregated and only one definite tuberculoid case - a woman who had recently come to the area - was found at large in the community, is taken as evidence that leprosy is under control in this area. This

illustration of the favourable effects of village segregation is in contrast to the conditions obtaining in the area where no measures for the control of leprosy had been put into operation, only a few cases,not specially selected,having been sent to a main territorial settlement at a distance and six others including only two lepromatous cases having been driven to stay in the'bush' outside the villages. With the exception of these six, then, all other cases recorded as having been seen on survey were living among healthy people, and the high child rate and high tuberculoid type rate - indicating increased opportunities for infection - show that leprosy is increasing in this area. Now that control measures are being instituted in this, the Agbo Clan; clinics have been opened in the segregation villages and these villages made more attractive in the other, the Edda Clan; the results of subsequent surveys in both clans should not only elicit a better response from the people but should also furnish interesting information on the progress of control measures in the one and the maintenance of the control of leprosy in the other.

Similarities between the sulphones and sulphonamides in chemical structure and in their effects on tuberculosis in experimental animals are referred to and the possibility of similar effects on leprosy discussed. Almost entire unanimity on the favourable effects of the sulphones on leprosy in man is apparent from a review of the literature on that subject. The literature on the use of the sulphonamides in leprosy, in vitro, in vivo in experimental animals and in man is detailed, varying results in all and only one successful trial in the last being recorded. The effects of the sulphones as represented by sulphetrone and the sulphonamides as represented by sulphamezathine on two roughly parallel series, each consisting of ten cases of lepromatous leprosy is described, tabulated and discussed. The favourable reports on the effects of the sulphones in leprosy are confirmed by the results obtained in the series treated by the oral administration of sulphetrone over a period of six months, and the one favourable report on the treatment of human leprosy with a sulphonamide is confirmed by the results obtained in the series treated by the oral administration of sulphamezathine over a period of similar duration. The toxic properties of both these drugs are stressed; sulphamezathine being considered to be more toxic than sulphetrone is therefore not suitable for routine administration in the treatment of leprosy, and sulphetrone should only be administered in a settlement where adequate supervision is available. From this trial and its confirmation of a previous report the activity of the sulphonamides in leprosy may be assumed, at least, not to have been disproved. Provided their greater toxicity is realised, the success of this experiment invites further research to establish this activity with a view to the synthesis of compounds of less toxicity from which important repercussions on the treatment and control of leprosy might be anticipated.

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Table 1. Sulphones and Sulphonamides: clinical improvement.

Clinical improvement:	Sulphones' cases	Total	Sulphonamides' cases	Total
Flattening nodules or papules	Nos. 4,8,9,10	4	Nos. 11,14,15,20	4
Lessening infiltration of skin	Nos. 1 - 8 & 10	9	Nos. 11,12 & 14 - 20	9
Subsidence of infiltration of nasal m.m.	Nos. 1-3,5-7&10	7	Nos. 11 - 15	5
Lessening of hypopigmentation	Nos. 1-3, 5-8	7	Nos. 12 & 14 - 19	7
Defined macules appearing	Nos. 3, 5 & 6	3	Nos. 11,15 & 17	3
Healing of fissures & ulcers of skin.....	Nos. 1,4,6 &8-10	6	Nos. 15,17,18 & 19	4
Healing of ulcers of nasal m.m.	Nos. 4 & 8 - 10	4	No. 16	1
Reduced thickening of nerves	Nos. 3,4 & 7	3	Nos. 13 & 15	2
Reduced anaesthesia of a limb or limbs.....	Nos. 1,2,5,6,&8	5	Nos. 18 & 19	2
Erythema fading	No. 3	1	Nos. 12 & 13	2
Reduced tenderness of nerves	Nos. 3,5,6,7,&10	5	No. 12	1
Resolution of macules	No. 7	1	No. 13	1
Signs of clinical improvement, totals		55		41

Average number of patients showing signs of clinical improvement in each group of signs, sulphones' cases approximately 4.6;
sulphonamides' cases approximately 3.4.

Table 2. Sulphones and Sulphonamides: possible toxic effects.

Possible toxic effects:	Sulphones' cases	Total	Sulphonamides' cases	Total
Fever, temp. 99 F. and over	Nos. 1,2,6,7 & 9	5	Nos. 16,17,19 & 20	4
Skin lesions, nodules, papules, macules, plaques and urticaria	Nos. 1,5 & 9	3	Nos. 16,17 &20	3
Swellings, extremities, genitalia, subcutaneous	Nos. 1,3, & 6	3	Nos. 12,17,19 & 20	4
Headache	Nos. 1-3 & 5-9	8	Nos. 11-13,16,18 &20	6
Pains, epigastric and abdominal	Nos. 1,2,5 &7-9	6	Nos. 13,18 & 19	3
Pains localised to bones, nodules, etc.	Nos. 1,2 & 5-10	8	Nos. 1 - 10	10
Pains, generalised	Nos. 1-3,5,6,9 &10	7	Nos. 13,14,16,17,19,20	6
Constipation	Nos. 1,2,7,8 & 9	5	No. 13	1
Exacerbations of severe iritis	No. 6	1	No. 12	1
Catarrh	Nos. 5,7 & 8	3	No. 12	1
Enlargement of spleen.	Nos. 6 & 9	2	- -	-
Onset of tenderness of nerves	Nos. 1 & 9	2	No. 12	1
Ulcers associated with reaction	No. 9	1	No. 20	1
Adenitis	No. 9	1	- -	-
Sialorrhœa	No. 1	1	- -	-
Gingivitis	- -	-	No. 15	1
Diarrhœa	Nos. 8 & 9	2	Nos. 13 & 17	2
Possible toxic effects, totals		58		44

Average number of patients showing possible toxic effects in each group of possible toxic effects, sulphones' cases approximately 3.4;
sulphonamides' cases approximately 2.6.

Table 3. Sulphones and Sulphonamides: blood concentrations; daily doses.

Case no.	Blood sulphone conc. in mg. % on 20/8/49.	Daily dose in gms.
1	(Treatment suspended,13/8) 2	3
2	5	3
3	4	4
4	3	3
5	3	3
6	3	3
7	3	3
8	4	3
9	(Developed reaction,22/8) 5	1.5
10	3	3
Average bd. sulphone conc.	3.5 mg.%. Average dose appr.	3 gms.

Case no.	Blood sulphonamide conc. in mg. % on 15/9/49.	Daily dose in gms.
11	2	0.5
12	3	0.5
13	3	0.5
14	2	0.5
15	2	1.0
16	2	0.5
17	3	0.5
18	2	0.5
19	2	0.5
20	2	0.338
Average bd. sulphonamide conc.	2 mg.%(appr.). Ave. dose(appr.)	0.5 gm.

Table 4. Sulphones and Sulphonamides: haemoglobin percentages (Sahli).

Case number.		% at commencement.	% after six months.
1	Sulphones	75	75
2		71	80
3		71	85
4		70	67
5		78	90
6		72	78
7		79	95
8		60	67
9		80	60
10		60	68
11	Sulphonamides	70	64
12		68	68
13		65	65
14		75	85
15		65	77
16		90	80
17		75	90
18		75	90
19		75	70
20		80	65

Table 5. Sulphones and Sulphonamides: Red Blood Cell Counts.

Case number.		At commencement.	After six months.
1	Sulphones	4,080,000	5,050,000
2		5,460,000	4,370,000
3		3,820,000	4,740,000
4		4,400,000	4,740,000
5		3,940,000	4,740,000
6		4,200,000	4,210,000
7		4,020,000	4,950,000
8		3,080,000	3,520,000
9		4,300,000	3,340,000
10		3,590,000	3,590,000
11	Sulphonamides	4,050,000	3,550,000
12		4,310,000	3,550,000
13		3,660,000	4,290,000
14		4,340,000	5,030,000
15		3,550,000	4,300,000
16		4,840,000	4,370,000
17		4,720,000	5,280,000
18		4,200,000	4,930,000
19		4,110,000	3,710,000
20		5,300,000	4,180,000

Table 6. Sulphones and Sulphonamides: White Blood Cell Counts.

Case number.		At commencement.	After six months.
1	Sulphones	8,333	8,800
2		9,999	6,400
3		10,400	10,400
4		5,333	9,000
5		7,533	8,200
6		10,400	7,600
7		6,866	6,800
8		6,000	7,468
9		5,733	8,000
10		7,600	6,733
11	Sulphonamides	5,466	5,266
12		4,133	8,133
13		8,800	5,533
14		7,000	5,333
15		7,400	10,400
16		5,733	6,800
17		6,666	10,666
18		6,066	5,000
19		6,400	7,933
20		6,866	7,933

Table 7. Sulphones and Sulphonamides: Erythrocyte Sedimentation Rate (mm./ hr.).

Case number.		At commencement.	After six months.
1	Sulphones	76	5
2		6	3
3		55	8
4		127	68
5		84	34
6		125	96
7		58.5	19
8		77.5	63
9		47	69
10		132	124
11	Sulphonamides	99.5	103
12		68.5	92
13		65.5	84
14		68	91
15		4.5	115
16		109	118
17		124.5	86
18		88.5	54
19		113	76
20		96	73

Table 8. Sulphones and Sulphonamides: patients' weights in pounds.

Case number.		At commencement.	After six months.
1	Sulphones	91	85
2		120	118
3		140	138
4		105	98
5		138	143
6		103	100
7		104	110
8		110	105
9		51	54
10		122	124
11	Sulphonamides	124	126
12		102	102
13		96	91
14		107	107
15		131	128
16		145	134
17		112	112
18		126	119
19		96	90
20		117	106

Table 9. Sulphones and Sulphonamides: nasal and skin bacillary counts.

Case number.		At commencement.	After six months.
1	Sulphones	3+	3+
2		3+	3+
3		3+	3+
4		3+	3+
5		3+	+s(plus scanty)
6		3+	3+
7		3+	3+
8		3+	3+
9		3+	3+
10		3+	3+
11	Sulphonamides	3+	3+
12		3+	3+
13		3+	2+
14		3+	3+
15		3+	3+
16		3+	3+
17		2+	2+
18		3+	-ve (Negative)
19		2+	3+ (One field)
20		3+	3+

Table 10. Sulphones and Sulphonamides: clinical stage of disease.

Case number.		At commencement.	After six months.
1	Sulphones	L3-N2	L2-N2
2		L2-N2	L1-N2
3		L2-N1	L1-N2
4		L3-N3	L2-N3
5		L2-N2	L1-N1
6		L2-N2	L1-N2
7		L2-N1	L1-N1
8		L3-N3	L2-N3
9		L3-N1	L3-N1
10		L3-N3	L3-N3
11	Sulphonamides	L3-N3	L2-N3
12		L3-N2	L2-N2
13		L2-N2	L1-N2
14		L2-N2	L1-N2
15		L3-N2	L3-N2
16		L3-N3	L2-N3
17		L2-N3	L1-N2
18		L2-N2	L1-N2
19		L2-N3	L1-N3
20		L3-N2	L3-N2

Case no. 1.

Ude Nwaneke, male of Uburu. Age 20 yrs. Admitted 29/6/42.

History. Contact: a close associate suffered from leprosy. Predisposing causes: followed yaws. Duration: seven years. Initial lesions: a macule on the outer side of the left elbow followed by another one on the anterior aspect of the left thigh. The leonine facies of nodular leprosy noted on admission resolved during seven years' treatment with Hydnocarpus oil.

On examination previous to administration of sulphetrone, development good. Lepromatous infiltration marked on forehead and cheeks, less marked on ears. Diffuse infiltration with hypopigmentation over the whole surface of the glabrous skin. Nose flattened. Fourth and fifth fingers of right hand ankylosed in flexion. During the course of sulphetrone administration, marked infiltration subsided leaving a crinkled appearance of the skin which began to regain its normal dark colour especially in the regions of the temples, cheeks and axillae, commencing at the periphery and spreading inwards. Slight infiltration of nasal mucosa subsided. A wound of the right sole, which developed indolent ulceration, enlarged from 1 c~m. to 2.5 c~ms. in diameter during treatment, then reduced to 1.5 x 1 c~m. in extent. Fissures on both heels healed. Both great auricular, ulnar, superficial peroneal and right medial calcaneal nerves remained thickened, and the right medial calcaneal nerve became tender to palpation following reaction to sulphetrone. Upper level of segmental anaesthesia progressed from the middle third to the elbow joint of the right forearm and from the lower to the middle third of the left thigh; but after a period of apparent progression to the left elbow joint when examined on 2nd. June, upper level, found before treatment started at the left wrist, had receded to the inner part of the left hand, involving this part and the 4th. and 5th. fingers. Similarly, on the right leg, the upper level of anaesthesia had receded from the knee joint to the middle third of the leg. Dosage of sulphetrone, started at 1 gm. daily on 1st. March, raised to 2 gms. on 8th. and 3 gms. on 15th. March which was the maximum dose. This dose was maintained, with a rest period from 28/4 to 23/5 and an additional one from 25/7 to 28/7 for sialorrhoea, until 14/8. Then administration was suspended until 23/8 owing to reaction: resumed on 23/8 at 0.5 gm. daily, the dose was raised to 1 gm. on 25/8, 1.5 gm. on 26/8 and 2 gms. on 29/8, this dose being maintained until cessation of treatment on 31st. Sept.* Toxic effects. Transient swelling of both ankles on 2/3. Abdominal and chest pains relieved by ol. ric. and sod. bic. on 24/3. Mild pain localised to the right buttock on 3/6 and generalised on 23/6 and 30/6. Fever, temp. 100°F. with headache on 2/7 was followed by headache on 13/7 and sialorrhoea with tenderness of oral mucosa on 24/7. Generalised pains and constipation on 11/8 followed by fever, temp. 100°F. on 12/8, and headache, swelling and pains in both testicles on 13/8. Painful, erythematous nodules then appeared on the posterior aspect of the right arm, chest and on the forehead on 15/8, started to subside on 18/8, had almost subsided by 20/8 and were merely residual by 23rd. August.

* Total sulphetrone administered amounted to 370.5 grams.

Case no. 2.

Okoro Uwem, male of Enna. Age 30 yrs. Admitted 4/10/48.

History. No contact or predisposing factors revealed.
Duration: 3 yrs. Initial lesion: a macule on the epigastrium spreading rapidly as small macules all over the body. No noticeable improvement during four months' treatment with Hydnocarpus oil.

On examination previous to administration of sulphetrone, development good. Diffuse lepromatous infiltration of forehead, cheeks and ears. Lepromatous macules scattered over the body, erythematous on back chest and flanks; hypopigmented on anterior trunk, buttocks, thighs, legs, arms and forearms. The nasal mucosa appears to be slightly infiltrated. During the course of treatment infiltration resolved entirely and erythema faded. A limited area of hypopigmentation remained on the malar region of the cheeks and also became more localised in other areas. On the flanks the macules changed in character to resemble clinically minor tuberculoid leprosy with pebble margin and healing centre, but they were not anaesthetic to light touch. Infiltration of the nasal mucosa, still appreciable when the patient was examined on 2nd. June, had resolved by 15th. September. Both great auricular, ulnar and superficial peroneal nerves remained thickened but were not tender throughout treatment. Anaesthesia of both hands, present at the beginning, was not found at the end of treatment. The upper level of segmental anaesthesia remained at the lower third of the right leg throughout, but receded from the middle third to the lower third of the left leg during treatment.

Dosage of sulphetrone, started at 1 gm. daily on 1st. March, was raised at weekly intervals to 2 gms., 3 gms. and 4 gms. which was the maximum dose given. This dose was maintained until 12th. July when it was reduced to 3 gms. following an elevation of temperature to 99 F., and this dose was continued until the end of treatment.

Total sulphetrone administered amounted to 503 grams.

Toxic effects. Apart from the slight elevation of temperature noted above, the only symptoms that might have been attributed to toxic effects of sulphetrone were mild generalised pains and headache four days before the onset of fever in July; epigastric pains associated with constipation and relieved by an alkaline powder and purgatives; pains localised to the limbs in the first month of treatment, and to the lumbar region, neck and shoulder in the last month.

Case no. 3.

Eke Ojoke, male of Ishiago. Age 35 yrs. Admitted 15/12/47.

History. No contact or predisposing factors revealed. Duration 2 yrs. Initial lesion: a macule on the outer side of the lower third of the left thigh followed by another on the lower left hypochondrium. No improvement during 14 months' treatment with Hydnocarpus oil.

On examination previous to administration of sulphetrone, development good. Diffuse lepromatous infiltration, marked on ears. Hypopigmentation of face, trunk, back of neck and limbs. Active, erythematous macules on back of chest. Slight infiltration of nasal mucosa.

During the course of treatment, when patient was examined on 2nd. June, it was noted that infiltration was lessening, erythema of macules on the back of the chest was fading and there was less hypopigmentation on the face, trunk, back of the neck and limbs. Normal, dark skin was appearing and discrete, light brown tinted macules forming on the trunk. No infiltration was noted on the nasal mucosa. An abscess of the lower third of the outer aspect of the right leg which followed an injection of hydnocarpus oil and which, with swelling of the leg and foot, was present when treatment with sulphetrone started, healed rapidly. Both great auricular and superficial peroneal nerves together with the left ulnar nerve were thickened at the beginning of treatment, but the left ulnar and right superficial peroneal nerves were reduced in thickness at the end of treatment. Thickening and tenderness to palpation were present at the beginning in the left medial calcaneal nerve, but when the patient was examined on 15th. September tenderness was only elicited on firm pressure. No definite anaesthesia was present anywhere on the body at the beginning, but anaesthesia was detected over the whole of the left hand and involving the inner part and the fourth and fifth fingers of the right hand, both feet and the lower thirds of both legs on 2nd. June. When the patient was examined on 15th. Sept. anaesthesia remained as noted on the right hand, was not detected at all on the left hand and the upper level had receded to just above the ankle joints on both legs.

Dosage of sulphetrone, started at 1 gm. daily on 1st. March, was raised to 2 gms. on 8th., 3 gms. on 15th. and to 4 gms. on 22nd. March. This was the maximum dose given. After the rest period which lasted from 28/4 to 23/5, a daily dose of 2 gms. was administered from 24th. to 27th. March. On 28th. March the dose was again raised to 4 gms. and this dose was maintained until treatment was completed on 31st. August.

Total dose of sulphetrone administered amounted to 548.5 grams.

Toxic effects. Apart from headache on 6th. March, 8th. March, and generalised pains on 26th. June and two abscesses developing on the right buttock and the left side of the back of the chest in March, no other symptoms were noted which could possibly be attributed to toxic effects of sulphetrone.

Case no. 4.

Eze Nwogo, male of Isu. Age 40 yrs. Admitted 3/9/31.

History. No contact or predisposing factors revealed. Duration 18 yrs. Initial lesion: on the upper part and left side of the umbilical region a macule appeared followed by another on the anterior aspect of the lower left thigh. Received certificate "symptom free" on 29/12/32, repeatedly renewed until readmitted with recurrence on 17/11/37.

On examination before administration of sulphetrone, development fair. Lepromatous nodules on ears, marked infiltration of forehead, diffuse hypopigmentation of face, trunk and limbs, crinkling of skin on back of chest and parakeratosis of legs. Bridge of nose flattened.

During administration of sulphetrone, in the third week of treatment (17th. March) nodules on ears had all flattened leaving areas of hyperpigmentation where they had been. In the same period an ulcer of the right heel became reduced in size to 1 cm. x 5 mm., one third of its original diameter, and by 27th. March had completely healed. Ulceration of the nasal mucosa, detected on 17th. March, had healed by 2nd. June, the surface then being dry and crusted. When the patient was examined on 15th. Sept. after completion of six months' treatment with sulphetrone, the marked infiltration had subsided leaving crinkling which had increased in extent and degree but was still most obvious on the back of the chest. Normal skin was appearing at the temples and on the forehead and cheeks. Marked thickening of both great auricular, ulnar and superficial peroneal nerves and of the left medial calcaneal and the median cutaneous nerve of the left forearm subsided during treatment. The right medial calcaneal nerve was still markedly thickened when the patient was examined on 15/9/49. Anaesthesia covering extremities at the beginning extended over shoulders and onto buttocks during treatment. A mask-like appearance of the face, present at the beginning, started to disappear, the normal contours becoming restored. Deformities were present in both hands.

Dosage of sulphetrone, started on 1st. March at 1 gm. daily was raised on 8th. to 2 gms. and on 15th. March to 3 gms. Apart from the rest period extending from 28th. April to 23rd. May and commencing on 24th. May until 27th. May when a dose of 2 gms. was given, the 3 gms. daily dose was maintained until the end of treatment on 31st. August. Total sulphetrone administered amounted to 422 grams.

Toxic effects. None except pain and slight inflammation in the left eye on 8th. March. This patient was singularly free from pains from the time the course of sulphetrone started.

Case no. 5.

Joseph Nwosibe, male of Uburu. Age 30 yrs. Admitted 1/7/46.

History. His brother suffered from leprosy. The disease followed swelling of the left knee. Duration: 5 yrs. Initial lesion: a macule on the outer side of the upper third of the right leg followed by another macule on the anterior aspect of the upper part of the left arm. No improvement on Hydnocarpus oil treatment, 2 years, 8 months. On examination before administration of sulphetrone, development good. Diffuse lepromatous infiltration most marked on ears with hypopigmentation on trunk and limbs. During treatment with sulphetrone, diffuse infiltration subsided entirely and normal skin appeared. Only one small macule with follicular hypopigmentation remained on the left shoulder and a few very faint diffusely hypopigmented macules remained on the central part of the lumbar region. At the beginning of treatment both great auricular, ulnar, superficial peroneal and medial calcaneal nerves were found to be thickened and the medial calcaneal nerves were also found to be tender to palpation. All these nerves remained greatly thickened throughout treatment but there was no tenderness to palpation of any of them when the patient was examined on 2nd. June and subsequently. Anaesthesia of both hands found at the beginning of treatment receded to exclude the left thumb by 2nd. June and to include only the fourth and fifth fingers and corresponding inner parts of both hands by 15th. Sept. Anaesthesia extended at first over both feet and legs to the lower thirds of both thighs. By 15th. Sept. these upper levels had receded to below the right knee and to the lower third of the left leg. Infiltration of the nasal mucosa noted on 17th. March was not detected on 2nd. June or subsequently. A fissure of the right heel persisted throughout treatment.

Dosage of sulphetrone, started at 1 gm. daily on 1st. March was increased to 2 gms. on 8th. and 3 gms. on 15th. March. On 22nd. March this dose was increased to 4 gms. which was the maximum dose. This dose was maintained until the rest period between 28th. April and 23rd. May, after which sulphetrone was re-started at a dose of 2 gms. daily from 24th. to 27th., raised to 4 gms. daily on 28th. May. This dose was maintained until a rest period had to be accorded to the patient because of cough and rhinitis between 12th. and 17th. July, after which a dose of 3 gms. daily was maintained until the end of treatment on 31st. August. Total sulphetrone administered amounted to 454 grams.

Toxic effects. In addition to the cough and rhinitis noted above, possible toxic symptoms were epigastric pain on 10th. March relieved by sod. bic. dr. 1, t.d.s.; mid umbilical pain relieved by ol. ric. and chenopodii m xv on 21st. April; headache twice in March, once in April and again in June; catarrh in March and June. Pains, generalised and localised to the waist in April and to the lumbar region in August and urticaria in July complete the list of possible toxic effects.

Case no. 6.

Okoro Nwoga, male of Oshiri. Age 45 yrs. Admitted 9/6/47.

History. No contact revealed. Onset followed swelling of both thighs. Duration 6 yrs. Initial lesion: a papule on the right cheek followed by others on the face. The patients general condition improved somewhat following admission and treatment with Hydnocarpus oil.

On examination before administration of sulphetrone, development fairly good. Diffuse lepromatous infiltration marked on forehead, and cheeks showed areas of more circumscribed infiltration measuring 3 cms. x 1cm. on each; 'fig leaf' appearance of ear lobes: mask-like face: hypopigmentation of trunk and limbs: parakeratosis of legs. Integuments of right eye swollen, closing the lids; iritis with miosis; inflammation of sclera and cornea and lachrymation. Nasal mucosa infiltrated, congested and thickened. Fissures on left sole. During treatment with sulphetrone, marked infiltration of forehead resolved completely; circumscribed infiltration on the right cheek became reduced to 2.5 x 1 c/m., and on the left to 1.5 x 1 c/m., and crinkling of the skin of the ear lobes became more marked. Normal skin began to appear most extensively on the temples, cheeks, axillae, under the breasts, on the flanks, the centre of the back of the chest and the lower lumbar region. Elsewhere hypopigmentation gave place to more defined macules. 'Mask face' changed, normal contours appearing. Parakeratosis of legs persisted. Fissures of left sole healed. Swelling round the right eye subsided and did not recur with recurring attacks of iritis. The pupil remained contracted showing little reaction to light. Thickening of the nasal mucosa lessened, congestion disappeared and at the end of treatment there was no infiltration. Both great auricular, ulnar, superficial peroneal and left medial calcaneal nerves remained thickened throughout treatment. The right ulnar nerve, tender on palpation on 24th. Feb. before treatment started, became less acutely tender by 17th. March, lost all tenderness by 2nd. June and remained so at the final examination on 15th. Sept. Anaesthesia of the hands was first noted during treatment on 2nd. June. Upper level of segmental anaesthesia remained just below the knee joint on the right leg but receded to the middle third of the left leg during treatment, from its previous position corresponding to the right.

Daily dose of sulphetrone, started at 1 gm. on 1st. March, was raised to 2 gms. on 9th. and 3 gms. on 15th. March. After the rest period from 28th. April to 23rd. May, 2 gms. was administered from 24th to 27th. May, increased to 3 gms. on 28th. May, and this dose was maintained until treatment was stopped for reaction to sulphetrone on 23rd. August. Treatment was resumed on 26th. August at 1 gm., increased to 1.5 gm. on 30th. and 2 gms. on 31st. August when the course finished.

Total sulphetrone administered amounted to 401 grams.

Toxic effects. Acute iritis of the right eye, subsiding after treatment started, recurred on 8/3 and had subsided by the end of April; recurred again between 27th. and 30th. June and on 29th. August. Reaction to sulphetrone was preceded by fever, temp. 100°F. on 23rd. August, 101°F. with spleen enlarged on 24th. Aug. followed by swelling of the left testicle and cord on 26th. Aug., lasting two days. Other possible toxic

Case no. 6, continued.

effects were, headache on 8 days in all (March, April, May and June); generalised pains (various); pains localised to waist, toes, neck and feet (various); cough, 1/6; praecodrial fullness relieved by ol. ric., 26/7.

Case no. 7.
Ivere Nwosibe, male of Ugulangu. Age 18 yrs. Admitted 1/3/48.
History. No contact or predisposing factors revealed.
Duration 3 yrs. Initial lesion: a macule on the right buttock followed by another one on the epigastrium. No marked improvement during one year's treatment with Hydnocarpus oil.
On examination before administration of sulphetrone, development fairly good: diffuse lepromatous infiltration marked on forehead, cheeks and ears; hypopigmentation of other parts of the body and numerous erythematous macules on the back of the chest; defined hypopigmented macules noted on buttocks and thighs: nasal mucosa inflamed and slightly infiltrated. During treatment with sulphetrone, marked infiltration almost resolved. Areas of normal skin appeared peripherally on the temples and cheeks spreading inwards with a defined margin until, at the end of the course of treatment, only the middle of the forehead and small parts of the malar regions of the cheeks under the eyes remained involved. Hypopigmented macules on the right buttock and both thighs resolved; elsewhere macules were resolving, but those on the back of the chest remained erythematous. The nasal mucosa was still inflamed on 2nd. June, but this and any evidence of infiltration had subsided by 15th. September. The right great auricular, both ulnar, superficial peroneal and medial calcaneal nerves were thickened before treatment started; both medial calcaneal and the right ulnar nerves were tender to palpation. At the end of treatment the ulnar nerves were not thickened and the right great auricular nerve only slightly thickened; tenderness to palpation was not elicited in the right medial calcaneal nerve on 17th. March or subsequently, in the left medial calcaneal nerve on 15th. Sept., and in the right ulnar nerve only slightly on 17th. March, not at all on 2nd. June.
Anaesthesia of the heels only, present at the beginning of treatment, extended over both feet and ankles by 2nd. June and remained thus on 15th. Sept.
Dosage of sulphetrone, started at 1 gm. daily on 1st. March, was increased to 2 gms. on 8th. and 3 gms. on 15th. March. This dose was maintained apart from the rest period between 28th. April and 23rd. May, dosage being resumed on 24th. May at 2 gms. until 28th. May when it was increased to 3 gms. This dose, the maximum given, was maintained until the end of treatment on 31st. August.
Total sulphetrone administered amounted to 420.5 grams.
Toxic effects. Only minor ones observed. Slight epigastric pain on 7th. March and 22nd. July relieved by sod. bic. dr. 1 t.i.d. Fever, temp. 101.2°F on 18th. March, relieved by ol. ric.,and paludrine 0.2 gm. Pains localised to the back of the neck on 29th. March, 12th. June, and to the left side of the neck on 13th. July, the left cheek on 28/5, elbows on 1/7 and 5/8; abdominal pains relieved by ol. ric. on 17/7 and 18/7. Catarrh relieved by aspirin and ephedrine on 4/4 and 22/5. Constipation relieved by ol. ric. on 6/4. Headache on 19/4,26/4, 24/5.

Case no. 8.

Omere Agude, male of Isu. Age 35 yrs. Admitted 27/9/48.

History. No contact or predisposing factors revealed. Duration:7 yrs. Initial lesion: a macule at the lower end of the left lateral sternal line followed by another on the left hip. No marked improvement during seventeen months' treatment with Hydnocarpus oil. On examination before administration of sulphetrone, development fairly good. Lepromatous nodules covering face and ears. Measurements of some nodules on face as follows:- at both lower alae nasi 1.5 cms. diameter; right cheek 2 x 1.5 cms.; left cheek 1.5 cms. diameter; right side of chin 1 cm. diameter. Diffuse infiltration with hypopigmentation of trunk and limbs. Hypertrophy of nipples. Bridge of nose flattened; nasal septum partly necrosed and ulcerated. Ulcers on outer sides of both ankles, each 3 x 2 cms. Deformities of fingers of both hands. During administration of sulphetrone, nodules on ears flattened by 17th. March. Nodules on face were flattening throughout treatment but showed no marked decrease in the diameters of the flattening areas. Diffuse infiltration with hypopigmentation continued to resolve, areas of normal skin appearing except on the back of the chest. Hypertrophy of the nipples persisted. Ulceration of the nasal septum healed. The ulcer on the right ankle healed but the one on the left ankle after apparent healing recurred and remained indolent at the end of treatment. The ear lobes assumed a 'fig leaf' appearance. Two ulcers first noted on 17th. March, one on the outer left sole measuring 1 cm. diameter and another on the plantar surface of the first toe of the left foot, 1.5 cms. x 2 cms., had both healed by 2nd. June. Both great auricular nerves, transverse branches of the left cervical plexus, both ulnar and superficial peroneal nerves remained thickened but were not tender throughout treatment. The upper level of segmental anaesthesia remained at the middle third of both arms throughout treatment: on the right thigh the original level at the middle third was retained, but it receded from the lower third of the left thigh to just below the left knee joint during treatment. Dosage of sulphetrone, started at 1 gm. on 1st. March was increased to 2 gms. on 8th. and to 3 gms. on 15th. March. This dose was maintained until the end of treatment apart from the rest period between 28/4 and 23/5, after which it was resumed at 2 gms. on 24/5 until 27th. May, raised to 3 gms. on 28th. May, suspended between 14th. and 18th. July for N.A.B. injection for yaws foot and again between 23rd. and 27th. July owing to absence. Total dose of sulphetrone administered, 389gms. Toxic effects. Only minor ones observed. Epigastric pain and constipation relieved by ol. ric., 13/3. Pain in the umbilical region relieved by ol. chenopodii m. xv, 9/6. Abdominal pain and diarrhoea relieved by ol. ric. 5/8. Pains localised to anterior tibiae, 19/3,25/3, 8/4; both ankles, 30/3; lower lumbar region 16/4; over sternum 18/4; waist 17/8. Catarrh relieved by ephedrine, 23/5, 19/6; headache relieved by aspirin 22/6, 31/8.

Case no. 9.

Chuku Ada, boy of Uburu. Age 10 yrs. Admitted 16/8/48.

History. No contact revealed. Followed yaws. Duration 3 yrs. Initial lesion: a nodule on the right buttock followed by others which spread rapidly all over the body. No improvement during six months' treatment with Hydnocarpus oil.

On examination before administration of sulphetrone, development only fair; poorly nourished. Numerous lepromatous nodules on forehead, cheeks, ears, arms and forearms, hands, buttocks, thighs, legs and feet. Diffuse lepromatous infiltration with marked hypopigmentation on both legs and the posterior aspects of both thighs and on the buttocks. Ulcers on the toes, one on the dorsum of the right foot at the fourth toe measuring 4 cms. diameter. Ulcerating nodules of legs. Nasal mucosa ulcerated. During treatment with sulphetrone, nodules already flattening on 17th. March. Nodules on upper part of pinnae reduced from 2 x 1 cm. to 1.225 x 0.5 cms. during treatment. Nodules on the peripheral parts of the face and on the trunk and limbs continued to flatten during treatment only those on the nose and cheeks remaining prominent. One nodule on the prepuce of the penis responded well. All ulcers healed except one on the left sole thought to be due to yaws for which disease the patient received 300,000 units of penicillin during treatment with sulphetrone, 20/3 to 24/3, florid secondary lesions then subsiding. Ulcers of nasal mucosa healed but infiltration persisted. Both great auricular, superficial peroneal and medial calcaneal nerves remained enlarged during treatment. The left superficial peroneal nerve was greatly thickened, but marked tenderness to palpation noted on 2nd. June subsided by 15th. Sept. Anaesthesia of feet and the lower third of both legs remained during administration of sulphetrone.

Dosage of sulphetrone. Difficulty was experienced in regulating dosage, perhaps because the patient was under-nourished and irregular in attending for treatment and he showed intolerance when the dose was raised to or above 1.5 gm. daily for three or four weeks' administration. Started at 0.5 gm. on 1st. March, the dose was raised to 1 gm. on 8th. and 1.5 gm. was given on 15th. but the patient complaining of headache the dose was reduced to 1 gm. on 16th. March. On 17th. March the dose was raised to 1.25 gm. and to 1.5 gm. on 23rd. March, this dose being maintained until 12th. April when it was raised to 2 gms. The drug was withheld on 19th. April because of a papular eczematous rash on the anterior aspect of the chest and on the buttocks noted on 17th. April and not resumed until 24th. May as with other patients following the rest period, at a reduced dose of 0.225 gm. This dose was raised to 0.5 gm. on 28th. May and to 1 gm. on 5th. June, a dose which was maintained until the patient absented himself from treatment on 27th. June, not returning until 8th. July. Treatment was then continued with a dose of 0.5 gm. raised to 1 gm. on 9th. and to 1.25 gm. on 19th. July, and to 1.5 gm. on 13th. August. This dose was reduced following pains in both legs on 21st. and temperature elevation to 99°F on 22nd. to 0.5 gm. on 21st., raised to 0.75 gm. on 22nd. August.

Case no. 9, continued.

After two days' rest during which the temperature rose to 99.4°F.on 23rd. administration was resumed at a dose of 0.225 gm. on 25th. Aug. This dose was repeated on 26th. Aug. but administration had to be stopped because the temperature rose to 101°F. that day and 101.4°F. on 27th. Aug. and on 29th. Aug., rising to 103°F. on 30th. Aug., but falling to 100°F. on 31st. August. No recurrence was noted in elevation of temperature and the patient remained well after 5/9/49. Total sulphetrone administered amounted to 133.8 grams.

Toxic effects. The most serious are recorded above. The eczematous rash noted on 17th. April was followed by a painful subcutaneous swelling over the sacrum on 18th. April. A zinc oxide powder was applied to the eczema and ichthyol and glycerin to the sacrum and by 22/4 the condition was clearing; eczema drying, oedema subsiding and ulcers healing. On 25/4 an acute neuritis of the left superficial peroneal nerve was noted along with a blister the size of half-a-crown on the outer side of the left heel. Elevation of temperature noted on 21st. and 23rd. Aug. was followed by a small new nodule on the anterior aspect of the right thigh and pains in the nodules on the nose and cheeks. Elevations of temperature between 26/8 and 30/8 were accompanied by enlargement of the spleen to percussion, pains, generalised and localised to the tibiae with tenderness over the tibiae; and followed on 31st. August by enlargement and tenderness of the submaxillary, axillary and inguinal glands. There was a considerable reduction in the percentage of haemoglobin and in the erythrocyte count (tables 4 and 5). Other possible toxic effects were epigastric pain relieved by sod. bic. on 9/3, ol. ric. and a bismuth powder on 20/5 and ol. ric. on 19/8; headache on 5 days in March, 2 days in April, 5 days in May, 3 days in June, 2 days in July and 2 days in August; pains localised to the ankle joints, 31/3, to the left foot, 3/4, the right eye 23/5, left ear 17/6, left leg 22/6, right shoulder 23/7 and fingers on 5/8; generalised pains on 30/7: constipation on 15/3 and 23/7; diarrhoea on 25/6.

Case no. 10.

Okoro Omaha, male of Ugulangu. Age 25 yrs. Admitted 24/1/44.

History. No contact or predisposing factors revealed. Duration 20 yrs. Initial lesion: a macule on the left, followed by another on the right infra-clavicular region. No improvement during five years' treatment with Hydnocarpus oil.

On examination before administration of sulphetrone, development good. Lepromatous nodules covering face, ears, trunk and limbs; diffuse infiltration marked on trunk, especially on the back of the chest. Nose flattened. Deformities of toes. During treatment with sulphetrone, nodules already flattening on ear lobes when patient examined on 17th. March. Flattening nodules on ears and forehead remained 1 cm. diameter throughout treatment. One nodule on the face became reduced from 3 cms. x 2 cms. to 2.5cms. x 1.5 cms. during treatment: in other parts flattening continued with little change in diameter. Nodules on the ears and extremities had resolved when the patient was examined on 15/9, and diffuse infiltration was resolving even on the back of the chest. Nodules of the nasal mucosa with ulceration and crusting noted on 17/3 had resolved by 2/6, and a purulent discharge noted on the latter date had ceased and there was no infiltration by 15/9. Crusted fissures on the anterior and outer aspect of the left ankle, an ulcer of the left sole measuring 3 x 1 cms. and another of the right heel measuring 5 x 4 cms. all noted on 2/6, had healed by 15/9. The right great auricular nerve, the left ulnar nerve and both superficial peroneal nerves remained thickened throughout treatment. The left ulnar nerve, tender to palpation before treatment started, became only slightly tender by 17/3, and on 2/6 no tenderness was elicited. There was tenderness on palpation over the right medial calcaneal nerve at the beginning of treatment, not elicited on 2/6: the nerve was not palpable owing to thickened tissues round the ankle joint. The upper level of segmental anaesthesia appeared to extend during treatment from its original level at the lower third of both arms and the middle third of both thighs to the shoulder joints in the former and the right buttock and upper third of the left thigh in the latter case when the patient was examined on 2/6. By 15/9 the original levels had been regained.

Dosage of sulphetrone, started at 1 gm. daily on 1st. March, was raised to 2 gms. on 8th., 3 gms. on 15th. and 4 gms. on 23rd. March. This dose was maintained until the rest period starting on 28/4, during which a drop in the percentage of haemoglobin necessitated doubling the dose of pil. ferri and administering 'NeoHepatex' 2c.c. intramuscularly on 24/5 when treatment was resumed at 2 gms. daily. This was raised to 3 gms. on 29/5 and although the haemoglobin continued to rise this dose was not exceeded. Total sulphetrone administered, 455 grams.

Toxic effects. Apart from the drop in haemoglobin, little of note. Fever, temp. 99°F. on 23/7 with cough, relieved by paludrine 0.1 gm. and did not recur. Swelling of the left foot was apparently due to epidermophytosis and relieved by 'Merfenil' and ichthyol and glycerin. Pains localised to lower back chest, 16/4; waist, 15/5, 16/5, 30/6; knees, 18/5: generalised, 17/5.

Case no. 11.

Agwu Uba, male of Umudomi, Onitsha. Age 45 yrs. Admitted 13/9/48.

History. No contact or predisposing factors revealed. Duration 10 yrs. Initial lesion: a macule on the left iliac region followed by another on the left infraclavicular region. No noticeable improvement during five months' treatment with Hydnocarpus oil.

On examination before administration of sulphamezathine, development fairly good. Lepromatous nodules on forehead, cheeks and ears; more than ten in number, the largest being 1 cm. in diameter. Diffuse lepromatous infiltration, markedly erythematous on the right inframammary region and the back of the chest. Mucosa of both nostrils infiltrated. Deformities of fingers of both hands and toes of both feet. During administration of sulphamezathine, nodules on the face were flattening by 17/4. The left great auricular, both supraclavicular, ulnar, medial cutaneous of forearm, superficial peroneal and medial calcaneal nerves remained thickened. Anaesthesia of both hands was detected at the beginning and end of administration, but the upper level of anaesthesia detected at the beginning at the middle of both legs had extended to the level of both knee joints by 19/9. By this date all nodules had flattened leaving dark, hyperpigmented areas of the same diameter, and infiltration was lessening. The nasal mucosa was dry and crusted and showed no evidence of infiltration. Defined macules were noted on the chest, no longer erythematous, but hypopigmented with crinkling. There was no tenderness of nerves throughout.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3 and daily from 21/3 with one weeks' rest following three weeks' administration. The second rest period starting on 28/4 was prolonged; because of a drop in the percentage of haemoglobin beyond the time necessary to correspond with the long rest granted to patients on the sulphones, until 28/5 when daily administration of 0.5 gm. was re-started and continued as above until the end of the course on 15/9. The dose of oil ferri was doubled and 'NeoHepatex', 2 c.c. intramuscularly administered, followed by a rise in haemoglobin percentage.

Toxic effects. Anaemia as indicated above. Patient complained of pains in fingers, 18/5; in lumbar region, 1/7; in back of neck, 8/7; in right knee, 29/7; both legs, 20/8; and headache, 26/8.

Case no. 12.

Nwite Nworie, male of Isu. Age 25 yrs. Admitted 31/5/48.

History. No contact revealed. Onset followed pain in the left shoulder. Duration: 4 yrs. Initial lesion: a macule on the posterior aspect of the left shoulder followed rapidly by another on the left breast, then becoming diffuse. No noticeable improvement during nine months' treatment with Hydnocarpus oil.

On examination before administration of sulphamezathine, development good. Diffuse lepromatous infiltration marked on forehead and ears, erythematous on the lower part of the back chest; hypopigmentation on trunk and limbs. Voice very hoarse. Bilateral inguinal adenitis. Both ulnar, superficial peroneal and right medial calcaneal nerves were thickened. The left medial calcaneal nerve was not palpable but there was tenderness to pressure in that area. Upper level of anaesthesia was found at the middle of both forearms and both legs. No deformities. At the end of the six months' course, the marked lepromatous infiltration had entirely subsided and islands of normal skin were appearing all over the trunk. No erythema remained. The voice was clearer. Nasal 'blocking' formerly complained of had been relieved and the nasal mucosa was dry and not infiltrated. Inguinal adenitis had almost subsided. The nerves mentioned above remained thickened but there was no tenderness on pressure over the left medial calcaneal nerve. Anaesthesia noted above remained unaltered. The pupil of the left eye was contracted, reacting sluggishly to light, and the cornea was slightly congested.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3 and daily from 21/3 with one weeks rest following three weeks' administration. The second rest period starting on 28/4 was extended to 28/5 as with case number 11 because of a drop in the haemoglobin percentage. Following administration of 'Anahaemin' 1 c.c. intramuscularly and doubling the dose of pil. ferri the haemoglobin percentage increased satisfactorily and administration was resumed on 28/5 at 0.5 gm. daily as above and continued until the completion of the course. Total sulphamezathine administered, 56.5 grams.

Toxic effects. Anaemia as noted above. Iritis of the left eye starting on 13/4, continuing with periods of increased activity but improving from 16/8. Swelling of the left ankle on 19/3 and again on 9/7 when there was also tenderness of the right medial calcaneal nerve. Pains in legs on 18/3; left knee on 29/7 and 6/8; right shoulder on 29/3. Headache 3 days in May, 7 in June, 2 in July and 2 in Sept. Catarrh relieved by ephedrine on 30/5 and 31/8.

Case no. 13.
Ogo Nwanjoku, female of Isu. Age 50 yrs. Admitted 1/11/48.
History. No contact revealed. Onset followed yaws. Duration 4 yrs. Initial lesion: a macule on the left iliac region followed by another on the left infrascapular region. The only improvement during four months' treatment with Hydnocarpus oil was healing of ulcers of fingers.
On examination before administration of sulphamezathine, development fair. Lepromatous macules on cheeks, forehead, right temple, anterior chest above breasts, abdomen, back of neck and covering back of trunk and limbs. Macules on the chest and abdomen were erythematous and, on the anterior aspect of the chest and on the abdomen presented a defined margin. The nasal mucosa appeared to be slightly infiltrated. Both great auricular, left ulnar, left superficial peroneal and left medial calcaneal nerves were thickened, the left medial calcaneal nerve being also tender to palpation. Anaesthesia was detected over both hands and forearms and both feet and legs to just above the knee joints. After cessation of sulphamezathine administration, on 19/9 the macules were found to be resolving well, to be hypopigmented the erythema having faded to a dull brown colour with mottled patches of hyperpigmentation appearing indicative of resolution. The nasal mucosa was not infiltrated. There was now no thickening of the left ulnar and superficial peroneal nerves : slight thickening of both great auricular and left medial calcaneal nerves was still present, the latter still being tender to palpation. There was no change in the distribution of anaesthesia.
Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration. The second rest period was started on 28/4 and extended until 23/5, after which administration was resumed as from 21/3 above. Total sulphamezathine given, 56 grams.
Toxic effects. Fever, temp. 100°F. on 17/4 possibly due to septic ulcers developing on the left sole with groin adenitis. Epigastric pain associated with constipation on 15/3 relieved by ol. ric. and again on 19/7 relieved by ol. ric. and a bismuth powder. The patient complained of generalised pains on 19/3, 25/3, 14/5 and 12/6; pains localised to the anterior tibiae on 22/3 and 11/4; umbilical pain relieved by ol. chenopodii m xv, 23/6; pains in hands and feet, 30/6; in legs and arms 9/7; waist 26/8; in fingers and legs 31/8; in arms and legs 8/9; headache on 29/5 and 28/8; diarrhoea on 24/6.

Case no. 14.
Abai Oke; male of Ukawu. Age 35 yrs. Admitted 23/9/47.
History. No contact or predisposing factors revealed.
Duration: 7 yrs. Initial lesion: a macule on the outer side of the right ankle followed by another on the right infrascapular region. Noticeable improvement during seventeen months' treatment with Hydnocarpus oil: resolution of nodules on right ear.
On examination before administration of sulphamezathine, development fairly good. Two lepromatous papules on the posterior outer edge of the left pinna, each 2 m/m. in diameter. Diffuse lepromatous infiltration marked on ears, forehead, nose, cheeks and chin; hypopigmentation on other parts with crinkling on the trunk and limbs. The nasal mucosa appeared to be slightly infiltrated. The right great auricular, both ulnar, superficial peroneal and medial calcaneal nerves were thickened. There was anaesthesia of the fourth and fifth fingers of both hands and the inner aspects of both hands and wrists, both feet and the lower halves of both legs.
After cessation of sulphamezathine administration, when the patient was examined on 19/9 both papules had flattened; one had entirely resolved and the other was just appreciable, the flattened area measuring 2 m/m. in diameter as at the beginning. Infiltration had entirely resolved and no hypopigmentation was present. Areas of anaesthesia remained unchanged. As is usual in cases of rapid resolution, hyperpigmentation was evident on the sites of former infiltration on the ear lobes, forehead and cheeks. The nasal mucosa was not infiltrated. Nerve thickening remained as formerly with the addition of the left great auricular nerve, both this and the right one being markedly thickened, but no tenderness of nerves was detected. No active lesions were noted. The patient acknowledged improvement in his condition as early as the third week of administration.
Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration. The second rest period extended from 28/4 to 23/5, after which administration was resumed as from 21/3 above. Total sulphamezathine given, 59 grams.
Toxic effects. Nil, and only two complaints: pains (generalised) 22/5; localised in lumbar region 28/5.

Case no. 15.

Nwosibe Okoro, male of Uburu. Age 45 yrs. Admitted April, 1929.

History. His mother had leprosy. Onset followed fever. Duration: 21 years. The patient appeared to improve during the first ten years' treatment with Hydnocarpus oil but relapsed after that period, his condition continuing to deteriorate following reaction in 1944. Initial lesion: a macule on the anterior aspect of the lower third of the left leg followed by nodules which spread rapidly.

On examination before administration of sulphamezathine, development fairly good. Many nodules scattered over the body on face, ears, trunk and limbs; some ulcerating on arms and legs. Diffuse lepromatous infiltration. An ulcer about 4 cms. in diameter was present on the right sole. The nasal mucosa was infiltrated. A nodule was present on the left eyelid. Both great auricular nerves were thickened and both ulnar, superficial peroneal and medial calcaneal nerves were thickened and tender. During administration of sulphamezathine, thickening of both great auricular nerves lessened and both ulnar nerves became no longer thickened as did also the left superficial peroneal nerve. Both ulnar, superficial peroneal and medial calcaneal nerves remained tender to palpation. The upper level of segmental anaesthesia remained at the middle third of the right, and at the elbow joint of the left forearm. In the legs a peculiar arrangement was found, the upper level sloping from the outer side at the knee joint to the middle of the inner side of the right leg, and from the inner side at the knee joint to the middle of the outer side of the left leg; these levels remaining unchanged. On examination after administration of sulphamezathine, on 19/9, nodules were resolving especially on ears, face, buttocks and limbs. More were ulcerating and some, having discharged purulent material for a time, were drying up and healing with scarring particularly on the hands and arms. Some more superficial nodules now collapsed on pressure; deeper discrete nodules had taken on a lighter colour and aggregated nodules as on the buttocks appeared as lightish purple plaques. Diffuse infiltration was resolving and normal skin appearing with a defined margin spreading inwards most noticeable on the temples and cheeks. The ulcer on the right sole had healed. The nasal mucosa was not infiltrated. The nodule of the left eyelid was flattening. A defined macule had appeared on the right umbilical region. Healthier toe nails were growing. The patient acknowledged improvement as early as the third week of treatment, nodules on cheeks and ears flattening.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration apart from the second rest period extending from 28/4 to 23/5. The dose was raised to 1 gm. daily (0.5 gm. b.d.) on 22/6 and maintained until cessation on 15/9. Total sulphamezathine administered, 83 grams.

Toxic effects. The patient complained of gingivitis, 26/4; pains in the feet, 8/9, and ankles, 9/9.

Case no. 16.
Chuku Obu, male of Uburu. Age 40 yrs. Admitted 1935.
History. No contact or predisposing factors revealed.
Duration 15 yrs. Initial lesion: thickening on the forehead spreading slowly over the face then to the posterior aspect of the chest. No improvement during 14 years' treatment with Hydnocarpus oil.
On examination before administration of sulphamezathine, development good. Diffuse lepromatous infiltration with hypopigmentation, infiltration being marked on the forehead, cheeks, ears, abdomen, the anterior aspect and the centre of the posterior aspect of the chest. Pronounced activity with erythema of infiltrated areas. Thickening of both ulnar and both superficial peroneal nerves. The upper level of segmental anaesthesia was detected at the lower third of both arms, the lower third of the right thigh and the left leg at the knee joint. There was marked deformity of the fingers of both hands and toes of both feet. On examination after cessation of administration of sulphamezathine, on 19/9, marked infiltration was subsiding on the face and ears; much reduced on the anterior aspect of the abdomen. Islands of normal skin were appearing on all affected parts except the centre of the face, producing a mottled appearance. Both nostrils were dry and crusted and there was healing ulceration of the right side of the nasal septum. Anaesthesia was found to have increased to cover the lower third of the left thigh. The patient acknowledged improvement as early as the third week of administration, infiltration of the forehead was noted to be lessening on 17/4, and at the end of the course the patient expressed his sense of well being and renewed strength in the phrase, "I can run like a horse."
Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration apart from the second rest period which extended from 28/4 to 23/5: resumed on 24/5, the dose was maintained until the end of the course on 15/9. Total sulphamezathine given, 55.5 gms.
Toxic effects. Fever, temp. 99.4°F. on 28/8, followed by pains in the right shoulder with fever, temp. 101°F. on 30/8, 98.8°F. on 31/8, headache on 1/9 and temp. 103°F. on 3/9, not recurring; but headache again on 4/9 and 5/9 and definite subsidence of infiltration noted on 13/9. Headache also complained of on 9/6, 10/6 and 6/8. Generalised pains on 26/5, 27/5 and 1/7. Pains in shoulders on 30/6. Urticaria on 19/8.

Case no. 17.

Oji Nwogo, male of Isu. Age 18 yrs. Admitted 23/9/47.

History. No contact revealed. Onset followed yaws. Duration: 10 yrs. Initial lesion: a nodule over the right patella followed by a macule on the left cheek. Some subsidence of marked lepromatous infiltration on nose, cheeks and ears was noted during seventeen months' treatment with Hydnocarpus oil.

On examination before administration of sulphamezathine, development good. Diffuse lepromatous infiltration with slight thickening not very noticeable on forehead, nose, cheeks and ears; hypopigmentation and lepromatous macules on limbs and trunk. No infiltration of nasal mucosa. The left great auricular, both ulnar, superficial peroneal and medial calcaneal nerves were thickened. The upper level of segmental anaesthesia was found at the right wrist, the middle third of the left forearm, the middle of the right thigh and the middle third of the left leg. There was deformity of four fingers of the left hand. Two small ulcers were present, one on the left sole and another on the second toe of the right foot, 1 c~~m~~. or less in diameter, and there were several fissures on both soles. After six months' administration of sulphamezathine, the infiltration with thickening of the skin had entirely subsided and only macules with hypopigmentation of both thighs remained: macules were flat and hypopigmented but more clearly defined than previous to sulphamezathine administration. One on the chest and another on the left arm showed evidence of central resolution. There was no infiltration of the nasal mucosa. Anaesthesia and nerve thickening remained as before and there was no tenderness on palpation of nerves. The ulcers and the fissures had all healed.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration, apart from the second rest period which extended from 28/4 to 23/5 and when administration was suspended following reaction on 30/7: re-started at 0.113 gm. on 2/8, repeated on 5/8 and 6/8, raised to 0.225 gm. on 7/8, continued until 9/8, another rest period intervening, resumed at the same dose on 16/8, raised to 0.338 gm. on 19/8 and 0.5 gm. on 20/8, this dose being continued until administration ceased on 15/9.

Total sulphamezathine administered, 57.225 gm.

Toxic effects. Fever, temp. 102°F. and pains in legs on 27/7. Old macules freshening on right side of neck, anterior upper chest and right side of abdomen on 30/7. Macules fading on 8/8 and reaction subsiding, there being only faint diffuse hypopigmentation on 19/8. Hypopigmentation lessening on 21/8. Other complaints were, pains and swelling in the right hand on 29/3 to 31/3: generalised pains on 2/4, 22/5, 23/5, 25/6 and 20/7: pains in the anterior tibiae on 15/4 and 4/9; in legs on 6/9; in the left foot on 21/7 and the back of the neck on 17/8: urticaria on 14/6; diarrhoea on 11/8.

Case no. 18.

Nwankwa Ngwu, male of Onicha. Age 25 yrs. Admitted 16/2/48.

History. No contact revealed. Onset followed swelling of the left thigh. Duration: 3 yrs. Initial lesion: a macule on the left umbilical region followed by another on the anterior aspect of the left thigh. Some subsidence of diffuse lepromatous infiltration which had been marked on the forehead, cheeks and ears, took place during one year's treatment with Hydnocarpus oil.

On examination before administration of sulphamezathine, development good. Diffuse lepromatous infiltration still more noticeable on the forehead, cheeks and ears; hypopigmentation on the face, trunk and limbs, and erythematous macules on the back of the chest. No infiltration of nasal mucosa. Both great auricular, ulnar, superficial peroneal and left medial calcaneal nerves thickened. Anaesthesia of both feet and legs with upper level at the knee joints. Ankylosis in flexion of the second, third, fourth and fifth fingers of the right hand. Several fissures of soles and both ankles measuring up to two inches in length. After administration of sulphamezathine, when the patient was examined on 19/9, infiltration of face and ears had subsided entirely. Wider areas of normal skin were appearing and macules were resolving but still numerous and erythematous on the chest. The nasal mucosa was not infiltrated. The upper level of segmental anaesthesia had receded to the middle thirds of both legs, but now the fourth and fifth fingers of both hands and the corresponding medial parts of both hands and the inner aspects of both wrists were involved. The patient now had free movements of the second, third and fourth fingers of the right hand, only the fifth finger remaining ankylosed. The fissures on the soles and ankles had all healed.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration apart from the second rest period extending from 28/4 to 23/5, and resumed thereafter as from 21/3.

Total sulphamezathine administered by 15/9, 59.5 gm.

Toxic effects. Nil of note. Complaints: pains over the umbilicus on 29/7, relieved by ol. ric. Headache on 16/4 and 30/7; pains in the right knee joint on 20/3, the lower left chest on 18/8 and both arms on 24/7; slight elevation of temperature above his normal to 98°F. on 20/8. The patient also complained of yaws foot, treated by N.A.B. 0.45 gm. during a rest period on 16/7.

Case no. 19.

Una Nwude, female of Okposi. Age 20 yrs. Admitted 31/1/49.

History. No contact or predisposing factors revealed.
Duration: 3 yrs. Initial lesion: a macule on the right cheek followed by another on the outer side of the right ankle. Attended Okposi Clinic previous to admission to Uburu Settlement on the above date because of severe neuritis of both ulnar nerves.

On examination before administration of sulphamezathine, development fairly good. Diffuse lepromatous infiltration with marked thickening on forehead and ears; hypopigmentation on cheeks, trunk and limbs. Bridge of nose flattened. No infiltration of nasal mucosa. Marked thickening and acute tenderness of both ulnar nerves especially on the left side. Both great auricular nerves were thickened and both superficial peroneal nerves were thickened but not tender to palpation. The upper levels of segmental anaesthesia were detected at both elbow joints and the middle of both thighs. There were deformities of the 2nd., 3rd. and 4th. fingers of the left hand. A fissure on the left sole measured 7.5 c~~m~~s . During administration left ulnar neuritis was troublesome, right ulnar neuritis less so, but the pains increased during rest periods when sulphamezathine and accessory medication was suspended. After administration of sulphamezathine, on 19/9, marked thickening had resolved, areas of normal skin were widening and defined macules appearing. There was no infiltration of the nasal mucosa. The fissure had healed. The upper level of segmental anaesthesia had receded to the middle of the right forearm but advanced to the lower third of the left arm: levels on the thighs remained as above. The nerves were still thickened as previous to administration and the left superficial peroneal nerve was now tender to palpation. Both ulnar nerves were still very tender to palpation, but the patient said the pains were now less severe.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration apart from the second rest period extending from 28/4 to 23/5, and resumed thereafter as from 21/3.

Total sulphamezathine administered, 58.5 gm.

Toxic effects. Fever, temp. 100°F. with an evanescent subcutaneous swelling in the left breast on 21/3, but no recurrence. Epigastric pains relieved by ol. ric. on 18/3. Severe pains in the ulnar nerves on 20/3, 15/4 and 24/6; slight on 2/8: generalised pains on 20/8: pains localised to the lower sternum on 30/6; the right cheek on 24/8; the arms on 6/9; and the left ear on 13/9 and 14/9.

Accessory medication. D.C.L. medicinal yeast was administered in doses of dr. ii b.d. until 27/5, not reduced to dr. i b.d. on 23/4 as with others because of apparent benefit to neuritis. Injections of a few c.c's of 2 percent 'Planocaine' into the ulnar nerves to relieve severe neuritis were given, two in June into the right; and one in April, 2 in May and 1 in July into the left ulnar nerve, after which injections were not required.

Case no. 20.

Nwamini Agada, male of Okposi. Age 20 yrs. Admitted 7/3/49.

History. No contact or predisposing factors revealed. Duration: 8 yrs. Initial lesion: a macule on the left cheek followed by another on the anterior aspect of the left thigh. Admitted to Settlement from Okposi Clinic because condition worsening under treatment with Hydnocarpus oil. Had reaction three times in 1946 with increased activity of nodules and swelling of feet.

On examination before administration of sulphamezathine, development good. Numerous lepromatous nodules on face, ears, upper back chest, buttocks and extensor and flexor surfaces of limbs. The largest single nodule was 2.5 c/m. in diameter. Diffuse lepromatous infiltration was marked on the upper anterior surface of the chest. The nasal mucosa was infiltrated. Both the ulnar, superficial peroneal and medial calcaneal nerves were thickened. There was anaesthesia of the feet and ankles only. There was no ulceration. During administration nodules on ears, arms and legs became bullous, bursting and discharging purulent material and flattening, and infiltration became less marked on the chest. After administration stopped, when the patient was examined on 19/9, the nodules were not discharging but now flattening on the ears, buttocks and limbs; still active on the face. On the chest, infiltration was subsiding. Signs of reaction to sulphamezathine were decreasing, the former 'raspberry' plaques becoming nodules with a burnished appearance on the surface and faded to a measly rash on the upper back chest. The left great auricular nerve was found to be thickened in addition to the others previously noted. There was no tenderness of nerves on palpation. The upper level of segmental anaesthesia had extended to the lower third of both legs and was found at the wrist joints of both hands not previously involved. The nasal mucosa was infiltrated and showed a purulent discharge, crusting and ulceration of the right side of the nasal septum, but nodulation of the mucosa, previously noted, was not detected. The patient had recently developed an ulcer of the inner side of the right foot after walking some miles. He said that his nose, formerly 'blocked' was now clear, and his companions said he no longer snored at night.

Dosage of sulphamezathine, started at 0.5 gm. on 15/3, repeated on 17/3 and 19/3, was continued daily from 21/3 with one week's rest following three weeks' administration. The second rest period extended from 28/4 to 23/5. Administration was suspended on 2/6 because of pin head sized papules on the forearms which proved to be evanescent; resumed on 5/6; raised on 21/6 to 1 gm. daily (0.5 gm. a.m. and p.m.); stopped on 5/7 for swelling and pain in feet and legs; resumed on 10/7, 0.5 gm. given followed by more swelling, so stopped; resumed on 2/8, 0.113 gm. given, followed by severe pains the same afternoon, so stopped: resumed at his own request on 13/9, 0.225 gm., followed by 0.338 gm. on 14/9, but fever, temp. 100.4°F. with weakness and itching caused administration to be suspended on 15/9 when the course finished.

Case no. 20, continued.

Total sulphamezathine administered, 40.63 gms.
Toxic effects. The initial favourable response with subsidence of nodules on peripheral parts but the failure of the nodules on the centre of the face to respond led us to consider it advisable to increase the dose from 0.5 gm. to 1 gm. daily. Previously the only possible toxic effects had been as follows:- Headache 4 days in March and one day in May; catarrh 1 day in May and in June and August; 'pin head' papules on 2/6; pains in legs on 24/6 and 25/6; generalised pains on 1/7; and pains in the shins on 3/7. But on 5/7, two weeks after the dose had been raised, there was swelling and pain in the feet and legs; on 6/7 the thighs and abdomen had an oedematous, infiltrated appearance; on 7/7 there were raised, hard, 'raspberry' plaques, nearly confluent on the thighs and abdomen, and the nasal mucosa was markedly congested with obstructed breathing which subsided on 8/7 when the swelling of the feet also subsided, but the shins remained painful. On 9/7 the plaques were extending over the back of the trunk and arms and on 10/7 swellings recurred, subsiding on 14/7. On 22/8 the 'raspberry' plaques had become small nodules, subsiding and erythema fading. On 30/8, following an injection of N.A.B. for yaws foot, evanescent erythematous plaques appeared on the chest, arms and abdomen. On 19/9 all signs of reaction were decreasing.

Case no. 21.
Aba Nwekwe, male of Uburu. Age 50 yrs. Admitted 1942.
History. No contact revealed. Onset followed dysentery.
Initial lesion: a macule on the middle of the anterior aspect of the left thigh followed by another on the right thigh, then others all over the body.
Examined on 28/6/48, development fairly good. Sub-type m.t. Stage N3. Uniformly enlarged macules scattered over trunk, face and limbs, but one macule on the upper anterior aspect of the left thigh showed healing in the centre. Segmental anaesthesia noted with the upper level at the middle third of both forearms, the right knee joint and the middle third of the left leg. No nerve thickening noted.
17/1/49. Reaction in all macules: dose of hydnocarpus oil reduced from $7\frac{1}{2}$ c.c's to $\frac{1}{2}$ c.c.
28/2/49. Neuritis of both ulnar nerves.
7/3/49. Macules now definitely M.T.
21/3/49. Given Antimonii et Potassii Tartras gr. ii (0.12 gm.) intravenously, repeated on 28/3 and 11/4.
In April nasal and skin smears were definitely positive (++ by Muir's, 1948, estimation). Between April and May the reaction subsided, erythema disappearing and the macules flattening and scaling. Ulceration of limbs followed and the patient died on 18/7/49.

This case illustrates change from a minor to a major tuberculoid sub-type and the infectivity of the Major Tuberculoid sub-type in reaction. The devastating results of reaction in the tuberculoid type are likewise apparent.

Case no. 22.

Echem Etuki, male of Itigeve. Age 30 yrs. Admitted 28/7/48.

History. His father died with leprosy. Duration 7 months. This patient was first seen on survey at Itigeve in December, 1947, when a diagnosis of suspected tuberculoid leprosy was made from one small macule, of pebble formation and hypopigmented on the middle of the back of the chest to the left of the spine, measuring 2.5 c/m/s. by 1.225 c/m/s. in extent. When admitted at the clinic, anaesthesia of the feet and ankles was the only other sign of leprosy. Perhaps doubting the diagnosis in so small a lesion the patient stopped attending the clinic after 21/12/48. Re-admitted on 26/7/49 he showed three small macules about the same size as the first and lateral to it. Anaesthesia to light touch was now detected in the first macule only. By 23/8/49 some regression was noted in all macules.

This case illustrates how leprosy may have been acquired by close contact in the family; the development of tuberculoid leprosy from a tiny macule with pebble papules; the value of the survey in bringing these cases to light; and the rapid response to Hydnocarpus oil therapy in early tuberculoid cases. Maximum dose 2½ c.c's.

Case no. 23.

Obassey Chuku, adolescent man of Uburu. Age 16 yrs. Admitted 16/2/48.

History. No contact revealed. Duration 1 yr.

Initial lesion: a macule on the posterior aspect of the left buttock followed rapidly by others scattered over the trunk, face and limbs.

Examined on 16/2/48, development good. Hypopigmentation with slight thickening of forehead, flat hypopigmented macules on cheeks, chin, trunk, arms and legs; diffuse hypopigmentation on the buttocks, the extensor surfaces of the arms and forearms and the flexor surfaces of the legs. No nerve thickening and anaesthesia of heels only.

Diagnosed Indeterminate (undifferentiated), suspected early lepromatous infiltration having been excluded by bacteriological examination with negative smears. This diagnosis was confirmed by later developments in this case, for, on 15/8/49 no infiltration was in evidence and the macules were resolving especially on the back and on the buttocks. The maximum dose of Hydnocarpus oil was 5 c.c's.

Case no. 24.

Uzo Nwanoke, female of Uburu. Age 23 yrs. Admitted 1938.

History. No contact or predisposing factors revealed. Onset followed fever. Initial lesion: a macule on the right lumbar region spreading slowly.

Examined on 17/6/41 when a girl of about 16 years of age, the patient had two macules with raised edges but otherwise uniformly enlarged on the right lumbar region, both anaesthetic to light touch. The only other evidence of leprosy was loss of discrimination between test tubes containing hot and cold water over a small area on the medial aspect of the left ankle.

The patient's subsequent progress was slow: she continued to attend the clinic, married and was pregnant twice, in 1942 and again in 1943. She first complained of a cough on 1/10/45 and again of cough and fever on 12/1/48, when, on examination of the sputum, the tubercle bacillus was found, and signs of a cavity were detected at the apex of the left lung. Negative smears for M.leprae obtained on 21/1/48. Examined again on 20/1/48, development poor. One macule had resolved, and only a puckered scar remained where the original macule had been. This area was still anaesthetic to light touch and the part of the medial aspect of the left ankle where there had been loss of discrimination between hot and cold was now anaesthetic to light touch. There was no nerve thickening. The patient was diagnosed as belonging to the minor tuberculoid sub-type, now in the arrested stage, having shown no evidence of regression to the 'anergic' or lepromatous state but remained in the 'allergic' or tuberculoid state over a period of seven years. Nevertheless she died of pulmonary tuberculosis in October, 1948.

Case no. 25.
Okorie Ebu, female of Nera, Onitsha. Age 40 yrs.
History. No contact revealed. Duration 1 year and 3 months.
Complaint: An itchy nodular rash appearing on the back and front of the chest, upper arms and anterior aspects of the forearms, knees, thighs and behind the knees and on the dorsum of the feet following the birth of a child.
Examined 13/6/49. Development good. The nodules are erythematous and scaly with bleeding when the scales are scraped off. No anaesthesia and no nerve thickening detected.
Biopsy was performed and the specimen sent to the Medical Research Institute, Yaba. The histological report, dated, 12/8/49 declared the section to reveal tuberculoid leprosy and that no bacilli were found in it.
On further examination of the patient on 15/8/49 a small area of anaesthesia was detected on the outer side of the dorsum of the left foot and ankle; the only typical clinical evidence of leprosy present, from which, had it been discovered earlier, it would still have been unwise to make a diagnosis of leprosy.

Case no. 26.

Akpa Nwachuku, male of Uburu. Age 30 yrs. Admitted 1939.

History. No contact revealed. Onset followed fever.
Initial lesion: a macule on the middle of the lumbar region followed rapidly by another on the left side of the chest. Duration 13 yrs.
Examined 12/7/48. Diagnosed resolving lepromatous infiltration and minor tuberculoid macules, evidence of the former being present in marked 'fig leaf' appearance of both ears; infiltrated appearance of forehead and cheeks; diffuse hypopigmentation of the anterior aspect of the upper part of the chest, buttocks and limbs; and the flattened bridge of the nose. The latter was evidenced by definite tuberculoid macules with healing centre and spreading, raised, pebble-like edge on the epigastrium, right and left lumbar and mid umbilical regions of the abdomen. Upper level of segmental anaesthesia at both elbows and middle thirds of both thighs. Both great auricular, ulnar and superficial peroneal nerves thickened. The fifth finger of the left hand was ankylosed in flexion, the only deformity.
On 8/8/49 the minor tuberculoid element definitely predominated. The upper level of segmental anaesthesia had receded to the lower third of the left and the middle of the right forearm. Two of the macules on the abdomen were anaesthetic to light touch and all macules were analgesic to the two pin test, even those on the face.
22/9/49. All smears from nose, skin and ears were negative.

This case illustrates the presence of signs of resolving lepromatous leprosy in a patient of the minor tuberculoid sub-type clinical evidence of which is recorded over a period of 13 months, confirmed bacteriologically at the end of 14 months.

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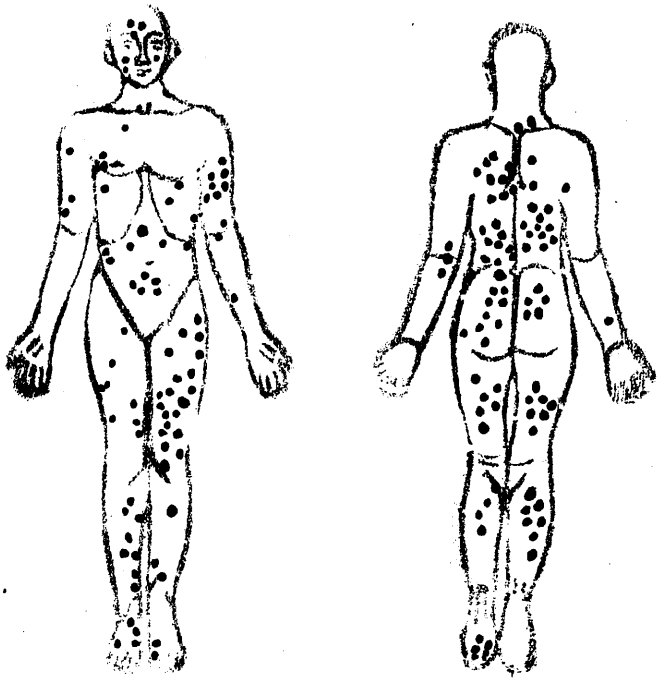
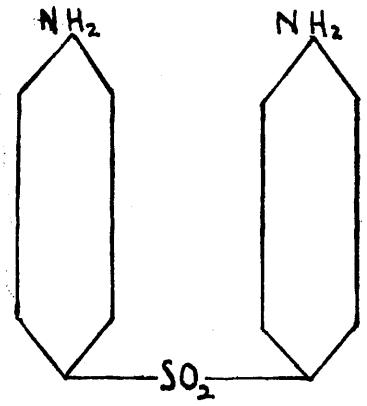
Figure 1.



Initial lesions from 170 cases, a few of which coincide.

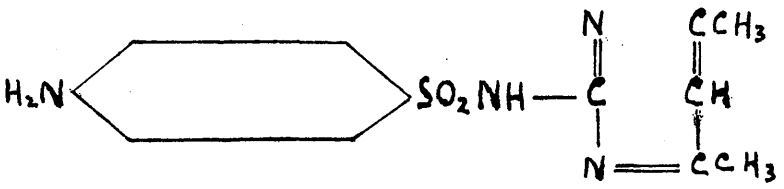
Figure 2.

SULPHANILAMIDE.



4,4'-DIAMINODIPHENYLSULPHONE.

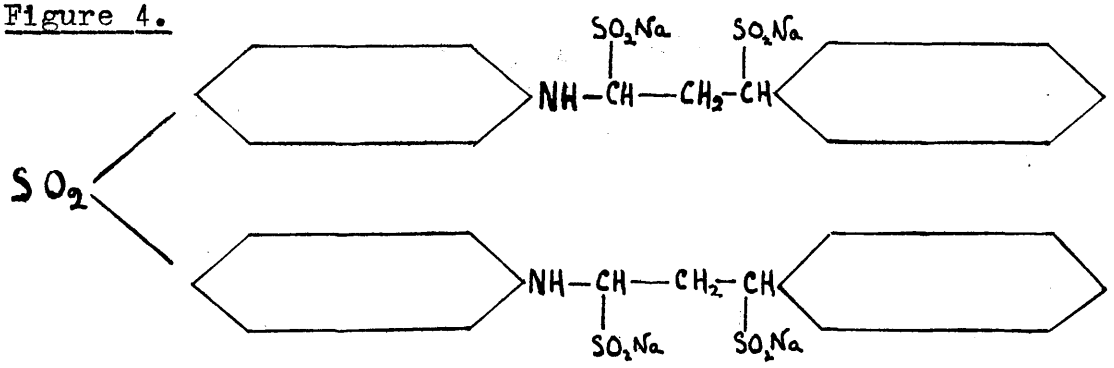
Figure 3.



2-(p-aminobenzenesulphonamido)4:6-dimethylpyrimidine.

SULPHAMEZATHINE.

Figure 4.



sodium 4:4'-bis-(γ-phenylpropylamino)-diphenylsulphone-α:γ:α':γ'-tetrasulphonate.

SULPHETRONE.

CHURCH OF SCOTLAND MISSION LEPROSY SCHEME FOR SOUTHERN OGOJA PROVINCE

SEPTEMBER, 1949.

ROAD MAP OF OGOJA PROVINCE.

CHURCH OF SCOTLAND MISSION AREA WITHIN ADMINISTRATIVE (DIVISIONAL) BOUNDARIES.